Historical and physical parameters as predictors of severe hyperkalemia in male cats with urethral obstruction

Justine A. Lee, DVM, DACVECC and Kenneth J. Drobatz, DVM, MSCE, DACVECC, DACVIM

Abstract

Objective: To evaluate selected historical and physical parameters as predictors of hyperkalemia in male cats with urethral obstruction.

Design: Retrospective study.

Setting: Veterinary teaching hospital.

Animals: Two hundred and twenty-three male cats.

Interventions: None.

Measurements and main results: The metabolic derangements of 223 male cats that presented with urethral obstruction from 1997 through 1999 were reported in a companion article. Approximately 12% of the cats had multiple, life-threatening metabolic derangements. In the present study, historical and physical parameters were evaluated as predictors of hyperkalemia ($K^+ \ge 8.0 \text{ mmol/L}$) in cats with urethral obstruction. The 4 historical parameters significantly associated with hyperkalemia were: first time obstruction, outdoor status, anorexia, or vomiting. The 5 physical parameters significantly associated with hyperkalemia were: rectal temperature, heart rate, respiratory rate, pulse quality, and the presence of arrhythmia. Of the physical parameters, a rectal temperature below 95–96.6°F (35–35.9°C) or a heart rate below 120 b.p.m. were the most accurate predictors. When used in combination (i.e., evidence of bradycardia and hypothermia), the specificity for hyperkalemia was 98–100%.

Conclusions: Rectal temperature and heart rate were the best parameters for predicting hyperkalemia in this population.

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Keywords: feline, heart rate, potassium, respiratory rate, temperature

Introduction

Urethral obstruction in male cats is a relatively common presenting complaint to veterinarians.^{1,2} Owners tend to recognize early that a cat's inability to urinate can be a life-threatening condition as the majority of cats with

From the Department of Clinical Studies, School of Veterinary Medicine, Matthew J. Ryan Veterinary Hospital, University of Pennsylvania, Philadelphia, PA.

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Dr. Lee's current address is Department of Small Animal Clinical Sciences, College of Veterinary Medicine, University of Minnesota, St. Paul, MN.

Dr. Justine A. Lee, Department of Small Animal Clinical Sciences, College of Veterinary Medicine, University of Minnesota, 1365 Gortner Avenue, St. Paul, MN 55108.

E-mail: leexx586@umn.edu

a urethral obstruction are presented with relatively normal physical examination and clinicopathologic findings.¹ Based on our previous evaluation, approximately 1 out of 10 cats with urethral obstruction are critically ill.¹ Hyperkalemia is considered to be the most common life-threatening complication of this condition and has been studied in selected clinical populations and experimental studies.^{3–7} Hyperkalemia primarily affects the cellular resting membrane potential and results clinically in cardiac conduction abnormalities and associated electrocardiographic (ECG) changes.^{5,8} The severity of these changes has been correlated with the concentration of potassium, but the correlation is inconsistent, limiting the use of ECG changes for the detection of hyperkalemia.^{5,9,10}

Over the past decade, there has been continuous improvement in the quality of critical care; bedside testing and point-of-care measurement of electrolyte and acid-

Address correspondence and reprint requests to:

base parameters has become widely available in veterinary medicine and promises to provide valuable information to guide therapy in critically ill cats with urethral obstruction. However, the cost of these analyzers is a limiting factor for some general practitioners, leaving ECG analysis and physical examination parameters as important practical means to determine the presence of hyperkalemia in this population. There have been no previously published studies on the rigorous assessment of historical and physical parameters in predicting and treating hyperkalemia in cats with urethral obstruction; therefore, the purpose of this study was to evaluate these parameters as alternative or adjunctive predictors of hyperkalemia when measurement of serum potassium concentrations is not readily available.

