Exploring the potential of self-monitoring kidney function after transplantation : from patient acceptance to replacing outpatient care

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CHAPTER 4

Application of a point of care creatinine device for trend monitoring in kidney transplant patients: fit for purpose?

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ABSTRACT

The StatSensor® Xpress-i™, a point-of-care system for blood creatinine measurement, offers patients the possibility of self-monitoring creatinine. In this study, the analytical performance of the StatSensor® for both detecting current renal function and monitoring renal (dys)function in kidney transplant patients was examined.

Accuracy of the StatSensor® with capillary and venous whole blood was evaluated and compared to an isotopic dilution mass spectrometry (IDMS)-traceable enzymatic creatinine test in venous serum (n=138). Twenty Li-heparin samples were compared to the IDMS reference method performed by a Joint Committee for Traceability in Laboratory Medicine (JCTLM)-listed reference laboratory (RfB, Bonn, Germany). To evaluate StatSensor®'s suitability to monitor kidney function, both venous and capillary samples were obtained in 20 hospitalized transplantation patients. Venous samples were analyzed with an IDMS-traceable enzymatic test, capillary samples were measured using the StatSensor®. For all 2-day intervals, percentage change in creatinine was compared between both methods.

The StatSensor® did not meet total allowable error criterion of 6.9%. Average overall CV for the StatSensor® was 10.4% and 5.2% for capillary and venous whole blood results, respectively. Overall CVa for the central laboratory serum creatinine method was <1.5%. For monitoring renal (dys)function, total agreement of the StatSensor® with an IDMS-traceable enzymatic test was 68% using a 10% Δchange. No significant differences were found between the changes observed by both methods.

Capillary blood testing with the StatSensor® is not advisable for determining current renal function with a single creatinine measurement in kidney transplant patients, mainly due to excessive analytical imprecision. However, our results suggest that capillary blood testing with the StatSensor® can be used for daily trend monitoring of kidney function after renal transplantation.

INTRODUCTION

In the last decade significant improvements in kidney transplant outcome have been achieved thanks to advances in the management of immunosuppression [1]. However, patients continue to be at risk for rejection, mainly in the first year after transplantation. The most important parameter for rejection is deterioration of the renal function, measured by the serum creatinine concentration. As early detection of a rejection episode is mandatory to minimize permanent damage to the kidney graft, kidney transplant patients have their serum creatinine checked on average 20 times during the first year post-transplantation. If patients were enabled to monitor kidney function at home, this would have important advantages.

First, home monitoring could improve speed of rejection detection. Second, the high number of necessary outpatient visits could be reduced. This would be an advantage, as the frequent visits are a burden to the recovering patient. Further, it would be beneficial for healthcare as decreasing number of outpatient appointments alleviates the burden to healthcare capacity. Third, transferring part of care to the home setting corresponds to the idea of 4 P Medicine [2]. 4 P Medicine aims at decentralizing healthcare by means of delivering P*redictive*, P*reventive*, P*ersonalized* and P*articipatory* medicine. It has repeatedly been shown that self-monitoring is of clinical benefit for patients with hypertension [3, 4] and thrombosis [5–7]. Further, several studies in different disease populations show that patients prefer self-monitoring to regular care [7–14] and that patients who self-monitor experience higher levels of quality of life [8, 10, 13, 15] and more empowerment [7, 8, 11, 12, 14] than patients who do not.

Recently, a handheld creatinine meter (StatSensor® Creatinine Xpress-i™) has become available. It is cleared by the US FDA for hospital use by healthcare professionals and the device is used among radiology patients to detect contrast-induced nephropathy [16–18]. In the future, the availability of this device may offer kidney transplant patients the possibility to self-monitor their blood creatinine levels at home.

However, before an in vitro diagnostic (IVD) device can be advocated for adequate home-based patient care, it must be thoroughly tested to guarantee its robustness and clinical reliability. Two previous studies on the performance of the StatSensor® creatinine meter concluded that its' results can deviate from centralized enzymatic method values to a small [19] or even large amount [20]. However, in both articles the possible value of StatSensor® for use in clinical practice is recognized, depending on the specific test purpose. The importance of taking the purpose of a test into consideration when evaluating its' performance has recently been advocated by a multidisciplinary group of the European

Federation of Clinical Chemistry and Laboratory Medicine (EFLM) [21]. For kidney function, one can distinguish between diagnosing and monitoring purposes, recognizing that both may require different levels of robustness as well as different criteria for performance assessment.

