ABSTRACT

Background. It was reported that the glomerular filtration rate (GFR) equation based on serum creatinine underestimated the GFR in potential kidney donors. Recently, the Japanese GFR equation based on standardized serum cystatin C was reported. Therefore, we assessed the performance of the equation in potential kidney donors.

Methods. Forty-five potential kidney donors from 2 hospitals were included. GFR was measured (mGFR) using inulin renal clearance. Serum creatinine was measured using the enzymatic method. Serum cystatin C was measured using a nephelometric immunoassay (Siemens) and calibrated to the standardized value traceable to ERM-DA471/IFCC using an equation reported previously. The estimated GFR (eGFR) was calculated using the Japanese GFR equation based on serum creatinine (eGFRcreat) and the Japanese GFR equation based on serum cystatin C (eGFRcys). Bias (mGFR - eGFR) and accuracy (P30) of the equations were evaluated.

Results. Inulin clearance, eGFRcreat, and eGFRcys were 91.0 ± 18.2, 78.5 ± 18.8, and 93.3 ± 16.3 mL/min/1.73 m², respectively. Bias of eGFRcreat was 12.4 ± 15.8 mL/min/1.73 m² and significantly different from zero, indicating underestimation of GFR. Bias of eGFRcys was −2.3 ± 16.3 mL/min/1.73 m² and was not significantly different from zero, suggesting better performance. But, the precision (standard deviation [SD] of bias) and accuracy (P30: Percentage of participants with eGFR within 30% of mGFR) of eGFRcys were not superior compared with eGFRcreat. Accuracies (P30) of eGFRcreat and eGFRcys were 87% (95% confidence interval [CI], 74–94) and 82% (95% CI, 69–91), respectively.

Conclusion. Bias of eGFRcys was better compared with eGFRcreat. But, the precision (SD of bias) and accuracy of eGFRcys were not superior compared with eGFRcreat in potential kidney donors.
Table 1. Characteristics of the Potential Kidney Donors

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>45</td>
<td>14 (31%)</td>
<td>31 (69%)</td>
</tr>
<tr>
<td>Age (y)</td>
<td>56 ± 11</td>
<td>50 ± 11</td>
<td>58 ± 10</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>161 ± 9</td>
<td>171 ± 7</td>
<td>156 ± 6</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>60 ± 11</td>
<td>70 ± 10</td>
<td>55 ± 7</td>
</tr>
<tr>
<td>BSA (m²)</td>
<td>1.62 ± 0.18</td>
<td>1.81 ± 0.14</td>
<td>1.53 ± 0.11</td>
</tr>
<tr>
<td>BMI</td>
<td>23 ± 3</td>
<td>24 ± 4</td>
<td>23 ± 2</td>
</tr>
<tr>
<td>Serum creatinine (mg/dL)</td>
<td>0.70 ± 0.17</td>
<td>0.83 ± 0.13</td>
<td>0.64 ± 0.14</td>
</tr>
<tr>
<td>Serum cystatin C (mg/L)</td>
<td>0.80 ± 0.11</td>
<td>0.74 ± 0.09</td>
<td>0.69 ± 0.12</td>
</tr>
<tr>
<td>mGFR (mL/min/1.73 m²)</td>
<td>91.0 ± 18.2</td>
<td>94.7 ± 15.7</td>
<td>89.3 ± 19.2</td>
</tr>
<tr>
<td>eGFRcreat (mL/min/1.73 m²)</td>
<td>78.5 ± 18.8</td>
<td>79.8 ± 16.2</td>
<td>78.0 ± 20.2</td>
</tr>
<tr>
<td>eGFRcys (mL/min/1.73 m²)</td>
<td>93.3 ± 16.3</td>
<td>95.8 ± 14.5</td>
<td>92.2 ± 17.2</td>
</tr>
<tr>
<td>eGFR-MDRD (mL/min/1.73 m²)</td>
<td>101.9 ± 25.1</td>
<td>100.9 ± 20.2</td>
<td>102.4 ± 27.3</td>
</tr>
</tbody>
</table>

Note: Data were expressed as means ± SD or number (%). Abbreviations: BSA, body surface area; BMI, body mass index.

Creatinine underestimated GFR in potential kidney donors [5,6]. Therefore, we assessed the performance of the equation based on serum cystatin C in potential kidney donors.

METHODS

Forty-five potential kidney donors from 2 hospitals were included. GFR was measured (mGFR) by inulin renal clearance. Inulin renal clearance was measured from 3 sets of 30-minute urine collections during 2 hours in fasting and hydrated condition by the continuous infusion method. Details were reported previously [7]. Serum creatinine was measured using IDMS (isotope dilution mass spectrometry) traceable enzymatic method in a single laboratory. Serum cystatin C was measured using nephelometric immunoassay (Siemens) and calibrated to the standardized value traceable to ERM-DA471/IFCC using an equation reported previously [4]. Osaka University Graduate School of Medicine Health Science Ethics Committee approval was obtained for the present study.

GFR Equations

The estimated GFR (eGFR) was calculated using the Japanese GFR equation based on serum creatinine (eGFRcreat) [3], the IDMS-MDRD (Modification of Diet in Renal Disease) Study equation (eGFR-MDRD) [2], and the Japanese GFR equation based on serum cystatin C (eGFRcys) [4].

