Original Clinical Research Quantitative

Performance of StatSensor Point-of-Care Device for Measuring Creatinine in Patients With Chronic Kidney Disease and Postkidney Transplantation

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Abstract

Background: The StatSensor is a point-of-care device which measures creatinine in capillary whole blood. Previous studies reported an underestimation of the creatinine measurements at high creatinine concentrations and were performed in the prestandardization era for creatinine.

Objective: This accuracy-based study evaluates the use of this device in kidney-transplanted patients and those with chronic kidney disease (CKD).

Design: Cross-sectional diagnostic accuracy study.

Setting: Nephrology outpatient clinic in an urban tertiary center.

Participants: Adults with CKD or a functioning kidney transplant.

Measurements: Duplicate StatSensor creatinine measurements were performed on capillary whole blood samples collected by direct fingerstick and SAFE-T-FILL collection device. Results were compared with simultaneous venous blood sampling for serum and plasma creatinine measured by an enzymatic method on the Roche Integra 400 mainframe analyzer with traceability to the ID-GC-MS (isotope dilution gas chromatography mass spectrometry) reference method.

Methods: Deming regression, Pearson correlation coefficient, and Bland-Altman analysis were used to assess accuracy and comparability between capillary whole blood measured by StatSensor and plasma creatinine measured by routine analyzer with traceability to the reference method. Estimated glomerular filtration (eGFR) rates were calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation and concordance with Kidney Disease Improving Global Outcomes (KDIGO) CKD stage classification was evaluated.

Results: There were 60 participants (mean age $= 61.9 \pm 15.0$ years, 55% men, 33% transplant, mean plasma creatinine $= 137 \pm 59$ μmol/L). Bland-Altman analysis indicated a positive mean bias of 12.7 μmol/L between StatSensor fingerstick creatinine measurement and plasma creatinine. Comparison of eGFR (CKD-EPI) calculated from the StatSensor fingerstick creatinine versus plasma creatinine showed misclassification across all KDIGO CKD stages. Postanalytical correction of the bias did not improve misclassifications. The use of mean of duplicate StatSensor creatinine results did not improve performance compared with the use of singlet results.

Limitations: Single center, limited participant numbers.

Conclusions: The results of our study suggest that the limiting characteristics of the StatSensor device are not only bias, but also imprecision. The level of imprecision observed may influence clinical decision-making and limit the usefulness of StatSensor as a CKD screening tool. If choosing to utilize it for either screening for or monitoring CKD, it is essential that clinicians understand the limitations of point-of-care devices and apply this knowledge to test interpretation.

Abrégé

Contexte: Le StatSensor est un appareil portatif conçu pour mesurer le taux de créatinine dans le sang capillaire total. Des études antérieures, réalisées avant la standardisation des mesures de la créatinine, ont rapporté une sous-estimation des mesures à des concentrations élevées.

Objectif: Cette étude centrée sur la précision a examiné l'utilisation de cet appareil chez des patients transplantés d'un rein et des patients atteints d'insuffisance rénale chronique (IRC).

Type d'étude: Étude transversale centrée sur la précision du diagnostic.

Cadre: La clinique ambulatoire de néphrologie d'un centre de soins tertiaires en milieu urbain.

Sujets: Des adultes atteints d'IRC ou transplantés avec un rein fonctionnel.

Mesures: Les mesures de créatinine par StatSensor ont été effectuées en double sur des échantillons de sang capillaire total prélevés par ponction digitale directe et à l'aide du dispositif de prélèvement SAFE-T-FILL. Ces résultats ont été comparés à un prélèvement veineux simultané pour la mesure des taux de créatinine sérique et plasmatique par la méthode enzymatique avec l'analyseur Integra 400 de Roche avec traçabilité à la méthode de référence ID-GC-MS.

Méthodologie: La régression de Deming, le coefficient de corrélation de Pearson et l'analyse de Bland-Altman ont été utilisés pour évaluer la précision et la comparabilité entre les mesures du sang capillaire total par StatSensor et la mesure de créatinine plasmatique obtenue par l'analyseur de routine avec traçabilité à la méthode de référence. Le débit de filtration glomérulaire estimé (DFGe) a été calculé avec l'équation CKD-EPI, puis la concordance avec la classification des stades KDIGO pour l'IRC a été évaluée.

Résultats: L'étude a inclus 60 patients (55 % d'hommes; âge moyen 61,9 ± 15,0 ans) dont 33 % étaient transplantés. Le taux moyen de créatinine plasmatique s'établissait à 137 ± 59 μmol/L. L'analyse de Bland-Altman indique un biais positif moyen de 12,7 μmol/L entre la mesure de créatinine obtenue avec StatSensor par ponction digitale et le taux de créatinine plasmatique. La comparaison entre le DFGe (CKD-EPI) calculé à partir des mesures obtenues par ponction digitale avec StatSensor et de la mesure de créatinine plasmatique a montré une classification erronée à tous les stades KDIGO pour l'IRC. La correction du biais après l'analyse n'a pas amélioré les erreurs de classification. L'utilisation de la moyenne des résultats obtenus par StatSensor sur les échantillons prélevés en double n'a pas amélioré les performances par rapport à l'utilisation de singulets.

Limites: Étude monocentrique, nombre de participants limité.

