Calculation of the estimated glomerular filtration rate using the 2021 CKD-EPI creatinine equation and whole blood creatinine values measured with Radiometer ABL 827 FLEX

Abstract

Objectives: Estimated glomerular filtration rate (eGFR) can be calculated using serum/plasma creatinine measured with automated chemistry analyzers. It is unclear whether eGFR can be calculated using creatinine values measured in whole blood (WB creatinine). The aim of this study is to determine the comparability between the eGFR calculated using WB creatinine and plasma creatinine.

Methods: Blood samples from 1,073 patients presented to the emergency department (ED), perioperative areas, intensive care unit (ICU) or nuclear medicine were used to determine the accuracy of WB creatinine. For each sample, WB creatinine was first measured with Radiometer ABL827 FLEX blood gas analyzer, then plasma creatinine was measured with Roche Cobas702 chemistry analyzer after samples were centrifuged. In a subset of 247 samples with the information of age and sex, whole blood eGFR (WB eGFR) and plasma eGFR were calculated using WB creatinine and plasma creatinine and the 2021 chronic kidney disease epidemiology collaboration (CKD-EPI) creatinine equation, respectively.

Results: WB creatinine correlated with plasma creatinine linearly with a slope of 1.06 and an intercept of −0.01. The coefficient of determination (R^2) was 0.99. WB eGFR correlated with plasma eGFR linearly with a slope of 0.95, intercept of −1.63, and R^2 of 0.97. Comparing to plasma eGFR, the sensitivity and specificity for WB eGFR to identify those with high risk (eGFR<30 mL/min/1.73 m^2) and low risk (eGFR>45 mL/min/1.73 m^2) for kidney injuries was 100 and 92.2%, respectively. The overall concordance in classifying the four stages of kidney damage between WB eGFR and plasma eGFR was 87.9%.

Conclusions: WB creatinine measured with Radiometer ABL827 Flex can be used to calculate eGFR using the 2021 CKD-EPI creatinine equation. The sensitivity and specificity for WB eGFR to identify those with high and low risks for potential kidney injuries are acceptable in patients needing rapid assessment of their kidney functions.

Keywords: estimated glomerular filtration rate (eGFR) calculations; point-of-care (POC); rapid assessment of kidney functions; the 2021 CKD-EPI creatinine equation; the EKFC equation; the revised Lund-Malmö equation; whole blood creatinine.

Introduction

In the emergency department (ED), perioperative areas, intensive care unit (ICU), imaging and nuclear medicine, rapid assessment of patients’ kidney functions using creatinine and/or estimated glomerular filtration rate (eGFR) prior to certain medications and/or procedures is necessary in order to prevent medication or contrast media induced acute kidney injuries [1]. Point-of-care (POC) devices can be used to obtain creatinine values in whole blood (WB) samples in a timely manner [2]. While estimated glomerular filtration rate (eGFR) can be calculated using plasma creatinine values and the chronic kidney disease epidemiology collaboration (CKD-EPI) equation [3, 4], it is unclear whether WB creatinine values can be used to calculate eGFR using the CKD-EPI equation. Recently, the joint task force of the National Kidney Foundation and the American Society of Nephrology (NKF-ASN) recommended laboratories in the United States to switch to the 2021 CKD-EPI creatinine equation without race variables to
calculate eGFR [5]. In this study, we used the 2021 CKD-EPI creatinine equation to calculate eGFR using WB creatinine values measured with Radiometer (Radiometer, Brea, CA, USA) ABL 827 FLEX blood gas analyzer (ABL827). Compared to plasma eGFR, the clinical sensitivity for WB eGFR to identify those with high risk (eGFR<30 mL/min/1.73 m²) for kidney injuries and the specificity to identify those with low risk (eGFR>45 mL/min/1.73 m²) for potential kidney injuries were determined. We also used the revised Lund-Malmö equation [6] and the European Kidney Function Consortium (EKFC) [7] equation to calculate both the WB eGFR and plasma eGFR. The performance of the three equations were compared using the bias, the interquartile range, and the 30% concordance between the results of WB and plasma eGFR.

Materials and methods

Patient samples

For the determination of the accuracy of WB creatinine measured with ABL827, we used 1,073 residual blood samples collected in lithium heparin tubes or heparinized blood gas syringes submitted from the ED, intensive care unit (ICU), nuclear medicine, and perioperative areas. In a subset of 247 samples, we recorded the age and gender of the patient in order to calculate eGFR. Among the 247 samples, 131 were males and 116 were females. The age range of the male patients was 20–101 years with a median of 58 years. The age range of the female patients was 19–101 years with a median of 60 years. Institutional review board waived the review of this study because these samples were de-identified discarded blood samples collected for patient care.

