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Symmetric dimethylarginine correlates with the urea, creatinine, potassium, and clinical scores in feline urethral obstructions

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ABSTRACT

Background: A urethral obstruction (UO) is an emergency commonly observed in male cats, which can result in significant clinical and laboratory alterations, leading to complications and death.
Objectives: This study aimed to correlate symmetric dimethylarginine (SDMA) with the urea, creatinine, potassium, and bicarbonate levels in cats with UO. In addition, the correlation between clinical score and time of obstruction was evaluated.
Methods: Thirty male cats were selected and allocated into a control group (CG, n = 13) and an obstruction group (OG, n = 17). The laboratory analyses were conducted before treatment (M0) and at different times after treatment (12 h [M12], 24 h [M24], and 48 h [M48]). Correlations were established between SDMA and creatinine, urea, bicarbonate, potassium, time of obstruction, and the clinical score.
Results: A strong correlation (r > 0.6) was observed between SDMA and creatinine, urea, and potassium in the OG. Furthermore, there was substantial agreement (kappa value) between SDMA and creatinine at M24. A higher clinical score was associated with a longer time of obstruction. In the OG, at M48, the SDMA and creatinine levels were 50% and 41.2% higher, respectively.
Conclusions: A correlation was observed between SDMA and creatinine in obstructed cats, and significant agreement between these values was observed 24 h after the unblocking treatment. A correlation among SDMA, urea, and potassium was observed. Approximately 9% more cats continued to have elevated SDMA levels after 48 h of treatment compared to creatinine. This suggests a slightly lower sensitivity of the latter biomarker but does not exclude the possibility of congruent and normalized values after a longer evaluation period.

Keywords: Biomarker; *Felis catus*; kidney; urethra

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Conflict of Interest

The authors declare no conflicts of interest.

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INTRODUCTION

Urethral obstruction (UO) induces post-renal azotemia, leading to a rapid and severe reduction of the glomerular filtration rate (GFR). Kidney interstitial inflammation and edema can also be observed, in addition to tubular atrophy, fibrosis, and apoptosis. Moreover, post-renal azotemia can evolve into an intrinsic acute kidney injury (AKI) [1].

Urinary output monitoring, renal biochemistry, and the onset of treatment are the available options to detect inappropriate urinary flow [2]. In veterinary medicine, renal function monitoring is a challenge, and the parameters used to assess this function are the GFR, serum creatinine (sCr), and symmetric dimethylarginine (SDMA) [3]. On the other hand, approximately 20% of creatinine excretion is tubular, and its levels may vary according to age, sex, lean muscle mass, muscle metabolism, and hydration [4], which does not allow a proper assessment.

SDMA has been suggested as a biomarker for evaluating the GFR [5,6]. SDMA is an amino acid formed by the methylation of arginine, which is released in the blood by the degradation of type II protein arginine methyltransferase [7] and excreted by the kidneys without signs of tubular reabsorption [8]. Compared to sCr, the SDMA serum concentration can detect earlier renal impairment. Furthermore, the SDMA concentrations are less affected, but not absent, by extrarenal factors such as age, sex, breed, lean body mass, and mitral regurgitation [6,8-10].

UO caused by feline lower urinary tract disease (FLUTD) can lead to a rapid decrease in GFR, increasing the serum SDMA concentration, similar to what occurs with creatinine. Nevertheless, in UO, SDMA follows the creatinine values, showing a significant reduction after decompression. Hence, these biomarkers cannot predict the renal function based on their concentration before decompression [11]. In AKI in cats, however, SDMA is useful when there is a sedimented AKI [12]. In the face of these findings, it is believed that in feline UO, SDMA may work as a biomarker for the early detection of chronic kidney disease (CKD) cats in which an irreversible kidney injury has been established after a long time of UO. The serum concentrations of SDMA in cats with UO have not been correlated with variables such as urea, potassium, bicarbonate, clinical score, and the time of obstruction. This study compared the behavior between SDMA and the variables above.

MATERIALS AND METHODS

Ethical aspects

This study was carried out in accordance with the ethical precepts recommended by the National Council for Animal Control and Experimentation (CONCEA) and was approved by the Institutional Animal Use Ethics Committee (CEUA) UNESP, Botucatu, Brazil, under protocol number 266/2018.

