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STANDARD ARTICLE

Variables of initial examination and clinical management associated with survival in small ruminants with obstructive urolithiasis

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Background: Obstructive urolithiasis is a common disease associated with a guarded prognosis in small ruminants.

Hypothesis/Objective: The results of physical examination, laboratory analyses, and clinical management of male small ruminants presented to 2 referral clinics were investigated to identify variables significantly associated with disease outcome, so as to provide better recommendations to animal owners regarding the management of these patients.

Animals: Two-hundred ten small ruminants (130 sheep and 80 goats) with confirmed diagnosis of obstructive urolithiasis.

Methods: Clinical findings (including diagnostic imaging) and laboratory results of the 210 animals were reviewed, and relevant information regarding clinical and laboratory variables recorded upon admission and clinical management was retrieved. The association of the different variables with nonsurvival was investigated by univariable and multivariable logistic regression models.

Results: Only 39% of all patients considered for treatment and 52% of those undergoing tube cystostomy survived to be released from the clinic. Nonsurvival was strongly associated with a very poor clinical condition upon presentation, obesity, castration, and evidence of uroperitoneum. Among blood variables, abnormal PCV, severely increased serum creatinine concentrations, and increased activity of the creatine kinase were associated with increased risk of nonsurvival. Presence of signs of colic or macroscopic appearance of urine was not significantly associated with outcome.

Conclusions and Clinical Importance: The prognosis of obstructive urolithiasis was guarded with survival rates of 39% (overall) to 52% (after tube cystostomy). Intact young males with normal body condition presented early in the course of disease had the best chances of survival.

KEYWORDS

goats, prognosis, sheep, urinary calculi

1 | INTRODUCTION

Obstructive urolithiasis occurs commonly in male small ruminants, which are at high risk of the disease because of their long narrow urethra with ischiatic arch, sigmoid flexure, and urethral process. The disease progresses from an early stage with slight disturbance of the

Abbreviations: BCS, body condition score; BUN, blood urea nitrogen; CK, creatine kinase; LCL, lower 95% confidence limit; OR, odds ratio; UCL, upper 95% confidence limit; WBC, white blood cell count general condition and without specific clinical signs to a stage in which affected animals show signs of colic and frequent attempts to void urine, and finally to an advanced stage of the disease with distinctly decreased demeanor, anorexia, and lethargy.[1–4] Complete obstruction can lead to uroperitoneum caused by a rupture in the urinary tract, leakage through the wall of the distended bladder, or to rupture of the urethra and SC infiltration of urine.[1,3,5] Retrograde catheterization of the urinary bladder with straight catheters is not possible in male small ruminants because of the presence of the urethal recess at the level of the ischiatic arch.[6–8] Even catheterization by use of angiographic catheters with a curved tip in intact adult male alpine goats was unsuccessful in 50% of attempts.[8] Treatment options are numerous, but all are to some extent unsatisfactory. The most promising treatment described to date is tube cystostomy with reported short-term survival rates of 76%-80%.[5,9] However, short-term survival rates seem lower, based on our clinical experience. Despite the expenditure associated with tube cystostomy (ie, general anesthesia and extended postoperative care), this treatment does not seem to achieve satisfactory success rates. Therefore, prognostic indicators are needed to support therapeutic decisions in the management of cases of obstructive urolithiasis in small ruminants, so as to identify those animals with a fair prognosis that should be given intensive treatment. The purpose of our study was to evaluate the prognostic value for survival of selected variables from clinical examination and clinicopathologic data recorded upon admission and of clinical management of small ruminants with obstructive urolithiasis at the Clinics for Ruminants of the Vetsuisse Faculty in Bern and Zurich.

2 | MATERIAL AND METHODS

2.1 | Animals

The medical records of male small ruminants presented with obstructive urolithiasis to the Clinics for Ruminants of the Vetsuisse Faculty in Bern and Zurich from 1990 to 2010 were retrieved for analysis. Signalment data included species, breed, castration status, and age. The animals were divided into 2 groups according to the short-term outcome of treatment: survivors (discharged from the clinics) and nonsurvivors (euthanasia or natural death occurring during hospitalization). Among surviving animals, information on long-term survival was gathered by telephone conversation with the owner or, in the event of relapse, upon readmission to the clinic, but long-term outcome was not included in risk factor analyses because of the limited number of entries (48) and numerous external factors that can influence long-term prognosis after the animal is released from the clinic.

2.2 | Clinical examination and diagnostic imaging

Medical history including clinical signs observed, disease duration, and previous treatments was obtained from the referring veterinarian, the animal's owner, or both. Clinical examination upon hospitalization consisted of a complete physical examination[10] and diagnostic imaging procedures. Transabdominal ultrasonography was performed with a 5 MHz sector probe. The general appearance (eg, shape and content echogenicity) and size of the urinary bladder at its largest diameter, as well as the presence or absence of free fluid in the abdomen, were recorded. Uroperitoneum was defined as the presence of anechoic free fluid in the abdominal cavity. Radiographs of the caudal abdomen were taken in lateral recumbency; presence of radiopaque uroliths and time of radiological examination (before or after surgery) were recorded.

