

## STANDARD ARTICLE

# Evaluation of the accuracy of an electronic point-of-care analyzer to quantify blood creatinine concentration in goats

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**Funding information**

AntheC Diagnostics (Zoasis Id: 121882, Oklahoma State University); McCasland Foundation (Clinical Professorship in the CVM)

**Abstract**

**Background:** There are no commercially available handheld blood creatinine analyzers validated in goats.

**Objectives:** The objective of the study was to validate the accuracy of a handheld point-of-care (POC) analyzer (Nova StatSensor) for quantifying blood creatinine concentration in goats. A secondary objective was to compare this POC against a chemistry analyzer to classify goats as normal or having mild or moderate azotemia.

**Animals:** Sixty-three goats admitted to a referral hospital.

**Methods:** Cross-sectional study. Venous blood was obtained, and creatinine concentration was measured by the POC in duplicate. Plasma was submitted for creatinine determination via the chemistry analyzer (gold standard).

**Results:** A total of 101 blood samples were collected from 63 goats. There was high repeatability for creatinine concentrations obtained by the POC (adjusted  $R^2 = .97$ ,  $P < .0001$ ). Correlation of POC concentrations with those reported by the chemistry analyzer was moderate (adjusted  $R^2 = .57$ ,  $P < .0001$ ). When correctly categorizing goats with mild azotemia, the POC demonstrated a sensitivity of 73.3% and a specificity of 88.3%. For moderate to severe azotemia, the POC had a sensitivity of 75.0% and specificity of 97.5%.

**Conclusion and Clinical Importance:** The Nova StatSensor POC provided above average accuracy for measuring blood creatinine concentration in goats compared with the gold standard test.

**KEYWORDS**

azotemia, renal, small ruminants, stall-side

## 1 | INTRODUCTION

Handheld point-of-care (POC) analyzers have gained popularity both in veterinary and human medicine over the last decade as they offer

rapid assessment of renal function, and acid-base, electrolyte, and blood glucose status of a patient. However, agreement of POC results with standard laboratory methods continues to be a concern.<sup>1-6</sup> The Nova StatSensor blood creatinine POC is approved for use in humans in North America and is primarily used in patients with chronic kidney disease or those being monitored closely while in intensive care hospital settings.<sup>7-9</sup> At this time,

**Abbreviations:** OSU-VTH, Oklahoma State University Veterinary Teaching Hospital; POC, point-of-care.

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there are no published reports regarding the use of this POC in animal species. Currently, there is no specific blood creatinine POC for goats commercially available although different devices, mainly VetScan ISTAT analyzers, have been used. A handheld blood creatinine POC such as the Nova StatSensor would be beneficial to small ruminant veterinarians for correctly classifying goats as normal or having azotemia, as well as improving overall case management both in veterinary clinic settings and in the field. However, the accuracy of this POC for measuring creatinine in blood of goats remains unknown.

The main objective of this cross-sectional study was to validate the accuracy of the Nova StatSensor blood creatinine POC for quantifying the blood creatinine concentration in goats presented to Oklahoma State University Veterinary Teaching Hospital (OSU-VTH) between June 2018 and June 2019. A secondary objective was to compare this POC against a standard chemistry analyzer to categorize goats as normal or having mild or moderate azotemia. We hypothesized that the POC would generate blood creatinine concentrations comparable to those obtained via the chemistry analyzer (gold standard).

## 2 | MATERIALS AND METHODS

The current study was performed after completion of a preliminary analytical evaluation protocol that characterized the precision, linearity, and accuracy of the creatinine POC using a panel of goat blood samples with normal, moderately elevated, and high creatinine concentrations. The study was conducted by Nova Biomedical staff, according to a standard protocol.<sup>7</sup>

### 2.1 | Experimental design

A cross-sectional study was conducted on a total of 63 goats which presented to the OSU-VTH between June 2018 and June 2019.

### 2.2 | Diagnostic testing

Data recorded included goat identification, age, breed, sex, presenting complaint, and clinical diagnosis based on case work up. Three milliliters of venous blood were collected in lithium-heparin vacutainers from either the right or left jugular vein using a 20-gauge 1-in. needle. The creatinine POC (StatSensor Point-of-Care Whole Blood Creatinine and eGFR Testing, Nova, Biomedical, Waltham, Massachusetts; measurement range: 0.3-12 mg/dL) was calibrated according to manufacturer's recommendations at least once in the 24 hours prior to sample testing (Data S1). Whole blood creatinine concentration was first measured by the creatinine POC (in duplicate). After the POC measurement (mean time between measurements, approximately 1 hour), whole blood was centrifuged (2400 rpm, 8 minutes, 25°C) and plasma was submitted for creatinine determination via Beckman Coulter AU680 Chemistry analyzer

(gold standard; measurement range: 0.2-50 mg/dL). Blood was collected once at presentation. Repeated blood sampling was performed on goats hospitalized for longer than 24 hours, but only 1 blood sample was collected in a 24-hour period. Data obtained were recorded in Excel throughout and analyzed at the end of the study. Using this POC to measure blood creatinine concentration was equivalent to one third the cost of running the gold standard laboratory test.