Animals and experimental groups

Thirty owned male cats of random ages were selected for this clinical prospective study. The animal selection occurred at the Veterinary Teaching Hospital of the São Paulo State University, Botucatu, from June 2018 to December 2018. The breed and body weight were not included as the selection criteria. The cats were allocated into two groups: the control group (CG, n = 13) and the obstruction group (OG, n = 17). The CG comprised healthy animals with no alterations in blood, urine, and imaging examinations. The OG comprised animals with

UO, with compatible blood, urinary, or imaging changes. None of the cats were receiving any medication prior to admission and selection.

In the CG, a single time was analyzed (M0), and four times were assessed in the OG (0 h [M0] and 12 h [M12], 24 h [M24], and 48 h [M48] after treatment). The first analysis (M0) was conducted two hours before treatment, followed by M12, M24, and M48. The time of obstruction (12, 24, 36, 48, and 60 h) registered in this study was in accordance with the data the owner provided before the onset of clinical management. Among the 17 cats with UO, the time of obstruction presented at hospital admission was registered (12, 24, 36, 48, and 60 h with three, five, three, five, and one cat in each time, respectively).

Inclusion and exclusion criteria

In the OG, the inclusion criterion was a complete UO first episode confirmed by the clinical history of strangury and distended urinary bladder in the physical examination, revealing pain upon abdominal palpation. The exclusion criteria were as follows: the administration of antimicrobial or anti-inflammatory drugs between seven to 14 days prior to hospital admission, diagnosis of urinary tract infection, performance of cystocentesis before emergency care attendance, and cats with a prior history of CKD or identified with signs of chronicity in the imaging examination. In addition, those with congenital malformations and neoplasms were excluded.

Clinical and physical evaluation

The clinical evaluation was performed prior to cystocentesis and urethral clearance. The body weight was registered, and the body condition score was evaluated using a 1 to 9 Royal Canin scale (**Supplementary Table 1**). A clinical score evaluation was developed based on the practitioners' experience and Collado et al. [13] by assessing variables such as appetite, emesis, mental condition, head position, and dehydration (**Supplementary Table 2**). The physical evaluation included the hydration status, heart rate (bpm), respiratory rate (per min), rectal temperature (°C), indirect systolic blood pressure (SBP) (mmHg), capillary filling time (CFT) (sec), mucosal coloring, and pulse strength. Indirect SBP was evaluated using a non-invasive method with an Ultrasonic Doppler 404 Flow Detector 811-B, Parks Medical Electronics, Aloha, OR, USA. The examination was performed in sternal recumbency on the emergency room table. The cuff size was selected so that the cuff width was 30–40% of the circumference of the forelimb [14]. The final SBP value was obtained according to IRIS (2023) guidelines [15].

Laboratory evaluation

A 5 mL blood sample was obtained by jugular venipuncture for complete blood count, serum biochemistry, SDMA, blood gas, and electrolytes analysis [16,17]. Blood collection tubes with anticoagulant – EDTA (EDTA.K2, FirstLab, Brazil), clot activator with gel (Medix, Brazil), and specific syringe for hemogasometry (Royal Tech®, Brazil) were used. The hemogram and platelet count were performed using commercially available kits in an automated device (Cobas® C111; Roche, Brazil). A slide examination of the samples was performed to confirm the equipment results. The serum biochemistry evaluation included urea, sCr, albumin, and phosphorus. Blood gas and electrolytes assay were conducted in a portable device (i-Stat 1 Handheld, Abbott, USA) using a commercially available kit (kit Cg8+, Abbott) to assess potassium (K^+), blood glucose, and bicarbonate (HCO_3). SDMA was measured using a specific device (Catalyst Dx®; IDEXX, USA), considering the reference interval for the serum SDMA in healthy cats [15] (0–14 μg/dL) (IDEXX Laboratories, Inc, USA).

In the urine analysis, a sample was obtained by cystocentesis (lateral recumbency) through the transabdominal puncture and centrifuged at 1,200 g for six minutes after 30 min from collection. The analysis was performed using reagent strips (Combur-Test; Roche), and the urinary protein-to-creatinine (UPC) ratio was then determined. The urine specific gravity (USG) was assessed by refractometry using a handheld refractometer (MEGABRIX Refractometer, Ionlab equip. sup. Laborat. Hosp. LTDA, Barigui, PR).