2.3 | Laboratory analyses

Blood analyses consisted of a CBC and serum biochemistry profile. Measured analytes were compared with published reference ranges for sheep and goats.[11] The variable "azotemia" was defined as increased blood urea nitrogen (BUN) concentration, serum creatinine concentration, or both. If urine could be collected, macroscopic appearance and pH were recorded.

2.4 | Clinical management

Amputation of the urethral process, if possible and indicated, was accomplished as part of the initial clinical examination, and urine flow after amputation of the urethral process was recorded. Decisions regarding further case management were made in agreement with the animals' owners based on clinical findings and results of laboratory analyses.

In advanced cases (eg, severely decreased general condition, markedly abnormal blood test results, and evidence of multiple uroliths on radiographs), the owners could decide to have their animals euthanized without further treatment. If treatment was initiated, therapeutic options consisted of, in order of increasing complexity, medical treatment (eg, antispasmodic, analgesic medications; fluid therapy), urethral process amputation (usually performed in the course of physical examination), and tube cystostomy. The use of these therapeutic procedures in combination has been described,[2] and several therapeutic steps indeed generally were implemented consecutively in our study.

Tube cystostomy was carried out as previously described.[9] Depending on the individual preferences of the surgeon and intraoperative findings, slight variations of the standard procedure occurred in some cases; anterograde flushing of the urethra was part of the procedure in most cases. Routine medical postoperative treatment included antibiotics, anti-inflammatory drugs, and supportive care. To confirm urethral patency before removal of the Foley catheter, it was intermittently occluded with a clamp 7-10 days after surgery.[5,9] The duration of hospitalization also was recorded.

All patients were treated and examined according to the standard procedures of the 2 clinics. Written informed consent for examination and treatment was obtained from all owners.

2.5 | Risk factor analysis

The aim of the statistical analyses was to identify variables at the time of admission that were significantly associated with short-term outcome (survival/nonsurvival). All statistical analyses were performed by commercial software (Number Crunch Statistical Software NCSS, Kaysville, Utah). Descriptive statistics for interval data were reported as mean ± SD for normally distributed data and as median and range (minimum-maximum) if normality was rejected. The Wilcoxon Rank Sum test was used to compare interval data between the 2 groups. Because of partly incomplete records, the total number of cases in any particular analysis did not always correspond to the total number of animals included in the study.

For further analyses, most interval variables were categorized as "normal," "increased," or "decreased" based on published reference ranges (Table 1).[11]

To investigate possible associations between single variables and outcome, a univariable analysis using logistic regression was conducted as a first step. The results are presented as odds ratio (OR), lower 95% confidence limit (LCL), upper 95% confidence limit (UCL), and probability value (*P* value). A *P* value of ≤0.05 was considered significant. In a second step, 2 models were designed for multivariable analysis. The clinical model contained selected variables based on clinical and statistical relevance (*P* ≤ 0.2 in the univariable analysis). The laboratory model contained selected blood test results based on statistical relevance (*P* ≤ 0.2 in the univariable model). Selected clinical variables were first also included in the laboratory model. The therapeutic procedure was included in both models to minimize the effect of tube cystostomy as a potential confounder. The aim of the clinical multivariable model was to identify the most important clinical variables associated with outcome, not to find the most parsimonious model. For the laboratory multivariable model, a backward elimination strategy was used to identify the simplest possible model. A *P* value ≤0.05 was considered significant in the multivariable models. Finally, a manual forward inclusion process was used to extend the clinical model with selected clinicopathologic data, so as to replicate a realistic clinical situation. The aim of this combined model was to assess the impact of an additional laboratory test result on outcome classification compared to the clinical variables alone.

TABLE 1 Categories used in statistical analyses and number of animals in the respective groups (n)

Parameter	Categories				
Duration of disease	Short duration		Longer duration		
	≤24 hours		*>24 hours*		
n = 198	n = 99		n = 99		
Age	Old		Young		
	>4 years		*≤4 years*		
n = 205	n = 50		n = 155		
Body condition score	1	2	3	4	5
	Thin	*Moderate*	*Good*	*Very good*	*Obese*
n = 201	n = 6	n = 11	n = 108	n = 55	n = 21
Stage of disease	Early stage	Painful stage		Advanced stage	
	No alteration in demeanor	*Colic, frequent straining, signs of pain*		*Severe lethargy, lateral recumbency*	
n = 199	n = 39	n = 90		n = 70	
Azotemia	Yes		No		
	Increased BUN and/or creatinine		*Normal BUN and creatinine*		
n = 192	n = 167		n = 25		
BUN concentration	Not increased	Mildly increased		Severely increased	
	≤reference value	*Increased but ≤ 216 mg/dL (36 mmol/L)*		*>216 mg/dL (36 mmol/L)*	
n = 192	n = 43	n = 104		n = 45	
Creatinine concentration	Not increased	Mildly increased		Severely increased	
	≤reference value	*Increased but ≤5.9 mg/dL (520 μmol/L)*		*>5.9 mg/dL (520 μmol/L)*	
n = 153	n = 11	n = 59		n = 83	
Degree of azotemia[a]	Mild	Moderate		Severe	
	BUN increased but ≤216 mg/dL (36 mmol/L) or creatinine increased but ≤5.9 mg/dL (520 μmol/L)	*BUN or creatinine above the critical value*		*BUN >216 mg/dL (36 mmol/L) and creatinine >5.9 mg/dL (520 μmol/L)*	
n = 167	n = 79	n = 43		n = 45	
Duration of clinic stay	Short stay		Longer stay		
	1–2 days		*>2 days*		
n = 209	n = 83		n = 126		
Therapeutic procedure	No tube cystostomy		Tube cystostomy		
	No treatment (mostly euthanasia) or medical treatment (including amputation of the urethral process)		*Tube cystostomy under general anesthesia*		
n = 210	n = 121		n = 89		

