Comparison between creatinine-based equations for estimating total creatinine clearance in peritoneal dialysis: a multicentre study

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Abstract
Background. It is crucial to assess the adequacy of peritoneal dialysis (PD) because of its influence on patient outcome. Collecting dialysate and urine for 24 h can be rather troublesome, so a simple and inexpensive alternative method for rapidly evaluating adequacy in PD would be very useful. Our study aimed to assess the performance of 12 different creatinine (Cr)-based equations commonly used to estimate GFR in predicting total Cr clearance (totCrCL) in PD.

Methods. Four Italian dialysis centres enrolled 355 PD patients with 2916 fluid collections. To rank the equations, their accuracy (median absolute percentage error, MAPE), precision (root mean square error, RMSE), agreement (k statistics), sensitivity and specificity (area under ROC curves, AUC, where x = 1 − specificity and y = sensitivity) were calculated with reference to the measured totCrCL.

Results. The Gates, Virga and 4-MDRD equations showed the best global performance as concerns accuracy (MAPE = 14.1, 16.3, 15.9% respectively), precision (RMSE = 13.2, 13.3, 13.4), agreement (k = 0.425, 0.440, 0.375), sensitivity and specificity (AUC = 0.825, 0.826, 0.820), while the Cockcroft–Gault formula revealed a rather poor reliability.

Conclusions. Fluid collection remains the gold standard for assessing PD adequacy. Our study ascertained how 12 Cr-based equations performed in estimating totCrCL in PD patients with a view to enabling the most accurate and precise among them to be chosen for use in approximately assessing totCrCL.

Keywords: accuracy; adequacy; creatinine clearance; creatinine-based equations; peritoneal dialysis

Introduction
Peritoneal dialysis (PD) is a well-known and widely used renal replacement therapy, but it is crucial to assess the adequacy of PD because of its influence on patient outcome [1,2].

In addition to evaluating water and sodium balance, this assessment involves calculating the weekly urea clearance normalized according to body water (Kt/V), and the weekly creatinine clearance (CrCL) normalized to a body surface area of 1.73 m² (CrCL/1.73).

Although the NKF-K/DOQI Guidelines for Peritoneal Dialysis Adequacy 2001 recommend measuring the total solute clearance every 4 months [3], the adequacy of dialysis in patients on PD is often assessed only twice a year because it can be rather tiresome. It involves collecting dialysate (sometimes more than 25 L) and urine simultaneously for 24 h, combining and weighing the two fluids and sending samples to the laboratory together with a blood sample, then interpreting the results and calculating the adequacy indexes.

As a result, the same dialysis prescription may be applied for at least 4–6 months, during which time there may be a decline in a patient’s residual renal function, making their total solute clearance shift into a range that is no longer adequate.

It would be very useful to have simple, inexpensive tools requiring no fluid collection to enable adequacy of dialysis
to be assessed once a month or, more generally, every time a blood sample is taken, to monitor PD patients more closely, and especially those at risk of inadequate dialysis due to a large body size or rapidly deteriorating residual renal function.

A formula for estimating renal CrCl or the glomerular filtration rate (GFR) in uraemic patients is theoretically capable of predicting totCrCL in PD. Many such equations have been developed [4–15], but they have seldom been tested in PD patients in terms of their power to estimate their total CrCL (totCrCL) [16–18].

The rationale for using a GFR estimating (eGFR) equation in the case of PD is that patients on PD are in a near-steady metabolic state, with stable sCr concentrations (median % variability on same-day samples = 2% [17]).

A reliable equation could simply be recorded in a spreadsheet, multiplying the eGFR finding by 10.08 to convert as regards their totCrCL rating power in PD.

Subjects and methods

Four Italian dialysis centres were enrolled for this retrospective study, i.e. Lecco (Center 1, C-1, 110 patients), Bari (C-2, 110 patients), Camposampiero (C-3, 90 patients) and Padova (C-4, 45 patients). All 355 cases were past and present unselected PD patients who were included in the study up until 30 April 2008. There were no selection or exclusion criteria. Two patients were amputees and the series contained no African Americans. There were 128 patients on APD and 227 on CAPD.

Three types of sample were analysed separately, i.e. (i) the first (1st) urine and dialysate collections from each patient (n = 555) as an indication of their highest GFR; (ii) the last (last) collections as an indication of their lowest GFR (n = 296, obtained only for cases with at least two fluid collections) and (iii) the patients’ pooled fluid collections (n = 2916).

