References


Research letters

Estimating GFR in the oldest old: does it matter what equation we use?

SIR—In coming decades, the Western world will face an epidemic of ageing. This forthcoming ‘grey epidemic’ will lead to an explosion of chronic diseases like chronic kidney disease (CKD). CKD is an important public health problem for several reasons. First, the prevalence of CKD is high [1], especially among patients aged 70 years and older [2]. Second, knowledge of the actual glomerular filtration rate (GFR) of a patient has important consequences in terms of medication, as the dosages of many drugs should be adapted according to renal function [3]. Finally, the cost and the burden of renal replacement therapy are high.

Measurement of the GFR is the gold standard index of overall kidney function. Several equations derived from endogenous filtration markers were developed to estimate this GFR. However, the most accurate method for estimating GFR, especially in elderly patients, is topic of on-going debate [4]. A recent systematic review [5] showed that the modification of diet in renal disease (MDRD) equation [6] does not differ appreciably from the Cockcroft–Gault equation [7] in terms of the accuracy with which GFR is estimated and that there is limited but promising evidence concerning serum cystatin C level as a biomarker of kidney function in the oldest of the old [8, 9]. In the absence of well-validated equations, a variety of equations are currently used in research as well as in clinical practice to estimate GFR in the elderly.

Therefore, this study was designed to determine differences in GFR estimated according to various equations in elderly patients and to investigate the clinical relevance of these differences at an individual patient level.
Methods

The BELFRAIL study (BF_C80+) is a prospective, observational, population-based cohort study of subjects aged 80 years and older in three well-circumscribed areas in Belgium. The full study design including power calculation has been described in detail [10]. Briefly, between 2 November 2008 and 15 September 2009, 29 general practitioner (GP) centres were asked to recruit consecutive patients aged 80 years and older. Only three exclusion criteria were used: severe dementia, palliative situations and medical urgency. Clinical research assistants performed a standardised measurement of weight and height. Blood samples were collected in the morning. The study protocol was approved by the Biomedical Ethics Committee of the Medical School of the Université Catholique de Louvain, Belgium (B40320084685).

Laboratory analyses

Serum samples obtained after centrifugation within <4 h of collection were stored at −80°C until analysis. Serum concentration of creatinine and cystatin C was measured using a Unicel DxC 800 Synchron instrument (Beckman Coulter, Inc., Brea, CA, USA). We calibrated our creatinine assays against an isotope dilution mass spectrometry (IDMS) traceable method.

GFR estimating equations

We used four different equations to estimate the GFR: the Cockcroft–Gault equation (CGgfr) [7], the abbreviated Modification of Diet in Renal Disease study equation (MDRDgfr) [6], the Chronic Disease Epidemiology collaboration equations (CKD-EPIgfr) [11] and the CKD epidemiology collaboration 2 Cystatin C equation (CKD2cystCgfr) [9].

Data analysis

Individual differences in eGFR were analysed in three ways. First, matches and mismatches at an individual patient level were analysed using Kappa statistics after classifying patients according to CKD stages using various equations. Second, relative differences between eGFR values (percentage differences from the mean of two eGFRs) for the same patient were computed. Finally, Bland–Altman plots were constructed to visualize individual (relative) differences. Data analyses were performed using SPSS 16.0 software (SPSS, Inc., Chicago, IL, USA) and MedCalc 11.3.3 software (MedCalc Software, Mariakerke, Belgium).

Results

In total, 567 patients were included in the BELFRAIL cohort, of which 36.9% were male. The mean study population age was 85 ± 3.9 years. Blood tests were conducted on 553 patients, and data were available to calculate all four eGFRs for 536 patients. The general characteristics of the study population were published earlier [10].

Differences in the estimated prevalence of CKD between equations were analysed. Using the CGgfr the prevalence of an eGFR <60 ml/min/1.73 m² was 29%, 34% had eGFR between 45 and 60 ml/min/1.73 m², 27% between 30 and 45 ml/min/1.73 m² and 10% eGFR <30 ml/min/1.73 m². For the MDRDgfr, these prevalences were 56, 24, 14 and 6%; for the CKD-EPIgfr, these prevalences were 52, 24, 17 and 6% and for the CKD2cystCgfr, these prevalences were 52, 24, 17 and 6%.

Furthermore, there were differences in CKD stage according to the eGFR at individual patient level; especially between the CGgfr equation and the other eGFRs (see Table 1). Moreover, when analyses were limited to patients with an eGFR <30 ml/min/1.73 m², differences were observed between equations (38–58% of estimates matched). Only estimates derived using the MDRD equation and the CKD-EPI equation matched well (82% of cases) for CKD stages 4 or 5.