Conclusion: Nos résultats suggèrent que les caractéristiques de limitation du StatSensor ne constituent pas qu'un biais, mais également une imprécision. Ce degré d'imprécision peut influencer la prise de décision clinique et limiter l'utilité du StatSensor comme outil de dépistage de l'IRC. Il est essentiel que les cliniciens soient conscients des limites de ces dispositifs et qu'ils appliquent ces connaissances à l'interprétation des résultats s'ils choisissent de les utiliser pour dépister ou surveiller l'IRC.

Enregistrement de l'essai: Sans objet, il ne s'agissait pas d'un essai clinique.

Introduction

Patients with chronic kidney disease (CKD) require frequent laboratory blood tests for assessment and monitoring of their kidney function. Point-of-care testing via fingerprick capillary blood sampling represents a minimally invasive way of evaluating renal function and may be useful in patients living in remote areas, those with difficult venous access, and in children. Furthermore, point-of-care measurements allow a rapid estimation of kidney function, which may be valuable in time-sensitive situations, such as prior to contrast studies, and in facilitating rapid diagnosis and clinical decision-making. It

is essential to evaluate the performance of any diagnostic device to ensure test results are precise, accurate, and reliable prior to clinical use.

The StatSensor (Nova Biomedical) is a point-of-care device which measures creatinine from a capillary whole blood sample. Previous studies have evaluated the performance of the StatSensor in capillary and venous whole blood specimens from healthy, CKD, dialysis, acute care, intensive care, and oncological patients with the intended use for assessing radiographic contrast-induced nephropathy[1-5] and screening for CKD in resource-limited settings.[5,6] These studies suggested a moderate correlation in lower creatinine

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concentrations and a significant underestimation (or negative bias relative to a reference method) of approximately 30% in higher creatinine concentrations (>150 μmol/L) when compared with central laboratory methods. The underestimation affecting higher creatinine concentrations has been postulated to be due to assay interference by disease-related factors, such as urea in end-stage kidney disease.[2,3,6]

During the last decade, improvements in creatinine measurements were made with the Creatinine Standardization Program created by the National Kidney Disease Education Program (NKDEP) Laboratory Working Group in collaboration with the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) and the European Communities Confederation of Clinical Chemistry (now European Federation of Clinical Chemistry and Laboratory Medicine).[7-9] Prior to standardization of creatinine methods, biases were reported to be 30% to 40% between different methods.[7,10] Based on biological variation data, the desirable and minimum analytical total error (TE), where TE = bias (%) + (1.96 × CV (%)) and CV = coefficient of variation (standard deviation/mean, %), performance goal for the measurement of creatinine is 7.6% and 11.4%, respectively.[7] The measurement of creatinine in clinical laboratories in British Columbia (BC), Canada, underwent regional standardization in March 2004 and reduced the average TE from 23.9% to 8.7% and average analytical bias from 16.5% to 2.7%.[11] The accuracy of creatinine testing (defined as the minimization of total analytical error) by clinical laboratories in BC is monitored by an external accuracy-assigned serum-based proficiency testing program (CEQAL). Recent performance data from this program in June 2020 indicated that 93% of the creatinine methods in the province were meeting a TE performance goal of 8.9% or less (data on file with the Provincial Renal Agency). In 2009, updates to the equation estimating glomerular filtration rate (eGFR) have also been made from the Modification of Diet in Renal Disease (MDRD) equation to Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation, where the accuracy of eGFR is improved for values greater than 60 mL/min/1.73 m^2.[12,13]

Since previous evaluations of the StatSensor were performed in the prestandardized era and using the MDRD or creatinine clearance equations, this study aims to evaluate the performance of the StatSensor device and compare with post-standardized isotope dilution mass spectrometry (ID-MS)–calibrated enzymatic creatinine method on the Roche Integra 400 analyzer. This was assessed by comparing capillary specimen collection methods (direct fingerstick vs SAFE-T-FILL collection device), reducing imprecision (singlet vs duplicate measurements), and correcting bias (by applying postanalytical bias correction). The study also aims to assess the feasibility of using the StatSensor to screen for or monitor CKD in patients with varying degrees of kidney dysfunction, by assessing concordance rates of Kidney Disease Improving Global Outcomes (KDIGO) CKD classification based on eGFR calculated by the CKD-EPI equation.

Methods

Study Conduct and Participants

Ethics approval was obtained from Providence Health Care Research Institute Research Ethics Board of the University of British Columbia (H17-02488-A001). Patients older than the age of 18 years with CKD or with a functioning kidney transplant attending outpatient clinic appointments between April and October 2018 at St. Paul's Hospital were recruited on a voluntary basis to participate. Patients were excluded if they were younger than 18 years of age, currently receiving dialysis treatment, pregnant, unable to give consent, or utilized a substitute decision maker. Written informed consent was obtained from all participants. Patient demographic data, test results, and residual samples were identified by a unique study number only. Patient demographic data included height, weight, age, and ethnicity for the calculation of eGFR by CKD-EPI equation.[13] Participants were recruited based on previous central laboratory plasma creatinine to include values spanning normal kidney function and CKD ranges to optimize the evaluation of the StatSensor analyzer performance. A sample size of 60 was selected for feasibility purposes.