Obstruction group treatment

Cystocentesis was previously performed in all cats. For urethral clearance, the cats were anesthetized with 5 mg/kg of propofol (Provive® 1%; União Química Farmacêutica Nacional S/A, Brazil) administered intravenously. The penis was adequately exposed and massaged, and an investigation for the presence of urethral plugs or calculi was conducted. After trichotomy and antisepsis of the prepuce area, a semiflexible urethral catheter (TomCat, Provar, Brazil) was used for urethral hydropulsion with a 0.9% NaCl solution. The urinary bladder was irrigated to remove the plugs and sediments. The urethral catheter was fixed and maintained for 48 h in a closed sterile system.

The clinical treatment was instituted simultaneously with urethral clearance. Electrolytic imbalances were adjusted with Ringer's lactate fluid therapy (Isofarma Industrial Farmacêutica Ltda., Brazil). Pain control was established with 2–4 mg/kg tramadol hydrochloride (Tramadol Hydrochloride, 50 mg/mL, União Química Farmacêutica Nacional S/A, Brazil), intramuscularly every 12 h.

Statistical analysis

The normal distribution and homoscedasticity of the data were estimated using Shapiro–Wilk and Barlett tests, respectively. Data without normal distribution were log-transformed. The non-normal data after the log transformation were analyzed using a non-parametric test. The SDMA, K^+, and HCO_3 between CG and OG variables were compared using an unpaired t-test. The SDMA variable in the OG among the times was compared using repeated measures over time (Mauchly's Sphericity Test). The comparisons were adjusted using a Tukey's test. The results are presented as mean ± SD of the mean.

A Mann–Whitney test was performed to compare the CG and OG within each time for the sCr, urea, UPC, and USG levels. In addition, a Wilcoxon test was used to compare the times within the OG. The results are presented as median (minimum and maximum) values.

The correlation between the SDMA and sCr, urea, K^+, HCO_3^-, time of obstruction, and clinical score at M0 was evaluated using Pearson's or Spearman's correlation analysis. The correlation coefficients were defined as strong ($r > 0.6$), moderate ($0.6 \leq r \geq 0.4$) or weak ($r < 0.4$) [18]. Kappa concordance analysis was used to verify the concordance of the results of diagnostic tests at M12, M24, and M48. The Kappa coefficients were estimated per point and the interval with 95% confidence and were considered significant when the zero value was not included in the interval. The results for the clinical scores are presented as frequencies. The statistical analysis was performed using GraphPad Prism Version 8 software (GraphPad Software Inc., USA) and the SAS statistical suite, version 9.1 (SAS Institute, Inc., USA). The differences were statistically significant for $p < 0.05$.

RESULTS

The data obtained from 13 cats in the CG and 17 cats in the OG were analyzed. The mean age and body weight of the CG cats were 3.5 years (1.0–8.5 years) and 3.5 kg (2.3–5.0 kg). In the OG, mean age and body weight were 4.1 years (0.5–12.0 years) and 3.8 kg (2.0–4.2 kg), respectively. Among cats in both CG and OG, the breeds were represented by Domestic Short, Medium, and Long Hair (n = 25; 83.33%), Persian (n = 3; 10%), Siamese (n = 1; 3.33%), and Angora (n = 1; 3.33%). Cats in the OG were evaluated according to the clinical condition score assessment, upon which higher scores represented a worsened clinical condition. Within the OG, 29.4% (n = 5), 23.5% (n = 4), 17.6% (n = 3), and 11.8% (n = 2) of the cats scored 7, 2, 1, and 3, respectively. Scores of 6, 9, and 10 were assessed in one cat each.

Table 1 lists the mean ± SD and range for variables, such as SDMA, sCr, urea, HCO_3, K^+, UPC, and USG of each group. At M48, half of the cats in the OG revealed SDMA values above the reference interval. A similar result was also found in the evaluation of creatinine at this time, with levels above the reference range in 41.2% (n = 7) of the animals.