The statistical analysis was performed to rank the equations most reliable in estimating totCrCL using the 2916 pooled fluid collections for the definitive classification.

Twelve Cr-based equations were considered for their power to estimate totCrCL: Edwards–White (Edwards [4]), Mawer [5], Jeliffe [6], Cockcroft–Gault (Cockcroft) [7], Bjornsson [8], Hull [9], Gates [10], Salazar [11], Davis–Chandler (Davis [12], Levey (4-MDRD) [13], Rule [14] and Virga [15] (see Appendix). The result of all equations other than Salazar, Davis–Chandler (Davis) [12], Levey (4-MDRD) [13], Rule and especially those at risk of inadequate dialysis due to a large body size or rapidly deteriorating residual renal function.

In all tables, the best results are shown in bold font.

Cr levels (mg/dL) were measured in all fluid samples as follows: using an enzymatic method and a Hitachi 717 instrument in C-1; using a modified Jaffé kinetic method on a Dimension RXL Siemens instrument in C-2; according to the rate-blanked and compensated, modified Jaffé kinetic method using the Hitachi Modular analyzer in C-3 and using the Jaffé kinetic method on a Modular DP Roche instrument in C-4.

Statistics

Continuous variables were expressed as means ± standard deviations (SD) or medians with the 25th–75th centiles (or 2.5th–97.5th for errors) if data distribution was not normal.

Normality of distribution was assessed with the Kolmogorov–Smirnov test.

For each equation studied, we assessed the systematic errors, accuracy, relative accuracy, predictive power, precision, sensitivity and specificity, and degree of agreement.

Absolute bias, as a measure of systematic error, was defined from the median error and relative bias from the median percentage error: these two parameters represent the average tendency of a given equation to under- or over-estimate the real totCrCL measured value.

Accuracy was considered as the median absolute percentage error (MAPE).

The relative accuracy was defined as the percentage of patients whose estimates came within 10%, 30% and 50% above and below the measured GFR and the ±30% value was used to rank the equations.

The predictive power was assessed with the non-parametric Spearman Rho correlation analysis (Rho) (estimated versus measured totCrCL).

Precision was assessed by calculating the root mean square error (RMSE), the square root of the response variable minus the fitted value: the smaller the RMSE, the better the formula’s precision.

The area under the receiver operating characteristic (ROC) curves (AUC) was calculated for each equation to assess its sensitivity and specificity using a totCrCL of 50 L/week 1.73 as the cut-off for adequacy. ROC curves were calculated for each equation using x = 1 − specificity and y = sensitivity: the greater the AUC, the higher the sensitivity and specificity of the equation considered (an AUC = 1.0 means a perfect sensitivity and specificity, while 0.5 means no discrimination).

Cohen’s k value [20,21] was calculated as a measure of agreement between the measured and estimated totCrCL, interpreting the agreement in relation to five totCrCL categories, i.e. < 30, 30–50, 50–60, 60–70, 70–85 and >85 L/week 1.73. The k values range between 0 (no agreement, better than chance) and 1 (perfect agreement). The k value was interpreted as follows: k = <0.20 → ‘poor’; k = 0.21–0.40 → ‘fair’; k = 0.41–0.60 → ‘moderate’; k = 0.61–0.80 → ‘good’ and k = 0.81–1.00 → ‘very good’ [21,22].

To establish the real estimative value of these equations, we considered the coefficient of variability deriving from differences in single fluid collections, drawn from our published data [23] (in three dialysate and urine collections taken within 7 days from 24 PD patients, the coefficient of variability for totCrCL was 6%). From the within-subject and inter-subject variances for totCrCL (53.68, SD = 7.33 and 75.01, SD = 8.66, respectively), we obtained the total variance (128.69, SD = 11.34), so the (within/total variance)*100, i.e. 41.71%, represents the proportion of the total variability due to the variability of the single fluid collections.

The null hypothesis was rejected for all tests with two-tailed alpha values below 0.05.

The statistical analysis was performed using the JMP 4.0.0 statistical software (SAS Institute Inc., Cary, NC, USA), and the Instat 3.05 statistical software (GraphPad Software Inc., San Diego, CA, USA).

Results

The weekly totCrCL was calculated as the arithmetic sum of weekly peritoneal CrCl and GFR.

Blood samples for the CrCL calculations were drawn at 8.00 for CAPD and at 14.00 for APD.