Sample Collection

Capillary whole blood specimens were collected by 2 methods: direct fingerstick and SAFE-T-FILL collection device. The standard method of use is direct fingerstick capillary whole blood testing, which, in this study, was performed using a BD Microtainer Contact-Activated Lancet (BD Diagnostics, Franklin Lakes, New Jersey), and immediate measurement of creatinine in duplicate by the StatSensor (Nova Biomedical, Waltham, Massachusetts). To monitor the effect of collection technique, additional drops of capillary whole blood (approximately 0.1 mL) were collected using the SAFE-T-FILL heparinized capillary blood collection device (RAM Scientific, Nashville, Tennessee), and creatinine were measured in duplicate by the StatSensor within 2 hours of collection. Simultaneously, one gel-free serum tube and one lithium heparinized plasma tube of venous blood were collected using a butterfly needle with vacutainer attachment (BD Diagnostics). Following collection and processing, specimens were aliquoted and stored at –70°C until further analysis.

Method Principle

Creatinine in capillary whole blood was measured by the StatSensor (Nova Biomedical) via a multi-enzyme (creatinine amidohydrolase, creatine amidohydrolase, and sarcosine oxidase) test strip with amperometric biosensor detection.[14] The whole blood creatinine concentrations are vendor-calibrated to reflect plasma concentrations.[14]

The Roche Integra 400 (Roche Diagnostics, GmbH, Mannheim, Germany) enzymatic colorimetric creatinine method (creatininase, creatinase, sarcosine oxidase, and

peroxidase) was used to measure serum and plasma creatinine for each patient who had StatSensor creatinine measurements. The between-run CV of the Roche Integra 400 creatinine method is less than 3% at both 86 and 350 µmol/L and meets vendor-claimed precision.

All laboratory analyses were performed by an independent technologist who was not involved with collection of the samples and was not aware of the results of the capillary blood sample testing.

Postanalytical Bias Correction of Serum and Plasma Creatinine Results Using Isotope Dilution Gas Chromatography Mass Spectrometry (ID-GC-MS)

Prior to comparison with the StatSensor creatinine results, the plasma creatinine results were adjusted via a postanalytical bias correction. The purpose of the correction was to align the Roche Integra plasma creatinine results with an ID-GC-MS reference method (CEQAL, Vancouver, BC). The ID-GC-MS method had been calibrated to establish traceability to the National Institute of Standards and Technology (NIST) standard reference material human frozen serum (SRM 967a). Six heparinized plasma samples were measured in duplicate on both the Roche and the ID-GC-MS reference method (Supplementary Figure 1). The samples were selected to span the clinical measuring range and the resulting regression equation was utilized to correct the Roche Integra plasma and serum creatinine results performed on all study patients. None of the study patient samples were measured directly with the ID-GC-MS method.

Data and Statistical Analysis

For imprecision, 2 levels of quality control materials (reference value of 73 and 117 µmol/L) were analyzed on the StatSensor in duplicate, twice daily prior to patient testing during the study period of 29 days. Precision was assessed by calculating the CV, which is equal to the standard deviation divided by the mean, for each level of quality control.

For method comparison and bias assessment, both singlet measurement and mean of duplicate measurements were separately included in the statistical analyses for each sample type (capillary whole blood, plasma, and serum) and collection type (direct fingerstick and SAFE-T-FILL collection device). Method comparison analyses included Deming regression, Pearson correlation coefficient, and Bland-Altman difference plot (cp-R statistical program, version 0.4, Vancouver, BC, Canada).[15] The resulting regression from method comparisons of capillary fingerstick versus plasma and capillary SAFE-T-FILL versus plasma was used for postanalytical bias correction for capillary whole blood creatinine results.

Estimated GFR was calculated using the CKD-EPI equation[13] from both the plasma creatinine and StatSensor-derived whole blood creatinine concentrations. Clinical

Table 1. Study Participant Demographics.

Number of patients	60
Age, years, mean ± SD (range)	61.9 ± 15.0 (27-94)
Sex	
Male, No. (%)	33 (55.0)
Female, No. (%)	27 (45.0)
Weight, kg, mean ± SD (range)	79.3 ± 18.2 (45.2-124.8)
Body mass index, kg/m², mean ± SD (range)	28.0 ± 5.9 (16.8-51.3)
Kidney	
Native, No. (%)	40 (66.7)
Transplant, No. (%)	20 (33.3)
Ethnicity	
Nonblack, No. (%)	57 (95.0)
Black, No. (%)	3 (5.0)
Plasma creatinine, µmol/L, mean ± SD (range)	137 ± 59 (50-357)
eGFR (plasma), mL/min/1.73 m², mean ± SD (range)	50 ± 20 (15-112)
eGFR, No. (%)	
≥90 mL/min/1.73 m²	2 (3.3)
60-89 mL/min/1.73 m²	15 (25.0)
30-59 mL/min/1.73 m²	35 (58.3)
15-29 mL/min/1.73 m²	8 (13.3)
<15 mL/min/1.73 m²	0 (0)

Note. eGFR = estimated glomerular filtration rate.

concordance in eGFR was evaluated by the accuracy in KDIGO CKD stages classification.[16] Sensitivity, specificity, positive predictive value, and negative predictive values were calculated for the ability of the StatSensor to detect CKD, as defined by an eGFR value of less than 60 mL/min/1.73 m².[17]