Although the MDRDgfr and CKD-EPIgfr estimates matched well, 40.1% of MDRDgfr estimates differed by more than 30% from the CGgfr estimates, whereas only 11.2% of the CKD-EPIgfr estimates differed by more than 30% from the CGgfr estimates. An additional analysis (data

### Table 1. Individual relative differences and mismatches after classifying the study population according to CKD stages using eGFRs calculated using different equations

<table>
<thead>
<tr>
<th>Method</th>
<th>Kappa (95% CI)</th>
<th>Total matches (%)</th>
<th>&gt;1 Category mismatch</th>
<th>Match &lt;30 ml/min or not (%)</th>
<th>Difference &lt;10%</th>
<th>Difference 10–20%</th>
<th>Difference 20–30%</th>
<th>Difference &gt;30%</th>
</tr>
</thead>
<tbody>
<tr>
<td>CG-MDRD</td>
<td>0.324* (0.267–0.377)</td>
<td>277 (51.7)</td>
<td>17</td>
<td>27/60 (45.0)</td>
<td>9.9</td>
<td>22.8</td>
<td>27.2</td>
<td>40.1</td>
</tr>
<tr>
<td>MDRD-CKD-EPI</td>
<td>0.934* (0.905–0.961)</td>
<td>517 (96.5)</td>
<td>0</td>
<td>31/38 (81.5)</td>
<td>52.1</td>
<td>39.3</td>
<td>6.5</td>
<td>2.0</td>
</tr>
<tr>
<td>MDRD-CKD2cystC</td>
<td>0.497* (0.438–0.556)</td>
<td>371 (69.2)</td>
<td>11</td>
<td>21/42 (50.0)</td>
<td>22.9</td>
<td>25.4</td>
<td>18.2</td>
<td>21.9</td>
</tr>
<tr>
<td>CKD2cystCG</td>
<td>0.297* (0.242–0.352)</td>
<td>267 (49.8)</td>
<td>40</td>
<td>23/60 (38.3)</td>
<td>22.9</td>
<td>21.8</td>
<td>17.7</td>
<td>37.5</td>
</tr>
<tr>
<td>CKD2cystC-CKD-EPI</td>
<td>0.496* (0.437–0.555)</td>
<td>369 (68.8)</td>
<td>13</td>
<td>23/47 (48.9)</td>
<td>31.7</td>
<td>28.9</td>
<td>18.7</td>
<td>20.6</td>
</tr>
<tr>
<td>CKD-EPI-CG</td>
<td>0.370* (0.314–0.424)</td>
<td>294 (54.8)</td>
<td>14</td>
<td>33/57 (58.0)</td>
<td>32.6</td>
<td>29.9</td>
<td>26.3</td>
<td>11.2</td>
</tr>
</tbody>
</table>

MDRD, modification of diet in renal disease study equation; CG, Cockcroft–Gault equation; CKD2cystC, chronic kidney disease epidemiology collaboration 2 cystatin C equation and CKD-EPI, chronic kidney disease epidemiology collaboration equation.

*Significance ≤0.001.
not shown) showed that among patients for whom the relative difference between the CGgfr and MDRDgfr estimates was above 30%, 66.5% had an MDRDgfr $\geq 60$ ml/min. These and other differences were visualised in Blant–Altman plots (Figure 1).

**Discussion**

Two important findings emerged from this study. First, a major difference in the estimated prevalence of impaired renal function was observed between estimates derived using the CG equation and those derived using the other equations. These differences are in agreement with those of a large study on institutionalized patients in Canada. Garg *et al.* [2] reported that the estimated prevalence of impaired renal function in a subgroup of patients aged $\geq 80$ years was 28% for men and 38% for women according to the MDRD equation and 62 and 63% for men and women, respectively, according to the CG equation. Second, we found large differences in eGFR between equations at individual patient level. Previously, Pedone...
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et al. [12] analysed creatinine-based GFR estimations in 7,747 patients older than 65 years. The authors reported a Kappa coefficient for the agreement between CGgfr and MDRDgfr-based classification of 0.44 (CI 0.43–0.45). Froissart et al. [13] reported individual differences for a subgroup of patients aged ≥65 years. They observed 68% agreement for CKD stage between CGgfr estimates and ‘true GFR’ (Cr-EDTA clearance) and 70.8% agreement between MDRDgfr estimates and true GFR. In this study, 13 and 22% of the patients had a relative difference of >30% between true GFR and the MDRDgfr and CGgfr estimates, respectively. In our study, agreement between CGgfr and MDRDgfr estimates was only 52%. So the differences between MDRDgfr and CGgfr estimates at individual level and at mean level was only 52%. The authors reported that 13% had a relative difference of >30% between the MDRDgfr estimate and the gold standard value and that 13% had a relative difference of >30% between the CKD2Cystgfr estimate and the gold standard value. Our study showed that 22% of patients had a relative difference of >30% between the MDRDgfr and CGgfr estimates.

Although the MDRDgfr and CKD-EPIgfr estimates matched well, differences in the eGFR >60 ml/min/1.73 m² were large (see Figure 1). This finding is in line with earlier research [14].