The weekly peritoneal CrCl (pCrCL, L) was calculated as follows: [(dialysate Cr/crCl) × drainage volume] × 7. Peritoneal CrCL was measured using the 24-h dialysate collection.

The weekly glomerular filtration rate (GFR, L) was calculated as follows: [(renal urea Cl + renal CrCl) × 7].

The weekly GFR was added to the weekly pCrCL to obtain the weekly totCrCL, which was normalized to a BSA of 1.73 m². We considered totCrCL as the arithmetic sum of weekly peritoneal CrCL and GFR, according to the NKF-DOQI Clinical Practice Guideline for Peritoneal Dialysis Adequacy [3].

We considered a totCrCL <50 L/week 1.73 as a sure sign of inadequate dialysis.
The characteristics of the population studied as at the first and last fluid collections are summarized in Table 1: the mean GFR and totCrCL values were lower in the last than in the first collections, while the pCrCL was higher.

Table 2 shows the median values for the measured and estimated totCrCL (L/week 1.73) in the first, last and all fluid collections: the Hull equation showed the median totCrCL in the first, last and all fluid collections: the Hull equation showed the median totCrCL.

Table 3 ranks the equations by accuracy: the Gates equation came out best for both predictive power and precision.

Although the errors did not show a Gaussian distribution, we report the mean pure and percentage errors (for the best six equations) to enable a comparison to be drawn with other published studies.

Mean error (L/week 1.73): Virga = –1.9 ± 17.5, Hull = +1.9 ± 23.5, Gates = +3.8 ± 14.5, 4-MDRD = –4.8 ± 14.9, Mawer = +8.8 ± 23.7, Jeliffe = +9.5 ± 16.7.

Mean percentage error (%): Hull = +2.7 ± 35.6, Virga = –2.8 ± 26.4, Gates = +4.2 ± 21.5, 4-MDRD = –5.9 ± 21.8, Mawer = +14.7 ± 36.2, Jeliffe = +17.1 ± 26.9.

Table 4 shows the calculated relative accuracy, and the Gates equation ranks the best (i.e. it has the highest proportion of estimates within 30% above or below the measured totCrCL).

Table 5 lists the equations in order of their predictive power (Spearman’s Rho coefficient) and precision, as assessed from the RMSE: the Gates equation came out best for both predictive power and precision.

Table 6 shows the results for Cohen’s statistics, represented by the k value and its 95% confidence interval (95% CI) and the interpretation of the degree of agreement between measured and estimated totCrCL. Virga’s equation revealed the best k index, with the following agreement...
Comparison between creatinine-based equations for estimating total creatinine clearance in PD

Table 4. Percentage of estimates within 10%, 30% and 50% above or below the measured totCrCL in first, last and all fluid collections