Materials and Methods

The medical records database of the Matthew J. Ryan Veterinary Hospital of the University of Pennsylvania (MJR VHUP) was searched for records with the diagnosis of feline urethral obstruction between the years of 1997–1999. Inclusion criteria included any previously untreated male cat that was presented to MJR VHUP with clinical signs consistent with a urethral obstruction and that had a large, firm, non-expressible urinary bladder. Records were excluded if the patient was female, canine, if the medical record was incomplete, if the cat showed signs of feline lower urinary tract disease (FLUTD) without obstruction, or if another underlying disease was diagnosed (e.g., bladder neoplasia).

The medical records were reviewed for signalment, previous medical history (including previous history of urethral obstruction), indoor or outdoor lifestyle, body weight, clinical signs, physical examination findings, renal function tests (blood urea nitrogen [BUN] and creatinine), and blood gas and electrolyte analysis. These results were presented in a companion manuscript.¹

Blood collection and method of potassium measurement

At admission, $200 \,\mu\text{L}$ of blood was collected from the hub of the intravenous catheter into a microhematocrit tube containing 5 IU of lithium heparin resulting in a total concentration of 40 IU of lithium heparin/mL. From this blood sample the following parameters were immediately measured: pH; pCO₂; pO₂; concentrations of sodium, potassium, chloride, ionized calcium (*i*Ca²⁺), glucose, lactate; or calculated: bicarbonate and base excess.^a

Parameters assessed for association with hyperkalemia

Historical parameters including occurrence of a previous urethral obstruction, indoor/outdoor lifestyle, anorexia, and vomiting were evaluated for association with hyperkalemia. In addition, 5 physical parameters including rectal temperature, heart rate, respiratory rate, pulse quality, and the presence of arrhythmias were also evaluated individually for their association with hyperkalemia. Rectal temperature and heart rate were combined in various ways to assess their combined association with hyperkalemia.

Statistical methods

Univariate logistic regression was used to assess the association between a history of previous urethral obstruction, vomiting, anorexia, and physical examination parameters with severe hyperkalemia (defined as a K^+ concentration $\geq 8.0 \text{ mmol/L}$). The coefficient of variation for potassium for the Nova Stat M was 0.01. Receiver-operating curves (ROC) were generated to assess the test characteristics of the parameters that were significantly associated with hyperkalemia. For rectal temperature, heart rate, and respiratory rate, a test was considered positive if the value of the parameter was below the selected cutoff point. For example, for the parameter rectal temperature (cutoff point of 99°F [37°C]), a temperature below 99°F (37°C) would be considered positive for hyperkalemia and a temperature above that would be considered negative for hyperkalemia. Because the values of these parameters decrease as potassium increases, the reciprocal of the parameter was graphed for the ROC curve. This method allowed us to generate traditional convex ROC curves, rather than a concave curve. Areas under the curve and associated 95% confidence intervals (CIs) for selected physical parameters were calculated using the trapezoidal rule and compared with each other.¹¹ Additionally, sensitivity, specificity, accuracy, likelihood ratio positive, likelihood ratio negative, and positive and negative predictive values were calculated for selected temperature, heart rate, and summed heart rate and temperature cutoffs points. Continuous variables were evaluated for normality by visual inspection of scatter plots and the Shapiro-Wilk test. Mean and standard deviation or median and range were used to describe continuous variables depending if the data were normally or not normally distributed, respectively. Percentages with associated CI were used to describe categorical variables. For all evaluations, a P-value of <0.05 was considered significant. All statistical calculations were performed using a statistical software package.^b

Results

Six hundred and sixty-seven feline records were coded with a diagnosis of feline urethral obstruction during the period of 1997–1999. Two hundred and twentythree of these met the inclusion criteria. The most common reasons for exclusion were due to incomplete medical records or evidence of FLUTD without obstruction.