Measurement of creatinine

WB creatinine was measured with ABL827. We have four ABL827 analyzers with one located in the ED Laboratory, two in the Anesthesia Laboratory for patients in radiology or perioperative areas, and one in the rapid response area of the central laboratory for ICU patients. As part of our quality assurance program to verify the accuracy of WB creatinine, we use a randomly selected patient sample to compare the WB creatinine values with plasma creatinine values for each ABL827 analyzer three times a day (on day, evening, and night shift, respectively) daily. For each selected sample, WB creatinine was measured with ABL827 first, then the sample was centrifuged for 3 min at 4,400 g to separate plasma from cells and plasma creatinine was measured with Roche (Roche Diagnostics, Indianapolis, Indiana, USA) Cobas 702 chemistry analyzer (Cobas702) within 1 h of the WB creatinine measurement. In a three month period, we collected 1,073 comparison dates from the four ABL827 analyzers.

The Cobas702 uses a cascade of enzymatic reactions to convert creatinine to creatine by creatinase, creatine to sarcosine by creatinase, and sarcosine to glycine by sarcosine oxidase (SOD). The end-product of the reactions is hydrogen peroxide, which can then be measured by spectrophotometry when it reacts with 4-aminophenazone to produce a color change [8]. Because of the equilibrium between creatine and creatinine in aqueous solutions, the signal from creatine should be deducted from the measurement for creatinine. The Cobas702 enzymatic creatinine method uses creatinase, SOD and catalase to destroy endogenous creatine during incubation in R1 [8]. The enzymatic reactions for creatinine are initiated after creatine is consumed, and the concentration of creatinine is determined using the standards that has the calibration traceability to NIST SRM 967 using isotope-dilution mass spectrometry (IDMS). The coefficient of variation (CV) was 2.1, 1.4, and 0.8%, respectively, in plasma samples with creatinine concentration of 0.55, 0.97, and 2.04 mg/dL. The ABL827 creatinine method uses two electrodes with one (electrode B that contains creatinine amidohydrolase, creatine amidohydrolase and SOD) detecting the end-product (Hydrogen peroxide) of both creatinine and creatine, and the other (electrode A that contains only creatine amidohydrolase and SOD) detecting the end-product of the reaction for creatine only. Hydrogen peroxide is measured with an amperometric method. After the signal from electrode A is deducted from electrode B, the concentration of creatinine is determined using calibration standards that are traceable to NIST SRM 914 [9, 10]. The CV was 1.6, 1.3, and 0.9%, respectively, in whole blood samples containing 0.69, 2.81, and 5.14 mg/dL of creatinine.

Effect of hematocrit on WB creatinine

Three additional samples with creatinine levels of 1.06, 1.16, and 1.18 mg/dL, respectively, were used in this experiment. After measuring WB with ABL827 and hematocrit (Hct) with Sysmex XN9000, each sample was centrifuged at 500 g for 5 min to gently separate the cells from plasma. Samples with different Hct were prepared by mixing three parts of the cells with one part of the plasma from Samples 1, 2, and 3, respectively. Then WB creatinine and plasma creatinine were measured in these samples in the same way as described earlier.

Effect of bilirubin on plasma creatinine

Whole blood samples containing 20, 40, and 100 mg/dL of bilirubin were made by spiking aliquots of a whole blood sample with various amounts of bilirubin stock solution. The expected concentration of creatinine in each sample was calculated to adjust for volume change. WB creatinine was measured with ABL827 in duplicate and plasma creatinine was measured with Cobas702 in duplicate. The difference between WB and plasma creatinine was calculated for each sample containing different level of bilirubin to show the effect of bilirubin on the difference.

Calculation of eGFR

The 2021 CKD-EPI creatinine equation without race variables [5] was programed in Microsoft Excel (Microsoft, Redmond, WA). WB and plasma eGFR were calculated using WB and plasma creatinine values, respectively:
where $\text{creatinine}$ is in mg/dL; $\min(\text{creatinine}/\kappa)$ denotes the minimum of creatinine/plasma creatinine or eGFR. P10 and P30 accuracy for WB eGFR is defined as the median of the individual differences between WB and plasma eGFR with plasma eGFR, respectively. As a comparison, WB and plasma eGFR were also calculated using the revised Lund-Malmö [6] equation, and the EKFC equation, respectively.

