Original Article

jfms Journal of Feline Medicine and Surgery

Evaluating feline lower urinary tract disease: Doppler ultrasound of the kidneys

Journal of Feline Medicine and Surgery
1–9

DOI: 10.1177/1098612X221145477
journals.sagepub.com/home/jfm

This paper was handled and processed by the American Editorial Office (AAFP) for publication in *JFMS*

SAGE

Gabriela CL Evangelista, Lorraine RSM Dornelas, Cristiane CV Cintra, Fabrício L Valente, Evandro S Favarato, Leandro A da Fonseca and Emily CC Reis

Abstract

Objectives Ultrasonography is used in the evaluation of urinary disorders, and the resistivity index (RI) and pulsatility index (PI) have been successfully used to detect early hemodynamic changes in the course of kidney diseases in humans and dogs. The aim of this study was to investigate RI and PI in cats with feline lower urinary tract disease (FLUTD).

Methods Twenty-nine client-owned cats were selected and divided into a control group (CG; n = 10), a group of animals with obstructive FLUTD (OG; n = 11) and non-obstructive FLUTD (nOG; n = 8). Clinical, laboratory and ultrasound evaluations were performed in all cats.

Results RI and PI values for cats in the CG were below the upper limit of normal suggested in other studies, while cats with FLUTD showed significantly higher values in the assessment of RI ($P = 0.027$ and $P = 0.034$, respectively) and PI ($P = 0.044$ and $P = 0.048$, respectively) of the right and left kidneys.

Conclusions and relevance Alteration in renal blood flow was observed in cats with lower urinary tract disorders, even in the nOG group. To the best of our knowledge, this is the first report of renal blood flow changes related to non-obstructive FLUTD.

Keywords: Resistivity index; pulsatility index; FLUTD; renal; resistive index; vascular resistance

Accepted: 18 November 2022

Introduction

Feline lower urinary tract disease (FLUTD) refers to conditions that affect the bladder and urethra of cats, and result in clinical signs such as dysuria, pollakiuria, urinating in inappropriate locations and hematuria.[1–3] Several underlying etiologies are related to FLUTD, including obstruction of the urinary tract; when no specific cause is found, these patients are diagnosed with feline interstitial cystitis (FIC).[4–7] In the early 1990s, FIC was reported to be similar to human interstitial cystitis (IC)/painful bladder syndrome (PBS), a clinical syndrome of unknown etiology that causes pelvic pain characterized by recurrent urinary frequency and urgency, similar to that reported in cats.[4,6,8–11] Under the One Health concept, cats were suggested as a natural model for IC/PBS and thus studies on the pathophysiology and modalities of diagnosis and treatment could be useful for both.[4,5,9]

Ultrasonography is the modality of choice for imaging the urinary tract.[12] The association of conventional ultrasonography with Doppler mode allows for the evaluation and detection of hemodynamic changes that can affect renal function.[13,14] Resistivity index (RI) and pulsatility index (PI), calculated from the systolic and diastolic velocity values obtained by the wave spectrum, represent the resistance of the vascular wall to blood flow during organ perfusion.[15,16] These indexes have been used in the evaluation of renal perfusion in humans[17–19] and dogs,[20–22] as well as horses[23,24] and cats.[22,25] Some studies

Department of Veterinary Medicine, Federal University of Viçosa, Viçosa, Brazil

Corresponding author:
Emily CC Reis DVM, PhD, Department of Veterinary Medicine, Federal University of Viçosa, Avenue Peter Henry Rolfs, s/n, University Campus, Viçosa, Minas Gerais 36570-900, Brazil
Email: emily.carlo@ufv.br

have evaluated the upper normal limit of renal RI and PI in non-sedated cats.[16,22,25–36] For RI, values of 0.64,[25] 0.68,[33] 0.69,[30] 0.70,[16,26] 0.71[36] and 0.72[31] were suggested; for PI, the suggested values were 1.06,[26] 1.23[31] and 1.29.[16] As yet, there is no consensus on normal RI and PI values, or values for kidney diseases in cats.[37]

Evaluation of vascular resistance by means of Doppler ultrasonography has been widely studied in recent years in several clinical conditions in human and veterinary medicine.[15,38] However, to date, there have been no reports of renal Doppler ultrasound assessment in cats with FLUTD. Thus, we aimed to compare the RI and PI in cats with FLUTD and healthy cats. Our main hypotheses were that (1) RI and PI would be higher in cats with FLUTD than in healthy cats; and (2) that cats with obstructive FLUTD would have higher RI and PI values than cats with FLUTD without obstruction.