Results

Patient Demographics

Sixty patients with varying kidney dysfunction participated. Mean age was 61.9 ± 15.0 years, 55% were men, and one-third were kidney transplant recipients (Table 1). The mean enzymatic (with postanalytical bias correction) plasma creatinine was 137 ± 59 µmol/L, ranging from 50 to 357 µmol/L. The mean eGFR derived from CKD-EPI using plasma creatinine (with postanalytical bias correction) was 50 ± 20 mL/min/1.73 m², ranging from 15 to 112 mL/min/1.73 m². Capillary whole blood creatinine from direct fingerstick and SAFE-T-FILL collection device creatinine was 153 ± 73 (range = 60-432) and 163 ± 90 (range = 77-488) µmol/L, respectively (Table 2).

Imprecision by Quality Control Materials

Coefficient of variation (CV) ranged from 5.8% to 9.5% at 73 µmol/L and from 6.8% to 11.3% at 117 µmol/L creatinine.

Table 2. Creatinine and eGFR in Serum, Plasma, and Capillary Whole Blood (Direct Fingerstick and SAFE-T-FILL).

	Vendor calibration mean $\pm$ SD (range)	Postanalytical bias correction mean $\pm$ SD (range)
Serum creatinine, μmol/L	142 $\pm$ 61 (55-368)	138 $\pm$ 59 (54-357)
Plasma creatinine, μmol/L	141 $\pm$ 61 (51-369)	137 $\pm$ 59 (50-357)
eGFR[a] (plasma), mL/min/1.73 m^2	NC	50 $\pm$ 20 (15-112)
Capillary (fingerstick) creatinine, μmol/L	153 $\pm$ 73 (60-432)	137 $\pm$ 62 (57-373)
eGFR[a] (fingerstick), mL/min/1.73 m^2	45 $\pm$ 18 (13-102)	50 $\pm$ 20 (15-105)
Capillary (SAFE-T-FILL) creatinine, μmol/L	163 $\pm$ 90 (77-488)	136 $\pm$ 65 (73-371)
eGFR[a] (SAFE-T-FILL), mL/min/1.73 m^2	43 $\pm$ 19 (11-88)	50 $\pm$ 19 (14-90)

Note. eGFR = estimated glomerular filtration rate; NC = not calculated; CKD-EPI = Chronic Kidney Disease Epidemiology Collaboration.
[a]eGFR was calculated from CKD-EPI equation.[13]
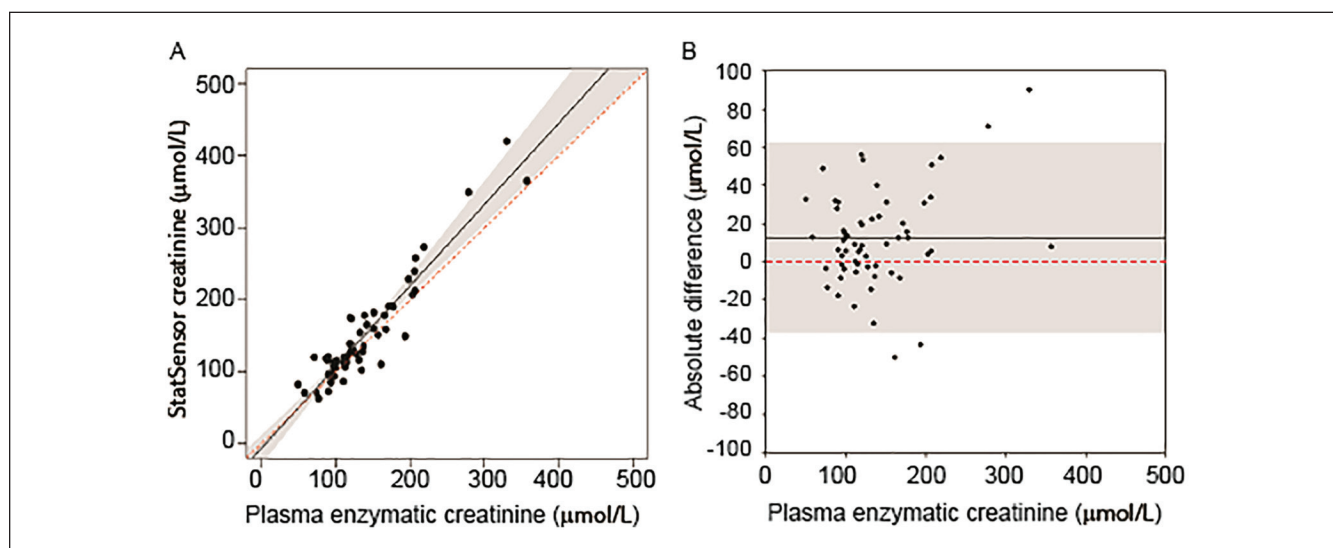
Figure 1. Comparison of direct fingerstick StatSensor creatinine and Roche plasma enzymatic creatinine (ID-GC-MS aligned). (A) Deming Regression Plot. Shaded area represents 95% CI. StatSensor Cr = 1.129 (95% CI = 0.931-1.293), plasma enzymatic Cr = −6.188 (95% CI = −26.498 to 18.25), R^2 = 0.883, n = 60. Solid line, linear best fit determined by 1/x-weighted Deming regression; dashed line, line of identity y = x and (B) Bland-Altman difference plot. Shaded area represents 95% CI. Solid line, mean bias = 12.7 (95% CI = −38.4 to 64.3); dashed line, no difference.
Note. ID-GC-MS = isotope dilution gas chromatography mass spectrometry; CI = confidence interval.