<table>
<thead>
<tr>
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<tbody>
<tr>
<td></td>
<td>10%</td>
<td>30%</td>
<td>50%</td>
<td>10%</td>
<td>30%</td>
<td>50%</td>
<td>10%</td>
<td>30%</td>
<td>50%</td>
<td></td>
</tr>
<tr>
<td>Gates</td>
<td>33.2%</td>
<td>79.7%</td>
<td>93.5%</td>
<td>31.4%</td>
<td>82.8%</td>
<td>94.6%</td>
<td>35.0%</td>
<td>86.3%</td>
<td>97.3%</td>
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<tr>
<td>4-MDRD</td>
<td>26.2%</td>
<td>78.9%</td>
<td>93.2%</td>
<td>30.7%</td>
<td>80.1%</td>
<td>94.9%</td>
<td>31.9%</td>
<td>84.3%</td>
<td>97.3%</td>
<td></td>
</tr>
<tr>
<td>Virga</td>
<td>29.6%</td>
<td>73.5%</td>
<td>89.9%</td>
<td>29.7%</td>
<td>72.6%</td>
<td>90.9%</td>
<td>32.5%</td>
<td>77.6%</td>
<td>94.0%</td>
<td></td>
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<tr>
<td>Jeliffe</td>
<td>29.0%</td>
<td>68.5%</td>
<td>86.5%</td>
<td>31.1%</td>
<td>76.6%</td>
<td>88.5%</td>
<td>31.9%</td>
<td>73.5%</td>
<td>89.8%</td>
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<tr>
<td>Mawer</td>
<td>25.7%</td>
<td>65.4%</td>
<td>83.4%</td>
<td>25.7%</td>
<td>62.8%</td>
<td>84.1%</td>
<td>28.3%</td>
<td>76.7%</td>
<td>85.9%</td>
<td></td>
</tr>
<tr>
<td>Hull</td>
<td>23.7%</td>
<td>65.4%</td>
<td>85.1%</td>
<td>23.6%</td>
<td>60.5%</td>
<td>88.9%</td>
<td>23.1%</td>
<td>65.0%</td>
<td>88.3%</td>
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<tr>
<td>Edwards</td>
<td>29.9%</td>
<td>60.3%</td>
<td>77.7%</td>
<td>23.0%</td>
<td>54.3%</td>
<td>80.1%</td>
<td>21.3%</td>
<td>57.8%</td>
<td>81.2%</td>
<td></td>
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<tr>
<td>Cockcroft</td>
<td>21.4%</td>
<td>56.3%</td>
<td>75.8%</td>
<td>21.6%</td>
<td>53.4%</td>
<td>74.0%</td>
<td>21.3%</td>
<td>57.8%</td>
<td>81.2%</td>
<td></td>
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<tr>
<td>Salazar</td>
<td>29.6%</td>
<td>68.5%</td>
<td>86.5%</td>
<td>29.6%</td>
<td>72.6%</td>
<td>90.9%</td>
<td>32.5%</td>
<td>77.6%</td>
<td>94.0%</td>
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</tr>
<tr>
<td>Davis</td>
<td>29.0%</td>
<td>65.4%</td>
<td>86.5%</td>
<td>21.1%</td>
<td>67.6%</td>
<td>86.5%</td>
<td>21.3%</td>
<td>70.8%</td>
<td>81.2%</td>
<td></td>
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<tr>
<td>Bjornsson</td>
<td>26.5%</td>
<td>65.4%</td>
<td>83.4%</td>
<td>25.7%</td>
<td>62.8%</td>
<td>84.1%</td>
<td>28.3%</td>
<td>76.7%</td>
<td>85.9%</td>
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Table 5. Spearman’s non-parametric Rho correlation coefficient (measured versus estimated totCrCL) and root mean square error (RMSE)

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<th>Spearman’s Rho coefficient</th>
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<th>Root mean square error</th>
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<tr>
<td>Gates</td>
<td>0.715 0.630 0.705</td>
<td>18.13 15.45 13.15</td>
<td></td>
</tr>
<tr>
<td>4-MDRD</td>
<td>0.707 0.647 0.695</td>
<td>18.55 15.30 13.39</td>
<td></td>
</tr>
<tr>
<td>Virga</td>
<td>0.717 0.647 0.704</td>
<td>17.99 15.53 13.28</td>
<td></td>
</tr>
<tr>
<td>Salazar</td>
<td>0.717 0.647 0.704</td>
<td>18.13 15.45 13.15</td>
<td></td>
</tr>
<tr>
<td>4-MDRD</td>
<td>0.707 0.647 0.695</td>
<td>18.55 15.30 13.39</td>
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</table>

The equations were ranked according the results for ‘all’ values.

Table 6. Cohen’s k statistics for strength of agreement of measured versus estimated totCrCL

