Comparison of the MDRD and the CKD-EPI equations to estimate the glomerular filtration rate in the general population

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ABSTRACT

Background and objective: The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation has been proposed as a replacement for the Modification of Diet in Renal Disease (MDRD) equation to estimate the glomerular filtration rate, but this equation has not yet been evaluated in the general population.

Patients and methods: Cross-sectional analysis of a random sample of 858 participants from the general population aged 50 – 75 years without known kidney disease. The prevalence of low eGFR (<60 mL/min/1.73 m²) was assessed with the MDRD and the CKD-EPI equations in the overall sample and in normoalbuminuric individuals.

Results: With the MDRD equation the median eGFRs (interquartile range) in men/women were 63.3(12.2)/56.7(9.4) mL/min/1.73 m², and with the CKD-EPI equation 66.6(14.2)/61.3(11.6) mL/min/1.73 m², respectively. The prevalence of low eGFR in men/women was 35.2%/68.5% and 25.1%/45.7% with the MDRD and the CKD-EPI equations, respectively. Normoalbuminuric women without risk factors for CKD experienced the most pronounced reduction in the number of cases with low eGFR with the CKD-EPI equation. The prevalence of renal impairment in this subgroup still remained even greater than that in men with diabetes, hypertension, or cardiovascular disease.

Conclusions: Compared with the MDRD, the CKD-EPI equation generates a substantial reduction in the prevalence of renal impairment in subjects with diabetes, hypertension, cardiovascular disease, and in subjects without risk factors. The prevalence of renal impairment in normoalbuminuric females may be still overestimated with the CKD-EPI equation.

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Comparación de las ecuaciones MDRD y CKD-EPI en la estimación de la tasa de filtrado glomerular en la población general

Resumen

Fundamento y objetivo: La ecuación Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) ha sido propuesta para sustituir a la actualmente recomendada Modification of Diet in Renal Disease (MDRD) para el cálculo de la tasa de filtrado glomerular (TGF), si bien no ha sido aún evaluada en la población general. Pacientes y Método: Estudio transversal de una muestra aleatoria de 858 individuos de la población general con edades entre 50 – 75 años sin enfermedad renal conocida. Comparación de la prevalencia de una TGF <60 mL/min/1.73 m² calculada con las ecuaciones MDRD y CKD-EPI en toda la muestra y en el subgrupo de individuos normoalbuminurínicos (cociente albúmina/creatinina < 30 mg/g).

Resultados: Con la ecuación MDRD la mediana de la TFG (rango intercuartílico) en varones/mujeres fue de 63.3 (12.2)/56.7 (9.4) mL/min/1.73 m², y con la ecuación CKD-EPI 66.6 (14.2)/61.3 (11.6) mL/min/1.73 m², respectivamente. La prevalencia de una TFG baja en varones/mujeres fue del 35.2 – 68.5%, y del 25.1 – 45.7% con las ecuaciones MDRD y CKD-EPI, respectivamente. El grupo de mujeres normoalbuminurínicas sin factores de riesgo para enfermedad renal crónica presentó la mayor reducción en la prevalencia de una TFG baja con la ecuación CKD-EPI. Sin embargo, la prevalencia en este grupo se mantuvo incluso más elevada que en el de los varones con diabetes, hipertensión o enfermedad cardiovascular.
Introduction

The overall prevalence of chronic kidney disease (CKD) is estimated at up to 11% of adults in the United States and 6% in Europe. Patients with CKD are at risk for not only progression to end stage renal disease but, and far more frequently, for the development of cardiovascular disease (CVD). Therefore, early identification of CKD by reliable methods is an important part of preventive health strategies.

