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Assessment of preoperative and postoperative l-lactatemia and clinical outcomes in goats undergoing tube cystostomy: A retrospective study of 34 cases (2015-2020)

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Abstract

Background: Urolithiasis in small ruminants has a poor long-term prognosis, and long-term clinical outcomes are variable and unpredictable.

Objectives: To assess the accuracy of preoperative and postoperative blood l-lactate concentrations in predicting a negative outcome in goats undergoing tube cystostomy.

Animals: Thirty-four male goats undergoing tube cystostomy.

Methods: Retrospective study. Medical records of goats undergoing tube cystostomy from 2015 to 2020 were reviewed. Clinical variables recorded included signalment, procedures before surgery, urolith location and type, duration of hospitalization, and heart rate. PCV, plasma total protein, potassium, preoperative and postoperative blood l-lactate concentrations, preoperative and postoperative creatinine concentrations, and relative changes in blood l-lactate and creatinine concentrations over time were measured using heparinized blood. A negative outcome was defined as death or euthanasia from urolithiasis complications at 6 months after discharge. Negative outcomes as a function of independent clinical variables were evaluated using χ^2 or Fisher's exact tests, and multivariate logistic regression. $P < .05$ was considered significant.

Results: Median (95% confidence interval) preoperative, postoperative, and the relative change over time of blood l-lactate concentrations were 3.3 mmol/L (2.2, 4.8), 1.0 mmol/L (0.7, 1.3), and 0.4 mmol/L (−3.5, 3.2), respectively. Preoperative ($P = 1$), postoperative ($P = .14$), and the relative change over time ($P = .63$) of blood l-lactate concentrations were not significant predictors of a negative outcome. Furthermore, all other clinical variables measured were not significant predictors of a negative outcome ($P > .05$).

Conclusions and Clinical Importance: Veterinarians should advise clients that clinical outcomes after tube cystostomy in goats are likely unpredictable.

Abbreviations: DT, duration of treatment; DT_{creat}, creatinine relative change over time; DT_{lact}, l-lactate relative change over time; LAC, l-lactate; PosCREAT, postoperative creatinine; PosLAC, postoperative l-lactate; PreCREAT, preoperative creatinine; PreLAC, preoperative l-lactate; ROC, receiver operating characteristic; TP, plasma total protein.

KEYWORDS
calcium carbonate, cystolithiasis, heart rate, potassium, struvite, urethrolithiasis

1 | INTRODUCTION

Urolithiasis is a common disease in small ruminants with a poor long-term prognosis and unpredictable clinical outcomes. Medical management is often unrewarding with many goats requiring surgery due to failure to establish patency of the urethra, stricture formation, or reobstruction. Surgical methods for treating obstructive urolithiasis include tube cystostomy, urethrotomy, perineal urethrostomy, bladder marsupialization, and vesiculopreputial anastomosis.[1-4] Multiple publications have focused on clinical outcomes associated with clinical variables on presentation and various surgical techniques that might predict survival.[4,5] Normal plasma potassium concentrations (<5.2 mEq/L), lack of peritoneal effusion, and an intact urethral process on admission are associated with increased survival.[5] The type of urolith, age at castration, and appearance of the bladder on ultrasound and in surgery are not associated with postoperative outcome.[5]

l-Lactate is a marker of tissue hypoxia, or hypoperfusion, secondary to hypovolemia. l-Lactate has been used as an indicator of tissue necrosis and is a predictor for organ viability and outcome in many species including humans, dogs, and horses.[6-10] Goats with urolithiasis might present dehydrated, hypovolemic, and with varying degrees of urinary bladder or urethral necrosis depending on the location, severity, and duration of the obstruction. Peer reviewed studies on the use of blood l-lactate concentrations as a prognostic indicator in small ruminants diagnosed with urolithiasis cases are lacking. The objectives of this study were to assess the accuracy of preoperative and postoperative blood concentrations of l-lactate in predicting a negative outcome in goats undergoing tube cystostomy. We hypothesized that the likelihood of a negative outcome in goats with urolithiasis can be predicted by blood l-lactate concentrations on admission, postoperatively, or by the relative change in blood l-lactate concentrations over time.