### 2.3 | Statistical analysis

Sample size calculation was based on showing a statistically significant difference between quantitative data results from 2 methods measuring creatinine concentration in whole blood (creatinine POC) and plasma (chemistry analyzer) using a paired *t* test. Accepting an alpha of .05, enrolling 100 goats gave an 80% probability of detecting a difference as small as 1 mg/dL, assuming a SD within the population of 3.5 mg/dL.

Linear regression and correlation were performed using Microsoft Excel<sup>®</sup> to compare results generated by the POC between immediately duplicated measurements of each sample. A Bland-Altman plot was created to assess concordance of the difference in blood creatinine concentration by chemistry analyzer minus concentration by POC against the mean of the 2 values.<sup>10</sup> Because the differences between the 2 methods were not normally distributed, "Level of Agreement" lines were not included. Results were assigned to 1 of 3 categories: 0.5 to 2 mg/dL (normal); 2 to 4 mg/dL (mild azotemia); and >4 mg/dL (moderate to severe azotemia). Freeware available online (vassarstats.net) was used to calculate Kappa statistic for agreement of the 2 tests in assignment to the 3 categories. Values of *P* < .05 were considered significant.

### 2.4 | IACUC protocol

All procedures used for blood collection and animal handling were reviewed and approved by the Oklahoma State University Institutional Animal Care and Use Committee (Protocol VM 18-11).

## 3 | RESULTS

Animals: 63 goats, ranging in age from 1 day to 10 years (mean: 3 years), were enrolled in the study. Goat breed included 44 Boer (70%), 7 Nubian (11%), 4 Pygmy (6%), 3 Nigerian dwarf (4%), 2 Kiko-Boer (2%), 1 Boer-cross (2%), 1 Lamancha (2%), and 1 of mixed breed (2%). Gender included 31 does (49%), 24 wethers (38%), and 8 bucks (13%). Presenting complaint and clinical diagnosis at time of blood collection for creatinine measurements are provided in Table 1.

A total of 101 venous blood samples were collected on 63 goats (average of 1.4 blood sample per goat per visit). Duplicated measurements were available for 90 of the 101 measurements. The correlation (ie, repeatability) was high for the creatinine POC (adjusted

**TABLE 1** Presenting complaint and clinical diagnosis at time of blood collection on 63 goats sampled during 72 different visits at Oklahoma State University Veterinary Teaching Hospital (101 blood samples total) for measurement of blood creatinine concentration by the Nova StatSensor creatinine point-of-care and plasma creatinine concentration by the Beckman Coulter AU680 chemistry analyzer (gold standard)

