Letter to the Editor

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Analytical and diagnostic performance evaluation of five creatinine POCT devices in the identification of patients at risk for post-contrast acute kidney injury (PCAKI)

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To the Editor,

We read with great interest Snaith and colleagues' paper on point-of-care (POCT) creatinine testing [1]. Iodine-based contrast agents are commonly used in medical imaging to provide accurate diagnosis. The advantages of their use must always be weighed against the risk of potential adverse reactions, as the administration of contrast agents can lead to post-contrast acute kidney injury (PCAKI) [2, 3]. Recently, an updated version of the European Society of Urogenital Radiology (ESUR) guidelines (version 10) has been published, which defines PCAKI as a rise in the serum creatinine concentration of more than 0.3 mg/dL (26.5 μ mol/L) or a 50% rise from baseline within 48–72 h after receiving intravascular contrast agents [4].

The ESUR guidelines recommend calculating the estimated glomerular filtration rate (eGFR) from the serum creatinine before receiving contrast agents in all patients. At-risk patients, which are patients with an eGFR <45 mL/min/1.73 m² (intra-arterial administration with first pass renal exposure or ICU patients) and eGFR <30 mL/min/1.73 m² (intravenous or intra-arterial administration with second pass renal exposure), can be identified and followed by

nephroprotective procedures to avoid PCAKI. An eGFR is often unknown for ambulant patients. As stated by [1], POCT can quickly provide an estimation of the kidney function.

In this study, we performed an analytical and diagnostic evaluation of five POCT creatinine devices: i-STAT (Abbott, USA), StatSensor (Nova Biomedical, USA), epoc (Siemens, UK), ABL90 Flex Plus (Radiometer Benelux, The Netherlands) and STAT Profile Prime+ (Nova Biomedical, USA) in the identification of PCAKI at-risk patients, according to the new ESUR guidelines.

In addition to the manufacturer's iQC material, three patient samples (low, medium, high) were used as iQC material to estimate imprecision. One normal creatinine lithium heparin whole blood sample was selected and two spiked whole blood samples were prepared with a target of 1.5 (clinical decision cut-off) and 3.0 mg/dL. For method comparison, 20 fresh whole blood samples were spiked covering the concentration range of 0.75–4.75 mg/dL. Before analysis, the spiked blood samples were gently mixed for 6 h at room temperature to allow for equilibration. Furthermore, routine lithium heparin whole blood samples of hemodialysis patients before and after dialysis were included, providing a minimum of 40 samples for method evaluation. As a reference method the enzymatic creatinine analysis on the cobas c501 analyzer (Roche, Germany) performed in the central laboratory was used.

To determine the total imprecision of the creatinine analysis of the different POCT devices, each QC material was analyzed 5 times. The coefficient of variation (CV) was calculated in accordance with the CLSI EP5-A2 protocol. For the method comparison, spiked whole blood samples and routine lithium heparin samples of the hemodialysis patients were analyzed on the different POCT devices. After POCT analysis, the samples were centrifuged and determined on the cobas c501 analyzer. The time between POCT analysis and cobas analysis was no longer than 30 min. Bland-Altman plots, Passing-Bablok regression analysis and diagnostic K-agreements were determined for all creatinine-assays in accordance with the reference method. POCT creatinine results were used to calculate an

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eGFR using the CKD-EPI formula to quickly identify at-risk patients prior to administration of contrast agents. The clinical interpretation of these eGFR-results is categorical, with cut-offs based on the new ESUR guidelines (30 and 45 mL/min/1.73 m², cfr. supra). Categorical agreement between the eGFR-results derived from the POCT analysis and the central laboratory analysis was calculated, expressed as unweighted kappa (*K*). To calculate eGFR with the CKD-EPI formula, creatinine results were interpreted in two different scenarios (50-year-old male and 80-year-old woman). In addition, the influence of hematocrit was investigated on the different devices. Therefore, we manipulated three whole blood samples (low, medium, high level), to obtain samples with a hematocrit of 30%,

40% and 60% for each creatinine concentration. Every sample was analyzed with the different POCT devices and the central laboratory creatinine method.