Table 1. SDMA, sCr, urea, bicarbonate (HCO_3^-), potassium (K^+), UPC ratio, and USG values of the cats in the OG and CG

Variables	Group	Time	No.	Mean ± SD	Minimum and maximum	Reference interval	% Cats below reference interval	% Cats above the reference interval
SDMA (μg/dL)	OG	M0	17	48.0 ± 7.3	8–100	0–14	0	82.4
		M12	16	37.9 ± 7.0	6–88		0	75.0
		M24	17	29.7 ± 6.1	7–63		0	58.8
		M48	16	18.3 ± 3.3	7–52		0	50.0
	CG	M0	13	8.2 ± 0.5	6–12		0	0
sCr (mg/dL)	OG	M0	16	9.4 ± 1.5	0.7–18.6	0.5–1.5	0	87.5
		M12	17	6.0 ± 1.2	0.9–15.5		0	70.6
		M24	17	5.3 ± 1.3	0.9–15.5		0	58.8
		M48	17	3.2 ± 1.1	0.8–16.6		0	41.2
	CG	M0	13	1.3 ± 0.1	0.8–1.5		0	0
Urea (mg/dL)	OG	M0	17	284.7 ± 35.4	42.2–467.9	42–64	0	82.4
		M12	17	223.7 ± 31.7	36.1–404.4		5.9	82.4
		M24	17	219.2 ± 37.8	37.2–489.3		5.9	76.5
		M48	17	164.2 ± 38.3	35.6–554.2		5.9	64.7
	CG	M0	13	51.2 ± 2.0	44.7–63.1		0	0
HCO_3^- (mmol/L)	OG	M0	13	16.8 ± 1.2	9.2–24.7	17–23	61.5	7.7
		M12	15	18.6 ± 0.9	14.2–24.5		33.3	6.7
		M24	15	18.2 ± 0.8	13.0–24.7		33.3	6.7
		M48	15	18.1 ± 0.8	11.7–22.8		26.7	0
	CG	M0	10	18.5 ± 0.4	16.9–20.1		10.0	0
K^+ (mEq/L)	OG	M0	16	7.1 ± 0.6	3.1–11.3	3.7–5.4	12.5	81.3
		M12	16	5.7 ± 0.5	3.0–9.7		6.3	43.8
		M24	15	5.2 ± 0.4	3.4–8.2		13.3	33.3
		M48	17	5.1 ± 0.4	2.4–9.0		5.9	29.4
	CG	M0	11	4.4 ± 0.1	4.0–4.7		0	0
UPC	OG	M0	14	1.6 ± 0.2	0.3–2.8	0–0.4	0	92.9
		M12	16	1.7 ± 0.3	0.2–4.3		0	81.3
		M24	16	1.65 ± 0.3	0.2–5.3		0	81.3
		M48	17	1.3 ± 0.2	0.2–3.2		0	88.2
	CG	M0	10	0.1 ± 0.1	0.1–0.2		0	0
USG[a]	OG	M0	17	1.033 ± 3.6	1.012–1.055	1.035–1.060	64.7	0
		M12	16	1.032 ± 3.5	1.012–1.055		75.0	0
		M24	16	1.027 ± 3.1	1.016–1.050		68.8	0
		M48	16	1.028 ± 3.1	1.016–1.055		62.5	0
	CG	M0	12	1.055 ± 0	1.055		0	0

SDMA, symmetric dimethylarginine; sCr, serum creatinine; UPC, urine protein-creatinine ratio; USG, urine specific gravity; OG, obstruction group; CG, control group.
[a]Values > 1.050 are not specified by the urinalysis reagent test; therefore, the values above this threshold are represented by 1.055.

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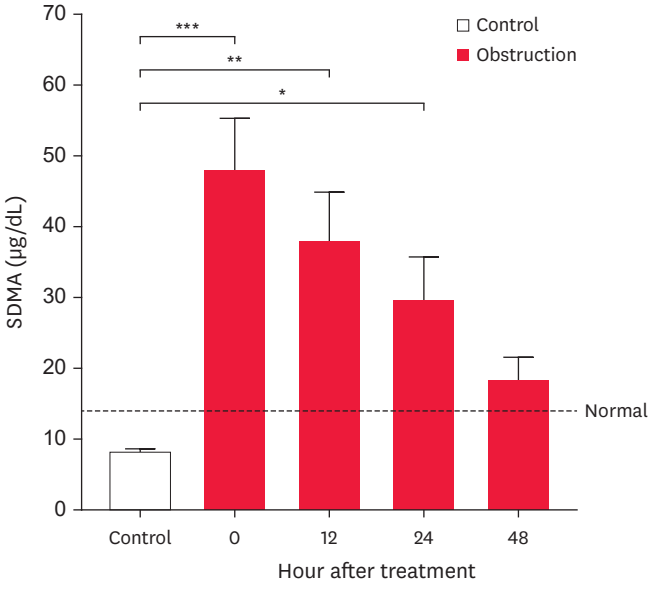

Fig. 1. SDMA values comparison between CG and OG at M0, M12, M24, and M48.
SDMA, symmetric dimethylarginine; CG, control group; OG, obstruction group.
$^{*}p < 0.05$, $^{**}p < 0.01$ and $^{***}p < 0.001$.