The revised Lund-Malmö [6] equations are as follows:

$$\text{eGFR} = e^{(-0.0159 \times \text{age} + 0.68 \times \ln(\text{age}))}$$

For male and $\text{Cr} < 150 \mu\text{mol/L}$, $X = 2.50 - 0.012(150 - \text{Cr})$

For female and $\text{Cr} < 150 \mu\text{mol/L}$, $X = 2.50 - 0.926 \times \ln(\text{Cr}/150)$

For male and $\text{Cr} > 180 \mu\text{mol/L}$, $X = 2.56 + 0.00968 \times (180 - \text{Cr})$

For male and $\text{Cr} > 180 \mu\text{mol/L}$, $X = 2.56 - 0.926 \times \ln(\text{Cr}/180)$

Where $\text{Cr}$ represents creatinine concentration in $\mu$mol/L. The revised Lund-Malmö equation was programed in Excel. Creatinine values were converted from mg/dL to $\mu$mol/L first. $X$ factor was then calculated for each plasma and WB creatinine value. Then the WB or plasma eGFR was calculated using the $X$ factor and the revised Lund-Malmö equation.

The EKFC [7] equations are as follows:

For age $2−40$ years old, if $\text{Cr}/Q < 1$,

$$\text{eGFR} = 107.3 \times (\text{SCr}/Q)^{−0.32}$$

For age $2−40$ years old, if $\text{Cr}/Q \geq 1$,

$$\text{eGFR} = 107.3 \times (\text{SCr}/Q)^{−1.132}$$

For age $>40$ years old, if $\text{Cr}/Q < 1$,

$$\text{eGFR} = 107.3 \times (\text{SCr}/Q)^{−0.32} \times 0.990^{(\text{Age}−60)}$$

For age $>40$ years old, if $\text{Cr}/Q \geq 1$,

$$\text{eGFR} = 107.3 \times (\text{SCr}/Q)^{−1.132} \times 0.990^{(\text{Age}−60)}$$

Where $Q$ values are:

For male $2−25$ years old, $\ln(Q) = 3.200 + 0.259 \times \text{Age} − 0.543 \times \ln(\text{Age}) − 0.00763 \times \text{Age}^2 + 0.0000790 \times \text{Age}^3$

For female $2−25$ years old, $\ln(Q) = 3.080 + 0.177 \times \text{Age} − 0.223 \times \ln(\text{Age}) − 0.00596 \times \text{Age}^2 + 0.0000686 \times \text{Age}^3$

For male $>25$ years old, $Q = 80 \mu\text{mol/L}$

For female $>25$ years old, $Q = 62 \mu\text{mol/L}$.

The EKFC [7] equation was programed in Excel. The unit of creatinine was converted from mg/dL to $\mu$mol/L. $Q$ value was calculated based on age and gender of each patient. Then WB and plasma eGFR was calculated using the equation specific for age and creatinine values, respectively.

The median, bias, interquartile range of the difference between WB and plasma eGFR, and the P10 and P30 accuracy were obtained based on the eGFR calculated using each of the three equations (the 2021 CKD-EPI creatinine equation, the revised Lund-Malmö equation, and the EKFC equation).

**Statistical analysis**

Linear regression analysis of Microsoft Excel and Bland–Altman Difference Plot (programed in Excel) were used to compare WB creatinine with plasma creatinine and WB eGFR with plasma eGFR, respectively. Whenever applicable, the mean and standard deviation (SD), and the coefficient of variation (CV) were derived using Excel. The bias was defined as the median of the individual differences between WB and plasma creatinine or eGFR. P10 and P30 accuracy for WB eGFR is defined as the percentage of WB eGFR that were within the ±10% and ±30% of plasma eGFR, respectively. The interquartile range of the difference between WB and plasma eGFR was defined as the range between Q3 (the difference value at the 75th percentile) and Q1 (the difference value at the 25th percentile) when the difference values between the WB eGFR and plasma eGFR (WB eGFR − plasma eGFR) were sorted and segmented into four parts.