The aim of this study was two-fold. First, to assess the suitability of the StatSensor® for detecting current renal function of kidney transplant patients with a single creatinine measurement, by evaluating the metrological traceability and exchangeability of StatSensor® results compared to an isotopic dilution mass spectrometry (IDMS) traceable enzymatic creatinine central laboratory method. Second, to assess the suitability of the StatSensor® for monitoring creatinine trends in kidney transplant patients with serial creatinine measurements, by evaluating the concordance of sequential StatSensor® results to sequential results of the reference laboratory method around the cut-off level used for early identification of kidney rejection in kidney transplant patients.

MATERIALS AND METHODS

Ethics approval

This study was performed at the Leiden University Medical Centre (LUMC). It was part of the pilot study Teletransplant which protocol was approved of by the LUMC Medical Ethics Committee.

Materials

The StatSensor® Xpress-i™ Creatinine Hospital Meter (Nova Biomedical, Waltham, MA, USA) is a handheld point-of-care (POC) device developed for measuring creatinine in capillary (finger prick) whole blood as well as venous and arterial whole blood. Serial numbers of the StatSensor® devices used were 149010610225, 149024910321, 149025210321, 149025910321, 149027410321 and 149027610321. The StatSensor strip technology utilizes a gold-based multiwell, multilayer technology that corrects for the influence of interfering substances that can be present in the whole blood matrix of hospitalized patients. Creatinine is measured enzymatically with signal detection method based on amperometry.

According to the product insert, test results are traceable to National Institute of Standard and Technology (NIST) SRM 967. Two batches of strips with LOT numbers 4910348249 and 4911013249 were used. During the evaluation study, five levels of calibrators were used (n=2) which were analyzed on six different StatSensor® devices with two batches of strips (see Supplemental Data, 1 that accompanies the article http://www.degruyter.com/view/j/cclm.2015.53.issue-10/cclm-2014-

0932/cclm-2014-0932.xml?format=INT). Serum creatinine in the hospital central laboratory is performed with an IDMS-traceable enzymatic method on the Roche Modular P800, Cat Nr. 11875566216 (Reagent 1) and 11875582216 (Reagent 2) for the Creatinine Plus assay and Cat Nr. 10759350190 for the C.f.a.s. (calibrator for automated systems) calibrator (Roche Diagnostics, Mannheim, Germany).

Methods

Evaluation of StatSensor®'s performance for detecting current renal function of kidney transplant patients

The analytical performance of the StatSensor® was evaluated and compared to the performance of an IDMS traceable enzymatic creatinine central laboratory method using specimens of kidney transplant patients who had their regular outpatient hospital appointment in July 2011. All patients received a letter about the study and the informed consent procedure. We used a 'yes, unless' principle, with all invited patients enrolled unless they declined participation.

Participation comprised of the donation of an extra tube of blood and the performance of two capillary creatinine measurements. After collecting venous blood samples for routine analyses (including analysis of serum creatinine concentration), an additional lithium heparin tube was taken. Participating patients then visited a doctors' assistant to measure capillary whole blood creatinine with the StatSensor® on the spot. Five different StatSensor® devices were randomly used. Capillary punctures were performed in duplicate (middle and ring finger). Based on the average of the duplicate StatSensor® measurements, patients were grouped into three creatinine categories: 50–100, 100–200 and >200 µmol/L. The first 30 patients allocated to one of these categories were selected for further analysis. In addition, eight patients with large differences between the duplicate measurements were selected for further assessment. In our central laboratory, creatinine was repetitively measured (2- and 5-fold) by an experienced technician in lithium heparinized blood on the patient-specific StatSensor® meters, i.e., the ones used for testing the capillary finger pricks. Residual lithium heparinized whole blood was centrifuged at 2750 *g* for 15 min at room temperature (RT). The obtained plasma was used to determine creatinine according to the central laboratory method. Residual plasma was stored at –80 °C. All lithium heparinized blood was analyzed within 4 h from blood drawing. A subset of 20 stored plasma samples was sent to the Reference Institute for Bioanalytics (RfB) in Bonn, Germany for objective evaluation of StatSensor® bias as compared to the Joint Committee for Traceability in Laboratory Medicine (JCTLM)-listed IDMS reference method (www.bipm.org/BIPM

database). Selection of 20 samples occurred based on sampling across creatinine devices used for capillary creatinine testing (n=5 for 149010610225, 149024910321, 149025210321 and 149025910321) and capillary creatinine test results, with all levels represented.