2 | MATERIALS AND METHODS

2.1 | Animals

Published reference blood l-lactate concentrations were not available for goats; thus, reference ranges for sheep were considered. Sample size calculation was based on detecting a minimum plasma lactate concentration of 1.3, that is considered within the reference range reported in sheep,[11] power of 80%, type 1 error of 5%, and a SD of 2.1 for blood lactate concentrations in goats diagnosed with urolithiasis based on preliminary studies, using a statistical software (JMP v15, SAS Institute, Cary, North Carolina). The minimum sample size required was 23 goats. A retrospective review of the medical record database was conducted at The University of California, Davis, Veterinary Medical Teaching Hospital between January 2015 and March 2020. Goats admitted and diagnosed with urolithiasis based on clinical examination, ultrasonography, and radiographic examination that underwent temporary tube cystostomy were enrolled. Only goats where temporary tube cystostomy surgery alone was successful were included. Successful temporary tube cystostomy was defined as normograde and retrograde flushing of normal saline through the urinary bladder and urethra without resistance, and absence of uroliths in the urethra or urinary bladder after surgery. Goats that underwent temporary tube cystotomy in combination with other surgical procedures such as urethrotomy were excluded. Information recorded included breed, age, use (production or pet), weight, sex, and time to presentation after clinical signs were observed by the owner. Clinical examination variables of interest recorded on presentation included heart rate. The research did not require approval from the institutional animal care and use committee.

2.2 | Sample collection

After completion of the clinical examination, whole blood was collected from the jugular vein in heparinized syringes for determination of PCV, plasma total protein (TP), preoperative creatinine (PreCREAT), potassium, and preoperative l-lactate (PreLAC) concentrations. PCV was determined using a microhematocrit centrifuge (Unico, Dayton, New Jersey), TP concentrations were determined using a handheld optic refractometer (ADE Advanced Optics Inc, Oregon City, Oregon), potassium and l-lactate concentrations in blood were determined using a commercial blood gas analyzer (ABL90 FLEX blood gas analyzer, Radiometer, Brea, California), and creatinine concentrations in blood were determined using a portable point of care blood analyzer (i-STAT 1 and CHEM8+ test cartridge, Abbott, Princeton, New Jersey).

Medical management of the goats included placement of a transabdominal catheter (Bonnano Suprapubic catheter, Becton Dickinson, Franklin Lakes, New Jersey) to drain the urinary bladder, intravenous administration of crystalloid fluids, and pain management. When applicable, amputation of the urethral process was performed before tube cystostomy. The duration of treatment (DT) between blood sample collection on presentation and immediately after temporary tube cystotomy was recorded. Postoperative blood creatinine (PosCREAT) and postoperative blood l-lactate concentrations (PosLAC) were determined immediately (within 10 minutes) after tube cystostomy surgery. Temporary tube cystostomy, by placement of a Foley catheter (Silicone Coated Latex Foley Catheter, Covidien, Tullamore, Ireland) was performed under general anesthesia as previously described.[12]

Location of the uroliths was determined based on ultrasonographic examination, radiographic examination, and findings during temporary tube cystostomy surgery. Uroliths collected during surgery were submitted to either the Minnesota Urolith Center or the Gerald

V. Ling Urinary Stone Analysis Laboratory at UC Davis for identification. In instances where laboratory analysis of uroliths was unavailable, visual appearance of uroliths was used for identification. Duration of hospitalization, clinical outcomes at discharge from hospital, at the time of Foley catheter removal, and 6 months after discharge were recorded.