**Results**

**Correlation between WB and plasma creatinine**

The range of creatinine from the 1,073 samples used in this study was 0.08–13.7 mg/dL (to convert to $\mu$mol/L, multiply by 88.4), which enabled us to compare values of WB creatinine with plasma creatinine in a wide range. The linear regression between WB creatinine and plasma creatinine yielded a slope of 1.06 (95% CI: 1.055–1.070), an intercept of −0.014 (95% CI: −0.027 to 0.000), and the coefficient of determination ($R^2$) of 0.99 (Figure 1A). The mean bias between WB and plasma creatinine was 0.06 mg/dL. Bland-Altman plot (Figure 1B) showed that 34 (3.2%) samples had the difference of (WB creatinine − plasma creatinine) above the mean + 1.96SD line, ranged from 0.4 to 1.25 mg/dL. And 17(1.6%) samples had the difference below the mean−1.96SD line, ranged from −0.27 to −0.57 mg/dL. Among the 17 samples, 8, 5, and 4 samples had creatinine values >1.7 mg/dL, between 1.2 and 1.7 mg/dL, and <1.2 mg/dL, respectively. Among the 34 samples above the mean + 1.96SD line, 27 had creatinine greater than 1.7 mg/dL and seven had creatinine values less than 1.2 mg/dL. As reflected in the slope of the regression (WB-plasma creatinine=0.06×plasma creatinine−0.04), the bias of WB creatinine increases as creatinine increases. There were 11 samples with creatinine values greater than 7 mg/dL, and among them, the difference of (WB-plasma) creatinine greater than 0.5 mg/dL in eight samples and greater than 1.0 mg/dL in five samples. It clearly showed that the bias between WB and plasma creatinine became larger when creatinine was high (Figure 1B). However, the percent difference at high creatinine was close to 6.7%, which was the mean of the percent difference (Figure 1C).

**Effect of hct on WB creatinine**

Values of WB creatinine and plasma creatinine for samples with different Hct are shown in Table 1. In samples with Hct ranged from 12.5 to 49.4%, the differences between WB and plasma creatinine were no more than 0.3 mg/dL, indicating Hct did not cause significant difference in WB creatinine measured with ABL827.
Effect of bilirubin on plasma creatinine

As shown in Table 2, WB creatinine values did not change in samples with 20, 40, and 100 mg/dL of bilirubin, whereas, plasma creatinine values decreased drastically by 13, 21, and 53%. Therefore, the plasma creatinine values will be falsely low in samples with high bilirubin, resulting in a high bias between WB creatinine and plasma creatinine.

Comparison of WB eGFR with plasma eGFR calculated using the 2021 CKD-EPI creatinine equation

In the 247 samples, WB eGFR ranged from 4 to 143 mL/min/1.73 m² with a median of 63 mL/min/1.73 m², and plasma eGFR ranged from 4 to 140 mL/min/1.73 m² with a median of 70 mL/min/1.73 m². WB eGFR correlated with plasma eGFR...
Table 1: Effect of hematocrit (Hct) on the measurement of WB and plasma creatinine.

<table>
<thead>
<tr>
<th>Sample</th>
<th>Hct</th>
<th>WB creatinine, mg/dL</th>
<th>Plasma creatinine, mg/dL</th>
<th>WB-plasma creatinine, mg/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12.5</td>
<td>1.16</td>
<td>1.05</td>
<td>0.11</td>
</tr>
<tr>
<td>1A</td>
<td>23.7</td>
<td>1.1</td>
<td>0.98</td>
<td>0.12</td>
</tr>
<tr>
<td>2</td>
<td>21.1</td>
<td>1.18</td>
<td>1.12</td>
<td>0.06</td>
</tr>
<tr>
<td>2A</td>
<td>42.1</td>
<td>1.17</td>
<td>1.1</td>
<td>0.07</td>
</tr>
<tr>
<td>3</td>
<td>23.6</td>
<td>1.06</td>
<td>0.85</td>
<td>0.21</td>
</tr>
<tr>
<td>3A</td>
<td>49.4</td>
<td>1.02</td>
<td>0.84</td>
<td>0.18</td>
</tr>
</tbody>
</table>

Samples 1A, 2A, and 3A were prepared by mixing three parts of cells with one part of plasma from samples 1, 2, and 3, respectively.

The linear regression: eGFR(WB)=0.95 (95% CI:0.93 to 0.97)×eGFR(Plasma)–1.63 (95% CI: –3.42 to 0.16) with a R² of 0.9654 (Figure 2A). The mean and SD of the difference between WB and plasma eGFR was –5 mL/min/1.73 m² and 7 mL/min/1.73 m². The Mean–1.96SD and Mean+1.96SD of the difference was –19 mL/min/1.73 m² and 8 mL/min/1.73 m², respectively. Bland-Altman plot for eGFR values less than 90 mL/min/1.73 m² was shown in Figure 2B. There were three points below the line of the Mean-1.96SD, and one point above the Mean+1.96SD line. The WB and plasma creatinine values and eGFR as well as the age and gender of these four patients are provided in Table 3. In Sample 1 and Sample 2, because of the discrepant WB and plasma creatinine values (WB creatinine around 0.9–1.0 mg/dL and plasma creatinine around 1.3 mg/dL), WB eGFR misclassified these two patients below or near 45 mL/min/1.73 m², whereas their plasma eGFR were above 60 mL/min/1.73 m².