History and clinical signs

The majority of cats were exclusively indoors (173/208 [83%]), CI 77–88%). Thirty-four cats (16%), CI 12–22%) had access to both indoors and outdoors, and only 1 cat (0.5%), CI 0–3%) was exclusively outdoors. The majority of cats were presented for their first occurrence of ure-thral obstruction (161/216 [75%]), CI 68–80%). Anorexia was noted in 115 of 191 cats (60%), CI 53–67%) and vomiting in 104 of 204 cats (51%), CI 44–58%).

Physical examination parameters

The median rectal temperature (*T*) was 38.0° C (100.4° F) (n = 174, range: $32.2-40.1^{\circ}$ C [$90-104.2^{\circ}$ F]). Sixty-eight cats (39%, CI 32-47%) were hypothermic ($T < 37.8^{\circ}$ C [100° F]), 87 (50%, CI 43-58%) were normothermic ($T \ge 37.8^{\circ}$ C $< 39.2^{\circ}$ C [$\ge 100^{\circ}$ F $< 102.5^{\circ}$ F]), and 19 (11%, CI 7-17%) were hyperthermic ($T \ge 39.2^{\circ}$ C [102.5° F]).

The median heart rate was 187 beats per minute (b.p.m.) (n = 187, range: 40–296 b.p.m.). Twelve percent of cats had a heart rate less than 140 b.p.m. (n = 22, CI 7–17%) and were considered mildly bradycardic, 6% (n = 12, CI 3–11%) had moderate bradycardia, with a heart rate between 100 and 140 b.p.m., and 5% (n = 10, CI 2–10%) of cats had severe bradycardia, with a heart rate of 100 b.p.m. or less.

The median respiratory rate was 36 breaths per minute (b.p.m.) (n = 180, range: 8–120 b.p.m.). Twentysix of 171 cats (15%, CI 10–21%) were assessed to have weak pulses. Sixty-six of 176 cats (38%, CI 30–45%) were reported to be depressed. Sixty-four of 170 cats (38%, CI 30–45%) were considered to be weak. Twentyone of 189 cats (11%, CI 7–16%) had arrhythmias on presentation to the emergency room.

Clinical pathology

Seventy-six percent of cats (151/199, CI 69–82%) had a potassium concentration <6.0 mmol/L. Twelve percent (24/199, CI 8–17%) had a potassium concentration \geq 6.0 mmol/L but <8.0% mmol/L, 12% (23/199, CI 7–17%) had a potassium concentration \geq 8.0 mmol/L but <10.0 mmol/L, and 0.5% (1/199, CI 0–3%) had a potassium concentration \geq 10.0 mmol/L. Additional parameters including renal function tests (BUN and

creatinine), blood gas and electrolyte analysis (packed cell volume, total solids, blood glucose, venous acidbase status, lactate, iCa²⁺, sodium, potassium, chloride),^a medical treatment for hyperkalemia, fluid therapy, duration that the urinary catheter was in place, duration of hospitalization, and outcome were previously reported.¹

Association of medical history and physical parameters with severe hyperkalemia

Four historical and clinical sign parameters including first-time diagnosis of urethral obstruction, indoor/ outdoor lifestyle, anorexia, or vomiting were significantly associated with hyperkalemia (P < 0.005) (Table 1). Cats with a first-time occurrence of urethral obstruction or indoor/outdoor status (vs. indoor exclusively) were significantly more hyperkalemic. However, the performance of these parameters was relatively poor in coridentifying whether the animal rectly was hyperkalemic or not, with accuracy ranging from 46 to 80% (Table 2).

Five physical exam parameters including rectal temperature, heart rate, respiratory rate, and the presence of arrhythmias or weak pulses on physical examination were significantly associated with severe hyperkalemia (Table 1). There were very few cases that had weak pulses or detectable arrhythmias on physical examination to provide sufficiently narrow CI to warrant further analysis using these parameters.