Imprecision is comparable with previously published evaluations of the StatSensor ranging between 3.3% and 13% with creatinine concentrations between 73 and 600 μmol/L[1-6] and meets the vendor claims.[18]

Method Comparisons and Bias Correction

Serum and plasma creatinine concentrations were measured by Roche Integra 400 enzymatic method. The difference between plasma and serum creatinine measurements on this analyzer was negligible (Table 2 and Supplementary Figure 1). The plasma creatinine concentrations measured by enzymatic method (with postanalytical bias correction based on ID-GC-MS) will be used as reference for comparison with capillary whole blood for the remainder of the study.

Capillary whole blood collected by direct fingerstick and SAFE-T-FILL collection device was analyzed on the StatSensor and the results were compared with those from the Roche enzymatic plasma creatinine method (with postanalytical bias correction) (Table 2). For direct fingerstick,
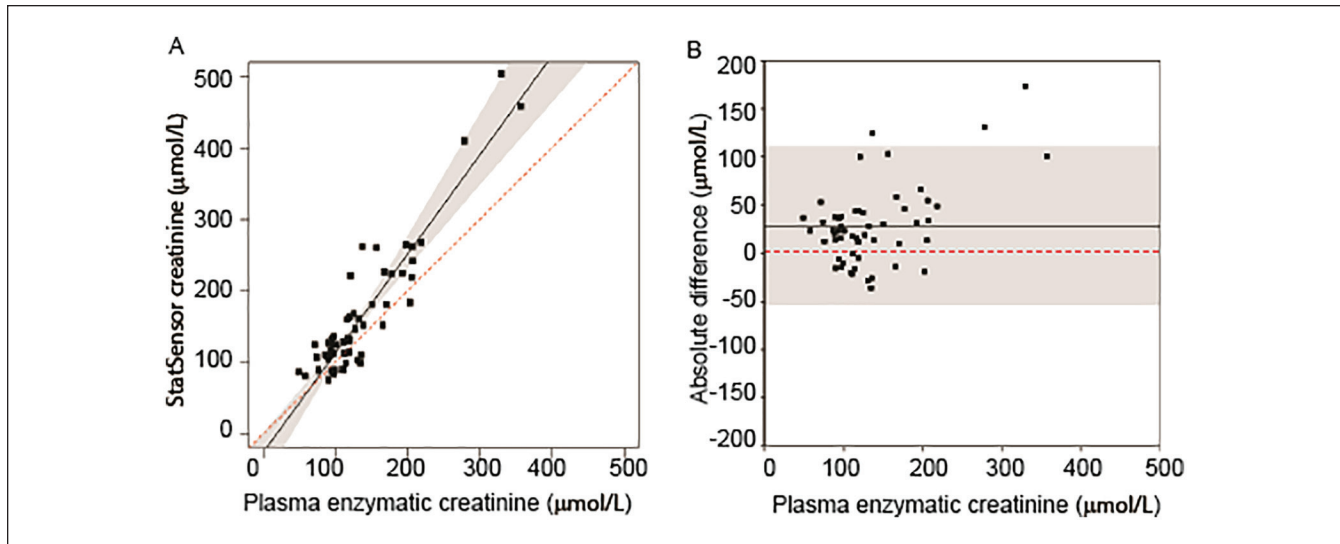
Figure 2. Comparison of SAFE-T-FILL StatSensor creatinine and Roche plasma enzymatic creatinine. (A) Deming Regression Plot. Shaded area represents 95% CI. StatSensor Cr = 1.385 (95% CI = 1.121-1.679), plasma enzymatic Cr = −25.483 (95% CI = −62.941 to 6.149), R^2 = 0.847, n = 55. Solid line, linear best fit determined by 1/x-weighted Deming regression; dashed line, line of identity y = x and (B) Bland-Altman difference plot. Shaded area represents 95% CI. Solid line, mean bias = 29.6 μmol/L (95% CI = −26.0 to 128.8); dashed line, no difference.
Note. CI = confidence interval.

Deming regression (Figure 1A) showed moderate to good agreement with a slope of 1.129 (95% confidence interval [CI] = 0.931-1.293), intercept of –6.188 (95% CI = −26.498 to 18.25), and R^2 = 0.883. Bland-Altman analysis demonstrated a mean positive bias of 12.7 μmol/L (95% CI = −38.4 to 64.3) or 7.8% (95% CI = −26.4 to 44.5) (Figure 1B). For SAFE-T-FILL collection device, Deming regression (Figure 2A) showed moderate agreement with a slope of 1.385 (95% CI = 1.121–1.679), intercept of –25.483 (95% CI = −62.941 to 6.149), and R^2 = 0.847. Bland-Altman analysis revealed a larger mean positive bias using SAFE-T-FILL device of 29.6 (95% CI = −26.0 to 128.8) μmol/L or 16.6% (95% CI = −23.2 to 57.3) (Figure 2B).