The difference of WB and plasma creatinine in Sample three and Sample four did not cause misclassifications because both were greater than 60 mL/min/1.73 m² with creatinine near or below 1 mg/dL. In most people, WB creatinine values less than 1.0 mg/dL would suggest normal to mildly compromised kidney functions, and creatinine values greater than 1.7 mg/dL would suggest severely compromised kidney functions. Therefore, discrepant WB and plasma creatinine values in the region of 0.9 mg/dL to 1.3 mg/dL are critical because small variations in creatinine may cause big change in GFR due to the hyperbolic relationship between eGFR and creatinine.

Chronic kidney disease (CKD) can be classified in four stages based on values of GFR. We evaluated the concordance (Table 4) between WB and plasma eGFR in the four categories of CKD: ≥60 mL/min/1.73 m² (CKD stages 1 and 2), 45–59 mL/min/1.73 m² (CKD stage 3A), 30–44 mL/min/1.73 m² (CKD stage 3B), and <30 mL/min/1.73 m² (CKD stages 4 and 5). WB eGFR correctly identified all 48 samples with plasma eGFR <30 mL/min/1.73 m². Therefore, the sensitivity for WB eGFR to detect those with severely decreased kidney functions was 48/48=100%. WB eGFR had correctly identified 15 out of 19 samples with plasma eGFR in the range of 30–44 mL/min/1.73 m², and put the other four in the category of eGFR>30 mL/min/1.73 m². When plasma eGFR was between 45 mL/min/1.73 m² and 59 mL/min/1.73 m², WB eGFR had correctly identified 15 out of 28 samples. When plasma eGFR was ≥60 mL/min/1.73 m², WB eGFR had correctly identified 139 out of 152 samples, and put 12 in the eGFR category of 45–59 mL/min/1.73 m² and one in the 30–44 mL/min/1.73 m² category. Therefore, the specificity for identifying those with low risk for kidney injuries (≥45 mL/min/1.73 m²) was 166/180=92.2%. The overall concordance of WB and plasma eGFR in these four categories was 217/247=87.9%. The P10 and P30 accuracy of WB eGFR was 64.8 and 98.4%, meaning 64.8 and 98.4% of WB eGFR values were within ±10% and ±30% of plasma eGFR, respectively.

Comparison of different eGFR calculations

The linear regression between the WB and plasma eGFR calculated using the revised Lund-Malmö equation (LM) was: eGFR(WB-LM)=0.93×eGFR(plasma-LM)–0.35, with R²=0.9678. The linear regression between the WB and plasma eGFR calculated using the EKFC equation was: eGFR(WB-EKFC)=0.94×eGFR(plasma-EKFC)–0.75, and R²=0.9651. The bias, the interquartile range of the
difference between WB and plasma eGFR, and the P10 and P30 accuracy for the three equations (the 2021 CKD-EPI creatinine equation, the revised Lund-Malmö equation, and the EKFC equation) are given in Table 5, respectively.

The results showed that the performance of these three calculations were very close regarding the bias, the interquartile range, and the P10 and P30 between the WB and plasma eGFR. When the plasma eGFR obtained using

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**Figure 2:** Comparison of WB eGFR and plasma eGFR calculated using the 2021 CKD-EPI creatinine equation.

(A) Comparison of WB eGFR and plasma eGFR. Linear regression analysis yielded: eGFR (WB) = 0.95 × eGFR (plasma) – 1.63, R² = 0.9654. (B) Difference between WB and plasma eGFR vs. the mean of WB and plasma eGFR for mean eGFR values less than 90 mL/min/1.73 m². The solid line represents the mean bias of −5 mL/min/1.73 m², and the upper and lower dashed lines represent 8 mL/min/1.73 m² and −19 mL/min/1.73 m², the ±1.96 SD of the difference of WB and plasma eGFR, respectively.

<table>
<thead>
<tr>
<th>Patient sample</th>
<th>Creatinine</th>
<th>eGFR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Index</td>
<td>Age, years</td>
<td>Sex</td>
</tr>
<tr>
<td>1</td>
<td>61</td>
<td>F</td>
</tr>
<tr>
<td>2</td>
<td>70</td>
<td>F</td>
</tr>
<tr>
<td>3</td>
<td>66</td>
<td>M</td>
</tr>
<tr>
<td>4</td>
<td>65</td>
<td>F</td>
</tr>
</tbody>
</table>
the revised Lund-Malmö equation was compared with that obtained using the 2021 CKD-EPI creatinine equation, the regression was: eGFR(plasma-LM)=0.81×eGFR(plasma-CKD-EPI)+6.4, and R²=0.8038. When the plasma eGFR obtained using the EKFC equation was compared with that obtained using the 2021 CKD-EPI creatinine equation, the linear regression was: eGFR(plasma-EKFC)=0.81×eGFR(plasma-CKD-EPI)+8.6, R²=0.8298 (Figure 3). The median of plasma eGFR calculated using the 2021 CKD-EPI creatinine equation, the revised Lund-Malmö equation, and the EKFC equation was 70 mL/min/1.73 m², 62 mL/min/1.73 m², and 64 mL/min/1.73 m², respectively. The comparisons between the three calculations showed that the eGFR calculated using the 2021 CKD-EPI creatinine equation was higher than that using the other two equations in samples used in the present study.