Male: eGFRcreat (mL/min/1.73 m²) = 194 × Cr−1.094 × age−0.287

eGFRcys (mL/min/1.73 m²) = (104 × Cys−1.019 × 0.996 Cr)−0.742

eGFR-MDRD (mL/min/1.73 m²) = 175 × Cr−1.154 × age−0.203

Female: eGFRcreat (mL/min/1.73 m²) = 194 × Cr−1.094 × age−0.287 × 0.739

eGFRcys (mL/min/1.73 m²) = (104 × Cys−1.019 × 0.996 Cr)−0.742

eGFR-MDRD (mL/min/1.73 m²) = 175 × Cr−1.154 × age−0.203 × 0.742

Statistical Analysis

Root mean square error was calculated as the square root of the sum of squared errors of the estimate(N]). Difference between eGFR and mGFR or whether the bias of GFR equation (mGFR minus eGFR) was significantly different from zero was analyzed using a paired t test. The difference of biases between eGFRcreat and eGFRcys was evaluated using an independent t test. Accuracy of the equation was expressed by percentage of the subjects with eGFR within ±20% (P20) and ±30% (P30) of mGFR. The accuracy was evaluated using chi-square tests. Statview version 4.02 (SAS Institute Cary, NC, United States) was used for statistical analysis.

RESULTS

Clinical characteristics of the study population are shown in Table 1. There was no significant difference between eGFRcys and mGFR in 45 potential kidney donors (89.3 ± 19.2 and 91.0 ± 18.2 mL/min/1.73 m², respectively). Contrary, eGFRcreat was significantly lower than mGFR (78.5 ± 18.8 and 91.0 ± 18.2 mL/min/1.73 m², respectively; P < .001). These results were confirmed in male (N = 14) and female subjects (N = 31). Figure 1 shows the relationship between mGFR and eGFRcreat and eGFRcys and mGFR.
eGFR in potential kidney donors. The eGFRcreat underestimated GFR in most subjects compared with eGFRcys. The MDRD Study equation overestimated GFR in Japanese potential kidney donors. eGFR using the MDRD Study equation was significantly higher than mGFR (101.9 ± 25.1 and 91.0 ± 18.2 mL/min/1.73 m², respectively; P < .05). We previously reported that the MDRD Study equation overestimated GFR about 20% in mostly chronic kidney disease (CKD) subjects [3]. The equation is not suitable in Japanese subjects probably due to the difference of muscle mass between the Japanese and white populations [3]. Therefore, bias and accuracy of the MDRD Study equation were not analyzed. Biases of eGFRcreat and eGFRcys are shown in Table 2. Bias of eGFRcreat in total subjects was 12.4 ± 15.8 mL/min/1.73 m², which was significantly different from zero (P < .001). The bias was significantly higher than the value of bias of eGFRcys (P < .01). These results were the same in male (N = 14) and female subjects (N = 31). RMSE of eGFRcys was lower compared with eGFRcreat in total, male, and female subjects.

Precision (standard deviation [SD] of bias) of eGFRcys was not better than eGFRcreat in total and female subjects. Accuracy of P30 of eGFRcys was not better than eGFRcreat in total female subjects. Accuracy of P20 of eGFRcys was better than eGFRcreat, although the difference was not significant.

**DISCUSSION**

eGFRcreat was significantly lower than mGFR in the potential kidney donors (78.5 ± 18.8 and 91.0 ± 18.2 mL/min/1.73 m², respectively). This result was consistent with previous reports [5,8]. Serum creatinine level is affected by not only kidney function but also skeletal muscle mass and protein intake. The Japanese GFR equations were derived from mainly CKD subjects. Higher muscle mass or higher protein intake in potential kidney donors compared with CKD subjects may be the possible explanation of the underestimation of eGFRcreat in potential kidney donors. eGFR using the MDRD Study equation was significantly higher than the mGFR. We previously reported that the MDRD Study equation overestimated GFR about 20% in mostly CKD subjects [3]. The MDRD Study equation without ethnic coefficient is not suitable in Japanese subjects. Difference of skeletal muscle mass and protein intake between the Japanese and white populations may contribute to the results.

There was no significant difference between eGFRcys and mGFR in 45 potential kidney donors (89.3 ± 19.2 and 91.0 ± 18.2 mL/min/1.73 m², respectively). Bias of eGFRcys was significantly lower compared with eGFRcreat in total, male, and female subjects, suggesting better performance compared with eGFRcreat. Serum concentration of creatinine was affected by muscle mass. Contrary, serum concentration of cystatin C was less influenced by muscle mass, leading to lower bias of eGFR based on serum cystatin C. The precision (SD of bias) of eGFRcys was not better compared with eGFRcreat in total and female subjects. Accuracies (P30) of eGFRcreat and eGFRcys were 87% (95% confidence interval [CI], 74–94) and 82% (95% CI, 69–91), respectively. Significantly better accuracy of eGFRcys was not detected in the present study. Serum cystatin C is a marker of GFR. However, factors other than GFR influence serum cystatin C levels [9–11]. Cystatin C levels were influenced by thyroid function [12,13]. Although factors affecting serum cystatin C level have not been evaluated in potential kidney donors, some factors may influence the performance of eGFRcys.

In conclusion, bias of eGFRcys was significantly better compared with eGFRcreat. But, the precision (SD of bias) and accuracy of eGFRcys were not superior compared with eGFRcreat. GFR estimating equations have some limitations. Measurement of GFR is important to assess the GFR of potential kidney donors.

**REFERENCES**