Evaluation of StatSensor®'s performance for monitoring creatinine trends in kidney transplant patients

To evaluate the suitability of the StatSensor® device for trend self-monitoring, tightly monitored patients with expected changes in levels of creatinine have to be selected. In theory, dialysis patients are an ideal population, considering the raise in creatinine during the days immediately following a dialysis session. However, their high levels of serum creatinine pose a problem, as earlier studies showed a significant negative bias of the StatSensor® at high creatinine concentrations [19, 20]. Another group of kidney patients in which changes in levels of creatinine can be expected, are recently transplanted patients. During the first days after kidney transplantation, the serum creatinine usually decreases rapidly due to the well-functioning kidney graft. Although only an increase of creatinine levels is relevant for the detection of kidney deterioration, it does not matter for the analysis whether creatinine levels rise or fall. Therefore, we can use this population for validating creatinine trend monitoring. For this analysis, 20 newly transplanted patients still being under hospital management were recruited for assessing the ability of StatSensor® for detecting changes in levels of creatinine over time (trend monitoring).

StatSensor® capillary creatinine measurements were performed twice per day (at 6.00 a.m. and 20.00 p.m.) on consecutive days following transplantation. According to routine clinical practice, serum was collected once a day for creatinine measurement by the central laboratory method. Both venous and capillary punctures were performed by professional nurses working at the transplantation ward.

Data analysis

For the analytical performance study, analytical coefficients of variation (CV) for StatSensor® were calculated from replicate determinations. Predefined quality requirements that we aimed at were based on desirable performance criteria derived from biological variation [22]. A split sample comparison was planned in order to study traceability of StatSensor® test results to NIST SRM 967. Equivalence of StatSensor® and central laboratory test results was evaluated using a two-instrument comparison procedure (EP Evaluator, Rhoads). Methods produce clinically exchangeable results if (Y-X) <total allowable error (TEa) for at least 95% of the results. In addition, reference change values

(RCVs) were calculated as 2.8 * (CV_a +CV_b), where CV_a means desirable analytical CV, and CV_b means intra-individual biological CV (CV_a =2.2%; CV_b =4.3%; TE_a =6.9%) [22].

For the evaluation of StatSensor®'s performance for determining creatinine trends in kidney transplant patients, a >10% increase in serum creatinine was considered to be clinically relevant. A general guideline is that an abrupt increase in the serum creatinine of greater than 50 percent should be promptly evaluated [23]. However, from professional experience, we know that an increase of 10% may indicate early symptoms of graft failure warranting further analysis or intensified follow-up of recently transplanted kidney patients. To calculate the degree of creatinine change, linear regression analysis was applied to analyze creatinine results generated during every 2-day interval with a maximum of five consecutive StatSensor® capillary creatinine measurements. The percentage creatinine change per day was obtained by dividing the slope by the average value (Figure 1). This calculation was also performed for the serum creatinine values determined by the central laboratory within the same time intervals. Only intervals which had at least four capillary creatinine values and three serum creatinine values available were selected. Agreement in levels of change as measured by the two methods was investigated by calculating the correlation between the percentage change in capillary creatinine and percentage change in venous serum creatinine for all selected 2-day intervals.

RESULTS

StatSensor®'s performance for detecting kidney function in kidney transplant patients

A total of 133 kidney transplant patients were included and 138 StatSensor® measurements were performed in duplicate (some patients visited the outpatient clinic twice during the period of inclusion). A mean difference of 20.21 µmol/L was found between the StatSensor® whole blood creatinine and the Roche Modular P800 serum creatinine (n=138) across the measuring range, with limits of agreement (defined as mean ±1.96 SD) varying between –58.8 and +34.1 µmol/L (see Supplemental Data, Figure 1).