Detection of severe hyperkalemia using medical history and physical examination parameters

Test characteristics for the 5 categorical variables significantly associated with hyperkalemia were calculated (Table 2). Test characteristics for continuous variables were calculated for multiple cutoff points (Tables 3–7). The table of test characteristics for respi-

Table 1: Results of univariate logistic regression analysis of the 9 variables that were significantly (P < 0.05) associated with severe hyperkalemia (>8.0 mmol/L)

Variable	n	OR	95% CI	<i>P</i> -value*
Previously blocked	195	0.12	0.01-0.92	0.0056
Anorexia	173	6.4	1.4–28	0.0028
Vomiting	186	3.2	1.2-8.5	0.0120
Indoor/outdoor	188	1.9	1.1–3.1	0.0150
Weak pulses	154	33.2	10.5–105	< 0.0001
Temperature	156	0.54	0.42-0.68	< 0.0001
Heart rate	169	0.96	0.94-0.97	< 0.0001
Respiratory rate	163	0.94	0.90-0.98	0.0003
Arrhythmia	172	22	6.9–64.4	< 0.0001

*P = < 0.005 statistically significant.

n, number; OR, odds ratio; CI, confidence interval.

Variable	Sensitivity (%)	Specificity (%)	Correctly classified (%)	LR+	LR –	PPV (%)	NPV (%)
Previously diagnosed	4	85	65	0.2	1.3	2	85
Indoor and outdoor	36	86	80	2.6	0.7	26	91
Vomiting	75	52	55	1.6	0.5	19	93
Weak pulses	65	95	90	12.2	0.4	68	94
Arrhythmia	48	96	89	11.9	0.5	65	92
Anorexia	90	40	46	1.5	0.3	17	97

Table 2: Categorical variable test characteristics for detection of hyperkalemia

LR+, likelihood ratio positive; LR-, likelihood ratio negative; PPV, positive predictive value; NPV, negative predictive value.

Table 3: Diagnostic characteristics of rectal temperature for detecting hyperkalemia (>8.0 mmol/L)

Temperature	Sensitivity (%)	Specificity (%)	Correctly classified (%)	LR+	LR –	PPV (%)	NPV (%)
35°C/95°F	25	99	88	32.9	0.8	86	88
35.9°C/96.6°F	46	95	88	10.1	0.6	80	89
37°C/98.6°F	67	90	86	6.8	0.4	54	93
37.9°C/100.3°F	83	57	61	2.0	0.3	27	95
38.2°C/100.7°F	96	51	58	1.9	0.1	27	99
38.9°C/102.1°F	100	19	31	1.2	0.0	19	100

LR+, likelihood ratio positive; LR -, likelihood ratio negative; PPV, positive predictive value; NPV, negative predictive value.

ratory rate is not shown because respiratory rate had the lowest area under the curve and was not considered sufficiently predictive when compared with temperature or heart rate. Approximate optimal cutoff points for the use of rectal temperature, heart rate, respiratory rate, and summed heart rate and temperature as predictors of hyperkalemia ($K^+ > 8.0 \text{ mmol/L}$) were determined using ROC curves (Figures 1-4). Test characteristics for varying heart rates at two different rectal temperature cutoffs were also determined (<37.8°C [100°F] and <37.2°C [99 °F]) (Tables 6 and 7). Area under the ROC curves for heart rate alone was 0.834 (CI, 0.728-0.939), rectal temperature alone was 0.844 (CI, 0.753-0.936), respiratory rate alone was 0.705 (CI 0.592-0.818), and summation of heart rate and rectal temperature was 0.845 (CI, 0.745-0.945). Areas under the ROC curve were not significantly different from each other (P = 0.08).

Discussion

There are several explanations as to why certain portions of the medical history might be useful predictors of hyperkalemia in male cats with a urethral obstruction. Cats that had a history of urethral obstruction were less likely to have hyperkalemia. These owners may be more diligent in observing their cat's urinary habits and may have a better understanding of the serious nature of the condition. Therefore, owners of these cats may present them to a veterinarian at an earlier stage before hyperkalemia can develop. Indoor cats were less likely to be hyperkalemic when compared with outdoor cats, as it is more difficult for owners to observe their outdoor cat's urinary habits. Finally, cats that were anorectic or were vomiting were more likely to have hyperkalemia, as these signs are consistent with severe uremia, acid-base, and electrolyte disturbances.