Clinical Concordance by eGFR

To evaluate the clinical usefulness of StatSensor as a device for CKD screening programs, eGFR calculated from whole blood creatinine collected by direct fingerstick (Figure 3A) and SAFE-T-FILL collection device (Figure 3B) was compared with eGFR calculated from plasma creatinine. The stages of CKD as defined by KDIGO were used to evaluate concordance.[17] Estimated GFR derived from the StatSensor direct fingerstick using the CKD-EPI equation correctly classified 41 of the 60 patients (68.3%) and misclassified 19 patients (31.7%) by one CKD stage. KDIGO CKD stage was underestimated in 13 patients (21.7%) and overestimated in 6 patients (10%) (Figure 3A, Supplementary Table 1A). A similar pattern was observed when SAFE-T-FILL collection device was used, where 30 of 55 patients (54.5%) were correctly classified, and 25 patients (45.5%) were misclassified

by one stage; CKD stage was underestimated in 21 patients (38.2%) and overestimated in 4 patients (7.3%) (Figure 3B, Supplementary Table 1C).

Impact of Bias Correction and Duplicate Measurements in eGFR Concordance

To evaluate the impact of analytical bias and imprecision on CKD stage misclassification, whole blood creatinine results were bias corrected and measured in duplicate. The bias-corrected results improved the CKD stage classification moderately from 68.3% to 81.7% for direct fingerstick sampling (Supplementary Table 1B) and from 54.5% to 67.3% for SAFE-T-FILL collection device (Supplementary Table 1D). The means of duplicate measurements for both direct fingerstick and SAFE-T-FILL device were analyzed and did not improve the rates of CKD stage misclassification compared with singlet measurements (Supplementary Figure 2).

Clinical Sensitivity and Specificity

Clinical sensitivity and specificity for detecting eGFR less than 60 mL/min/1.73 m^2 from direct fingerstick were 86.1% and 82.4%, respectively (Table 3). Correction of the positive bias in StatSensor creatinine measurements yielded similar clinical sensitivity of 88.4% and specificity of 76.5% in detecting CKD. Although positive predictive value was greater than 90% and negative predictive value was 72.2%, the test may have limited utility for the purposes of excluding CKD. When blood was collected via the SAFE-T-FILL device, similar sensitivity and positive predictive values
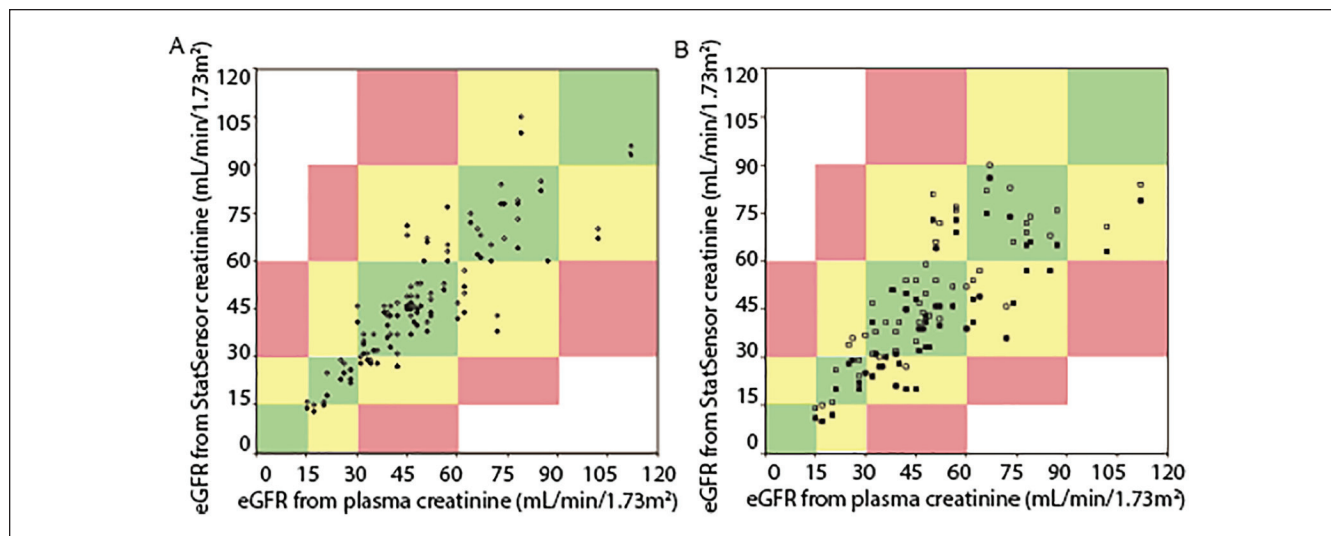
Figure 3. Clinical concordance of eGFR calculated by the CKD-EPI equation between capillary whole blood StatSensor creatinine in singlet compared with plasma enzymatic creatinine. (A) Direct fingerstick and (B) SAFE-T-FILL capillary collection device.
Note. Uncorrected creatinine value (filled circle), bias-corrected creatinine value (unfilled circle), eGFR calculated using StatSensor creatinine value compared with eGFR calculated using reference creatinine value results in same Kidney Disease: Improving Global Outcomes CKD stage (green), discrepancy by 1 stage (yellow), discrepancy by 2 stages (red). CI = confidence interval; eGFR = estimated glomerular filtration rate; CKD-EPI = Chronic Kidney Disease Epidemiology Collaboration.