To investigate equivalence of test results produced by StatSensor® and the central laboratory, 30 patients with StatSensor® creatinine results fitting into one of three categories (50–100, 100–200, >200 µmol/L) were selected. In addition, eight patients with the most marked differences between the duplicate capillary measurements (mean difference 42.5 ± 9.93, range 29 µmol/L) were selected. For each patient, a StatSensor® capillary whole blood creatinine result, a StatSensor® venous lithium heparin whole blood creatinine result, a venous lithium heparin plasma creatinine result as measured with the central laboratory method and a serum creatinine result as measured with the central

laboratory method was available. For the capillary blood measurements, the mean creatinine level was 161 ± 86 µmol/L. For the lithium heparin samples, the mean creatinine level was 150 ± 80 µmol/L for StatSensor® measurements and 154.4 ± 81.1 for the central laboratory methods. The cor- responding mean serum creatinine level according to the central laboratory method was 172 ± 82 µmol/L. The average error index(Y-X)/TE_a between the StatSensor® capillary result and central laboratory serum creatinine result was –0.96 with a range of –6.61 to 5.42. The difference between the StatSensor® and the central laboratory method was within the TE_a for only 15 out of 38 (39.5%) specimens. The largest error index occurred at a concentration of 107.5 µmol/L (see Figure 2A). Average overall CV_a for StatSensor (n=38) was 10.4% and 5.2% using the capillary respectively venous whole blood results (Table 1), which is far above the desirable imprecision of 2.2% [22]. For the central laboratory serum creatinine method, overall CV_a is <1.5%, and thus well below the desirable imprecision. As RCVs depend on the analytical imprecision of the method used, different RCVs will be found depending on the method used. RCVs for StatSensor® in capillary and heparinized venous whole blood are 35% and 23%, respectively, compared to 15.5% for the central laboratory method.

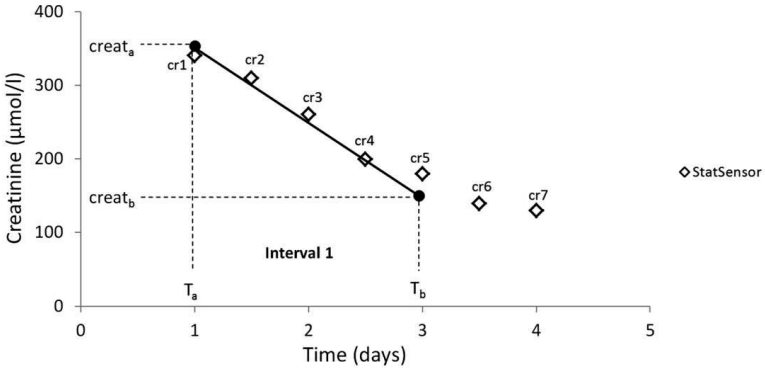

Figure 1: Regression line was calculated for every 2-day period (day 1– 3, day 2– 4, day 3– 5, etc.). Percentage change was calculated by creatinine change per day (creatb-creata)/(Tb-Ta) divided by the mean of the creatinine values (cr1+ cr2+ cr3+ cr4 + cr5)/5. This calculation was also performed for serum creatinine.

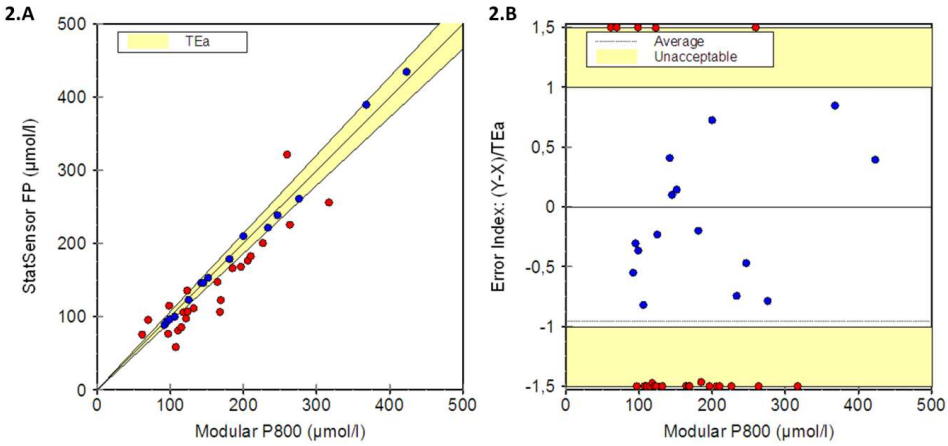

Figure 2: Routine method comparison.

Method comparison between creatinine measured in finger prick (FP) whole blood using StatSensor® and creatinine in serum using an IDMS-traceable Modular P800 assay (Roche) (left) with corresponding error indices (right). Blue dots meet the TE_a criterion of 6.9%; red dots do not meet the TE_a criterion.