There was a difference in the SDMA values between the OG and CG at M0, M12, and M24 (**Fig. 1**). Although there was no difference between M0 in the CG and M48 in the OG ($p > 0.06$), the SDMA value in the OG was higher than 14 μg/dL, which has clinical relevance [15]. The mean SDMA values decreased with time in the OG, but they were still above the reference interval.

The mean value for urea was higher in the OG at M0, M12, and M24 than in the CG. In addition, the mean value for sCr was higher in OG only at M0 and M12. Moreover, similar to SDMA results, the mean values for both biomarkers were above the reference interval at M48. Unlike the others, however, there was a significant decrease in the mean creatinine concentration between M0 and M48 in OG. (**Fig. 2A and B**). The potassium values were higher in the OG at M0 than in the CG (**Fig. 2C**). No difference in HCO_3^- was observed between OG and CG at any time (**Fig. 2D**), but the mean value was below the reference interval at M0 for OG, indicating clinical significance.

Between OG and CG, significantly higher UPC values were observed in the OG at all times ($p < 0.001$) (**Fig. 3A**). Similarly, USG showed significantly lower values in the OG than in the CG at all times (**Fig. 3B**).

SDMA showed a strong positive correlation with sCr, urea, and K^+ but no correlation with bicarbonate. The clinical score and time of obstruction showed a strong positive correlation with SDMA at M0 (**Table 2**).

The clinical score and time of obstruction also showed strong positive correlation with sCr ($r = 0.75$, $p < 0.0001$) ($r = 0.62$, $p = 0.009$), urea ($r = 0.81$, $p < 0.0001$) ($r = 0.87$, $p < 0.0001$), and moderate positive correlation with K^+ ($r = 0.53$, $p < 0.0045$) ($r = 0.86$, $p < 0.0001$), respectively.

SDMA showed Kappa concordance with sCr and urea at M24 (**Table 3**).

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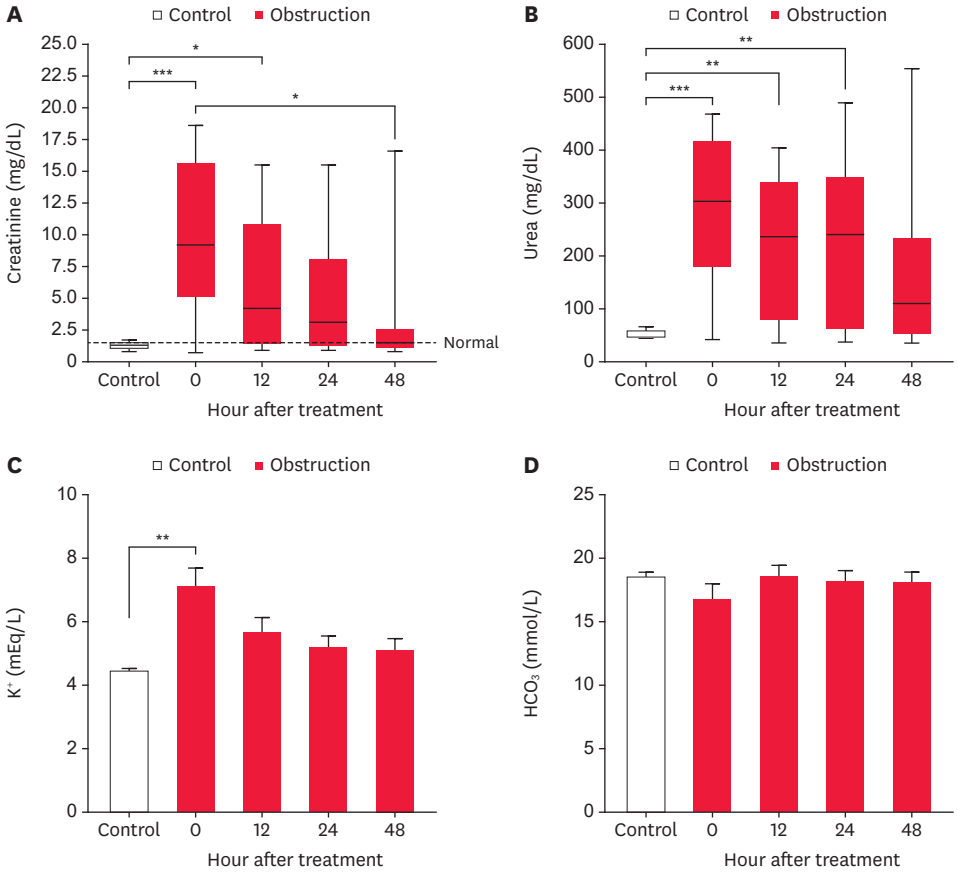