[a] For the degree of azotemia, 5 animals for which no creatinine value was available were assigned to the group "severe azotemia" based on strongly increased blood urea nitrogen (BUN) concentration values (276-516 mg/dL or 46-86 mmol/L).

The variables preliminarily were screened for correlations among one another. For variables with correlation coefficients >0.8, only 1 of the variables was included in the models. Interactions were not included in the models.

3 | RESULTS

3.1 | Animals

Of 270 small ruminants originally presented with urolithiasis, 210 (130 sheep and 80 goats, 49 of them pigmy goats) were suitable for analysis of the diagnostic and therapeutic procedures. Animals euthanized immediately after diagnosis at the owner's request (for considerations unrelated to medical reasons or specific prognosis of the individual animal, mostly exclusively financial in nature; 55 animals) or animals with surgical treatments other than tube cystostomy (eg, cystotomy without Foley catheter, urethrostomy or treatment with Walpole solution; 5 cases) were excluded from the study.

Ninety percent of the sheep (n = 117) were intact males, whereas 82.5% of the goats were castrated, 93.9% and 64.5% (46 and 20), respectively, for pigmy goats and other breeds. The median age was 3 years (range, 3 months to 10 years) for sheep and 4 years (range, 1.5 months to 12 years) for goats. A significant association was found between age and castration status ($P < 0.001$). The median age was significantly different ($P = 0.003$) between the surviving and nonsurviving groups, 2.5 years (1.5 month to 10 years) and 3.5 years (3 months to 12 years), respectively. The body condition of the animals was scored in categories 1 (thin) to 5 (obese), and the median body condition score (BCS) of the overall population was 3 (range, 1-5; interquartile range, 3-4).

3.2 | Outcome

Of the 210 animals included in the study, 82 (39%) could be discharged from the hospital, whereas 128 animals (61%) died or were euthanized during hospitalization. Follow-up determined that 40 animals were alive, 17 without relapse 6 months after discharge from the clinic, and 37 were alive 1 year after discharge, among these 15 without recurrence (6 had been treated conservatively and 9 with tube cystostomy). Information about the cause of death after discharge from the hospital was available for 24 animals, of which 13 had been euthanized because of relapse (9 after tube cystostomy and 4 after conservative treatment). Four animals had not survived because of complications associated with tube cystostomy. The remaining 7 animals had died of causes unrelated to urolithiasis.

3.3 | Clinical examination

Surviving animals had shown clinical signs before referral to the clinic for a significantly ($P = 0.005$) shorter time with a median of 1 day (range, 0-40 days), whereas the median duration of disease for nonsurviving animals was 2 days (range, 0-10 days).

Results of clinical examination, including whether urination was restored after urethral process amputation and results of diagnostic imaging procedures, are presented in Table 2. Ultrasonographic examination was performed in 189 of the 210 animals. Mean (±SD) bladder size on ultrasonography, noted for 138 animals, was 9.7 cm (±2.9). Hyperechoic material in the urinary bladder was observed in 24 cases and free fluid in the abdomen in 29 cases. Of the 29 animals with suspicion of uroperitoneum on ultrasonographic examination, 22 were euthanized without surgical treatment and 7 received tube cystostomy, of which 3 survived. Radiographs were performed less often than ultrasonography (n = 42). Radiopaque uroliths were visible on 27 radiographs. Of these animals, 25 did not survive and 2 with calculi in the urethra could be discharged, 1 after amputation of the urethral process and 1 after tube cystostomy, respectively. Twenty-one animals examined radiographically received surgical treatment, in 13 of these the radiographs had been taken before surgery, and in 8 cases after surgery (because of persistent obstruction after clamping the Foley catheter).

The variables of clinical examination significantly associated with outcome are summarized in Table 3. Species, treatments, or observations by the veterinarian before referral, as well as heart and respiratory rates upon clinic admission, were not significantly associated with the outcome in the univariable analysis. The high rate of death or euthanasia in the first days of hospitalization was reflected in the association of a short clinic stay (≤2 days) with increased risk of nonsurvival (OR,19.5; $P < 0.001$). In the clinical multivariable model, castrated animals, those with a BCS of 4 or 5, severe lethargy or evidence of uroperitoneum on ultrasound examination had significantly increased ORs for nonsurvival whereas those treated with tube cystostomy had a significantly decreased relative risk of nonsurvival.