Metrological traceability

Twenty plasma creatinine samples over a range of 60.0–317.9 µmol/L were analyzed by the German Reference laboratory RfB, using a JCTLM-listed, internationally recognized creatinine IDMS reference method, and by StatSensor® (mean of duplicate measurements). Linear regression and difference plots were calculated from the RfB IDMS plasma creatinine target values (X) and the StatSensor® capillary test results (Y): Y=0.7942*X+14.637, R^2 =0.9096 (see Figure 3A, left). The mean difference between the two methods was –16.1 µmol/L, with an upper limit of agreement [+2SD] of 28.07 µmol/L and a lower limit of agreement [–2SD] of –60.30 µmol/L (see Figure 3A, right). When plotting the central laboratory serum creatinine test results (Y) against the RfB IDMS plasma creatinine results (X) the linear regression was: Y=0.9981*X+1.886, R^2 =0.9981 (Figure 3B, left). The difference plot revealed a mean bias of 1.6 µmol/L, with a lower limit of agreement [–2SD] of –2.30 µmol/L and an upper limit of agreement [+2SD] of 5.50 µmol/L (Figure 3B, right). Whereas the central lab method meets the allowable bias of 3.4%, this is not the case for the StatSensor®.

Table 1. Analytical imprecision ($CV_{a)}$ and critical differences (RCV) using a StatSensor® whole blood creatinine device as compared to a serum central lab test performed on Modular P800 (Roche Diagnostics).

	StatSensor®		Modular P800	
	Capillary MF+RF[a]	Venous Li-Hep[b]	Venous Li-Hep[b]	Venous SST[b]
	Whole Blood (n=2)	*Whole Blood (n=2)*	*Whole Blood (n=5)*	*Serum (n=2)*
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Creatinine µmol/l	160.5 (85.7)	149.7 (79.6)	154.4 (81.1)	171.8 (82.0)
CV_a %	10.4 (10.2)	5.2 (4.4)	6.0 (2.3)	1.3 (1.0)
RCV %	35.3 (25.2)	22.5 (8.9)	22.7 (4.8)	15.5 (0.9)

[a] Middle and ring finger (MF and RF) capillary pricks were taken from 38 stable post-kidney transplant patients with creatinine values ranging between 50 - 450 µmol/l. [b] Venous blood was sampled in lithium heparin tubes (Venous Li-Hep) and in serum separation tubes (SST) for central lab analysis on both StatSensor® devices respectively Modular P800 according to manufacturers' instructions.

Evaluation of StatSensor®'s performance for monitoring creatinine trends in kidney transplant patients

Both capillary (twice per day) and venous blood samples were obtained from 20 kidney transplant patients for 6.28 (±2.99) consecutive days post-surgery. Some examples of post-transplantational creatinine courses measured by both StatSensor® and the central laboratory method (P-Modular) are shown in Figure 4. Eighty-two 2-days period trends (with 3 consecutive serum creatinine and at least 4 StatSensor® creatinine measurements) were obtained. According to expert opinion, an elevation of >10% in two subsequent creatinine measures is considered relevant for detection of kidney rejection. From Table 2, it can be seen that 33 out of 82 available intervals showed a >10% difference between subsequent intervals. The StatSensor® correctly identified a difference of >10% in 70% of these cases. Forty-nine intervals showed a difference of ≤10%, of which 67% was correctly identified as such by the StatSensor®. Total agreement was 68%. Figure 5 shows the calculated creatinine changes in venous (X-axis) and capillary blood (Y-axis). The correlation coefficient between both methods was 0.77 (95% CI

0.625–0.910). Deming regression analysis showed a slope of 0.889 (95% CI 0.753–1.026) indicating no statistically significant difference between changes observed by both methods.