The Modification of Diet in Renal Disease (MDRD) study equation has become the preferred method for estimating glomerular filtration rate (eGFR). This formula was initially developed in patients with known CKD, but has subsequently been widely used in the general population and in people with diverse cardiovascular risk profiles, even though there is no proof of its reliability as a screening test in people without known CKD. The MDRD equation provides unbiased and accurate estimates in a wide range of subgroups of patients when the eGFR is < 60 mL/min/1.73 m². For estimates equal or greater than 60 mL/min/1.73 m² the MDRD equation is not only less accurate but also less precise, especially in the absence of albuminuria and other markers of kidney damage. The MDRD has also been reported to be less precise in the absence of CKD than in cases with known disease, as eGFR values significantly overlap between patients with and without CKD and this compromises the use of eGFR to separate these two patient groups. However, clinicians continue using the MDRD equation for detecting renal impairment in everyday clinical practice, as measured GFR is not a suitable tool in this setting.

In an attempt to overcome some of the drawbacks of the MDRD equation, it has been suggested that screening for CKD should be targeted at subjects at risk, in whom an eGFR 1.73 m² the MDRD equation is not only less accurate but also less precise, especially in the absence of albuminuria and other markers of kidney damage. The MDRD has also been reported to be less precise in the absence of CKD than in cases with known disease, as eGFR values significantly overlap between patients with and without CKD and this compromises the use of eGFR to separate these two patient groups. However, clinicians continue using the MDRD equation for detecting renal impairment in everyday clinical practice, as measured GFR is not a suitable tool in this setting.

In an attempt to overcome some of the drawbacks of the MDRD equation, it has been suggested that screening for CKD should be targeted at subjects at risk, in whom an eGFR < 60 mL/min/1.73 m² could be considered a true-positive result. However, the assumption that in the absence of markers of kidney damage a correct interpretation of low eGFR can be ascertained by taking into account the presence or absence of risk factors for CKD has not been evaluated thoroughly. Another way to improve the accuracy obtained with the MDRD equation is the development of new estimative equations. Levey et al. have recently proposed a new equation to replace the original MDRD equation for the routine clinical use in the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) study. But although the CKD-EPI equation has improved in bias, its precision remains suboptimal. Until now there is limited information about the performance of this new equation in people from the general population, especially in people whose renal function is unknown and who do not have markers of kidney damage.

Our study compared the eGFR generated by the MDRD and the CKD-EPI equations in a random sample of individuals from the general population without known kidney disease. We also assessed whether there was a significant difference in the estimates of GFR among normoalbuminuric participants with and without risk factors for CKD.

Methods

Study population

This study was performed using the data from the Sanlúcar Study, the design of which is described elsewhere. It was a cross-sectional population-based study carried out in Sanlúcar de Barrameda, Spain, between July 2006 and February 2007. The study population was a random sample of 858 participants aged 50–75 years obtained from the local census, all of Caucasian origin. The investigation was carried out in accordance with the principles of the Declaration of Helsinki. Subjects who agreed to participate were included after being interviewed and informed about the nature, risks, and benefits of the study in the clinic and giving written consent.

Laboratory tests and estimates of GFR

Blood and urine samples were obtained from all participants in the early morning after overnight fasting. All participants were asymptomatic and without intercurrent illnesses at the time of testing. An ILAB-600 analyzer and standardized reagents (ITC Diagnostics, Itxas S.A., Barcelona, Spain) were used for measuring plasma glucose, total cholesterol, HDL-cholesterol, triglycerides, and glycylated hemoglobin. The Friedewald formula was used for calculating LDL-cholesterol.

Serum creatinine was measured using the Jaffe method with an alkaline picrate assay, giving a normal range up to 1.10 mg/dL in women and 1.30 mg/dL in men. This method was calibrated to be traceable to an isotope dilution mass spectrometry reference method. Albumin was measured in an early morning urine sample using a colorimetric method, and the results were expressed as milligrams of urinary albumin per gram of serum creatinine (ACR).

Estimated GFR was calculated with the re-expressed MDRD equation for standardized serum creatinine (1) and the CKD-EPI equation (2).

\[
GFR = 175 \times \text{age}^{-0.203} \times \frac{\text{Sc}}{0.742} 
\]
if female and Sc ≤ 0.70 mg/dL GFR = 144(Sc/0.7)−0.329(0.993)²ëGFR, (2) if female and Sc > 0.70 mg/dL GFR = 144(Sc/0.7)−1.209(0.993)²ëGFR, if male and Sc ≤ 0.90 mg/dL GFR = 141(Sc/0.9)−0.411(0.993)²ëGFR, if male and Sc > 0.90 mg/dL GFR = 141(Sc/0.9)−1.209(0.993)²ëGFR, where age is expressed in years and standardized serum creatinine (Sc) in mg/dL.