Heart rate (b.p.m.)	Sensitivity (%)	Specificity (%)	Correctly classified (%)	LR+	LR –	PPV (%)	NPV (%)
105	29	99	89.4	42.3	0.7	100	90
120	54	99	92.9	78.5	0.5	88	89
140	62	96	91.1	15.1	0.4	74	93
150	62	94	89.9	11.3	0.4	68	94
160	67	88	85.2	5.7	0.4	62	94
180	75	68	69.2	2.4	0.4	41	95
200	92	45	51.5	1.7	0.2	25	96
240	100	9	21.9	1.1	0.0	16	97

Table 4: Diagnostic characteristics of heart rate for detecting hyperkalemia (>8.0 mmol/L)

LR+, likelihood ratio positive; LR-, likelihood ratio negative; PPV, positive predictive value; NPV, negative predictive value.

Sensitivity (%)	Specificity (%)	Correctly classified (%)	LR+	LR –	PPV (%)	NPV (%)
100	20	33	1.2	0.0	15	100
96	41	50	1.6	0.1	18	99
92	48	55	1.8	0.2	19	98
88	57	62	2.0	0.2	22	97
79	62	65	2.1	0.3	22	96
75	83	81	4.3	0.3	38	96
67	94	90	12	0.4	61	95
54	99	92	68	0.5	87	94
29	99	88	37	0.7	78	91
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Table 5: Diagnostic characteristics of heart rate added to temperature for detecting hyperkalemia (>8.0 mmol/L)

LR+, likelihood ratio positive; LR -, likelihood ratio negative; PPV, positive predictive value; NPV, negative predictive value.

Table 6: Diagnostic characteristics of heart rate combined with temperature $<37.8^{\circ}C/100^{\circ}F$ for detecting hyperkalemia (>8.0 mmol/L)

Heart rate	Sensitivity (%)	Specificity (%)	Correctly classified (%)	LR+	LR –	PPV (%)	NPV (%)
<140	54.2	98	91	23	0.5	81	92
<120	25	99	87	31.5	0.8	85	87
<100	21	100	87	Infinity	0.8	100	87

LR+, likelihood ratio positive; LR -, likelihood ratio negative; PPV, positive predictive value; NPV, negative predictive value.

The use of these historical findings in detecting hyperkalemia was evaluated. While these historical parameters were significantly associated with hyperkalemia, the utility of these tests was poor in correctly identifying whether the animal was hyperkalemic or not, correctly classifying the cat's potassium status only 46–65% of the time. This may be due to incomplete medical histories from owners, making these historical findings inaccurate in predicating hyperkalemia. In addition, this may be due to lack of observation by the owner. Medical histories from owners can be nebulous and sometimes incomplete, making these historical findings inaccurate in predicating hyperkalemia.

In addition to these historical findings, physical examination parameters also provide information about the cat's potassium level. Of the 5 parameters (rectal temperature, heart rate, respiratory rate, pulse quality, and presence of arrhythmias) that were significantly associated with hyperkalemia, however, the small numbers of cases that had weak pulses or detectable arrhythmias noted in the medical record from the physical examination contributed to insufficiently narrow CIs. Therefore, rectal temperature, heart rate, and respiratory rate were the most accurate detectors of hyperkalemia. In addition, these parameters are relatively objective compared with assessing pulse quality and detecting arrhythmias on physical examination.