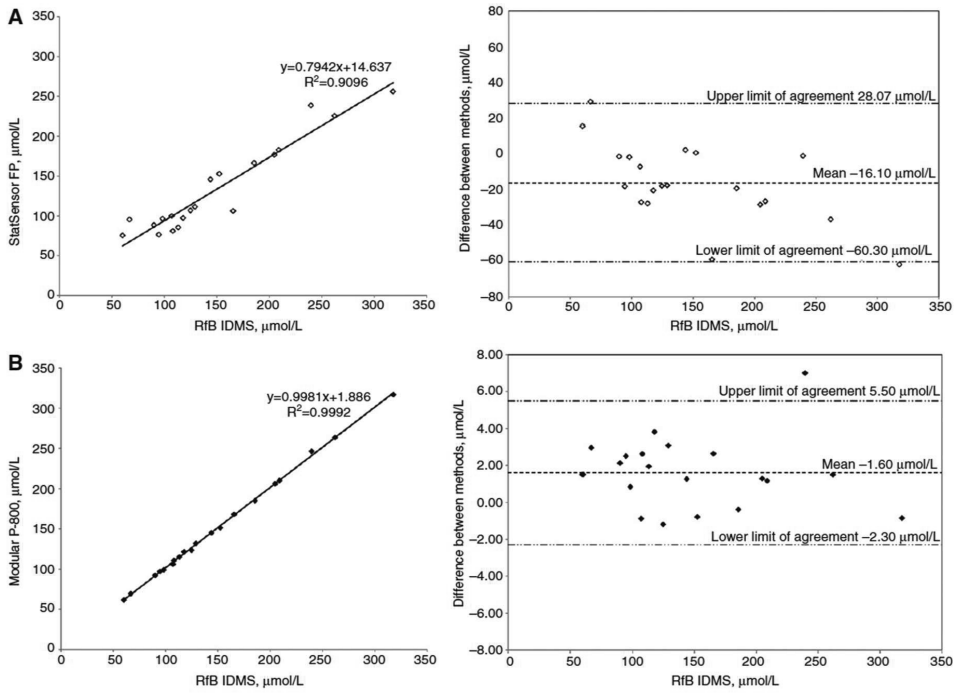

Figure 3: Reference standardization study.

(A) Linear regression (left) and difference plot (right) of creatinine measured in finger prick (FP) whole blood using StatSensor® (Y) and in Li-heparin plasma using the IDMS reference method, RfB, Bonn (X). (B) Linear regression plot (left) and difference plot (right) of creatinine measured in venous serum using Roche Modular P800 (Y) and in Li-heparin plasma using IDMS reference method, RfB, Bonn (X).

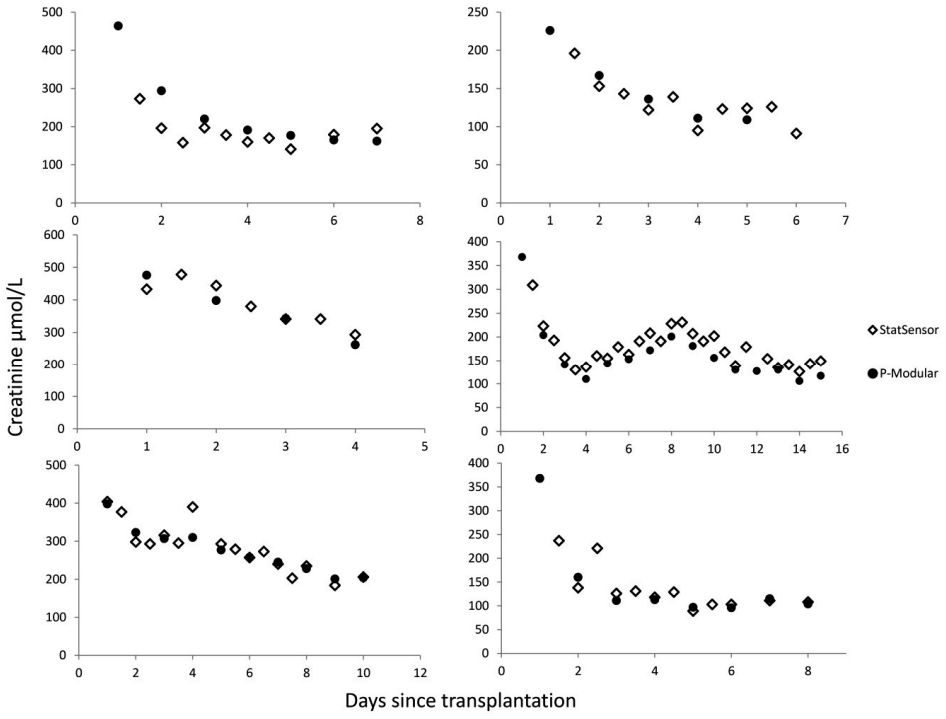

Figure 4. Examples of post-transplantational creatinine trends measured by StatSensor® (open) and Modular P800 (closed).

Table 2. Total agreement between serum creatinine on Modular P800 and finger prick whole blood creatinine on StatSensor® considering changes of >10% and ≤10% in serum creatinine in subsequent 2-day intervals.