Fig. 2. Comparison between CG and OG for sCr (A), urea (B), K^+ (C), and HCO_3^- (D) values at all times. The horizontal lines within the bars refer to the median values.
CG, control group; OG, obstruction group; sCr, serum creatinine.
*$p < 0.05$, **$p < 0.01$ and ***$p < 0.001$.

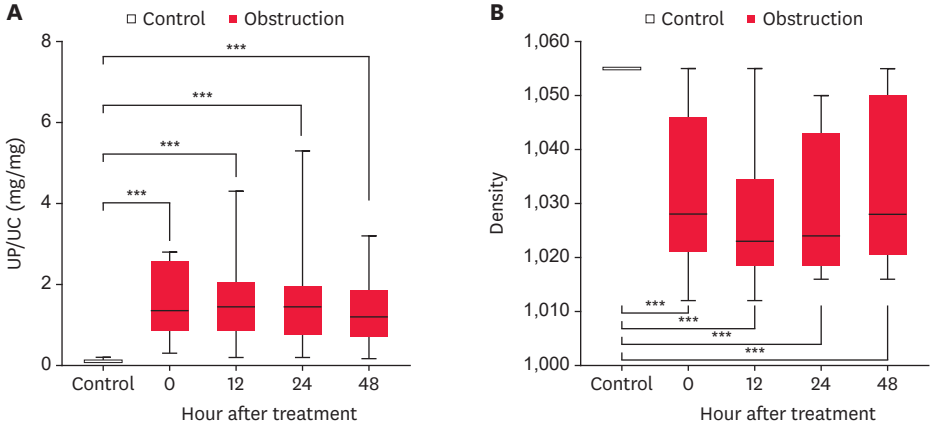

Fig. 3. Comparison between OG and CG at all times for mean UPC (A) and USG (B) values. The horizontal lines within the bars refer to the median values.
CG, control group; OG, obstruction group; UPC, urinary protein-to-creatinine; USG, urine specific gravity.
***$p < 0.001$.

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Table 2. Correlation between the SDMA and sCr, urea, potassium (K^+), bicarbonate (HCO_3), clinical score, and obstruction time at M0

Parameters	Spearman (rs)	Pearson ®	*p* value*	95% CI
SDMA vs. sCr	0.81		< 0.0001	0.71–0.87
SDMA vs. urea	0.86		< 0.0001	0.78–0.91
SDMA vs. K^+		0.78	< 0.0001	0.67–0.86
SDMA vs. HCO_3		−0.24	0.054	−0.46–0.01
SDMA vs. obstruction time		0.75	< 0.001	0.42–0.90
SDMA vs. clinical score		0.76	< 0.001	0.43–0.91
K vs. urea	0.38		0.079	−0.06–0.69
K^+ vs. sCr	0.50		0.016	0.09–0.77
K^+ vs. HCO_3		−0.38	0.075	−0.69–0.04
K^+ vs. obstruction time	0.86		< 0.0001	0.63–0.95
K^+ vs. clinical score	0.53		< 0.0045	0.18–0.77
HCO_3^- vs. sCr	0.12		0.581	−0.32–0.52
HCO_3^- vs. urea	0		> 0.999	−0.43–0.43
HCO_3^- vs. obstruction time		0.14	0.581	−0.36–0.58
sCr vs. urea	0.66		< 0.0001	0.38–0.83
sCr vs. obstruction time		0.62	0.009	0.18–0.85
sCr vs. clinical score	0.75		< 0.0001	0.52–0.88
Urea vs. obstruction time		0.87	< 0.0001	0.67–0.95
Urea vs. clinical score	0.81		< 0.0001	0.63–0.90

SDMA, symmetric dimethylarginine; sCr, serum creatinine; CI, confidence interval.
*Statistical difference for $p < 0.05$.