Mean and individual differences in CKD2cystCgfr estimates and eGFR based on creatinine levels were larger when using the CG equation than when using the MDRD and CKD-EPI equations. Stevens et al. [14] reported that 17% of patients older than 65 years had a relative difference of >30% between the MDRDgfr estimate and the gold standard value and that 13% had a relative difference of >30% between the CKD2Cystgfr estimate and the gold standard value. Our study showed that 22% of patients had a relative difference of >30% between the MDRDgfr and CKD2CystCgfr estimates.

Our study has some limitations because we had only one blood measurement for each patient. We cannot make definitive conclusions regarding CKD because multiple measurements are necessary to assess CKD. We had no data on proteinuria for detecting stage 1 or 2 CKD or for recognizing patients at higher risk of disease progression or complications in more advanced stages. We did not measure the true GFR using a gold standard method; as a result, we cannot conclude which would be the best way to estimate GFR in the very elderly.

In our study, a large representative sample of the oldest old was recruited. We were able to show that differences between equations used for estimating GFR have a significant impact on CKD classification in individual elderly patients. These equations differ greatly in distinguishing whether or not elderly patients have an eGFR of <30 ml/min/1.73 m². The large differences in GFR estimates for individual patients show that there is an urgent need for further research on methods for estimating GFR in elderly patients. Such research should compare existing equations and new equations based on creatinine or cystatin C levels with true GFRs measured using the (2) gold standard method and a representative sample of the oldest old. Until such results are available, eGFRs and CKD stage classification of the elderly based on eGFRs should be regarded with caution.

Key points

- The most accurate method for estimating GFR, especially in older patients, is topic of an ongoing debate.
- Differences in prevalence of CKD were observed using the CG equation compared with other equations.
- Major differences in eGFR were observed between the eGFR estimated by different equations at an individual patient level.
- These equations differ greatly in distinguishing whether or not older patients have an eGFR of <30 ml/min/m².

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References

SIR—A survey of UK geriatricians conducted in 2005 showed that only 4% had chosen their specialty while at university [1]. However, recent changes to UK postgraduate training mean that doctors are expected to form career plans earlier, starting while undergraduates [2–4]. Attitudes and perceptions about geriatric medicine formed by medical students are therefore increasingly important.

It is thought that students might be motivated to undertake a career in geriatrics following an attachment in the specialty [5, 6], or following personal experience of caring for older people [5, 7]. However, no attempt has been made at a national level to explore how students feel about geriatric medicine, or how their opinions are shaped by teaching and extra-curricular experience.

Against this background we set out to describe attitudes to, and perceptions of, geriatric medicine among the students of all UK medical schools.

Methods

A 39-question online survey was developed by medical students from the Universities of Nottingham and Oxford with support from an academic geriatrician. The questionnaire was then sent to the British Geriatrics Society (BGS) Education and Training Committee for expert content validation before piloting for usability with 30 students.

The resulting questionnaire comprised four sections headed: demographics, teaching, extracurricular and career. Question-styles were varied to include multiple choice, Likert scales and short answer questions. A copy of the questionnaire is available online [8].

A web-link to the survey was emailed to UK medical students using the British Medical Association and Royal Society of Medicine mailing lists, together reaching the majority of students. As an incentive to respond, a prize draw was advertised at the start of the questionnaire—participants were informed that this was for funding to attend a BGS scientific meeting and invited to submit their email address only after they had completed the survey. A reminder email was sent 3 weeks after the initial invitation.

Results

A total of 1,562 students responded from 29/31 UK medical schools, representing 4% of medical students [9]. The median number of respondents per school was 31 (range 1–185; mode 31). The average duration of time at medical school was 3.3 years with most responses from year 4 students and least from year 6 (25.2 and 5.7% of respondents, respectively). Of the total, 71% were female, 6.5% mature students and 8.9% graduate entry students, with no difference in response by these variables. Although incomplete responses were seen for several questions, no consistent pattern of non-response was evident.

Among the respondents, 565 (36%) students had completed a separate teaching module in geriatric medicine, 723 (46%) had undertaken a clinical placement in the specialty and 1,007 (65%) had been taught using cases focusing on older patients during problem-based learning. The mean scores for quality and enjoyment of teaching were 3.55 ± 1.01/5 and 3.42 ± 1.08/5, respectively (1 being poor and 5 excellent). Both were positively correlated with teaching by non-doctor team members, exposure to inspiring geriatricians, attachments in community geriatrics and separate teaching modules or dedicated clinical placements in the specialty (P < 0.05 for all; Spearman’s correlation coefficient). Also, 830 (53%) students stated they would like more teaching in geriatrics.

Of the total number, 1,193 (76%) respondents associated geriatrics with a positive impact on the lives of older people, 842 (54%) considered it to involve contact with likeable patients and 813 (52%) to be intellectually stimulating. However, 615 (39%) associated the specialty with low earning potential and 820 (52%) with low prestige within...