Table 3. Clinical Performance for Nova StatSensor Using an eGFR Decision Threshold of 60 mL/min/1.73 m^2.

	Calibration	Sensitivity, % (95% CI)	Specificity, % (95% CI)	Positive predictive value, % (95% CI)	Negative predictive value, % (95% CI)
StatSensor Direct Fingerstick	Vendor calibration	86.1 (72.1-94.7)	82.4 (56.6-96.2)	92.5 (81.4-97.2)	70.0 (51.8-83.5)
	Postanalytical bias correction	88.4 (74.9-96.1)	76.5 (50.1-93.2)	90.5 (80.0-95.8)	72.2 (52.3-86.1)
StatSensor SAFE-T-FILL	Vendor calibration	89.7 (75.8-97.1)	50.0 (24.7-75.4)	70.9 (57.1-82.4)	66.7 (41.2-85.1)
	Postanalytical bias correction	86.8 (71.9-95.6)	68.8 (41.3-89.0)	86.8 (76.0-93.2)	68.8 (47.7-84.2)

Note. Positive test when plasma creatinine determined eGFR < 60 mL/min/1.73 m^2. Negative test when plasma creatinine determined eGFR ≥ 60 mL/min/1.73 m^2. eGFR = estimated glomerular filtration rate; CI = confidence interval.

were calculated but with lower specificity and negative predictive values (Table 3).

Illustrative Cases

To consider the impact of analytical imprecision and bias on creatinine concentrations and the resultant eGFR calculations and CKD stage misclassification for individual cases, the mean of duplicate creatinine, eGFR, and corresponding CKD stage values from 4 illustrative cases from our data set are shown in Table 4.

These cases illustrate how the StatSensor may both over- and underestimate creatinine concentration when compared with the plasma enzymatic method to a degree that causes obvious misclassification of the severity of renal

dysfunction. Imprecision error was greatest when using the SAFE-T-FILL collection device, then direct fingerstick, and least by the central laboratory reference method. In 3 of these 4 patients, they remained misclassified after bias correction was applied. Imprecision in creatinine measurements with the StatSensor have implications for cost of retesting and monitoring as well as causing concern to the patient. This must be taken into consideration if clinicians are contemplating using the StatSensor or SAFE-T-FILL as part of a CKD screening program.

Discussion

Our study assessed the use of the StatSensor and SAFE-T-FILL collection devices compared with laboratory reference

Table 4. Effect of Recalibration on Interpretation of Patient Creatinine and eGFR Results.

Patient	Calibration	Plasma enzymatic			StatSensor direct fingerstick			StatSensor SAFE-T-FILL		
		Mean Cr, μmol/L (95% CI)	Mean eGFR, mL/min/1.73 m² (95% CI)	CKD stage	Mean Cr, μmol/L (95% CI)	Mean eGFR, mL/min/1.73 m² (95% CI)	CKD stage	Mean Cr, μmol/L (95% CI)	Mean eGFR, mL/min/1.73 m² (95% CI)	CKD stage
Patient A 68 yo, male, nonblack	Vendor calibration	193 (189-197)	30 (29-31)	III b	152 (149-154)	40 (39-41)	III b	201 (177-225)	29 (25-33)	IV
	Postanalytical bias correction	—	—	—	135 (133-137)	46 (45-47)	III a	163 (139-186)	37 (33-41)	III b
Patient B 66 yo, male, nonblack	Vendor calibration	278 (272-284)	20 (20-20)	IV	380 (349-411)	14 (12-15)	V	423 (409-436)	12 (11-12)	V
	Postanalytical bias correction	—	—	—	330 (298-361)	16 (14-18)	IV	323 (310-336)	16 (15-17)	IV
Patient C 75 yo female, nonblack	Vendor calibration	71 (70-73)	72 (70-74)	II	120 (119-120)	38 (38-38)	III b	119 (113-125)	39 (36-41)	III b
	Postanalytical bias correction	—	—	—	108 (108-109)	43 (43-43)	III b	103 (98-109)	46 (43-49)	III a
Patient D 60 yo, female, nonblack	Vendor calibration	131 (128-134)	38 (37-39)	III b	124 (117-132)	41 (38-44)	III b	118 (102-133)	45 (38-51)	III a
	Postanalytical bias correction	—	—	—	112 (104-119)	46 (43-49)	III a	102 (87-117)	51 (44-58)	III a

Note. eGFR = estimated glomerular filtration rate; CI = confidence interval; CKD = chronic kidney disease.

methods for potential use as part of CKD screening in remote settings. The StatSensor had poorer precision compared with the central laboratory method with a CV ranging between 5.8% and 11.3%, compared with a typical central laboratory CV of less than 3.3%, and with evident scatter in the Deming regression and Bland-Altman plots. The StatSensor imprecision observed in this study is similar to previous reports documenting a CV between 3.3% and 13%[1-6] and vendor-claimed CV between 3.4% and 8.7%.[18]