Presenting complaint at time of blood collection (# of goat blood samples tested)	Clinical diagnosis (# of goat blood sample tested)	Mean (median) [range] creatinine concentration—point-of-care analyzer (mg/dL)	Mean (median) [range] creatinine concentration—chemistry analyzer (mg/dL)
Apparently healthy (12)	Apparently healthy (12)	1.51 (1.42) [0.98-2.1]	1.1 (1.05) [0.4-1.9]
Neurologic signs (5)	<i>Parelaphostrongylus tenuis</i> (1) Copper toxicity with hepatic encephalopathy (1) Portosystemic shunt (1) Caudal brainstem mass (1) Cervical spinal cord mass (1)	1.55 (0.93) [0.64-3.39]	2.12 (0.7) [0.6-7.1]
Straining to urinate/obstructive urolithiasis (45)	Urolithiasis - partial obstruction (10) Obstructive urolithiasis and associated complications (35)	3.14 (2.7) [0.68-8.66]	4.32 (2.7) [0.7-28.2]
Weight loss (7)	Internal parasites (6) Abomasal impaction (1)	0.91 (0.93) [0.51-1.28]	0.69 (0.7) [0.3-1.1]
Bloat (5)	Grain overload (3) Free gas bloat (1) Frothy bloat (1)	3.35 (3.99) [0.78-5.69]	2.74 (3.2) [0.9-4.8]
Lameness (4)	Septic joint (2) Tendonitis (1) Distal interphalangeal joint ankylosis (1)	0.85 (0.88) [0.71-0.93]	0.63 (0.65) [0.5-0.7]
Respiratory distress (4)	Bacterial pneumonia (3) Aspiration pneumonia (1)	0.77 (0.82) [0.57-0.86]	0.78 (0.8) [0.4-1.1]
Down, unable to rise (4)	Head/neck trauma (1) Fractured pelvis (1) Hypo-magnesemia/phosphatemia/kalemia (2)	0.75 (0.57) [0.55-0.99]	0.8 (0.7) [0.6-1.2]
Pregnancy toxemia (6)	Pregnancy toxemia (6)	0.92 (0.81) [0.49-1.7]	0.97 (1.0) [0.7-1.2]
Off feed/lethargic (4)	Mastitis, metritis, pneumonia (2) Mastitis, metritis (1) Jugular thrombosis & intra-abdominal hematoma (1)	2.38 (2.38) [0.64-4.11]	2.03 (1.9) [0.6-3.7]
Miscellaneous (5) Neck swelling (1) Vaginal discharge (1) Infertility (1) Choke (1) Wellness exam (1)	Laryngeal trauma with emphysema -neck (1) Cystitis and pyelonephritis (1) Uterine foreign body (1) Esophageal diverticulum (1) Osteoarthritis - multiple joints (1)	1.08 (1.08) [0.89-1.24]	0.86 (0.8) [0.6-1.3]

$R^2 = .97$ ,  $P < .0001$ ; Figure 1). The Bland-Altman plot showed high concordance for creatinine concentrations within normal range and very good concordance for samples from goats with mild increase in creatinine concentration (Figure 2). The concordance declined as the creatinine concentration increased (Figure 2).

There was agreement in categorization for 87/101 observations, with a Kappa statistic of 0.74 (95% confidence interval, 0.61 to 0.86). The POC correctly assigned 61/66 goat blood samples into the “normal” category, with the other 5 being classified as mild azotemia by the POC but normal by the gold standard. The POC correctly classified 11/15 goat blood samples in the mild azotemia group, with 2 of the incorrectly classified ones being mischaracterized in the normal group and the other 2 being categorized as moderate to severe azotemia. The POC correctly classified 15/20 moderate to severe azotemia goat blood samples, with the 5 incorrectly classified ones being