An eGFR value less than 60 mL/min/1.73 m² was selected to define an abnormal GFR. Albuminuria was defined as an ACR ≥ 30 mg/g.

Risk factors for CKD

Type 2 diabetes, hypertension, and cardiovascular disease were the risk factors for CKD selected for the purposes of the study. Diabetes was diagnosed in participants being treated for diabetes and in those with fasting serum glucose ≥ 7.0 mmol/L. Hypertension was defined as already being treated with antihypertensive drugs or having a mean blood pressure of ≥ 135/85 mmHg following 24-h ambulatory blood pressure monitoring or 1 week of home blood pressure self-measurement. Patients with CVD were those with a documented diagnosis of a transient ischemic attack, ischemic stroke, stable angina, acute coronary syndrome, coronary revascularization, or peripheral arterial disease defined as an ankle–brachial index < 0.90.

Other cardiovascular and CKD risk factors were also considered. Subjects were classified as smokers (current smokers or smokers in the last year) or non-smokers (participants who never smoked or who stopped smoking a year ago). The Framingham risk score was used as an integrated tool of traditional cardiovascular risk factors.

As a reference group for comparing the performance of eGFR in subjects with risk factors for CKD, we defined a group of participants with no risk factors as the non-smoking, non-diabetic, and non-hypertensive participants with no history of CVD and a Framingham risk score < 10%.

Statistical analysis

Results are expressed as mean (95% confidence interval) for normally distributed continuous data, median (interquartile range) for continuous data without normal distribution, and frequencies (95% confidence intervals) for categorical data. Differences in the risk factor profile were compared between albuminuric and normoalbuminuric participants by categorizing an eGFR lower vs. greater than 60 mL/min/1.73 m² using the chi-square test for categorical variables, and ANOVA and Kruskal–Wallis test for normally and non-normally distributed continuous data respectively. A P-value < 0.05 was accepted as being statistically significant. SPSS for Windows, version 12.0 (Chicago, Illinois, USA) was used for the statistical analyses.

Results

GFR calculated with the MDRD equation

The general characteristics of the study sample are summarized in Table 1. The overall prevalence of renal impairment was 53%. Among them, 92.1% had an eGFR of 45–60 mL/min/1.73 m². There was a marked difference in the median eGFR and the prevalence of low eGFR by gender (Table 2). An important proportion of all cases with renal impairment was normoalbuminuric women, in whom the percentage of low eGFR was as high as in women with an ACR ≥ 30 mg/g (68.8% vs. 66.1%, respectively). Only 15.8% of cases with an eGFR < 60 mL/min/1.73 m² also had an ACR ≥ 30 mg/g, whereas up to 58.5% of participants with albuminuria also had a low eGFR.

The presence of albuminuria was associated with the most adverse risk factor profile regardless of the eGFR level. However, in the absence of albuminuria, no substantial difference in the risk factor profile was observed when comparing the groups with an eGFR ≥ or < 60 mL/min/1.73 m² (Tables 3 and 4). The values of the eGFR in the 735 normoalbuminuric participants, whether greater or lower than 60 mL/min/1.73 m², closely overlapped between individuals with and without risk factors for CKD (Figs. 1 and 2). In the subgroup of normoalbuminuric women with diabetes, hypertension, or cardiovascular disease, the range of eGFR values and the proportion of cases with an eGFR < 60 mL/min/1.73 m² were very similar to those in women with no risk factors (Fig. 3).

GFR calculated with the CKD-EPI equation

Compared with the MDRD, the most noteworthy result obtained with the CKD-EPI equation was a 16.9% absolute reduction of participants with an eGFR < 60 mL/min/1.73 m², a reduction that was greater in women than in men (22.8% vs. 10.1%). Overall, in 91.6% of cases with renal impairment, the estimates fell in the range of 45–60 mL/min/1.73 m². The subgroup of participants with the most pronounced reduction in the percentage of cases with low eGFR was the normoalbuminuric women with no CKD risk factors (29.8% absolute reduction).