Table 3. Kappa concordance analysis results between the SDMA, sCr, urea, and potassium (K^+) levels

Parameters	Level	SDMA		Kappa	95% CI
		Normal	Increased		
M12					
sCr	Normal	4.0	0	0.3	0.51–1.50
	Increased	0	12.0		
Urea	Normal	2.0	0	0.2	0.15–1.05
	Increased	2.0	12.0		
K^+	Normal	3.0	5.0	0.3	−0.23–0.76
	Increased	0	7.0		
M24					
sCr	Normal	6.0	1.0	0.8	0.27–0.97
	Increased	1.0	9.0		
Urea	Normal	4.0	0	0.6	0.13–0.92
	Increased	3.0	10.0		
K^+	Normal	6.0	4.0	0.2	0.06–0.93
	Increased	0	5.0		
M48					
sCr	Normal	8.0	4.0	0.2	0.07–0.92
	Increased	0	4.0		
Urea	Normal	6.0	0	0.2	0.27–1.22
	Increased	2.0	8.0		
K^+	Normal	8.0	5.0	0.2	−0.01–0.75
	Increased	0	3.0		

SDMA, symmetric dimethylarginine; sCr, serum creatinine; CI, confidence interval.

DISCUSSION

This is the first study to correlate the serum SDMA values with urea, sCr, HCO_3^-, K^+, clinical score, and time of obstruction in feline male patients with UO. As a biomarker, SDMA is more sensitive than sCr, being less influenced by extrarenal factors [4,18]. In the present study, a slightly higher percentage of cats maintained serum SDMA levels above the reference interval at M48 compared to sCr at the same time. This finding supports the idea that SDMA

may be a more sensitive biomarker of renal impairment. Studies have indicated that elevated SDMA levels can reflect the compromise of approximately 40% of nephron functionality, whereas elevated sCr would only be present with a compromise of approximately 75% of the renal functional mass [4]. Therefore, based on SDMA, at least one animal in this study would be identified as having some degree of renal functional loss after 48 h of UO, but this level is still below 75% because the creatinine values would remain within the reference interval.

In the present study, the correlation between SDMA and time of obstruction showed significance because higher SDMA values were positively correlated with a longer time of UO. On the other hand, a significant correlation between SDMA and time of obstruction was observed. Higher SDMA values were positively correlated with longer obstruction periods. This trend was also evident for sCr, urea, and potassium. While these findings were expected, they support the literature because previous studies had not yet demonstrated such correlations. In particular, Wilson et al. [11] reported considerably lower mean SDMA and sCr values before unblocking compared to the values presented here. Nevertheless, no data on the time of obstruction are available, which may have been pivotal in explaining the discrepancies in the results. Thus, prolonged UO leads to more severe renal involvement, resulting in a greater accumulation of compounds that should be excreted in the urine. Supporting these findings, the positive correlation between SDMA and the clinical score demonstrates that the time of obstruction reflects the severity of clinical presentation at emergency care. The creatinine, urea, and potassium values were positively correlated with the severity of presentation. Therefore, a longer time of obstruction may result in kidney damage and irreversible lesions, which can be monitored at some level through imaging alterations, renal biomarkers, and histopathology, which were not performed in this study [19,20]. In obstructive FLUTD, the clinical signs may vary considerably depending on the degree of obstruction, time of obstruction, and metabolic alterations [21]. In the present study, more severe clinical and laboratory alterations contributed to the higher clinical scores and significant electrolyte imbalance, so cats with more severe clinical signs were hospitalized and followed up until stabilization.

