Letter on the article “Plasma creatinine, Cockcroft and MDRD: Validity and limitations for evaluation of renal function in chronic kidney disease”

Assessment of glomerular filtration (GFR) rate is an important issue in geriatric practice. Indeed, even when they don’t have renal disease, many old subjects have an impaired renal function, which should be taken into account before prescribing drugs eliminated through the renal route or investigations requiring iodine injection. This point is crucial in subjects older than 80 years, because the effects of renal aging on GFR are more pronounced, and they are prone to experience care-related adverse effects.

In their review about GFR estimates, Flamant et al. indicated that the Modification of Diet in Renal Disease (MDRD) formula is more appropriate than the Cockcroft and Gault (CG) formula to assess renal function in the elderly [1]. On the contrary, based on our experience and literature, we think that CG formula gives a more precise estimation than the MDRD formula in very old patients. In a recent study [2], we have calculated the CG and MDRD formula in 121 patients aged of 86 ± 7 years, admitted in geriatric wards and who had an indwelling bladder catheter. The values calculated from the formulae were compared to creatinine clearance (mClCr) measured using carefully collected 24-hour urine samples. Bias of CG formula (estimated minus measured values) was −3.5 ± 22.5 mL/min, and that of MDRD was 20.1 ± 28.2 mL/min (P < 0.001). We also classified the patients according to renal impairment (no impairment if ClCr > 60 mL/min/1.73 m², moderate impairment if 60 > ClCr > 30 mL/min/1.73 m², and severe impairment if ClCr < 30 mL/min/1.73 m²) using mClCr and Cockcroft and MDRD formulae (table I). Concordance was moderate with the CG formula (kappa = 0.54) and poor with the MDRD formula (kappa = 0.28).

Others studies in very old patients have concluded that MDRD formula didn’t estimate the GFR better than the CG formula. In 48 patients aged 84 ± 6 years, van den Noortgate et al. [3] found a bias of −6.5 mL/min for the CG formula, and of 10.5 mL/min for the MDRD formula, using GFR isotopic measurement as the reference. In the same way, Lamb et al. [4]

Table I

Concordance in the diagnosis of renal impairment (Absent, Moderate, Severe) determined according to measured creatinine clearance (reference method) and Cockcroft-Gault (CG) and MDRD formulae with normalization for body surface.

<table>
<thead>
<tr>
<th>Renal impairment according to creatinine clearance</th>
<th>Renal impairment according to measured creatinine clearance, normalized for 1.73m², n (%)</th>
<th>Kappa value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Absent (n = 34) Moderate (n = 68) Severe (n = 19)</td>
<td></td>
</tr>
<tr>
<td>CG</td>
<td></td>
<td>0.54</td>
</tr>
<tr>
<td>Absent (n = 28)</td>
<td>20 (59) 8 (12) 0 (0)</td>
<td></td>
</tr>
<tr>
<td>Moderate (n = 74)</td>
<td>13 (38) 54 (79) 7 (37)</td>
<td></td>
</tr>
<tr>
<td>Severe (n = 19)</td>
<td>1 (3) 6 (9) 12 (63)</td>
<td></td>
</tr>
<tr>
<td>MDRD</td>
<td></td>
<td>0.28</td>
</tr>
<tr>
<td>Absent (n = 75)</td>
<td>30 (88) 41 (60) 4 (22)</td>
<td></td>
</tr>
<tr>
<td>Moderate (n = 42)</td>
<td>4 (12) 27 (40) 11 (56)</td>
<td></td>
</tr>
<tr>
<td>Severe (n = 4)</td>
<td>0 (0) 0 (0) 4 (22)</td>
<td></td>
</tr>
</tbody>
</table>

Absent (no impairment) if ClCr > 60 mL/min/1.73 m²; moderate impairment if 60 > ClCr > 30 mL/min/1.73 m²; severe impairment if ClCr < 30 mL/min/1.73 m².
found in 52 patients aged 80 ± 5 years a bias of −5.2 mL/min for the CG formula, and of 6.4 mL/min for the MDRD formula. Our results and the literature show that the CG formula underestimates the GFR and that the MDRD formula overestimates it. To conclude, these different studies show that the MDRD formula doesn’t estimate better the GFR in very old patients. On the opposite, it seems that the CG formula could be more appropriate (and easier to use) in this particular population, good classification of renal impairment was better than with the MDRD formula (table I). All these studies emphasize the fact that none of the two formulas is perfect to estimate the renal function and that more research is needed to find a better way to simply assess renal function in the elders.

Conflict of interest: none

References


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Authors’ response to the letter on the article ‘‘Plasma creatinine, Cockcroft and MDRD: Validity and limitations for evaluation of renal function in chronic kidney disease’’

Réponse des auteurs à la correspondance à propos de l’article « Mesure et estimation du débit de filtration glomérulaire : quels outils pour la prise en charge de la maladie rénale chronique ? »

Chauvelier et al. raise here the problem of Glomerular Filtration Rate (GFR) estimation in very old subjects. Based on their recent work in very old hospitalized patients, they argue that the 4-variables Modification of Diet in Renal Disease formula (MDRD) overestimates GFR in this population, and recommend the use of Cockcroft’s formula (Cockcroft) [1]. In this study, Pequignot et al. used a non standardized creatinine assay. Plasma creatinine assays have been largely modified within the past decades. A long quest for better specificity was marked by successive improvements such as ultrafiltration or dialysis of samples, widespread use of kinetic colorimetric methods and more recently through compensation for non-creatinine chromogens of colorimetric assays and progressive rise of enzymatic assays allowing standardization to Isotope Dilution Mass Spectrometry (IDMS) with reference to Standard Reference Materials (SRM). MDRD has been recently updated in order to be used with these standardized creatinine assays. On the other hand, Cockcroft has not been analytically re-evaluated as the creatinine assay evolved. As a consequence, GFR estimation performances using Cockcroft are directly dependant on which creatinine assay method is used, and the results of this study don’t remain valid with current standardized creatinine assay. The study by Pequignot et al. relies on the urinary creatinine clearance (U24CICreat) as reference for GFR value. It should be noticed that U24CICreat is only a poor estimator of GFR, as creatinine is partially excreted by tubular secretion. Nevertheless, it’s important to outline here that Cockcroft was established in comparison to U24CICreat, unlike MDRD, which was established in comparison to gold standard GFR measurements (Body Surface Area normalized urinary iothalamate clearance). This could partially explain the better performance of Cockcroft when U24CICreat is used as reference for renal function, but does not presume the respective performances of MDRD and Cockcroft when compared with measured GFR.