### Discussion

In our study, the mean bias between WB creatinine measured with ABL827 and plasma creatinine measured with Roche Cobas702 was 0.06 mg/dL and the slope of the linear regression was 1.06, indicating a slight overestimation of creatinine by ABL827. Korpi-Steiner et al. reported a slight underestimation of WB creatinine measured with ABL800 in samples with creatinine ranged from 0.45 mg/dL to 3 mg/dL, with a mean bias of −0.05 mg/dL and a slope of 0.95 [11]. Both slopes (1.06 vs. 0.95) and the bias (0.06 vs. −0.05) in the two studies were acceptable for method comparison studies. The range of creatinine in our study was notably larger, 13.7 mg/dL vs. 3 mg/dL, which may be the cause for the different slopes seen in the two studies. Consider different analyzers as well as different reagent or calibrator lots were used in the two studies (ABL827 vs. ABL800 and Cobas702 vs. Cobas Integra), the overall agreements between the WB creatinine values measured with ABL800 and the plasma creatinine values measured with the enzymatic creatinine methods on Roche Cobas were pretty good. The bias of WB creatinine can be estimated from the linear regression relationship: (WB-plasma creatinine)=0.06×plasma creatinine−0.04. Based on this formula, the difference should be around 0.3 mg/dL when plasma creatinine value was higher than 5 mg/dL, and the difference should increase to 0.6 mg/dL when creatinine increases to 10 mg/dL. If WB creatinine is greater than plasma creatinine by 0.8 or 1 mg/dL when plasma creatinine is less than 10, the difference would be larger than expected. Because the ABL827 and cobas702 use different methods to eliminate the contribution of creatine, we speculate that the systematic bias might be caused by the corrections for creatine. The Cobas702 uses enzymes (creatinate/SOD/catalase) to consume creatine before the initiation of creatinine reactions [8], whereas ABL827 uses one electrode to measure the signal from creatine and subtract it from the total reactions [10]. Both methods to correct for creatine may work fine when creatine was not very high. However, creatine may be high in samples with high creatinine because of the equilibrium between them [12]. If in our study, the ABL827 method underestimated creatine in samples with high creatinine, or the Cobas702 method over-corrected for creatine, values of WB creatinine would be higher than that of plasma creatinine. Vice versa, if in the study by Korpi-Steiner et al., the ABL800 overcorrected for creatine or their Cobas method underestimated creatine, WB creatinine would be lower than plasma creatinine. This is only a speculation that we do not have data to support it. Straseski et al. actually measured the concentrations of creatine in a control group and a “discrepent group” and found the means of creatine in the

### Table 4: Concordance of WB and plasma eGFR calculated using the 2021 CKD-EPI creatinine equation.

<table>
<thead>
<tr>
<th>WB eGFR, mL/min/1.73 m²</th>
<th>Plasma eGFR, mL/min/1.73 m²</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥60</td>
<td>45–59</td>
</tr>
<tr>
<td>60</td>
<td>19</td>
</tr>
<tr>
<td>30–44</td>
<td>0</td>
</tr>
<tr>
<td>&lt;30</td>
<td>0</td>
</tr>
</tbody>
</table>

### Table 5: The median, bias, interquartile range of the difference between WB and plasma eGFR, and the P30 accuracy for WB eGFR using the 2021 CKD-EPI creatinine equation [5], the revised Lund-Malmö [6] equation, and the EKFC equation [7], respectively.