Table 1

<table>
<thead>
<tr>
<th>General characteristics of the study sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>All (n = 858)</td>
</tr>
<tr>
<td>Women (n = 460)</td>
</tr>
<tr>
<td>Men (n = 398)</td>
</tr>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>Smokers</td>
</tr>
<tr>
<td>Diabetes</td>
</tr>
<tr>
<td>Hypertension</td>
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<tr>
<td>Body mass index ≥ 30 kg/m²</td>
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<tr>
<td>Framingham risk score&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Cardiovascular disease</td>
</tr>
<tr>
<td>Participants with no risk factors</td>
</tr>
<tr>
<td>Serum creatinine (mg/100 mL)</td>
</tr>
</tbody>
</table>

Data are mean (95% confidence interval) or percentages (95% confidence interval).
Table 2
Mean eGFR and percentage of low eGFR

<table>
<thead>
<tr>
<th></th>
<th>Women (n = 460)</th>
<th>Men (n = 398)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MDRD</td>
<td>CKD-EPI</td>
</tr>
<tr>
<td>Mean eGFR&lt;sup&gt;a&lt;/sup&gt;</td>
<td>56.8 (56.0 – 57.5)</td>
<td>61.4 (60.6 – 62.3)</td>
</tr>
<tr>
<td>Low eGFR&lt;sup&gt;b&lt;/sup&gt;</td>
<td>68.5 (64.0 – 72.7)</td>
<td>45.7 (41.0 – 50.3)</td>
</tr>
<tr>
<td>Low eGFR-ACR &lt;30&lt;sup&gt;c&lt;/sup&gt;</td>
<td>11.7 (8.4 – 15.8)</td>
<td>13.3 (9.0 – 18.7)</td>
</tr>
<tr>
<td>Low eGFR-ACR ≥30</td>
<td>88.3 (84.2 – 91.6)</td>
<td>86.7 (81.3 – 91.0)</td>
</tr>
</tbody>
</table>

<sup>a</sup> Mean (95% confidence interval), mL/min/1.73 m<sup>2</sup>.<sup>b</sup> eGFR < 60 mL/min/1.73 m<sup>2</sup> (percentage [95% confidence interval]).<sup>c</sup> ACR (mg/g).

Table 3
Risk factor profile according to the albumin/creatinine ratio and eGFR categories (MDRD equation)