2.3 | Data analysis

2.3.1 | Descriptive statistics

Data analysis was performed using statistical software (GraphPad Prism v 8.4.3, GraphPad Software, San Diego, California; JMP v15, SAS Institute). Normality of data points was assessed using the Shapiro-Wilk test. For data points that were normally distributed, mean ± SD were reported, whereas median and 95% confidence interval (95% CI) were reported for non-normally distributed data points. Descriptive data were reported for age, sex (intact or castrated), use (production or pet), time to presentation after clinical signs observed by owner (<6 hours or ≥6 hours), breed (small or large), bodyweight, heart rate, PCV, TP, blood potassium concentrations, procedures performed before surgery, DT, location of the uroliths (urinary bladder only or urinary bladder and urethra), and duration of hospitalization. The change in blood l-lactate or creatinine concentrations on presentation and after temporary tube cystotomy were compared using a Wilcoxon matched-pairs signed test. The relative change in blood l-lactate [(PosLAC − PreLAC) ÷ PreLAC] and creatinine [(PosCREAT − PreCREAT) ÷ PreCREAT] were calculated. The relative change over time for blood lactate [DT_{lact} = (PosLAC − PreLAC) ÷ DT] and creatinine [DT_{creat} = (PosCREAT − PreCREAT) ÷ DT] after initiation of treatment were calculated. Proportions of goats that survived to discharge, and at Foley catheter removal were recorded. Goats were presented for assessment of ability to urinate through the urethra, and removal of Foley catheters at 10 to 14 days after surgery. Clinical outcomes (positive outcome defined as alive or negative defined as euthanized due to complications associated with urolithiasis) at 6 months after discharge were recorded based on representation of the goat to the hospital or via phone call to the client or referring veterinarian.

2.3.2 | Logistic regression

To assess the effect of explanatory variables on a negative clinical outcome, univariate analysis was initially performed. In the univariate analysis age, bodyweight, heart rate, use of animal, time to presentation after clinical signs observed by owner, location of the uroliths, urolith type, DT, duration of hospitalization, PCV, TP, creatinine, potassium, PreLAC, PosLAC, PreCREAT, and PosCREAT concentrations were considered as explanatory variables. The indices DT_{creat}, DT_{lact}, and the relative change in creatinine and l-lactate were also considered as explanatory variables. The outcome variable of interest was a negative clinical outcome (death or humane euthanasia) at 6 months after surgery. Univariate analysis for categorical variables, including sex, use of animal, time to presentation after clinical signs observed by owner, and location of uroliths, was determined using χ^2 test after constructing 2 × 2 frequency tables. In cases where a cell in a 2 × 2 frequency table had <5 counts, a Fisher's exact test was used. Explanatory variables with $P \leq .2$ were considered for follow-up multivariate logistic regression analysis.

Two follow-up multivariate logistic models predicting a negative clinical outcome were considered. The first model was based on variables measured preoperatively only (model 1). The second model included both variables measured preoperatively and postoperatively (model 2). The outcome variable of interest for the multivariate logistic regression models was a negative clinical outcome at 6 months after surgery. Collinearity among the independent variables was assessed using Pearson's correlation coefficient. When multicollinearity was present, the correlated independent variables were not included in the same model. Final regression model analysis was assessed using likelihood estimation. $P < .05$ was considered significant.

When applicable, the accuracy of continuous variables that were significant in predicting a negative outcome were determined by the measurement of an endpoint that maximized both sensitivity and specificity by construction of receiver operating characteristic (ROC) curves.

3 | RESULTS

3.1 | Descriptive statistics

Thirty-eight male goats met the criteria for enrollment into the study. Four goats underwent temporary tube cystotomy and urethrotomy. Thus, 34 goats met the criteria for inclusion. Fifteen goats were small breeds (Nigerian dwarf and pygmy) and 19 were large breeds (Alpine, Angora, Boer, Tennessee fainting, Nubian, Oberhasli, San Clemente, Toggenburg or their cross breeds). Median (95% CI) age for all goats was 3.8 (2.0, 5.0) years. Mean ± SD bodyweight for small and large breeds were 38.4 ± 14.5 kg and 86.4 ± 24.1 kg, respectively. Three goats were raised for production purposes (showing or breeding) whereas 31 were pets. Three animals were intact, whereas 31 were castrated. Twelve and 20 goats were presented ≤6 hours and >6 hours after clinical signs were noticed by the owner, respectively. Time to presentation after clinical signs were noticed by the owner was not recorded in 2 goats. Uroliths were located in the urinary bladder only, and urinary bladder and urethra in 13 and 20 goats, respectively. Location of the uroliths was not reported in 1 goat. The descriptive statistics are summarized in Table 1.