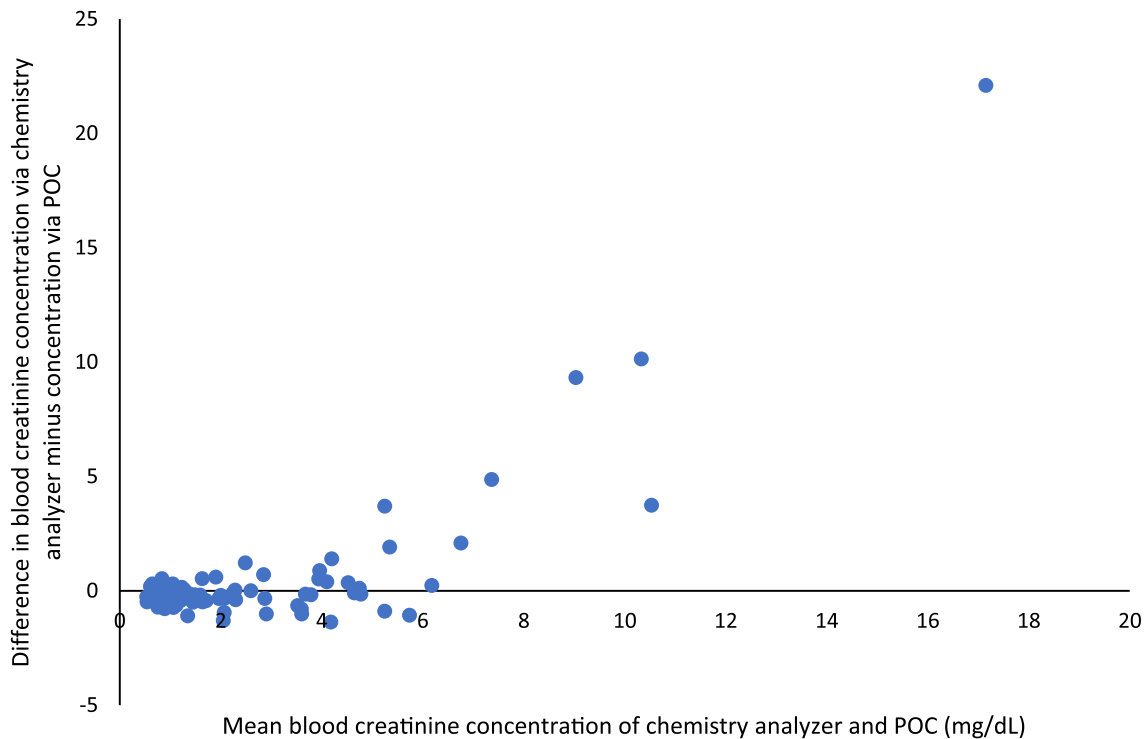
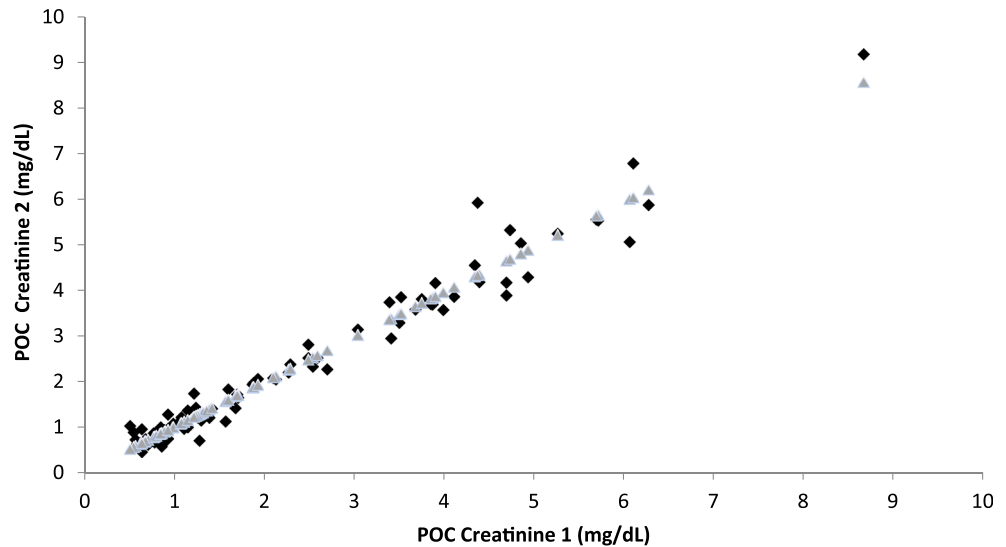
categorized as mild azotemia. The sensitivity and specificity of the creatinine POC ability to correctly categorize mild or moderate to severe azotemia are provided in Table 2. Although not recorded consistently (eg, data available for 43/101 blood samples tested), average hematocrit was 30%, and ranged from 14% to 54%.

## 4 | DISCUSSION

The objectives of this study were to validate the accuracy of the creatinine POC for quantifying the blood creatinine concentration in goats and to compare this POC against a chemistry analyzer to categorize goats as normal or having mild or moderate azotemia.

In this study, there was high repeatability for creatinine concentrations obtained by the POC. However, concordance between POC

**FIGURE 1** Correlation between blood creatinine concentration (n = 90/101 samples) measured in duplicates (POC 1 [black diamond], POC 2 [gray triangle] by the Nova StatSensor creatinine point-of-care (POC) in 63 goats



**FIGURE 2** Bland-Altman plot to assess concordance of the difference in blood creatinine concentration (n= 101 samples obtained from 63 goats) by chemistry analyzer (gold standard) minus concentration by the Nova StatSensor creatinine point-of-care against the mean of the 2 values. Because the differences between the 2 methods were not normally distributed, “Level of Agreement” lines were not included

concentration with those reported by the chemistry analyzer (gold standard) were deemed adequate only for creatinine concentration within normal or mild azotemia range, which refuted our initial hypothesis. As shown in Figure 2, the concordance declined as the creatinine concentration increased. This is similar to a human study that observed an increased discordance between creatinine concentrations obtained by POC vs standard chemistry analyzer, when >2.0 mg/dL.<sup>9</sup> This creatinine POC measures and corrects for varying hematocrit levels in blood. This POC was less precise than the

plasma enzymatic method with increased variability, partly due to the whole-blood matrix.<sup>9</sup> Observed POC performance on goat blood might be due to a difference between human and goat erythrocytes. Normal ruminant red blood cells are discoid, non-nucleated and lack the obvious central pallor seen in species with larger red blood cells (ie, humans and dogs).<sup>11</sup> Observed POC performance might also be due to hematocrit interference if outside the 30% to 60% performance range of hematocrit for this device.<sup>12</sup>