<table>
<thead>
<tr>
<th>mL/min/1.73 m&lt;sup&gt;2&lt;/sup&gt;</th>
<th>ACR &lt; 30 mg/g</th>
<th>eGFR ≥ 60</th>
<th>eGFR &lt; 60</th>
<th>ACR ≥ 30 mg/g</th>
<th>eGFR ≥ 60</th>
<th>eGFR &lt; 60</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>351 (40.9)</td>
<td>384 (44.7)</td>
<td>51 (6.0)</td>
<td>72 (8.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>60.0 (59.4 – 60.7)</td>
<td>62.0 (61.3 – 62.6)</td>
<td>63.1 (61.0 – 65.3)</td>
<td>64.6 (63.2 – 66.4)*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender (female)</td>
<td>36.2 (31.1 – 41.5)</td>
<td>72.4 (67.6 – 76.8)</td>
<td>37.3 (24.1 – 51.9)</td>
<td>52.1 (40.7 – 64.7)*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td>110 (107 – 114)</td>
<td>112 (108 – 115)</td>
<td>121 (106 – 137)</td>
<td>122 (111 – 133)***</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haemoglobin A1C (%)</td>
<td>6.0 (5.9 – 6.1)</td>
<td>6.0 (5.9 – 6.1)</td>
<td>6.3 (6.1 – 6.9)</td>
<td>6.5 (6.1 – 6.8)*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>143 (141 – 145)</td>
<td>142 (140 – 144)</td>
<td>153 (148 – 158)</td>
<td>157 (151 – 163)*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>79 (78 – 81)</td>
<td>80 (79 – 81)</td>
<td>81 (78 – 84)</td>
<td>84 (81 – 87)***</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body mass index (kg/m&lt;sup&gt;2&lt;/sup&gt;)</td>
<td>30.4 (29.9 – 30.9)</td>
<td>31.0 (30.5 – 31.5)</td>
<td>31.3 (30.0 – 32.7)</td>
<td>32.0 (30.7 – 33.2)***</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>105 (104 – 106)</td>
<td>103 (102 – 104)</td>
<td>108 (103 – 112)</td>
<td>107 (104 – 110)***</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cholesterol (mg/dL)</td>
<td>225 (221 – 230)</td>
<td>238 (234 – 242)</td>
<td>229 (215 – 243)</td>
<td>233 (222 – 244)***</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HDL cholesterol (mg/dL)</td>
<td>56 (55 – 57)</td>
<td>60 (58 – 61)</td>
<td>55 (51 – 59)</td>
<td>53 (50 – 56)*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDL cholesterol (mg/dL)</td>
<td>142 (138 – 146)</td>
<td>150 (146 – 154)</td>
<td>145 (133 – 157)</td>
<td>147 (137 – 156)***</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triglycerides (mg/dL)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>116 (83)</td>
<td>124 (83)</td>
<td>129 (116)</td>
<td>150 (106)*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Framingham risk score&lt;sup&gt;*&lt;/sup&gt;</td>
<td>52.3 (47.1 – 57.7)</td>
<td>72.1 (67.4 – 76.6)</td>
<td>37.3 (24.1 – 51.9)</td>
<td>43.7 (31.4 – 55.3)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data are percentages (95% confidence interval) or mean (95% confidence interval).

<sup>*</sup> P < 0.001.
<sup>**</sup> P < 0.01.
<sup>***</sup> P < 0.05.
<sup>###</sup> Median (interquartile range).

Table 4
Risk factor profile according to the albumin/creatinine ratio and eGFR categories (CKD-EPI)

<table>
<thead>
<tr>
<th>mL/min/1.73 m&lt;sup&gt;2&lt;/sup&gt;</th>
<th>ACR &lt; 30 mg/g</th>
<th>eGFR ≥ 60</th>
<th>eGFR &lt; 60</th>
<th>ACR ≥ 30 mg/g</th>
<th>eGFR ≥ 60</th>
<th>eGFR &lt; 60</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>484 (56.4)</td>
<td>252 (29.3)</td>
<td>64 (7.5)</td>
<td>58 (6.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>60.0 (59.1 – 60.7)</td>
<td>62.0 (61.3 – 62.6)</td>
<td>62.2 (60.4 – 64.4)</td>
<td>66.2 (64.5 – 67.9)*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender (female)</td>
<td>46.3 (40.5 – 52.1)</td>
<td>72.2 (64.6 – 79.0)</td>
<td>43.8 (31.4 – 56.7)</td>
<td>48.3 (35.0 – 61.8)*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haemoglobin A1C (%)</td>
<td>6.0 (5.9 – 6.1)</td>
<td>6.0 (5.9 – 6.1)</td>
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<td>6.4 (6.0 – 6.8)*</td>
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<td>Systolic BP (mmHg)</td>
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<td>142 (140 – 144)</td>
<td>154 (149 – 159)</td>
<td>157 (150 – 163)*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>80 (79 – 81)</td>
<td>79 (78 – 80)</td>
<td>82 (79 – 85)</td>
<td>84 (81 – 87)***</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body mass index (kg/m&lt;sup&gt;2&lt;/sup&gt;)</td>
<td>30.4 (30.0 – 30.9)</td>
<td>31.3 (30.7 – 31.9)</td>
<td>31.8 (30.5 – 33.1)</td>
<td>31.6 (30.3 – 33.0)***</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>104 (103 – 105)</td>
<td>104 (102 – 105)</td>
<td>108 (105 – 112)</td>
<td>106 (103 – 110)***</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cholesterol (mg/dL)</td>
<td>229 (225 – 233)</td>
<td>237 (232 – 243)</td>
<td>234 (221 – 247)</td>
<td>229 (218 – 241)***</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HDL cholesterol (mg/dL)</td>
<td>57 (56 – 59)</td>
<td>59 (57 – 61)</td>
<td>55 (51 – 58)</td>
<td>53 (49 – 56)**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDL cholesterol (mg/dL)</td>
<td>145 (141 – 148)</td>
<td>149 (145 – 154)</td>
<td>140 (139 – 160)</td>
<td>142 (132 – 153)**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triglycerides (mg/dL)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>116 (80)</td>
<td>127 (82)</td>
<td>133 (104)</td>
<td>158 (111)*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Framingham risk score&lt;sup&gt;*&lt;/sup&gt;</td>
<td>58.5 (52.6 – 64.1)</td>
<td>70.6 (64.6 – 76.2)</td>
<td>42.2 (29.9 – 55.2)</td>
<td>39.7 (27.0 – 53.4)</td>
<td></td>
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</tr>
</tbody>
</table>