3.4 | Laboratory analyses

The results of blood analyses are presented in Table 4. Azotemia was found in 167 animals (87.0%; increased BUN concentration in 149 animals, 77.6%; increased serum creatinine concentration in 142 animals, 92.8%).

Urine appearance and pH value were recorded for 60 animals. Median urine pH was 8 (range, 5-9). In 31 cases (51.7%), urine color was altered, mostly bloody (19 cases, 61.3%). Urine color was reported to be normal in 29 cases (48.3%).

Abnormalities in blood test results significantly associated with the outcome in the univariable analysis are given in Table 5. No significant association was observed for BUN concentration, sodium, phosphorus, plasma proteins, and WBC, but abnormalities in the values of creatinine, PCV, CK, potassium, chloride, as well as severity of azotemia were significantly associated with the outcome. In the multivariable laboratory model, abnormalities in the values of creatinine, CK, and PCV were significantly associated with the outcome. In the forward inclusion process of the clinical model, only abnormal PCV increased the model's accuracy for correctly classified outcomes (from 69.6% to 74.6%).

3.5 | Clinical management

Eighty-three animals remained hospitalized ≤2 days (64 for 1 day, 19 for 2 days), of which 77 (92.8%) were nonsurvivors (64 were euthanized and 13 died). Of the 31 animals registered as having

TABLE 2 Distribution of clinical parameters and associations with outcome (survival/nonsurvival)

Parameter	n	Variables	n	Survival %	Nonsurvival %
Castration status[m]	210	Intact	131	44.3	55.7
		Castrated[a]	79	30.4	69.6
BCS[m]	201	Normal (BCS = 3)	108	48.1	51.9
		Too high (BCS = 4 or 5)[a,b]	76	28.9	71.1
		Too low (BCS = 1 or 2)	17	23.5	76.5
Uroperitoneum[m]	193	Absent (ultrasound)	164	45.1	54.9
		Present (ultrasound)[a,b]	29	17.2	82.8
Stage of disease[c,m]	199	Early	39	53.8	46.2
		Painful	90	42.2	57.8
		Advanced[a,b]	70	25.7	74.3
Surgery[m]	210	Tube cystostomy	89	51.7	48.3
		No tube cystostomy[a,b]	121	29.8	70.2
Age	205	4 years and younger	155	45.2	54.8
		Older than 4 years[a]	50	20.0	80.0
General condition	199	Normal	43	77.7	92.3
		Moderate lethargy	130	40.0	60.0
		Severe lethargy[a]	26	55.8	44.2
Skin elasticity	157	Normal/slightly decreased	126	42.9	57.1
		Strongly decreased[a]	31	19.4	80.6
Urination upon admission	207	Normal amount	17	58.8	41.2
		Decreased amount	61	42.6	57.4
		No urination	129	34.1	65.9
Urination after amputation of the urethral process	69	Normal	23	73.9	26.1
		Improved (but not normal)[a]	24	29.2	70.8
		No difference[a]	22	27.3	72.7
Radiology findings	42	No urolith visible	15	80.0	20.0
		Urolith(s) visible[a]	27	7.4	92.6

Two-hundred ten animals were included in the study (82 survivors and 128 nonsurvivors).
n is the number of animals with records for a given parameter.
The parameters marked with superscript "m" were included in the final multivariable clinical model.
[a] Significantly associated with the outcome "nonsurvival" in the univariable analysis ($P \leq 0.05$).
[b] Significantly associated with the outcome "nonsurvival" in the multivariable analysis ($P \leq 0.05$).
[c] The 3 stages of disease are characterized by discrete unspecific clinical signs (early stage), frequent straining, expression of pain and moderate lethargy (painful stage), and severe lethargy with recumbency in final stages (advanced stage).

received no treatment after hospitalization, 29 (93.5%) belonged to the group of short clinic stay, they were euthanized for medical reasons (poor prognosis) after clinical examination or died before treatment could be initiated.

The administration of antispasmodic, analgesic drugs or muscle relaxants to 140 animals was mostly unsuccessful (88 cases of 95 with recorded outcome, 92.6%). Urethral process amputation was carried out in 91 animals; the amount of urine voided after amputation, recorded for 69 animals, was not significantly associated with the subsequent therapeutic decision (conservative versus surgical treatment, $P = 0.1$). Of the animals with normal urine flow after urethral process amputation, 26.1% still had to be taken to surgery afterward (in some cases, 1 day after urethral process amputation). Of those animals with some urine flow after surgery, 37.5% subsequently had surgery, and 54.4% of the animals with no urination after urethral process amputation received tube cystostomy.

One-hundred twenty-one animals were treated conservatively or by urethral process amputation only (36 survivors and 85 nonsurvivors), and 89 received tube cystostomy (46 survivors and 43 nonsurvivors). The group of nonsurgical treatment consisted of 76 sheep, 26 pygmy goats, and 19 other goats, and the group of surgical treatment consisted of 54 sheep, 23 pygmy goats, and 12 goats. Survival until release from the clinic was significantly higher for the surgical than for the nonsurgical group (46 of 89 animals or 51.6%, and 36 of 121 or 29.8%, respectively; $P = 0.001$) in the univariable analysis. No significant difference was found in long-term survival (≥6 months) between animals having received surgical (tube cystostomy) or conservative treatment (medical treatment, with or without amputation of the urethral process; $P = 0.77$, n = 48).