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<tbody>
<tr>
<td></td>
<td>k</td>
<td>95% C.I.</td>
<td>A</td>
<td>k</td>
<td>95% C.I.</td>
<td>A</td>
<td>k</td>
<td>95% C.I.</td>
</tr>
<tr>
<td>Virga</td>
<td>0.503</td>
<td>0.438–0.567</td>
<td>3</td>
<td>0.395</td>
<td>0.322–0.467</td>
<td>2</td>
<td>0.440</td>
<td>0.374–0.512</td>
</tr>
<tr>
<td>Gates</td>
<td>0.464</td>
<td>0.399–0.529</td>
<td>3</td>
<td>0.377</td>
<td>0.304–0.430</td>
<td>2</td>
<td>0.401</td>
<td>0.397–0.424</td>
</tr>
<tr>
<td>Hull</td>
<td>0.494</td>
<td>0.429–0.559</td>
<td>3</td>
<td>0.348</td>
<td>0.276–0.420</td>
<td>2</td>
<td>0.383</td>
<td>0.397–0.428</td>
</tr>
<tr>
<td>Cockcroft</td>
<td>0.495</td>
<td>0.429–0.560</td>
<td>3</td>
<td>0.330</td>
<td>0.259–0.401</td>
<td>2</td>
<td>0.379</td>
<td>0.374–0.419</td>
</tr>
<tr>
<td>Edwards</td>
<td>0.433</td>
<td>0.368–0.498</td>
<td>3</td>
<td>0.364</td>
<td>0.291–0.438</td>
<td>2</td>
<td>0.357</td>
<td>0.352–0.397</td>
</tr>
<tr>
<td>Jeliffe</td>
<td>0.476</td>
<td>0.409–0.542</td>
<td>3</td>
<td>0.308</td>
<td>0.238–0.378</td>
<td>2</td>
<td>0.365</td>
<td>0.343–0.388</td>
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<tr>
<td>Cockcroft</td>
<td>0.411</td>
<td>0.343–0.480</td>
<td>3</td>
<td>0.273</td>
<td>0.205–0.340</td>
<td>2</td>
<td>0.280</td>
<td>0.258–0.302</td>
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<tr>
<td>Davis</td>
<td>0.404</td>
<td>0.335–0.473</td>
<td>2</td>
<td>0.241</td>
<td>0.174–0.307</td>
<td>2</td>
<td>0.276</td>
<td>0.254–0.298</td>
</tr>
<tr>
<td>Salazar</td>
<td>0.408</td>
<td>0.339–0.477</td>
<td>2</td>
<td>0.254</td>
<td>0.187–0.321</td>
<td>2</td>
<td>0.272</td>
<td>0.251–0.294</td>
</tr>
<tr>
<td>Bjornsson</td>
<td>0.380</td>
<td>0.311–0.450</td>
<td>2</td>
<td>0.218</td>
<td>0.153–0.283</td>
<td>2</td>
<td>0.249</td>
<td>0.227–0.270</td>
</tr>
<tr>
<td>Rule</td>
<td>0.322</td>
<td>0.253–0.392</td>
<td>2</td>
<td>0.161</td>
<td>0.099–0.222</td>
<td>1</td>
<td>0.206</td>
<td>0.185–0.228</td>
</tr>
</tbody>
</table>


in the totCrCL categories (L/week 1.73): <50 = 377/520 (72.5%), 50–60 = 200/725 (27.6%), 60–70 = 165/675 (24.4%), 70–85 = 183/551 (33.2%) and >85 = 312/445 (70.1%). Only the Virga and Gates equation showed a ‘moderate’ agreement.

Table 7 summarizes the values for the AUC of the ROC curves relating to sensitivity and specificity, using a cut-off at totCrCL = 50 L/week 1.73: here again, the Virga and Gates equations performed the best (with the highest AUC).

Figure 1 shows the Bland–Altman test [24] results related to the Gates equation and the same sample: the mean difference was $-3.76 \pm 14.46$ L/week 1.73. For an averaged totCrCL <50 L/week 1.73, only 0.3% of the test results (2/611) are outside the range of the mean ± 2SD
Table 7. Area under curve (AUC) of ROC curves relating to sensitivity and specificity with cut-off at totCrCL = 50 L/week 1.73

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<tr>
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<th>First</th>
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<tbody>
<tr>
<td>Virga</td>
<td>0.836</td>
<td>0.797</td>
<td>0.826</td>
</tr>
<tr>
<td>Gates</td>
<td>0.831</td>
<td>0.795</td>
<td>0.825</td>
</tr>
<tr>
<td>4-MDRD</td>
<td>0.820</td>
<td>0.799</td>
<td>0.820</td>
</tr>
<tr>
<td>Bjornsson</td>
<td>0.843</td>
<td>0.781</td>
<td>0.813</td>
</tr>
<tr>
<td>Salazar</td>
<td>0.848</td>
<td>0.788</td>
<td>0.812</td>
</tr>
<tr>
<td>Cockroft</td>
<td>0.845</td>
<td>0.780</td>
<td>0.810</td>
</tr>
<tr>
<td>Edwards</td>
<td>0.786</td>
<td>0.780</td>
<td>0.798</td>
</tr>
<tr>
<td>Jeliffe</td>
<td>0.841</td>
<td>0.779</td>
<td>0.770</td>
</tr>
<tr>
<td>Hull</td>
<td>0.809</td>
<td>0.753</td>
<td>0.785</td>
</tr>
<tr>
<td>Mawer</td>
<td>0.814</td>
<td>0.736</td>
<td>0.785</td>
</tr>
<tr>
<td>Davis</td>
<td>0.801</td>
<td>0.748</td>
<td>0.778</td>
</tr>
<tr>
<td>Rule</td>
<td>0.816</td>
<td>0.748</td>
<td>0.773</td>
</tr>
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</table>

Figure 1. Bland–Altman test for the Gates equation.