Mean ± SD for heart rate and PCV for all goats on admission were 118 ± 30 beats/min and 38% ± 7%, respectively. Median (95% CI) for plasma TP and blood potassium concentrations on admission were 6.6 g/dL (6.3, 7.2) and 4.0 (3.7, 4.2) mmol/L. Median (95% CI) PreLAC and PosLAC concentrations in blood were 3.3 (2.2,

TABLE 1 Descriptive statistics for goats presented for temporary tube cystostomy (n = 34)

Variable		n	Mean ± SD	Median (95% CI)
Breed	Large	19		
	Small	15		
Age (y)		34		3.8 (2.0, 5.0)
Body weight (kg)	Large breeds	19	86.4 ± 24.1	
	Small breeds	15	38.4 ± 14.5	
Use of animal	Pets	31		
	Production	3		
Status	Intact	3		
	Castrated	31		
Time (h)	≤6	12		
	>6	20		
Location	Bladder only	13		
	Bladder and urethra	20		
	Urethra only	0		

Note: Large breeds = Alpine, Angora, Boer, Tennessee fainting, Nubian, Oberhasli, San Clemente, Toggenburg, or their crossbreeds. Small breeds = Nigerian dwarf and pygmy. Location of uroliths was not reported in 1 goat and time to presentation was not reported in 2 goats. For descriptive variables that were normally distributed, mean ± SD were reported whereas median and 95% CI were reported for non-normally distributed variable.
Abbreviation: 95% CI, 95% confidence interval.

TABLE 2 Logistic model (model 1) prediction of negative (euthanasia) clinical outcome with variables measured preoperatively in male goats undergoing temporary tube cystotomy (n = 34)

Variable	Estimate (95% CI)	SE	*P* value
Intercept	0.388 (−3.867, 4.813)	2.135	.86
Age (y)	0.136 (−0.176, 0.457)	0.155	.38
Heart rate (bpm)	−0.018 (−0.05, 0.009)	0.014	.21
Duration of hospitalization (d)	0.129 (−0.021, 0.321)	0.084	.12

Note: Variables included in model 1 were based on $P \leq .2$ in the univariate analysis. $P < .05$ is significant.
Abbreviation: 95% CI, 95% confidence interval.

4.8) mmol/L and 1.0 (0.7, 1.3) mmol/L, respectively. PreLAC concentrations were higher than PosLAC concentrations (3.3 vs 1.0; $P < .001$). Median (95% CI) PreCREAT and PosCREAT concentrations in blood were 3.0 (1.1, 6.6) mmol/L and 1.1 (1.0, 1.8) mmol/L, respectively. PreCREAT concentrations were higher than PosCREAT concentrations (3.0 vs 1.1; $P < .001$).

All goats were administered fluids IV, morphine (0.1-0.2 mg/kg IM or IV) for pain control, and acepromazine (0.02-0.06 mg/kg IV or IM) for reduction of urethral spasms before surgery. In 18, 6, and 4 goats, transabdominal catheter placement and urethral amputation process, transabdominal catheter placement only, and urethral process amputation only, respectively, were performed. In 6 goats, transabdominal catheter placement or urethral process amputation was not performed. Median (95% CI) DT was 9.3 (3.5, 17.5) hours. Urolith type was identified as calcium carbonate and other (silica, magnesium ammonium phosphate, amorphous calcium phosphate carbonate, amorphous magnesium calcium phosphate, or mixed urolith types) in 24 and 8 goats, respectively. Identification of urolith was not recorded in 2 goats. Median (95% CI) hospitalization time was 4 (4, 6) days, as a majority of goats were discharged with foley catheters in place. The goats then returned to the clinic for Foley catheter challenge, which occurred 10 to 14 days post tube cystostomy.

A total of 14 goats (41.2%) were euthanized for complications associated with urolithiasis by 6 months after surgery. Four goats were euthanized before discharge from hospital, whereas 1 was euthanized at Foley catheter removal. Reasons for euthanasia included reobstruction of the genitourinary tract (n = 9), urethral stricture formation or urethral rupture (n = 3), peritonitis (n = 1), and nephrolithiasis (n = 1).