4 | DISCUSSION

Retrospective analysis of 210 cases of obstructive urolithiasis presented to 2 referral clinics identified a lower treatment success rate (39% overall short-term survival and 52% after tube cystostomy) than described in the literature.[2,5,9] Overall survival rate might have been affected in part by the fact that all cases were included, except for

TABLE 3 Results of the univariable and multivariable analyses for clinical parameters

	Univariable analysis (see Table 2 for n)			Multivariable analysis (n = 135)		
Variable	**OR**	**LCL-UCL**	***P* value**	**OR**	**LCL-UCL**	***P* value**
Castrated animal	1.8	1.0-3.3	0.03	2.11	1.0-4.3	0.04
High BCS (4 to 5)	2.28	1.2-4.2	0.009	2.43	1.2-5.0	0.02
Uroperitoneum on ultrasonographic examination	3.9	1.4-10.8	0.008	3.55	1.0-11.7	0.04
Painful stage of disease	1.6	0.7-3.4	0.2	1.44	0.6-3.5	0.4
Advanced stage of disease	3.37	1.5-7.7	0.004	3.31	1.2-8.73	0.01
No tube cystostomy performed	2.52	1.4-4.5	0.001	2.12	1.1-4.1	0.04
Older than 4 years	3.29	1.5-7.0	0.002			
Severely decreased skin elasticity	3.12	1.2-8.1	0.02			
Moderate lethargy	1.9	0.9-3.8	0.07			
Severe lethargy	15.15	3.2-72.3	0.0006			
Decreased amount of urine voided at admission	1.92	0.6-5.7	0.24			
No urination at admission	2.76	1.0-7.7	0.05			
Urination only improved (not normal) after amputation of urethral process	6.88	1.9-24.8	0.003			
No difference in urination after amputation of urethral process	7.55	2.0-28.3	0.003			
Urolith(s) visible on radiographs	50.0	7.3-340.0	<0.0001			

Abbreviations: LCL, lower limit of 95% confidence interval; OR, odds ratio for nonsurvival; ULC, upper limit of 95% confidence interval.

patients for which economic factors alone defined the owners' decisions and the few animals that received surgical treatment other than tube cystostomy. The animals that were not treated (ie, those euthanized immediately after clinical examination because of poor prognosis or agonal state) were not considered in the survival rates in other studies.[2] Therefore, the low overall survival rate of 39% described here may reflect the outcome of obstructive urolithiasis more closely than studies in which patient selection led to exclusion of the most severe cases.[2] Indeed, even if the 29 animals euthanized immediately (without treatment) or that died shortly after admission are excluded, the overall survival rate still is lower than in other studies, at 45%. In the present study, no animal in need of treatment was left untreated (ie, all animals with obstructive urolithiasis either were treated as appropriate or euthanized). The 2 participating clinics do not see primary cases and uncomplicated cases of obstructive urolithiasis (ie, those resolving after administration of spasmolytic drugs or urethral process amputation) rarely are referred. Severity of disease therefore may have been to some extent higher in the study population than in the general population of affected small ruminants. Our results also found survival rates after tube cystostomy that are distinctly lower than the 68%-92% described in the literature.[5,9,12] This finding might be because of the fact that previous studies evaluated tube cystostomy as a surgical technique, which was not the objective of our retrospective study. Tube cystostomy mainly was included in the analyses because of its influence on outcome. Also, in the case of complications (obstruction of the tube or no restoration of urethral patency), patients in other studies often received further surgical treatment (eg, Foley catheter replacement and perineal urethrostomy). In our study, such animals mostly were euthanized at the owner's request (based on animal welfare concerns) if urine outflow was not restored within the expected time frame. Different designs and reported variables in the various studies do not allow estimation of whether the patient populations were comparable before surgery. Awareness of small ruminant owners and veterinarians about obstructive urolithiasis has been reported to be less than satisfactory in Switzerland,[4] which may have contributed to delayed referral for treatment. Duration of disease of >24 hours was significantly associated with an increased risk of nonsurvival.

The main aim of our study was to analyze clinical and clinicopathologic data obtained upon admission in 210 small ruminants with obstructive urolithiasis so as to determine OR for nonsurvival for variables that could be used as prognostic indicators to support decision making for subsequent clinical management. Overall, intact animals <4 years of age with clinical signs of ≤24 hours' duration, normal BCS, normal demeanor, no free fluid in the abdomen, and no uroliths visible on radiographs were significantly more likely to survive. Regarding laboratory variables, abnormalities in PCV, serum creatinine concentration (or severity of azotemia), and CK activity were most closely associated with nonsurvival.