$(-32.7/25.2)$. This range (mean ± 2SD) might seem clinically significant, but it is really far smaller when we take into account that 41.7% of the total variability is due to single fluid collections.

Figure 2 shows the ROC curve for Virga’s equation (AUC = 0.826) as regards sensitivity and specificity using a cut-off at totCrCL = 50 L/week 1.73 in the sample of 2916 fluid collections.

About 3% of patients were undernourished, since 12/355 (3.4%) patients had a BMI of < 18.5 kg/m² at the first fluid collection and 8/296 (2.7%) at the last. Recalculating the MAPE (i.e. Gates 14.2%, 4-MDRD 15.8%, Virga 16.4%), the percentage of estimates within 30% (Gates 86.0%, 4-MDRD 84.2%, Virga 77.3%) and the RMSE (Gates 13.13, Virga 13.14, 4-MDRD 13.36) without the malnourished patients did not modify the ranking of the equations considered.

To assess any effect of the different methods for assaying creatinine (enzymatic, Jaffé kinetic), or of the different centres, on the estimated totCrCL, we performed a statistical analysis using a mixed linear model:

$\text{eCrCL}_{ij} = \beta_0 + \beta_1 m\text{CrCL}_{ij} + \nu_{0i} + \epsilon_{0ij}$

where $\text{eCrCL}_{ij}$ is estimated totCrCL, $m\text{CrCL}_{ij}$ is measured totCrCL, $\nu_{0i}$ is error of method, $\epsilon_{0ij}$ is error of each subject. The coefficients calculated were

$\beta_0 = 7.94$ (95% C.I. = 6.20 − 9.69), standard error = 0.89 and

$\beta_1 = 0.82$ (95% C.I. = 0.80 − 0.85), standard error = 0.01.

The variance due to the centre = 0.11 and due to the method = 0.000, $P = 1.00$, demonstrated that the different methods for assaying creatinine and the different centres involved had no influence on the estimation of the totCrCL.

After removing the two patients who had undergone amputation (27 fluid collections), the ranking of the equations for all the parameters considered was substantially unchanged, e.g. MAPE (Gates = 14.2%, 4-MDRD = 16.0%, Virga = 16.3%), 30% relative accuracy (Gates = 86.2%, 4-MDRD = 84.2%, Virga = 77.6%), Rho correlation coefficient (Gates = 0.706, Virga = 0.706, 4-MDRD = 0.696), RMSE (Gates = 13.20, Virga = 13.31, 4-MDRD = 13.43), Cohen’s $k$ value (Virga = 0.435, Gates = 0.418, 4-MDRD = 0.395) and AUC (Virga = 0.826, Gates = 0.825, 4-MDRD = 0.819).

Discussion

Identifying patients on PD with a low total clearance (PD inadequacy) is a priority.

of at least 60 L/week 1.73 for high and moderate–high transporters, and 50 L/week 1.73 for low and low–moderate transporters, respectively, while the European PD Guidelines 2005 recommend a minimum totCrCL target of at least 45 L/week 1.73 [25].

Many issues may be involved when adequacy targets are not met, including (a) non-compliance with the prescribed dialysis dose (this is true of 40% of patients, according to Bernardini [26]); (b) deterioration in residual renal function (which may represent 50% of the total clearance [27]); (c) a low peritoneal permeability (which coincides with a lower peritoneal CrCL in CAPD [28]); (d) a patient’s large size (an average daily dialysis dose of 140 mL/kg is needed in anuric patients on CAPD, which means >3 L × 4 daily for a patient weighing 90 kg [29]).

Of course, more than one of these factors may be involved in a given patient.

A simple tool for judging the adequacy of PD by estimating totCrCL would be very useful.

The National Kidney Foundation (NKF) recommends estimating GFR from sCr measurements as a method for assessing kidney function: the Cockcroft and 4-MDRD formulas have been suggested for this purpose in the NKF-K/DOQI guidelines, for high and low GFR, respectively [30].

The MDRD formula stemmed from a study on the Modification of Diet in Renal Disease that measured patients’ GFR from renal 125I-iothalamate CL [31]: several different MDRD equations were developed, but the four-variable MDRD equation (4-MDRD, considering only age, sCr, gender and race) [13] is the most widely used. Although Cr assays are calibrated differently from the laboratory calibration that led to the development of the 4-MDRD equation, the differences in the estimates obtained using this equation (uncalibrated versus calibrated Cr assays) are presumably significant only for lower sCr levels, as demonstrated by Coresh et al. [32], so the lack of any assay standardization for measuring sCr concentrations will have a negligible influence on dialysis patients.