		Modular P800		
		Delta >10%	Delta ≤10%	Total
StatSensor®	Delta >10%	23	16	39
	Delta ≤10%	10	33	43
Total		33	49	82

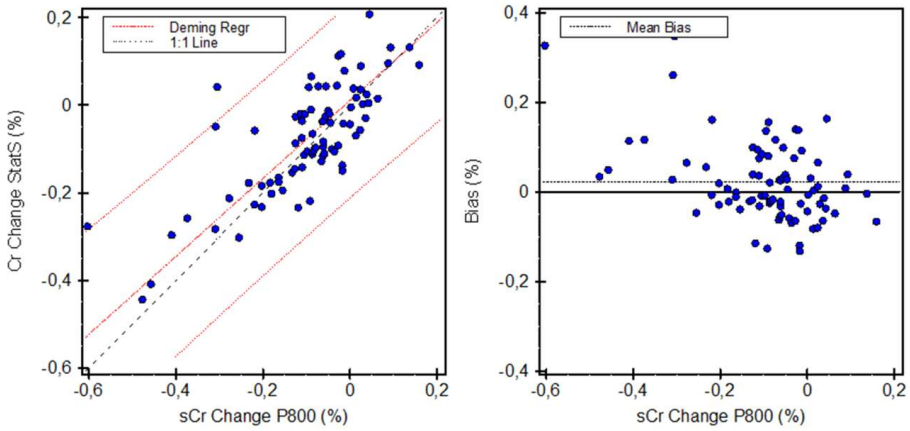

Figure 5: Agreement between blood creatinine changes in capillary finger prick (FP) whole blood measured with the StatSensor® (Cr change) and in venous serum measured with the Modular P800 (sCr change) has been evaluated. Both a Deming regression plot (left) and the corresponding difference plot (right) are presented.

DISCUSSION

In the current study, we examined the suitability of the StatSensor® Xpress-i™, a handheld POC system for creatinine measurement. We analyzed its performance for both detecting current renal function of kidney transplant patients with a single creatinine measurement and monitoring creatinine trends with serial creatinine measurements. From the reference standardization study it becomes clear that the traceability of capillary StatSensor® creatinine results to the creatinine reference system is inadequate. The split-sample comparison study showed that CV_a of the StatSensor® is excessive compared to the predefined desirable CV_a criterion based on biological variation [22], leading to 2.25-fold increased RCVs as compared to the central laboratory method (Table 1). Therefore, the StatSensor® device does not fulfill desirable nor minimum analytical performance criteria in case of using capillary blood. As such, the StatSensor® is not suitable for detecting current renal function of kidney transplant patients with a single creatinine measurement. These findings are in agreement with previous studies which showed insufficient analytical validity of the StatSensor® [19, 20] compared to IDMS-standardized enzymatic methods in the central laboratory. Improving the analytical performance of the StatSensor®, in line with IVD 98/79/EC directive and the ISO 15189 guideline, could improve the potential for using StatSensor® creatinine capillary testing for kidney diagnostic use. Figure 3B illustrates the perfect

agreement and negligible bias of 1.60 (–2.3– 5.5) µmol/L between central laboratory/Modular P800 and IDMS reference method, contrasting with the large scatter and excessive bias of –16.1 (–60.3–28.1) µmol/L for StatSensor® compared to IDMS reference methods as presented in Figure 3A. In the case of trend monitoring, the uncertainty of a single capillary blood creatinine test result is less critical. Detection of rejection episodes after kidney transplantation reflects a monitoring purpose for which the device should be able to detect trends in sequential measurements. In the present study, we examined the suitability of StatSensor® capillary blood testing to monitor changes in renal function. For recently transplanted patients, clinicians are especially interested in sudden increases in serum creatinine of >10% as this requires further analysis and/ or intensified follow-up. Therefore, the aim of this study was to assess whether a >10% change in serum creatinine (as measured by the central laboratory method) can also be detected when using StatSensor® for trend monitoring. For validating trend detection, it does not matter whether creatinine increases or decreases. Newly transplanted patients are a suitable population group, as their creatinine levels usually decrease rapidly during the first days after kidney transplantation. A reasonable correlation (R=0.77) between changes detected by the central laboratory and the StatSensor® was found. False-negative results lead to a delayed detection of rejection and should not or hardly occur. Although false-positive findings are less problematic, they lead to extra diagnostic interventions. In this study, the StatSensor® correctly identified a difference of >10% (true positive) in 70% and a difference of ≤10% (true negative) in 67% of all cases (total agreement 68%) within the time period monitored. Although these results indicate that StatSensor®'s ability to detect changes in kidney function needs improvement, the absence of a significant difference between changes observed by the central laboratory analyzer and the StatSensor® shows that it does have potential for monitoring creatinine.