Although others have reported that castration was associated (albeit not significantly) with survival after tube cystostomy,[5] castration generally is considered a risk factor for obstructive urolithiasis because of the smaller urethral diameter in castrated animals.[13] This conclusion was corroborated by our results in that castrated animals had a significantly higher risk of nonsurvival (OR = 1.8) than did intact animals. Because a significant association was found between age and castration status, the outcome also was significantly associated with the age of the animals. Indeed, the population was mostly composed either of young intact animals, mostly sheep used for breeding, or of older castrated goats, mostly kept as pets. Overfeeding concentrate, a well-established risk factor for struvite calculi formation,[7] was observed in both populations and was reflected in the large number of animals with BCS of 4 or 5. This variable was significantly associated with increased risk of nonsurvival in the univariable (OR = 2.29) and multivariable (OR = 2.43) analyses.

Animals that had been sick >24 hours were more often lethargic upon arrival (advanced stage of disease),[4] they also had significantly worse azotemia and were significantly less likely to survive. This

TABLE 4 Distribution of laboratory values and associations with outcome (survival/nonsurvival)

Parameter	n	Variables	n	Survival %	Range[a]	Nonsurvival %	Range[b]
Creatinine[m] (mg/dL)	142	Mildly increased (≤5.9)	59	45.8	0.9-5.5	54.2	0.9-5.7
		Severely increased (>5.9)[d,e]	83	25.3	6.2-20.0	74.7	6.1-35.1
PCV[m] (%)	188	Normal	112	42.9	27-38	57.1	24-38
		Abnormal[d,e]	76	27.6	14-47	72.4	15-59
CK activity[m] (IU/L)	175	Normal	69	49.3	29-233	50.7	46-245
		Increased[d,e]	106	31.1	216-10 465	68.9	214-7208
Potassium[m] (mmol/L)	183	Hypokalemia	69	47.8	2.4-4.5	52.2	2.7-4.6
		Normokalemia	82	36.6	4.5-6.5	63.4	4.6-7.8
		Hyperkalemia[d]	32	25.0	6.7-7.5	75.0	6.6-11.3
Chloride[m] (mmol/L)	180	Hypochloremia[d]	94	30.9	55-103	69.1	65-103
		Normochloremia	78	48.7	102-116	51.3	103-115
		Hyperchloremia	8	50.0	118-126	50.0	115-127
Azotemia[c]	167	Mild	79	48.1		51.9	
		Moderate[d]	43	27.9		72.1	
		Severe[d]	45	24.4		75.6	
BUN (mg/dL)	149	Mildly increased (≤216)	81	42.0	44.4-209.4	58.0	43.4-211.8
		Severely increased (>216)	68	29.4	219.0-426.0	70.6	220.8-694.6
Phosphorus (mmol/L)	125	Hypophosphatemia	63	33.3	0.32-1.16	66.7	0.41-1.18
		Normophosphatemia	48	45.8	1.22-2.79	54.2	1.20-2.84
		Hyperphosphatemia	14	35.7	2.58-4.35	64.3	2.46-4.21
Sodium (mmol/L)	187	Hyponatremia	82	35.4	136-148	64.6	119-148
		Normonatremia	101	41.6	147-159	58.4	148-159
		Hypernatremia	4	25.0	173 (1 value)	75.0	158-162
Plasma proteins (g/L)	180	Decreased	16	43.7	50.0-62.3	56.3	49.4-62.0
		Normal	131	37.4	60.8-81.5	62.6	61.0-82.0
		Increased	33	39.4	83.3-102.0	60.6	87.0-111.5
WBC (10^9/L)	170	Normal	139	39.6	4.7-19.3	60.4	4.6-19.5
		Abnormal	31	25.8	3.7-15.9	74.2	1.34-40.8

Two-hundred ten animals included in the study (82 survivors and 128 nonsurvivors).
n is the number of animals with records for a given parameter.
Parameters marked with superscript "m" were included in the final multivariable laboratory model.
[a] Range of observed values for the described categories of each parameter in survivors.
[b] Range of observed values for the described categories of each parameter in nonsurvivors.
[c] For definition of the degrees of azotemia see Table 1. Because "azotemia" is defined by combined values of BUN and/or creatinine, a range of observed values cannot be given for this parameter.
[d] Significantly associated with the outcome "nonsurvival" in the univariable analysis ($P \le .05$).
[e] Significantly associated with the outcome "nonsurvival" in the multivariable analysis, ($P \le .05$).

TABLE 5 Results of the univariable and multivariable analyses for clinicopathologic data

Univariable analysis (see Table 4 for n)				Multivariable analysis (n = 127)		
Variable	OR	LCL-UCL	*P* value	OR	LCL-UCL	*P* value
Severely increased creatinine	2.49	1.2-5.1	0.01	3.57	1.5-8.5	0.004
Increased or decreased PCV	1.96	1.0-3.7	0.03	4.1	1.6-10.3	0.003
Increased activity of CK	2.15	1.1-4.0	0.02	2.8	1.2-6.5	0.02
Hyperkalemia	3.13	1.4-7.0	0.005			
Hypochloremia	2.1	1.2-3.9	0.01			
Moderate azotemia	2.64	1.1-5.3	0.03			
Severe azotemia	2.86	1.3-6.9	0.01			
Severely increased BUN	2.18	0.99-4.8	0.051			