To be useful, an estimate has to be both accurate and precise.

Accuracy is defined as the ability of a measurement to match the actual value of the quantity being measured or the degree of conformity of a calculated quantity to its true value. Precision is the ability of a measurement to be reproduced consistently or the degree to which further calculations produce the same results.

The 4-MDRD equation performed in our study in much the same way as in a data set pooled from 10 studies and involving 5504 people with and without renal failure (the mean percentage error was −5.9% versus −5.8% and the ±30% relative accuracy was 84% versus 83% [33]), but this equation did not produce the best result in any of the parameters that we considered; it was less accurate than the Gates equation (15.9% versus 14.1%), based on the median absolute% error (Table 3), and it was less precise than the Gates and Virga equations (13.39 versus 13.15 and 13.28), as assessed using the RMSE (Table 5).

Although there is no agreement as to what predictive value can be considered clinically acceptable, we feel that, since the accuracy of the 4-MDRD equation is currently considered acceptable for uraemic patients in clinical nephrology, the same could apply to PD, and the predictive power of a more accurate equation, such as the Gates equation, would be even more acceptable.

No formula is more widely used to predict GFR, however, than the one proposed by Cockcroft even though the original aim of the Cockcroft formula was to predict CrCL [7].

Stirling et al. examined the Cockcroft equation’s power to estimate totCrCL in 35 PD patients, establishing a linear correlation coefficient of 0.82, but a mean overestimation of about 10 L/week [17]. The Cockcroft equation’s performance proved unsatisfactory in our study since seven equations did better in terms of accuracy and agreement, six offered a higher precision, and five a better sensitivity and specificity.

According to our results, the Gates and Virga equations performed best: the Gates formula offered the best accuracy, relative accuracy and precision, while the Virga equation revealed the best agreement, sensitivity and specificity. These results mean that the Gates equation is probably the most suitable for estimating totCrCL in PD, while the Virga formula is slightly more reliable for estimating totCrCL classes (i.e. > 50 L versus < 50 L).

The Gates equation has seldom been tested in the past and it has often been copied erroneously from the original paper.

The Gates equation was developed using a hundred 1.73 BSA-normalized CrCLs from 90 patients [10], while Virga’s equation was based on 530 CrCLs (1 per patient) to obtain a dual equation demanding BSA normalization [15].

Taking into account that the coefficient of variability of the totCrCL in PD patients, using three CL measurements over a 1-week period, was reportedly 6.0% [23] and 9.4% [34], the real MAPE of the equations studied could be calculated by subtracting the value of their variability: for example, 14%−6% = 8% (Gates). In fact, ~42% of the total variability is due to the variability in the single fluid collections (see Statistics).

Although fluid collection still represents the gold standard for assessing the adequacy of dialysis in PD patients, estimating their totCrCL by means of a Cr-based formula enables the nephrologist to implement a frequent, easy, approximate adequacy monitoring procedure at no additional expense.

Our study ascertained how 12 Cr-based equations performed in estimating totCrCL in PD patients with a view to enabling the most accurate and precise among them to be chosen for use in approximately assessing totCrCL albeit with the known limitations of all eGFR Cr-based formulas (i.e. they are not applicable to cirrhotic, paraplegic or amputated subjects, the malnourished, <18 years, pregnant women or, more in general, subjects in an unsteady metabolic state). Another very important limitation is represented by the possibility of changes in nutritional and muscle mass status inducing lower serum creatinine values and a consequently fictitious increase in the totCrCL estimate, even without any change in dialysis prescription.

Providing all such limitations are borne in mind, a rough estimation of adequacy of PD could be estimated monthly.

Conflict of interest statement. None declared.
Appendix

Edwards–White (mL/min) [4]

\[ \text{CrCL} = (94.3 + \text{sCr}) - 1.8 \text{ for males} \]
\[ \text{CrCL} = (69.9 + \text{sCr}) - 2.2 \text{ for females} \]

Mawer (mL/min) [5]

\[ \text{CrCL} = \frac{[\text{BW}^{0.293} - 0.203 \times \text{age}] \times [1 - 0.03 \times \text{sCr}]}{[14.4 \times \text{sCr}]} \text{ for males} \]
\[ \text{CrCL} = \frac{[\text{BW}^{0.253} - 0.175 \times \text{age}] \times [1 - 0.03 \times \text{sCr}]}{[14.4 \times \text{sCr}]} \text{ for females} \]