3.2 | Logistic regression

Based on the univariate analysis, age ($P = .18$), heart rate ($P = .09$), and duration of hospitalization ($P = .16$) were considered in model 1. Model 1 is summarized in Table 2. Age, heart rate, and duration of hospitalization were not significant predictors of a negative outcome.

TABLE 3 Logistic model (model 2) predicting a negative (euthanasia) clinical outcome with variables measured preoperatively and postoperatively in male goats undergoing temporary tube cystotomy (n = 34)

Variable	Estimate (95% CI)	SE	*P* value
Intercept	1.273 (−6.78, 10.56)	4.126	.76
Age (y)	−0.070 (−0.871, 0.604)	0.359	.85
Heart rate (bpm)	−0.035 (−0.116, 0.014)	0.029	.24
Duration of hospitalization (d)	0.263 (0.007, 0.686)	0.162	.11
PosLAC (mmol/L)	1.014 (−0.798, 6.999)	1.880	.59
Relative change in lactate (mmol/L)	0.354 (−3.516, 3.243)	1.473	.81
Relative change in creatinine (mmol/L)	0.810 (−2.248, 4.809)	1.658	.63

Note: Variables included in model 2 were based on $P \leq .2$ in the univariate analysis. $P < .05$ is significant. Relative change in lactate = [(PosLAC − PreLAC) ÷ PreLAC]. Relative change in creatinine = [(PosCREAT − PreCREAT) ÷ PreCREAT].
Abbreviations: 95%CI, 95% confidence interval; PosCREAT, postoperative creatinine concentrations; PosLAC, postoperative l-lactate concentrations; PreCREAT, preoperative creatinine concentrations; PreLAC, preoperative l-lactate concentrations.

Breed ($P = .5$), bodyweight ($P = .2$), sex ($P > .99$), animal use ($P = .56$), time to presentation after clinical signs observed by owner ($P = .47$), location of urolith ($P > .99$), urolith type ($P = .7$), presurgical procedures ($P = .6$), DT ($P = .64$), PreLAC ($P = 1$), PreCREAT ($P = .44$), potassium ($P = .88$), TP ($P = .72$), PCV ($P = .9$), DT_{lact} ($P = .63$), PosCREAT ($P = .22$), and DT_{creat} ($P = .22$) were not considered significant and therefore were not included in the multivariate logistic regression analysis.

In model 2, PosLAC ($P = .14$), relative change in lactate ($P = .2$), and relative change in creatinine ($P = .16$) were added to the variables considered in model 1. Model 2 is summarized in Table 3. Age ($P = .85$), heart rate ($P = .24$), duration of hospitalization ($P = .11$), PosLAC ($P = .59$), relevant change in lactate ($P = .81$), and relative change in creatinine ($P = .63$) were not significant predictors of a negative outcome (Table 3). All variables were not significant predictors of a negative outcome; therefore, assessment of accuracy of blood l-lactate or other variables using ROC curves was not performed.

4 | DISCUSSION

The results of our study indicate that preoperative and postoperative l-lactate concentrations in blood are not associated with or predictive of a negative outcome in goats diagnosed with urolithiasis undergoing tube cystostomy. Our study findings do not support our hypothesis. Similarly, all other clinical variables including signalment, procedures performed before surgery, urolith location and type, duration of hospitalization, heart rate, preoperative and postoperative blood creatinine concentration, blood potassium, PCV, plasma TP, heart rate, and the relative change in creatinine and lactate over time were not associated with a negative outcome.