**TABLE 2** Categorization of blood creatinine concentrations (n = 101 samples obtained from 63 goats) measured by the Nova StatSensor creatinine point-of-care when compared to plasma creatinine concentrations reported by the Beckman Coulter AU680 chemistry analyzer (gold standard) and further sorted into 3 categories (normal, mild, and moderate to severe azotemia)

Category assignment (blood creatinine concentration range)	# Goats correctly assigned by creatinine point-of-care	Nova StatSensor whole blood creatinine POC	
		Sensitivity	Specificity
Normal (0.5-2 mg/dL)	61/66		
Mild azotemia (>2 to 4 mg/dL)	11/15	73.3%	88.3%
Moderate to severe (>4 mg/dL)	15/20	75%	97.5%

In this study, the creatinine POC demonstrated a similar sensitivity or probability of detecting goats with mild and moderate to severe azotemia (73.3% vs 75%). This moderate sensitivity can be problematic especially when not being able to readily identify a dehydrated goat needing fluid therapy or one with obstructive urolithiasis. The specificity of the creatinine POC was high for goats with mild and very high for moderate to severe azotemia (88.3% vs 97.5%), making the probability of having false positives (testing a nonazotemic goat as azotemic) low.

There were several limitations in this study including lack of blinding, goat breed overrepresentation, nonrandomized categorization of creatinine concentrations, and blood components used to measure creatinine concentrations. Study personnel (M. B., L. W.) in charge of sample and data collection was not blinded to creatinine concentrations obtained by the chemistry analyzer. Assigning data collection to the study statistician (J. T.) could have reduced bias. Meat goats were overrepresented in this study with the majority of goats being Boer or Boer-cross, the latter being representative of our hospital case load. The group assignment to 3 categories (ie, 0.5-2 mg/dL [normal], >2 to 4 mg/dL [mild azotemia], >4 mg/dL [moderate to severe azotemia]) was arbitrary (nonrandomized). This was primarily based on reference range for creatinine concentration of our chemistry analyzer combined with the authors' clinical experience with sick goats including those with obstructive urolithiasis. Categorization of creatinine concentration into normal, prerenal, renal and postrenal azotemia would have been more clinically useful. Documentation of hematocrit, total solids, and urine specific gravity at arrival was not consistently recorded along with physical exam findings for each goat.

This cross-sectional study had uneven number of goat blood samples within each category: 66/101 (65%) in the normal category as compared to 15/101 (15%) in the mild azotemia, and 20/101 (20%) in the moderate to severe azotemia category. Increasing the length of the study could have allowed for more evenly distributed number of goats for group assignment.

Lastly, whole blood was used to measure creatinine concentration by the POC as compared to plasma by the chemistry analyzer. The authors are unaware of a difference or potential discrepancy between testing whole blood vs plasma for creatinine concentrations.<sup>13</sup> Conversion between blood creatinine molality detected and plasma creatinine molality reported is affected by device calibration that typically assumes

healthy mean values for plasma water mass, red blood cell water mass, and hematocrit.<sup>4</sup> The composition of whole blood and plasma varies in many disease states, which could challenge the analytic reliability of whole-blood biosensors in some goats.

In conclusion, the accuracy of Nova StatSensor POC for measuring blood creatinine concentration in goats is above average when compared with the gold standard test.

#### ACKNOWLEDGMENT

Funding was provided by Anhect Diagnostics (Zoasis Id: 121882, Oklahoma State University) and McCasland Foundation (Clinical Professorship in the College of Veterinary Medicine). We thank Nova BioMedical for providing a creatinine meter, reagents, and consumables for this study. Research abstract presented at the 2019 American Association Bovine Practitioners Annual Conference, St. Louis, Missouri (September 13, 2019).

#### CONFLICT OF INTEREST DECLARATION

Authors declare no conflict of interest.

#### OFF-LABEL ANTIMICROBIAL DECLARATION

Authors declare no off-label use of antimicrobials.

#### INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION

All procedures used for blood collection and animal handling were reviewed and approved by the Oklahoma State University Institutional Animal Care and Use Committee (Protocol VM 18-11).

#### HUMAN ETHICS APPROVAL DECLARATION

Authors declare human ethics approval was not needed for this study.

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

**How to cite this article:** Boileau MJ, Wagner L, Taylor JD. Evaluation of the accuracy of an electronic point-of-care analyzer to quantify blood creatinine concentration in goats. *J Vet Intern Med.* 2021;35:1164–1169. <https://doi.org/10.1111/jvim.16059>