Data are percentages (95% confidence interval) or mean (95% confidence interval).

<sup>*</sup> P < 0.001.
<sup>**</sup> P < 0.01.
<sup>***</sup> P < 0.05.
<sup>###</sup> Median (interquartile range).
However, the prevalence of a low eGFR in this subgroup remained almost double that of men, irrespective of the presence or absence of risk factors for CKD (Fig. 3).

Unlike with the MDRD equation, with the CKD-EPI equation normoalbuminuric women with diabetes, hypertension, or CVD had significantly lower levels of eGFR than women with no CKD risk factors (Fig. 3). However, the range of values of eGFR also overlapped between normoalbuminuric participants (men or women) with and without risk factors for CKD (Figs. 1 and 2). In the absence of albuminuria, no significant difference was observed between participants with an eGFR $\geq 60$ mL/min/1.73 m$^2$ in systolic or diastolic blood pressure, body mass index, waist circumference, serum glucose, or hemoglobin A1C. The level of HDL-cholesterol and the percentage of cases with a Framingham risk score $< 10\%$ were even greater among normoalbuminuric participants with low eGFR than among those with an eGFR $\geq 60$ mL/min/1.73 m$^2$.

**Discussion**

The main finding of this study is that the CKD-EPI equation, applied to the general population, generates higher eGFR values than the MDRD equation, decreasing the overall prevalence of low eGFR by 16.9% (36.1\% vs. 53.0\%). Normoalbuminuric women with no risk factors were the subgroup with the greatest reduction in the prevalence of apparent renal impairment. However, the prevalence of apparent renal impairment in this subgroup still remained very high, especially in women with no CKD risk factors, in whom the rate of low eGFR was even higher than in normoalbuminuric men with any risk factor for CKD. The first practical consequence derived using the new equation is likely to be a significant reduction in the number of people previously labeled as having stage 3 CKD. These people would not undergo further nephrological evaluation or overaggressive cardiovascular risk factor...
reduction and would not receive an ineffective reduction in the dosage of drugs excreted by the kidneys.20

The authors of the CKD-EPI equation reported a lower bias of the estimates higher than 60 mL/min/1.73 m²; this could explain the rise in the proportion of normoalbuminuric people without renal impairment, which we found when comparing the CKD-EPI and MDRD equations. However, the authors also stated that the precision of the equation was limited, and this may explain the extensive overlap in the values of the estimates between normoalbuminuric people with and without risk factors for CKD observed in our study.

One of the main reasons for using the CKD-EPI equation is to reduce the rate of false-positive diagnoses of stage 3 CKD obtained with the MDRD equation.20 This is a matter of special concern when screening people from the general population who lack markers of kidney damage.11 The MDRD in our study population produced very low estimates that fell below 60 mL/min/1.73 m² in more than a third of the men and in more than two thirds of the women. Paradoxically, these proportions were even greater among normoalbuminuric women regardless of the presence or absence of risk factors for CKD. Although we did not perform a direct measurement of the GFR, these results strongly suggest that the MDRD equation underestimated the real GFR in the individuals without albuminuria. The significant reduction in the prevalence of renal impairment we obtained with the CKD-EPI equation supports this idea. Consequently, the results of our study argue against the use of the MDRD study equation as estimate of the GFR in the general population when there are no markers of kidney damage. At least in women, focusing screening for CKD on individuals with risk factors for CKD will not help clinicians interpret low estimates generated with the MDRD equation or avoid false-positive diagnoses.