Two-hundred ten animals included in the study (82 survivors and 128 nonsurvivors).
Abbreviation: OR, odds ratio for nonsurvival.
Species (sheep, goat or pygmy goat), concentrations of creatinine, bilirubin, CK activity, chloride, potassium, and PCV were included in the original multivariable model.
The surgical procedure (tube cystostomy performed or not) was included in the original multivariable model as a potential confounder.

finding highlights the importance of restoring urine outflow as soon as possible. In addition to more severe azotemia, prolonged obstruction leads to a higher risk of uroperitoneum, and urinary bladder rupture can occur after 24-48 hours.[3] Uroperitoneum itself was found to be significantly associated with nonsurvival in our study (OR = 3.9), as previously reported.[5]

Signs of colic frequently have been described in previous reports on urolithiasis.[9,14,15] In our study population, signs of abdominal pain were observed in 45% of the affected animals upon admission and this variable was not associated with the outcome. However, colic had been reported more often (63%) by owners and veterinarians. Administration of spasmolytics and analgesics before referral, a more advanced stage of disease at clinic presentation, or both may have masked an association between the occurrence of colic and outcome.

Dysuria, stranguria, or urine retention, as well as abnormal urine also are expected in animals with obstructive urolithiasis.[5,14] Although 62% of our patients did not void any urine and 29% could pass only small amounts of urine, normal volume of urine was recorded in 8% of affected animals upon admission. Furthermore, urine color was reported to be normal in 48% of the 60 animals for which a description was available. These results show that animals with urolithiasis can, although this might only occur temporarily (eg, after treatment with spasmolytic drugs), pass a normal amount of macroscopically normal-appearing urine. In contrast, no urination upon presentation was associated with increased risk of nonsurvival, but this effect was not significant (OR = 2.76, P = 0.054).

Examination of the urethral process is an important step in the clinical management of small ruminants with suspected urolithiasis, because amputation of the urethral process can lead to resolution of obstruction in case of an isolated urolith.[14] In our study, partial (decreased urine flow) or no success after urethral process amputation was associated with significantly higher risk of nonsurvival (OR, 6.88 and 7.55, respectively) in the univariable analysis, compared to restoration of normal urine flow. However, records regarding visualization of the urethral process and response to amputation only were available for 33% of the study patients. Often, no attempts were undertaken to visualize the urethral process (eg, in severely lethargic animals) or were unsuccessful (eg, in obese animals), which are 2 factors in themselves associated with high risk of nonsurvival. Thus, the population in which this variable could be investigated was not necessarily representative. It will nevertheless be of interest for veterinary practitioners that normal urine flow was restored in 33% of the patients after urethral process amputation, and that these patients had a significantly higher short-term survival rate (73.9%) than animals for which only decreased or no urine flow was restored (29.2% and 27.3%, respectively). However, the long-term result of urethral process amputation has been reported to be poor because of persistent or recurrent obstruction.[2,16]

Ultrasonography is a useful aid in diagnosing urolithiasis and possible complications such as uroperitoneum.[17] Animals with evidence of uroperitoneum in our study had a significantly increased risk of nonsurvival (OR of 3.9 in the univariable and 3.55 in the multivariable analysis), which is in accordance with previous reports.[5] Some of the owners may have decided to have their animals euthanized based on evidence of uroperitoneum on ultrasonography, and thus the prognostic value of this factor is difficult to define.

Radiopaque uroliths can be visualized on plain radiographs in small ruminants.[18,19] Although the usefulness of plain radiographs to diagnose urolithiasis has been questioned[6] and a recent study has shown that struvite and amorphous magnesium calcium phosphate uroliths cannot often be detected on radiographs,[20] this method allowed for confirming the presence of uroliths in 64% of the patients that had radiographs taken in our study, but unfortunately the type of uroliths could not be determined. Presence of uroliths at radiography was associated with a very high risk of nonsurvival (OR = 50 in the univariable analysis). These figures must be interpreted with caution because they are mostly because, in the first years of the study, radiography was almost exclusively used for animals that had not been able to void urine normally after the expected recovery period after tube cystostomy. In those cases, radiologic examination was not performed for diagnostic purposes before treatment but to confirm persistent urethral obstruction. In later years, radiographs gained more importance in the diagnostic evaluation of urolithiasis. In the case of numerous large stones or urethral obstruction with small sand-like calculi over several centimeters, many owners elected euthanasia rather than further treatment because of poor prognosis. Radiographic examination should be recommended before surgery for small ruminants with suspected urolithiasis to avoid the costly and painful procedure if the prognosis is poor based on the nature of the obstruction.

An original aim of our study was to define threshold values for selected blood variables that would allow for reliable prognostic prediction. Unfortunately, likely because of the high variability of the observed results, such tentative cutoff values could only be identified for BUN and serum creatinine concentrations.