To strengthen StatSensor®'s performance, an important step should be the improvement of its analytical performance as this will impact its clinical (diagnosing and monitoring) performance too. In the meantime, two manoeuvres could offer a provisional solution. First, to decrease the number of false negative results, one could choose a cut-off percentage which is lower for StatSensor® results. For example, by lowering the StatSensor® cut-off percentage to >5%, the number of correctly identified relevant changes (>10% increase as determined by the central laboratory method) increases from 70% to 82%. However, this approach would result in an increased number of false positives. Second, with increasing the frequency of StatSensor® measurements, a more reliable trend will be obtained, as the confidence interval decreases proportionally to the square root of the number of performed measurements, given a normal distribution. At home, patients can measure their creatinine daily. By doing so, the chances of detecting rejection are increased and theoretically, the number of outpatient

visits can be safely reduced. To investigate this approach, we have implemented a randomized controlled trial (RCT) with StatSensor®'s monitoring performance being tested in a clinical setting. One of the other outcomes of this study will show whether the results produced by patients at home, will yield the same clinically acceptable results for monitoring creatinine trends as observed when hospital professionals perform the measurements.

Besides offering the possibility of lowering the number of outpatient visits, self-monitoring kidney function after kidney transplantation is expected to have other benefits. Studies in other patient populations show that patients monitoring and/or managing their own disease results in more cost-effective healthcare systems by enabling the management of chronic diseases outside institutions [24–29], improved health outcomes [4, 6, 7, 9, 30, 31] and higher patient satisfaction [7–15, 32–34]. Whether the possible benefits also apply to kidney transplant patients, has yet to be investigated.

In conclusion, the analytical validity assessment and comparison to an international JCTLM-listed IDMS reference method indicate that the StatSensor® is not suitable for detecting kidney (dys)function of kidney transplant patients in case of singlicate capillary blood measurements, i.e., more variation is observed with StatSensor® capillary blood results compared to StatSensor® venous blood results and plasma or serum central laboratory results. Further investigation is required to determine the nature of the variation in capillary blood. Nevertheless, our results show that the device has potential for trend monitoring in the context of daily follow-up for kidney function after kidney transplantation. In an ongoing RCT, the safety and clinical performance of the StatSensor® POC system for monitoring creatinine trends is further investigated.

The different conclusions concerning the suitability of the StatSensor® for detecting current kidney function with a single creatinine measurement versus monitoring creatinine trends with serial creatinine measurements in kidney transplant patients illustrate the importance of the interplay of the different components of the cyclical framework for the evaluation of medical tests and IVDs, which was described recently by a multidisciplinary group of the EFLM [21]. They state that the key components of test evaluation should be driven by the test purpose and test role in the clinical pathway, and that clinical effectiveness data should be fed back to refine analytical and clinical performances. This implies that the intended clinical applications and outcomes of the new test should determine its analytical performance requirements.

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SUPPLEMENTAL DATA

Table 1. Calibration performance of the creatinine Statsensor® device as determined by a clinical chemistry technician during the evaluation study. To that end, 5 calibrator levels were measured in duplicate on 6 different StatSensor® devices with two batches of strips. Averages, SD and overall CVs were calculated using basic statistics.

	Lot	**Range**	**Lot strips 4910348249**		**n=12**	**Lot strips 4911013249**		**n=12**
Creatinine	**Calibrators**	**µmol/L**	Mean µmol/L	SD µmol/L	**VC%**	Mean µmol/L	SD µmol/L	**VC%**
Level1	**5511017241**	**71-150**	**141**	**5**	**3.2**	**131**	**9**	**6.5**
Level2	**5511017242**	**133-248**	**207**	**11**	**5.2**	**200**	**12**	**6.2**
Level3	**5511017243**	**256-442**	**391**	**26**	**6.8**	**382**	**21**	**5.6**
Level4	**5511017244**	**433-698**	**558**	**20**	**3.6**	**564**	**46**	**8.2**
Level5	**5511017245**	**619-1061**	**816**	**20**	**2.5**	**807**	**27**	**3.3**