<table>
<thead>
<tr>
<th>eGFR equation</th>
<th>Bias in WB and plasma eGFR, mL/min/1.73 m²</th>
<th>Interquartile range, mL/min/1.73 m²</th>
<th>P30 accuracy, %</th>
<th>P10 accuracy, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>2021 CKD-EPI creatinine</td>
<td>−4</td>
<td>6</td>
<td>98.4</td>
<td>64.8</td>
</tr>
<tr>
<td>The revised Lund-Malmö</td>
<td>−4</td>
<td>5</td>
<td>98.4</td>
<td>67.2</td>
</tr>
<tr>
<td>EKFC</td>
<td>−3</td>
<td>5</td>
<td>98.4</td>
<td>66.8</td>
</tr>
</tbody>
</table>

CKD-EPI, chronic kidney disease epidemiology collaboration; EKFC, European Kidney Function Consortium.
two groups identical [13]. In any case, one can use a feature on ABL827 to align WB creatinine with plasma creatinine by adjusting the slope and/or the intercept on ABL827 [10]. Unlike the high positive bias observed in our study, Sstraskei et al. found large negative bias of WB creatinine measured with StatSensor (Nova Biochemical, Waltham, Massachusetts, USA) compared with plasma creatinine measured with Roche Cobas Modular in samples with high creatinine [13]. They suspected that some interfering substances present in samples from renal patients might caused the discrepancy. Given the fact that large positive bias was found with WB creatinine measured with ABL827, and large negative bias was found with WB creatinine measured with StatSensor in samples with high creatinine [13], we believe that the bias between WB and plasma creatinine was caused by the methodologies used to determine WB creatinine in each of the analyzers. Although the large discrepancies between WB and plasma creatinine in samples with high creatinine values is concerning, they may not be clinically significant because creatinine values greater than 2 mg/dL or 2.5 mg/dL would indicate low eGFR result (<30 mL/min/1.73 m²) for most people, suggesting kidney failures.

To investigate the causes for “larger than expected” bias of WB creatinine, we tested the effect of hematocrit and bilirubin on the measurements of WB and plasma creatinine, respectively. In our Hct study, we prepared samples with various Hct (ranged from 12.5 to 49.4%) and found no significant difference in WB and plasma creatinine values. The manufacturer also indicated that Hct has little effect on the measurement of creatinine when they changed Hct from 24 to 69% and compared WB creatinine values in these samples with that in a sample with Hct of 46% [10]. Therefore, Hct of WB samples was not a factor for larger than expected discrepant WB and plasma creatinine values observed in our study. Bilirubin on the other hand, caused significant decrease in plasma creatinine, but not in WB creatinine. One of our technologist noted “grossly icteric” in one of the samples included in this study, which had WB creatinine of 1.38 mg/dL and plasma creatinine of 0.85 mg/dL (results confirmed by repeat testing). Therefore, in samples containing high bilirubin, WB creatinine values will be higher than plasma creatinine values. Drugs like Rifampicin, Levodopa, and calcium dobesilate can cause artificially low plasma creatinine results [8]. However, we did not have information regarding our patients’ medications.

Patients with chronic kidney disease are at increased risk to develop acute kidney injuries associated with the use of certain medications or iodinated contrast medium administered intravenously for computerized tomography (CT) procedures [14–16]. In order to prevent contrast-induced nephropathy and acute kidney injury, creatinine and eGFR can be used to assess kidney functions in patients with risk factors, which include age older than 60 years, history of renal disease, hypertension, diabetes mellitus, or patients on Metformin [17]. Our institution uses different protocols for administering iodinated contrast medium for CT procedures based on patient’s creatinine or eGFR values as well as the risk factors. When eGFR is above 45 mL/min/1.73 m², or creatinine is below 1.7 mg/dL, standard Omnipaque 350 protocol is used. When eGFR is between 30 and 45 mL/min/1.73 m², or creatinine is between 1.7 and 2.5 mg/dL, standard Visipaque 320 with no volume or rate reduction is used for patients with no risk factors. When eGFR <30 mL/min/1.73 m² and creatinine

![Figure 3: Comparison of the plasma eGFR calculated using the revised Lund-Malmö equation (LM), and the EKFC equation with that calculated using the 2021 CKD-EPI creatinine equation (CKD-EPI). Solid circle: LM eGFR; Triangle: EKFC eGFR. The linear regression between the LM eGFR and the CKD-EPI eGFR was: eGFR(plasma-LM)=0.81×eGFR(plasma-CKD-EPI)+6.4, and R²=0.8298. The linear regression between the EKFC eGFR and the CKD-EPI eGFR was: eGFR(plasma-EKFC)=0.81×eGFR(plasma-CKD-EPI)+8.6, and R²=0.8038.](image-url)
>2.5 mg/dL, or for patients with risk factors and eGFR is between 30 and 45 mL/min/1.73 m² or creatinine between 1.7 and 2.5 mg/dL, no IV contrast medium should be administered. The result of the present study showed that the sensitivity for WB eGFR obtained with ABL827 to identify patients with severe kidney damage is as good as that for plasma eGFR. In creatinine range of 0.9 mg/dL to 1.3 mg/dL, WB eGFR tended to misplace a few patients to a worse stage of kidney damage than plasma eGFR. Therefore, one should always obtain a plasma creatinine and plasma eGFR when a WB eGFR does not appear to accurately reflect the status of a patient’s kidney functions or is not consistent with patient’s clinical presentation and the decision based on WB creatinine may prevent the patient from receiving the necessary medical procedures or medications.