The strong positive correlation between SDMA and sCr was expected because the values of both biomarkers increase as the GFR decreases [5-6,11]. The urinary flow obstruction leads to intrinsic and extrinsic injuries caused by post-renal azotemia, which may decrease the GFR and impair the renal function [22]. Previous studies revealed positive correlations between SDMA and sCr in mice [23], dogs [5,8], and humans [24]. In cats, SDMA and sCr showed a strong correlation in CKD [4,25,26]. Moreover, a strong correlation was found between both biomarkers and GFR [8,25,27]. A recent study assessed the serum SDMA and sCr in obstructed cats, showing a significant reduction in both biomarkers after urethral catheterization, suggesting that the pre-clearance values cannot predict the post-clearance renal function [11]. Despite the strong correlation between SDMA, urea, and sCr, the degree of renal function impairment could not be determined, and the assessment of GFR is still the gold standard for this purpose.

Similarly, a strong correlation between SDMA and urea was expected. In cats with UO, azotemia was the most common serum abnormality caused by renal function impairment [2]. On the other hand, the strong correlation between SDMA and potassium was attributed to the reduction of the GFR that disables potassium excretion by the kidneys [21,24]. Hyperkalemia may be significant in cases of UO because of metabolic acidosis and tissue catabolism [21]. As previously suggested, the severity of electrolyte abnormalities aggravates

the patient's clinical status [28]. The present study observed a moderate positive correlation between the clinical score and hyperkalemia. In addition, a visual analysis revealed a poorer clinical score in the longer-time obstructed cats, with consequently higher potassium levels.

A UO may lead to metabolic acidosis caused by the retention of metabolic acids, HCO_3^- consumption to stabilize the plasma pH, production of lactate associated with hypovolemia, hypoxia, and reduction in HCO_3^- tubular conservation during the post-obstructive period [21,28]. Therefore, the lack of correlation between the HCO_3^- and SDMA values may be explained, in part, by the distinct mechanisms through which these two biomarkers change during renal dysfunction. This is because SDMA is associated with a decline in GFR [4], while HCO_3^- follows the tubular involvement pathways, as mentioned earlier. In the present study, although no significant differences in HCO_3 levels were observed compared to CG, the results at M0 in the OG were clinically relevant. This is because the mean values of HCO_3^- at this stage fell below the reference interval. This presentation can be justified by the functional renal impairment at the time of animal inclusion and its impact on the body's acid-base balance [21, 28]. Moreover, HCO_3^- reduction was not verified, possibly due to the institution of Ringer Lactate Solution in the clinical treatment of the cats. A previous study with male cats induced to UO demonstrated that animals treated with Ringer Lactate Solution showed higher HCO_3^- values over 48 hours post-unblocking than those treated with Physiologic Saline Solution [29]. Another hypothesis is the time between the identification of UO and unblocking. Longer periods of obstruction culminate with more severe metabolic changes, such as lower HCO_3^- levels [30].

A UPC evaluation is indicated to determine the magnitude and significance of proteinuria. Cats with obstructive FLUTD often present with post-renal AKI [21], inflammation, and hematuria [31], making a proteinuria assessment unreliable. In the present study, proteinuria had no clinical application and would be useful only to investigate possible further irreversible damages caused by UO during serial evaluations. Considering the results of USG, although significant, it should be monitored for a longer time than that considered in this study. The hydration status, kidney, endocrine, and hepatic function may interfere with the USG values [32]. Therefore, the consequences of UO may be considered, and the values obtained after unblocking can be used to monitor these patients further. Nevertheless, electrolyte imbalances may account for more diluted urine [33], in conjunction with the possibility of post-obstructive diuresis [34], to which the animals in this study were subjected.

Nevertheless, the considerably low number of cats in each group, the non-measurement of GFR, and the inability to follow the cats' clinical evolution longer than the study period due to owners' lack of commitment are limitations of this study.

In conclusion, SDMA is correlated with sCr in obstructed cats, and there is agreement between both values after 24 h of unblocking management. Approximately 9% more cats continued to exhibit elevated SDMA levels after 48 h of management compared to sCr, suggesting a slightly lower sensitivity of the latter biomarker. On the other hand, this does not exclude the possibility of congruent values between the two biomarkers after a longer evaluation period. Furthermore, a longer obstruction time is associated with a more severe clinical presentation and a higher degree of laboratory abnormalities, with SDMA, sCr, urea, and potassium being correlated with the patient's clinical score.

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SUPPLEMENTARY MATERIALS

Supplementary Table 1

BCS assessment of the cats with obstructive FLUTD

Supplementary Table 2

Score assessment for clinical evaluation of male cats with urethral obstruction prior to initial clinical management

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