Jeliffe (mL/min 1.73 m²) [6]

\[ \text{CrCL} = \frac{[98 - \text{age} - 20/20]}{\text{Cr}} \text{ for males} \]
\[ \text{CrCL} = \frac{[98 - \text{age} - 20/20]}{0.90/\text{Cr}} \text{ for females} \]

Cockcroft–Gault (mL/min) [7]

\[ \text{CrCL} = \frac{[140 - \text{age} \times \text{BW}]}{72 \times \text{Cr}} \text{ for males} \]
\[ \text{CrCL} = \frac{[(140 - \text{age}) \times \text{BW}]}{(72 \times \text{Cr})} \times 0.85 \text{ for females} \]

Bjornsson (mL/min) [8]

\[ \text{CrCL} = \frac{[27 - (0.173 \times \text{age})] \times \text{BW}^0.07}{\text{Cr}} \text{ for males} \]
\[ \text{CrCL} = \frac{[25 - (0.175 \times \text{age})] \times \text{BW}^0.07}{\text{Cr}} \text{ for females} \]

Hull (mL/min) [9]

\[ \text{CrCL} = \frac{[(145 - \text{age} \times \text{Cr} - 3) \times \text{BW}/70]}{0.85 \text{ for males}} \]
\[ \text{CrCL} = \frac{[(145 - \text{age} \times \text{Cr} - 3) \times \text{BW}/70]}{0.85 \text{ for females}} \]

Gates (mL/min 1.73 m²) [10]

\[ \text{CrCL} = \frac{[89.4 \times \text{sCr}^{(-1.2)}] + [(55 - \text{age}) \times (0.447) \times \text{sCr}^{(-1.1)}]}{0} \text{ for males} \]
\[ \text{CrCL} = \frac{[60.0 \times \text{sCr}^{(-1.1)}] + [(56 - \text{age}) \times (0.300) \times \text{sCr}^{(-1.1)}]}{0} \text{ for females} \]

Salazar (mL/min) [11]

\[ \text{CrCL} = \frac{[137 - \text{age}] \times ([0.285 \times \text{BW}) + (12.1 \times \text{H}^2)/(\text{sCr} \times 51)]}{0} \text{ for males} \]
\[ \text{CrCL} = \frac{[146 - \text{age}] \times ([0.287 \times \text{BW}) + (9.74 \times \text{H}^2)/(\text{sCr} \times 60)]}{0} \text{ for females} \]

Davis–Chandler (mL/min) [12]

\[ \text{CrCL} = (140 - \text{age})/\text{Cr} \text{ for males} \]
\[ \text{CrCL} = [(140 - \text{age}) \times 0.85]/\text{Cr} \text{ for females} \]

4-MDRD (mL/min 1.73 m²) [13]

\[ \text{GFR} = 186 \times (\text{sCr}^{(-1.154)} + (\text{age}^{(-0.203)}) \text{ for males}. \]
\[ \text{GFR} = 186 \times (\text{sCr}^{(-1.154)} + (\text{age}^{(-0.203)}) \times 0.742 \text{ for females} \]
\[ \text{GFR} = 186 \times (\text{sCr}^{(-1.154)} + (\text{age}^{(-0.203)}) \times 1.212 \text{ for African-American} \]

Rule (mL/min 1.73 m²) [14]

\[ \text{GFR} = \frac{\text{Cr}}{(1.911 + (5.249/\text{Cr}) - (2.114/\text{Cr}^2) - (0.00686/\text{age})} \text{ for males} \]
\[ \text{GFR} = \frac{\text{Cr}}{(1.911 + (5.249/\text{Cr}) - (2.114/\text{Cr}^2) - (0.00686/\text{age})} - 0.205 \text{ for females} \]

Virga (mL/min) [15]

\[ \text{CrCL} = \frac{[69.4 - 0.59 \times \text{age} + 0.79 \times \text{BW}]}{\text{Cr}} - 3.0 \text{ for males} \]
\[ \text{CrCL} = \frac{[57.3 - 0.37 \times \text{age} + 0.51 \times \text{BW}]}{\text{Cr}} - 2.9 \text{ for females} \]

\( \text{BW} \), body weight (Kg); \( \text{Cr} \), serum creatinine (mg/dL), age (years); \( H \), height (meters).

References

Comparison between creatinine-based equations for estimating total creatinine clearance in PD 269


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