Hypothermia was an excellent, objective assessment of hyperkalemic status. The cause of hypothermia $(T < 37.8 \,^{\circ}\text{C} [100 \,^{\circ}\text{F}])$ in these cats has not been identified. Poor rectal perfusion due to cardiac dysfunction and hypovolemia may contribute to this finding. Additionally, hypothalamic temperature set point is reported to be decreased with uremia.¹² Additionally, a functional hypothyroidism may occur as the conversion of T_4 to T_3 in peripheral tissue is decreased in uremic patients.¹² A rectal temperature between 35 $^{\circ}$ C (95 $^{\circ}$ F) and 35.9 $^{\circ}$ C (96.6 $^{\circ}$ F) correctly characterized hyperkalemic status in 88% of the cats (Table 3).

Table 7: Diagnostic characteristics of heart rate combined with temperature <37.2°C/99°F for detecting hyperkalemia (>8.0 mmol/L)

Heart rate	Sensitivity (%)	Specificity (%)	Correctly classified (%)	LR+	LR –	PPV (%)	NPV (%)
<140	46	98	89	19.3	0.6	79	90
<120	25	99	92	50	0.8	86	89
<100	21	100	87	Infinity	0.8	100	87

LR+, likelihood ratio positive; LR-, likelihood ratio negative; PPV, positive predictive value; NPV, negative predictive value.

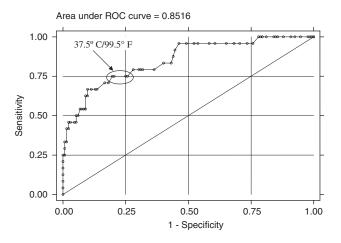


Figure 1: Receiver–operating curves (ROC) curve using rectal temperature for the prediction of hyperkalemia $(K^+ > 8.0 \text{ mmol/L})$.

Heart rate was also one of the most useful physical examination predictors of hyperkalemia. As heart rate increased, the likelihood of hyperkalemia decreased. The ratio of intracellular to extracellular potassium concentration is the major determinant of resting membrane potential. As this ratio decreases (increasing plasma potassium concentration), the resting membrane potential becomes less negative.⁸ Initially, cells may be hyperexcitable but conduction velocity slows. When resting and threshold potentials are equal, the cells can no longer depolarize and atrial arrest occurs. Sinoventricular conduction continues but at a slower rate.^{8,10,13} A heart rate of 120 b.p.m. (Figure 2 and Table 4) tended to have the best utility for correctly identifying hyper-kalemic status, being successful nearly 93% of the time.

A combined temperature and heart rate between 220 and 276 (Table 5) correctly characterized potassium status in 81–92% of the cats. However, the area under

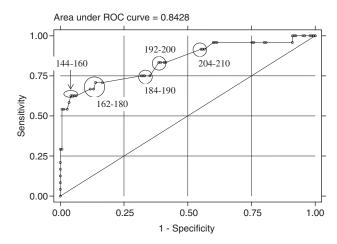


Figure 2: Receiver–operating curves (ROC) curve using heart rate for the prediction of hyperkalemia ($K^+ > 8.0 \text{ mmol/L}$).

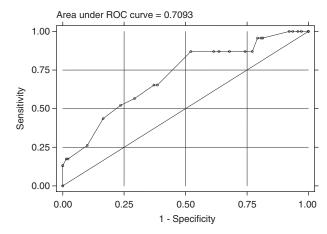


Figure 3: Receiver–operating curves (ROC) curve using respiratory rate for the prediction of hyperkalemia (K^+ >8.0 mmol/L).

the ROC curve for the summed heart rate and rectal temperature was similar to that for temperature or heart rate curves alone, suggesting that combining these two physical parameters does not provide additional discriminating power for the prediction of hyperkalemia (Figures 1, 2, and 4).