The new CKD-EPI equation increases the values of the estimates and decreases the rate of apparent renal impairment compared with the MDRD equation. However, some results in our study suggest that also there may be a particularly inaccurate correction factor for females in the CKD-EPI equation, and it is likely that the bias in this equation might not have improved in females to the same extent as in males. First, the prevalence of renal impairment among normoalbuminuric women remained much greater than in men, despite the women’s better cardiovascular risk factor profile. Second, the rate of renal impairment of normoalbuminuric women with no CKD risk factors was very high and even greater than in men with diabetes, hypertension, or CVD. Finally, the estimates extensively overlapped between normoalbuminuric women with no risk factor and women with diabetes, hypertension, or CVD.

The CKD-EPI equation shares another feature with the MDRD equation. In the absence of albuminuria no substantial difference in the cardiovascular risk factor profile was observed between the groups with an eGFR lower or greater than 60 mL/min/1.73 m². The association between risk factors for CKD and renal impairment depends not only on the accuracy of the equations, but also on the cut-off points selected to identify low eGFR.26 An isolated mildly depressed eGFR may confer a low cardiovascular risk that can be indistinguishable from that of an eGFR just over 60 mL/min/1.73 m² because the threshold of 60 mL/min/1.73 m² has been arbitrarily defined as identifying stage 3 CKD.11,27,28 In our sample, the large number of normoalbuminuric participants with an eGFR > 45 mL/min/1.73 m² significantly accounted for the very high prevalence of renal impairment, but most of these subjects had a very low cardiovascular risk profile. Using the threshold of 60 mL/min/1.73 m², 30–50% of older people could be misclassified as having renal impairment.29 To avoid this, it has been proposed that clinicians should focus on eGFR < 45 mL/min/1.73 m². The performance of the CKD-EPI equation for this lower threshold could not be analyzed in our cohort because of the low number of participants with this value.

Our study has several limitations. First, the lack of a direct measurement of GFR, which would have allowed us to compare the accuracy of the different formulas, prevents us from making a statement about the accuracy of either formula in the general population. It was not within our scope to compare the diagnostic performance of the estimates against a direct measurement of GFR, but rather to compare their performance in an unselected sample from the general population with different risk factor profiles and to investigate the factors that could affect such performance. Second, we only made one determination of serum

![Fig. 3 Percentage of low eGFR (95% confidence interval) within different risk factors for CKD.](http://www.elsevier.es)
creatinine and albuminuria, without further confirmation, and this might affect a rigorous classification of the participants into the categories of eGFR and albuminuria. However, we think that the impact of a single determination on our results is likely to be insignificant, considering that all samples were obtained in asymptomatic subjects in the early morning and given the relatively large sample size. Third, our population has one of the highest prevalences of obesity and diabetes in Spain.21 Our results may not be comparable with those of other populations with lower prevalence of obesity and diabetes. Lastly, in our cross-sectional analysis we described a very poor association between prevalent cardiovascular risk factor profile and normoalbuminuric renal insufficiency. The renal and cardiovascular outcomes of normoalbuminuric individuals with low eGFR defined with the new CKD-EPI equation should be assessed in prospective studies.

In conclusion, compared with the MDRD equation, using the CKD-EPI equation to estimate GFR generates a substantial reduction in the prevalence of renal impairment that has important practical consequences. Normoalbuminuric individuals, especially women, previously labeled as having stage 3 CKD with the MDRD equation would be the people most affected by the new estimations. The persistence of a disproportionately elevated prevalence of low eGFR among normoalbuminuric women, even without risk factors for CKD, suggests that an inaccurate correction factor for females may persist in the CKD-EPI equation.

Conflict of interest

The authors declare no conflicts of interest.

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