In contrast to our findings, increased blood l-lactate concentrations are significantly associated with a negative outcome in dairy cattle with a right displaced abomasum and uterine torsion.[13,14] Median l-lactate concentrations associated with a negative outcome for cattle with a right displaced abomasum and a uterine torsion are 5.88 mmol/L and 15.0 mmol/L, respectively.[13,14] Positive clinical outcomes for both studies are associated with blood l-lactate concentrations of 3.23 and 3.0 mmol/L,[13,14] which are consistent with the reported concentrations of 3.3 mmol/L in our study. Although the pathophysiology of a right displaced abomasum, uterine torsion, and urolithiasis are not directly comparable, levels of dehydration, hypovolemia, resulting tissue hypoxia, and tissue necrosis are sequalae to all 3 disease conditions. However, based on the findings of our study, the level of hypovolemia and subsequent tissue hypoxia or necrosis in obstructive urolithiasis cases is not as consequential as in other diseases, such as those associated with gastrointestinal stasis, sequestration of fluid, and circulatory impairment. Furthermore, the gross appearance of the urinary bladder during tube cystostomy is not associated with a negative outcome, despite a majority of urinary bladders being red-purple in color (22/34), with some maintaining abnormal color after decompression of the bladder (5/22).[5] Our study only included goats that had an intact urinary bladder on presentation. Therefore, analysis of blood l-lactate concentration in goats with urolithiasis and uroabdomen are warranted because of potential increased osmotic pull of extracellular fluid into the abdomen, hypovolemia, and severe tissue necrosis due to urinary bladder rupture.

Eighty-five percent of animals in our study survived after removal of the Foley catheter, consistent with findings in another study reporting 84% survival in a similar time frame.[5] In total, 9 of the 29 animals alive after foley catheter removal, were either euthanized or died by 6 months due to complications from urolithiasis (70% survival at 6 months after discharge). These findings are consistent with survival rates reported in previous studies.[5] Blood potassium concentrations in our study were not associated with a negative clinical outcome, in contrast to previous studies in which a potassium <5.2 mEq/L is associated with survival and hyperkalemia is associated with nonsurvival.[5,15] However, in the previous studies, potassium concentrations of both sheep and goats were included, which could have accounted for the difference with our study.[5,15] Goats diagnosed with

urolithiasis have a higher frequency of hyperkalemia,[16] in contrast to our study where mean blood potassium concentrations were within reference ranges. This difference could be because of varying degrees of anorexia and or duration of disease, thereby affecting potassium intake. Similar to previous studies, duration of disease, breed, urolith type, location of urolith, blood creatinine, PCV, plasma TP, and procedures performed before surgery were not associated with outcome.[5,17] Although heart rate was not associated with a negative outcome in our study, cattle with abomasal volvulus and heart rates ≥100 are likely to die or be euthanized.[18] The decrease in blood l-lactate and creatinine concentrations after surgery compared to measurements before surgery is expected because of intravenous administration of fluids and emptying of the bladder via the transabdominal catheter or cystostomy.

The main practical implication of our study findings is the inability to predict clinical outcomes based on analyte concentrations before and after surgery. These findings suggest that other factors are associated with complications and negative outcomes in goats undergoing tube cystostomy. Therefore, clinicians should be aware of the limitations of clinical examination findings and serum biochemical analytes before surgery in predicting clinical outcomes in goats undergoing tube cystotomy.

Limitations of our study include the drawbacks of a retrospective design including case selection bias, and recall bias by clinicians and clients. Similarly, multiple clinicians were involved in goat care over the 5-year period of this study adding increased variability in medical record detail, medical triage, and experience in surgical management. We did not report other clinical examination variables such as temperature, respiratory rate, and hydration status, as these variables vary among goats that have recently been transported to the hospital due to different times of day, year, and varying travel times. The results of this study are from a single institution, thereby limiting the external validity of our findings and recommendations in other clinical practices.

5 | CONCLUSIONS

Preoperative and postoperative l-lactatemia concentrations and other clinical variables are not practically useful in predicting a negative outcome in goats after tube cystostomy. Clinicians should advise clients that clinical outcomes following tube cystostomy in goats are unpredictable and many of the factors assessed on presentation cannot predict clinical outcomes.

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CONFLICT OF INTEREST DECLARATION

Munashe Chigerwe serves as Associate Editor for the *Journal of Veterinary Internal Medicine*. He was not involved in review of this manuscript. The other author has 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

Authors declare no IACUC or other approval was needed.

HUMAN ETHICS APPROVAL DECLARATION

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

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