Changes in respiratory rate may be reflective of stress, pain, response to hypoxemia, or acid–base status. As a cat's respiratory rate increased in this study, it was less likely to be hyperkalemic. A previous study on this same group of cats showed that pH and potassium concentration were negatively correlated.¹ The expectation from this relationship would be that cats that were hyperkalemic would have higher respiratory rates to compensate for the metabolic acidosis. Though arterial blood gas assessment was not performed in these cats, anecdotal evidence suggests that hypoxemia is not a major problem in cats with urethral obstruction mak-

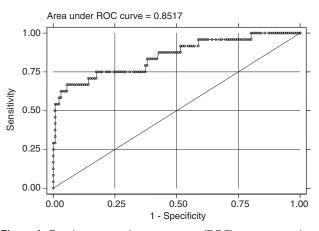


Figure 4: Receiver–operating curves (ROC) curve using combined heart rate and temperature for the prediction of hyperkalemia ($K^+ > 8.0 \text{ mmol/L}$).

ing it a less likely cause for the increased respiratory rate. This evidence suggests then that stress or pain may be the major contributors to the increase in respiratory rate in cats with urethral obstruction. Likewise, severely hyperkalemic, comatose cats may not be tachypneic due to obtundation from hyperkalemia and uremia. As a physical parameter, the area under the curve for respiratory rate was less than the other parameters suggesting it was the weakest discriminator for predicting hyperkalemia, but the area under the ROC curve for respiratory rate was not statistically significant from the others.

Based on this study, historical and physical parameters can be safely used at the veterinarian's discretion as predictors of hyperkalemia in cats with urethral obstruction. However, interpretation of diagnostic test results can be complex. Choosing a cutoff value that is more sensitive but less specific may increase the chances of treating a false positive, but will minimize the chances of not treating a false negative. Tables 2–7 provide a spectrum of different test characteristics for the parameters studied. A range of cutoff points was presented to assist the practitioner in interpreting the information successfully. For example, some practitioners may feel that treating a false positive is less risky than not treating a true positive. Therefore, he/she may choose a cutoff value that is more sensitive, but less specific. Similarly, a practitioner may think that treating a false positive inappropriately may carry greater risk than not treating a true positive; therefore, that practitioner would choose a cutoff value that is more specific, but less sensitive to minimize this risk. Finally, the tables include different test characteristics including sensitivity, specificity, likelihood ratio positive, likelihood ratio negative, positive predictive value, and negative predictive value, which provide alternative methods of interpreting the diagnostic test results. Appendix 1 provides definitions to assist in interpretation of these measurements.

As with the development of any diagnostic test, the generalizability of the test is dependent upon the characteristics of the population of patients that the test was developed in. This study was conducted in a university-associated emergency hospital but the caseload includes a full spectrum of referral and first-opinion cases. The population of cats with urethral obstruction in this study should not differ significantly from those presented to other veterinary hospitals. Confidence in the accuracy and utility of a diagnostic test can be improved by evaluation in one or more additional pop-We recommend repeating the study ulations. (specifically evaluating rectal temperature and heart rate as diagnostic tests) in a second population of male cats with urethral obstruction. This will allow corroboration and validation of the findings reported here. Evaluating a spectrum of cutoff points provides greater flexibility for the clinician to incorporate the findings into his or her own approach to these critically ill patients.

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Appendix 1

Sensitivity: Among the cats that were hyperkalemic, what proportion were test-positive (True positive rate)? *Specificity*: Among the cats that were not hyper-kalemic, what proportion were test-negative (True negative rate)?

Positive predictive value: Given a positive test, what is the probability of a cat being hyperkalemic?

Negative predictive value: Given a negative test, what is the probability of a cat not being hyperkalemic?

Likelihood ratio positive: Given a positive test, what is the chance (likelihood or odds) of the cat being hyper-kalemic?

Likelihood ratio negative: Given a negative test, what is the chance (likelihood or odds) of a cat being hyper-kalemic?

Correctly classified: Accuracy of the test. How many true positives and true negatives can a test correctly classify?

Footnotes

- ^a Nova Stat Profile M, Nova Biomedical, Waltham, MA.
- ^b Intercooled Stats 7.0 for Windows, College Station, TX.

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