Method comparison between StatSensor and laboratory enzymatic creatinine showed moderate to good correlation with an R^2 of 0.883 for direct fingerstick. Correlation for the SAFE-T-FILL collection device was slightly poorer with an R^2 of 0.847 which may have been due to preanalytical error; however, our study was not designed to assess this. While this degree of correlation has also been observed in other studies (R^2 range of 0.61-0.93),[1-3,6] our study demonstrated that the StatSensor both over- and underestimates creatinine in patients with advanced kidney dysfunction (>150 μmol/L). Results comparing duplicate creatinine measurements by the StatSensor and SAFE-T-FILL suggest repeatability may also be an issue. Previous studies have indicated that a change in eGFR of as little as 5 mL/min/1.73 m² annually has been associated with a 2-fold increase in mortality.[19,20] Increased risk of myocardial infarction, heart failure, and stroke has been observed in patients who have a drop in CKD stage within a year.[21] In this study, repeat measurements performed simultaneously on the same patient changed by greater than 3 mL/min/1.73 m² in 22 of the 60 (36.7%) patients, and greater than 5 mL/min/1.73 m² in 17 of the 60 (28.3%) patients. KDIGO stage misclassification occurred at all stages of CKD, where some patients were misclassified as

having milder disease while others were misclassified as having more severe disease. This may have clinical implications on patient management and would limit its use for screening purposes.

Our study demonstrated that the clinical sensitivity and specificity for the StatSensor in detecting CKD (as defined by an eGFR of less than 60 mL/min/1.73 m²) are 86.1% and 82.4% respectively, for direct fingerstick, and 89.7% and 50.0% for SAFE-T-FILL collection device. Shephard et al reported a similar sensitivity of 82.4% to 86.8% by the MDRD equation; specificity was substantially improved compared with our study, at 100%.[6] The investigators applied an observed bias correction of the meter creatinine results, relative to the reference standard, and thereby improved sensitivity from 86.8% to 96.2% for detecting an eGFR of less than 60 mL/min/1.73 m² by the MDRD equation.[6] Korpi-Steiner et al evaluated the performance of StatSensor in detecting CKD as defined by an eGFR of less than 60 mL/min/1.73 m² by the MDRD equation.[1] The authors likewise applied a bias correction of 25.8 μmol/L (0.28 mg/dL) to the creatinine measurements and improved the sensitivity from 16% to 59%. However, the study cohort in Korpi-Steiner et al had a much lower incidence of CKD compared with our study, with only 29% of patients having an eGFR of less than 60 mL/min/1.73 m², and only 1.5% with an eGFR of less than 30 mL/min/1.73 m². In addition, the prior study did not utilize direct fingerprick capillary sampling, as would be the case in clinical situations. While previous studies had been successful in applying a postanalytical bias correction to improve the sensitivity and specificity for StatSensor, a postanalytical bias correction in this study did not improve sensitivity and specificity, and only improved the eGFR clinical concordance moderately (68.3%-81.7% for

direct fingerstick sampling; 54.5%-67.3% for SAFE-T-FILL collection device). It is important to note that there are also differences in calibration, eGFR calculation, and patient population in these studies. If the previously published correction factors were applied to the current study patient measurements, it would have markedly decreased concordance. Overall, the inability to improve test characteristics with a postanalytical bias correction and the observation that the StatSensor creatinine measurements led to bi-directional CKD stage misclassification suggest that the limiting characteristic of the StatSensor may not be limited to bias, but also to imprecision.

Although most previous studies evaluating the performance of the StatSensor were performed in the prestandardization era, recently a study evaluated the StatSensor for the purposes of screening prior to intravenous contrast use.[22] The authors compared the creatinine measured by the StatSensor with those obtained from plasma laboratory method. In addition, CKD-EPI eGFR calculated from StatSensor and plasma creatinine were compared with GFR measure by iohexol plasma clearance. Their results showed good correlation between the StatSensor and laboratory methods ($r = 0.93$, $P < .0001$). The patient population did differ compared with our study, as these were patients who had an indication for iohexol measure of GFR and thus suggesting clinicians already may not have had adequate confidence in their eGFR. Patients in this study overall had better kidney function with a mean eGFR of 77 mL/min/1.73 m^2. In addition, the study collected singlet samples for the StatSensor, so did not evaluate reproducibility of test results.

Strengths of our study include the use of a study population with a wide range of creatinine results and collection of direct fingerstick blood samples in a method identical to that used in clinical practice. Limitations include limited sample size and restriction of study population to those who had known kidney disease. Given that we have studied only patients with a known history of kidney disease, we cannot directly comment on the performance of the StatSensor test in measuring creatinine in patients without kidney dysfunction, that is, this test may have a better specificity in identifying CKD if we had included such patients in our study. Similarly, pregnant women, children, and dialysis patients were excluded, so the results of this study cannot be generalized in any specific manner to those populations.

Conclusions

Point-of-care devices for measuring creatinine may be useful where laboratory-based measurements are not easily available. The StatSensor may be of use as a preliminary indicator of eGFR, which would require verification with formal laboratory testing. Most importantly, clinicians should be aware of the bias and imprecision of the StatSensor device relative to laboratory-based measurements, so that they are aware of the potential margin of error when making management decisions about their patients.

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