The imprecision was <5%CV for all POCT devices, with the exception of the STAT Profile Prime+ (i-STAT: 0.0%–3.0%; StatSensor: 1.1%–2.1%; epoc: 1.1%–2.7%; ABL90 Flex Plus: 0.0%–3.7%; STAT Profile Prime+: 2.5%–14.3%). Figure 1 shows the Passing-Bablok regression analysis plots and Bland-Altman plots of the creatinine results obtained on the POCT devices in comparison to the cobas results. The ABL90 Flex Plus had the best correlation with the laboratory creatinine analysis ($R^2=0.997$; mean difference of +2.8%) followed by the i-STAT ($R^2=0.997$; mean difference of −7.0%), epoc ($R^2=0.989$; mean

Figure 1: Passing-Bablok regression analysis and Bland-Altman chart of the results obtained on the POCT devices in comparison to the enzymatic cobas c501 results with respect to total allowable error (Ricos=8.9%).

(A) i-STAT (Abbott, USA); (B) StatSensor (Nova Biomedical, USA); (C) epoc (Siemens, UK); (D) ABL90 Flex Plus (Radiometer Benelux, Netherlands); (E) STAT Profile Prime+ (Nova Biomedical, USA).

Figure 1: continued

Table 1: Diagnostic *K*-agreements of eGFR between POCT devices and Cobas c501.

Kappa (95% CI)	i-STAT (Abbott)	StatSensor (Nova Biomedical)	Epoc (Siemens)	ABL90 Flex Plus (Radiometer)	STAT Profile Prime+ (Nova Biomedical)
50-year-old male	0.93 (0.84–1.00)	0.69 (0.52–0.86)	0.85 (0.71–0.99)	0.96 (0.89–1.00)	0.85 (0.71–0.99)
80-year-old woman	0.88 (0.75–1.00)	0.32 (0.12–0.52)	0.58 (0.36–0.81)	0.95 (0.86–1.00)	0.22 (0.05–0.38)

difference of -9.9%), STAT Profile Prime+ ($R^2=0.984$; mean difference of $+18.2\%$) and StatSensor ($R^2=0.957$; mean difference of $+22.8\%$). All at-risk patients were identified by all POCT devices. The *K*-agreements were much better for ABL90 Flex Plus and i-STAT than the other POCT devices (Table 1). Creatinine results on StatSensor, epoc and STAT Profile Prime+ increased 18%, 18% and 20%, respectively, with an increased hematocrit ($\pm 60\%$), compared to normal hematocrit, while this effect was not revealed on i-STAT and ABL90 Flex Plus. Decreased hematocrit ($\pm 30\%$) did not affect the performance of the creatinine assay of the different POCT devices.

To estimate the risk of PCAKI, the latest ESUR guidelines advise calculating the eGFR in all patients. If the kidney function is not known, an accurate, reliable and rapid POCT can improve service efficiency, resulting in better patient management [5]. In this study, the ABL90 Flex Plus and i-STAT analyzer showed the best precision, the lowest mean difference and the best diagnostic performance compared to the reference method. These findings were similar to previous reported studies [1, 6, 7]. Moreover, there was no effect of hematocrit on the measurement of these two analyzers. The results of samples with increased hematocrit seems to be less reliable for StatSensor, STAT Profile Prime+ and epoc. POCT testing is very vulnerable to pre-analytical sampling errors, which are not highlighted nor corrected by all commercial devices. Therefore, POCT analyses which are not affected by major pre-analytical errors or which do not report a result if such errors occur, are of great added value to POCT diagnostic care [8, 9].

Our study revealed that the screening of patients at risk of PCAKI may be feasible with POCT technology, as all at-risk patients were identified by all analyzers. However, the larger mean difference and minor *K*-agreement of StatSensor, STAT Profile Prime+ and epoc results in a lower specificity. This implies an underestimation of the kidney function of too many patients, which unnecessarily reduces the use of contrast agents and impacts the workflow of a radiology department with increased waiting times, less patient satisfaction and inefficient patient management. In conclusion, we agree with Snaith et al., that implementation of POCT creatinine measurement is feasible at the radiology ward for screening of at-risk patients for PCAKI. However, possible consequences

on workflow and patient turnaround time of radiology examinations has to be borne in mind for devices with low specificity before application in clinical practice.

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