Azotemia was the most commonly observed abnormality on blood analysis. Animals in the group with severe azotemia were significantly less likely to survive (OR = 2.86) than animals with mild azotemia. Severely increased serum creatinine concentrations were significantly associated with nonsurvival, whereas severely increased BUN concentrations were not (P = 0.051). This finding may be due to recycling of BUN concentration in the rumino-hepatic cycle.[21] Our results suggest that serum creatinine concentration is more reliable than BUN concentration for evaluating patients with suspected azotemia. The BUN and serum creatinine concentrations were significantly higher in the group with a duration of disease >24 hours, likely because of more severe dehydration caused by decreased water intake, development of uroperitoneum or both.[22]

Relative hypovolemia, assessed clinically by the skin tent test, has been described in association with urolithiasis and uroperitoneum.[22] In our study, severe dehydration was significantly associated with an increased risk of nonsurvival in the univariable clinical analysis (OR = 3.12). Abnormal PCV was significantly associated with nonsurvival in the univariable (OR = 1.96) and multivariable (OR = 4.1) laboratory models. Although skin elasticity or increased PCV generally are rather nonspecific, our results indicate that they can be used for prognostic evaluation of small ruminants with urolithiasis, likely because they are directly linked to disease duration and uroperitoneum. In contrast, abnormally low PCV has not been, to the best of our knowledge, described in relation to urolithiasis. In our results, both increased and decreased PCV was associated with increased risk of nonsurvival. Anemia in those patients probably was a consequence of concomitant disease (eg, hemonchosis) and not related to urolithiasis. Because anemia caused by infestation with endoparasites is a common problem in small ruminants,[23] these findings suggest that the presence of concomitant diseases may negatively influence the prognosis of animals with urolithiasis.

Besides azotemia, blood biochemistry abnormalities significantly associated with increased risk of nonsurvival included hyperkalemia and hypochloremia. Hyperkalemia can lead to cardiac dysfunction[24] and has been described as a risk factor for sudden death or anesthetic complications.[5] Lower survival rates for animals with hyperkalemia were confirmed in our study. This observation highlights the importance of correcting electrolyte imbalances, especially if surgery is to be performed under general anesthesia. Furthermore, hypokalemia, although not significantly associated with outcome, was observed more often than hyperkalemia (54 versus 44 cases of 183; normal serum potassium concentration in 85 animals). This finding confirms that the choice of fluids to be administered to small ruminants with urolithiasis should be based on blood biochemistry results if possible, because the serum potassium concentration cannot be predicted accurately based on clinical signs. Hypochloremia has been associated with abdominal sequestration of electrolytes and fluids in cases of uroperitoneum.[22] The negative prognostic value of hypochloremia thus is in accordance with the poor prognosis associated with uroperitoneum.

Hyponatremia, also described in relation to uroperitoneum,[22] and abnormal serum phosphorus concentration were not significantly associated with disease outcome in our study. However, hyponatremia was observed in 44% of the patients and abnormal serum phosphorus concentration in 62%. Thus, although these variables can be used for the diagnosis of obstructive urolithiasis, they do not appear to be of prognostic value.

To the best of our knowledge, increased CK activity has not been described in relation to the prognosis of small ruminants with urolithiasis. In our study, increased CK activity was significantly associated with increased risk of nonsurvival in the univariable and multivariable models. Prolonged recumbency can cause increased CK activity and is linked to other prognostic factors (eg, severe lethargy, long duration of disease, and dehydration). This variable mostly reflects disease severity and does not offer added value for the prognostic evaluation of small ruminants with obstructive urolithiasis.

The backward elimination strategy of the laboratory multivariable model indicated that severely increased serum creatinine concentrations, abnormal PCV, and increased CK activity were significantly associated with outcome. The forward inclusion process used to identify the single most useful laboratory variable to be assessed after clinical examination so as to increase prognostic accuracy did not allow for identifying any 1 variable that would markedly influence the percentage of animals classified correctly by the model. If an abnormal PCV was measured, the accuracy of the clinical model increased by 5%, from 69% to 74%. Thus, a negative outcome could be correctly predicted based on the relevant clinical variables combined with PCV measurement in approximately 3 of 4 cases.

The effect of treatment choice by the owner of the animals, especially regarding surgical or nonsurgical treatment, on disease outcome also was taken into account in the statistical analyses by including tube cystostomy as a confounding factor in all statistical models. Conservative treatment (ie, no tube cystostomy) was significantly associated with increased risk of nonsurvival in the clinical multivariable model, but not in the laboratory model. This result for the clinical model was expected, because the decision to proceed to surgery under general anesthesia primarily was made for animals in reasonably good general condition. This finding highlights a major limitation of our study (ie, the influence of perceived prognosis on therapeutic decisions), because recommendations of the clinicians to the owners were based on the same clinical and laboratory variables that also were evaluated with regard to their prognostic value. This potential bias however is inevitable in a retrospective study.

4.1 | Conclusion and clinical relevance

The evaluation of prognostic factors confirmed the importance of a complete clinical examination for rational management of small ruminants with obstructive urolithiasis. Some of the classical clinical signs of urolithiasis such as colic or abnormal macroscopic urine appearance, if present, were not significantly associated with outcome, whereas more nonspecific signs such as severe lethargy or abnormal PCV were significantly associated with increased risk of nonsurvival. Nevertheless, the classical risk factors castration and obesity were significantly associated with nonsurvival. All of these factors should be taken into consideration when discussing the clinical approach for small ruminants with urolithiasis with their owners, because the survival rate was not high in the population under study (39% overall, 52% after tube cystostomy).

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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

Authors declare no IACUC or other approval was needed.

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