When the 2021 CKD-EPI creatinine equation [5] was compared to the revised Lund-Malmö [6] equation and the EKFC equation [7] in the estimation of either the WB eGFR or the plasma eGFR, the bias, the interquartile range, and the P30 accuracy between WB eGFR and plasma eGFR did not show significant difference for the three calculations. However, eGFR calculated using the 2021 CKD-EPI creatinine equation was generally higher than that obtained with the revised Lund-Malmö equation or the EKFC equation (Figure 3). One of the features of EKFC equation is that it can be used to calculate eGFR in both adult and pediatric patients and it can handle age gap smoothly [7]. This superior feature was not apparent in our study because we only used adult samples.

The limitation of our study was that we did not use measured GFR (mGFR) as the standard for comparison. As we all know, eGFR calculated using creatinine has its own uncertainties because it is value represents that of a fitting curve derived from the comparison between mGFR and serum creatinine from all of the study participants [3]. Stojkovic et al. compared the WB eGFR obtained using StatSensor and the CKD-EPI equation with the mGFR obtained using iohexol as a filtration marker [18]. The slope of their Passing-Bablok regression was 1.15, and P30 was 81%. They concluded that WB eGFR obtained with StatSensor was acceptable in terms of detecting mild to moderate loss of kidney functions, defined as eGFR<60 mL/min/1.73 m² [18]. Korpi-Steiner et al. found that StatSensor had lower concordance and bigger variability when compared with plasma eGFR [11]. Straseski et al. also cautioned the use of WB creatinine measured with StatSensor to calculate eGFR because of its variability [13]. We also observed relatively larger lot-to-lot or user-to-user variations in WB creatinine measured with StatSensor (data not published). In our institution, we do not use WB creatinine measured with StatSensor to calculate eGFR. Perhaps the capillary samples used in the report by Stojkovic et al. helped with the accuracy and precision of the WB creatinine measured with StatSensor [18]. In the report by Stojkovic et al., a Passing-Bablok slope of 1.05, and a P30 of 95% were obtained when they compared plasma eGFR obtained with plasma creatinine measured with Roche Cobas analyzers with mGFR [18], and the concordance of plasma eGFR obtained with Cobas in classifying patients with CKD stages was 63% [18]. This showed that eGFR has uncertainties because eGFR does not necessarily represent the true GFR of a particular patient. As the overall comparison between WB and plasma creatinine was good, we are confident that WB creatinine values measured with ABL827 are comparable with plasma creatinine measured with Cobas702 and can be used to calculate eGFR using the 2021 CKD-EPI creatinine equation.

Conclusions

Values of WB creatinine measured with Radiometer ABL 827 FLEX correlated with that of plasma creatinine measured with Roche Cobas 702 very well. WB eGFR calculated using the 2021 CKD-EPI creatinine equation correlated linearly with plasma eGFR with a slope of 0.95. The sensitivity for WB eGFR to identify patients with severe loss of kidney functions (eGFR<30 mL/min/1.73 m²) was 100%. The specificity for WB eGFR to identify patients who are at lower risk for kidney injuries (eGFR>45 mL/min/1.73 m²) was 92.2%. Therefore, we conclude that WB creatinine measured with ABL 827 FLEX can be used to calculate eGFR using the 2021 CKD-EPI creatinine equation. However, caution should be practiced when evaluating eGFR values obtained from WB creatinine values around 0.9–1.3 mg/dL because a small variation in WB creatinine can misplace the patient’s eGFR into a different category of kidney damage. We suggest obtaining a plasma creatinine/eGFR when a WB creatinine/eGFR is not consistent with patient’s kidney functions and the decision based on WB creatinine/eGFR may prevent the patient from receiving the necessary medical procedures or medications. Finally, one should always interpret eGFR values in the clinical context of a patient.

Impact statement

The results of this study showed that whole blood creatinine measured with Radiometer ABL827 Flex can be used to calculate eGFR using the 2021 CKD-EPI creatinine equation. The sensitivity and specificity for whole blood eGFR to
detect high and low risks for potential kidney injuries are acceptable. Patients present to the emergency department, perioperative areas, intensive care units, and nuclear medicine who need rapid assessment of their kidney functions will benefit from this study because their kidney functions can be assessed in a timely manner when both WB creatinine and WB eGFR are available at the point-of-care.

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