Materials and methods

Case selection

From April 2019 to March 2020, adult pet cats were selected from the routine care of a veterinary teaching hospital (ethics committee approval 07/2019). All cats were client-owned and there was no restriction regarding sex or breed. Inclusion criteria for the control group (CG) were cats taken to the hospital for a check-up or neutering and that were considered to be healthy, without abnormalities on physical and laboratory examination, and without a prior history of or clinical signs associated with FLUTD. The study group included cats that presented with clinical signs of FLUTD, including pollakiuria (increased frequency of urination), hematuria, periuria (inappropriate urination), dysuria (difficulty or painful urination), stranguria and/or obstruction of the outflow of urine. This study group was subdivided into obstructive (OG) and non-obstructive (nOG) FLUTD, based on clinical evaluation. Cats with nephrolithiasis, ureterolithiasis, polycystic kidney disease or other ultrasonographic findings of chronic kidney disease (ie, irregular contour, decrease or absence of corticomedullary differentiation, and decreased renal volume) were excluded from both groups.

Hematological evaluation, measurement of blood urea nitrogen (BUN) and creatinine, electrolyte concentrations (phosphorus, potassium, sodium), complete urinalysis and abdominal ultrasound were performed at admission. Blood samples were obtained by puncturing the cephalic or jugular veins; urine samples were obtained by cystocentesis, spontaneous urination or via urethral catheterization, at the clinicians' discretion. Urinalysis included dipstick analysis, microscopic urine sediment evaluation and measurement of urine specific gravity (USG) using a portable refractometer (Uricon; Atago). When evaluating the urine sediment, hematuria was defined as the presence of >5 red blood cells/high-power field (HPF), pyuria was defined as the presence of >5 white blood cells (WBCs)/HPF and bacteriuria was defined as positive or negative for presence/field. These evaluations were performed by a single clinical pathologist.

Ultrasound evaluation

After abdominal fur had been clipped, CG and nOG cats were left in the examination room for a period of 10–15 mins for environmental adaptation and to reduce their stress. Cats with FLUTD were stabilized (eg, fluid therapy, analgesics, decompressive cystocentesis or placement of the urinary catheter) prior to performing the abdominal ultrasound. All ultrasonographic examinations (Mylab 30 [Esaote], equipped with an 8.0 MHz microconvex transducer) were performed by the same investigator (GCLE). Cats were manually restrained, without sedation, in dorsal or lateral recumbency, according to the animal's temperament.

Initially, a complete scan of the abdominal cavity was performed to exclude other anatomic conditions and then the urinary tract was assessed. Criteria used in the evaluation were similar to those described by Nevins et al.[39] For evaluation of the kidneys, renal length, dilation of the renal pelvis, echogenicity of the renal cortex relative to the spleen, echogenicity of the medullary relative to the renal cortex, corticomedullary definition and the presence of retroperitoneal fluid were recorded. For evaluation of the bladder, wall thickening, bladder repletion, the presence of cystolithiasis, echogenicity of the urine, sediment and the presence of peritoneal fluid close to the bladder were assessed.

After the evaluation of morphological aspects, renal vascular architecture was evaluated. Color Doppler was used concomitantly with the B-mode image for detecting intrarenal vessels (Figure 1). With the image of the

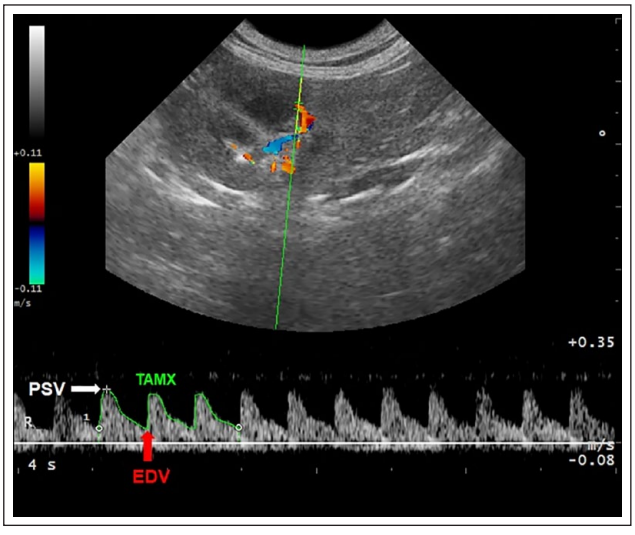

Figure 1 Measurement of the resistivity index (RI) and pulsatility index (PI) in an intrarenal artery. Doppler waveform showing delimitation for peak systolic velocity (PSV), end-diastolic velocity (EDV) and time average maximum velocity (TAMX)

kidney preferably in the dorsal plane, pulsed Doppler was activated, and the sample volume was adjusted by measuring 1–2 mm and positioned in the center of a chosen vessel. The Doppler angle did not exceed 40°, the wall filter was set at 50 Hz, gain-adjusted to 58% and the pulse repetition frequency was kept as low as possible to avoid aliasing (1.4–2.8 kHz). Doppler spectrum comprised a minimum of three similar successive waveforms obtained for arcuate or interlobar arteries. The mean RI and PI for each kidney was determined by averaging waveforms in distinct regions within each kidney (cranial, middle and caudal). Indices were calculated using the software on the ultrasound device after manual delimitation using the equipment's built-in calipers: peak systolic velocity (PSV), end-diastolic velocity (EDV) and time average maximum velocity (TAMX). RI and PI were calculated automatically by the equipment using the following formulas:

- RI = (PSV – EDV)/PSV
- PI = (PSV – EDV)/TAMX

Data analysis

Quantitative measurement of B-mode images for echogenicity was assessed using a grayscale histogram using specific software (ImageJ; National Institutes of Health). Areas (2 mm^2) were selected in the renal cortex, liver and splenic parenchyma, and the average number of pixels was used for comparison.

Results obtained from laboratory evaluation (hematocrit, total plasma protein, leukocytes and serum levels of urea, creatinine, phosphorus, potassium and sodium) and from urinalysis (USG, pH, protein, erythrocytes, leukocytes and bacteria) were analyzed for differences between groups, along with the parameters obtained from ultrasound evaluation (RI, PI, renal length, renal pelvis measurement, echogenicity of the renal cortex relative to spleen, echogenicity of the medullary relative to renal cortex, corticomedullary definition, bladder wall measurement, bladder repletion, presence of cystolithiasis, echogenicity of the urine, sediment dependent portion and the presence of peritoneal fluid).

Shapiro–Wilk and Brown–Forsythe tests were used to verify the normality and homogeneity of variances, respectively. Comparison between groups was carried out using a one-way ANOVA. Tukey's test was performed when the ANOVA premises were fulfilled. Otherwise, the Kruskal–Wallis test with Dunn's post-hoc test was applied. Spearman's correlation coefficient was used to investigate the correlations between the RI and PI, and the different parameters evaluated. Statistical analyses were performed using SigmaPlot 11.0. For all tests, a level of 5% was considered to be significant.

Results

Selected animals

Initially, 33 cats were considered for inclusion. Four cats were excluded for uncooperative behavior during the examination, resulting in 29 cats being included. Clinical data are summarized in Table 1.

Laboratory evaluation

Blood samples were collected from all cats and urinalysis was only performed on 21 animals due to a small amount of urine in the bladder at the time of collection. Results of the hemogram, biochemistry and urinalysis are summarized in Table 2.

WBC levels were higher in OG cats than in CG and nOG cats, while BUN, creatinine and phosphorus were higher in OG cats than in CG cats. Regarding urinalysis, glucose, ketone bodies, bilirubin and cylinders were absent, while rare transitional epithelial cells were found

Table 1 Clinical data summary

	CG (n = 10)	nOG (n = 8)*	OG (n = 11)	*P* value
Sex	6 CM, 4 SF	3 CM, 5 SF	6 CM, 4 M, 1 F	0.054
Breed	6 DSH, 3 DLH, 1 Persian	7 DSH, 1 DLH	10 DSH, 1 DLH	0.971
Age (years)	5.3 ± 3.3	3.0 ± 2.0	3.6 ± 2.46	0.200
BW (kg)	4.95 ± 0.57	4.4 ± 0.96	4.05 ± 0.93	0.150
HR (bpm)	182 ± 28	172 ± 12	167 ± 32	0.416
RI right kidney	0.63 (0.60–0.71)	0.78 (0.61–0.81)	0.72 (0.58–0.92)	0.027†
RI left kidney	0.65 (0.54–0.68)	0.73 (0.61–0.75)	0.69 (0.54–0.93)	0.034†
PI right kidney	1.03 (0.94–1.43)	1.51 (1.04–2.26)	1.36 (0.86–3.85)	0.044†
PI left kidney	1.03 (0.88–1.23)	1.35 (0.97–1.61)	1.35 (0.82–3.20)	0.048†

Data are presented as n or mean ± SD
*Five with feline interstitial cystitis and three with cystolithiasis
†Significant difference by Kruskal–Wallis test ($P < 0.05$) followed by the Dunn's test between the groups.
CG = control group; nOG = non-obstructive feline lower urinary tract disease group; OG = obstructive feline lower urinary tract disease group; CM = castrated male; SF = spayed female; M = entire male; F = entire female; DSH = domestic shorthair; DLH = domestic longhair; BW = body weight; HR = heart rate; bpm = beats/min; RI = resistivity index; PI = pulsatility index

Table 2 Laboratory results

Parameter	CG	nOG	OG	Reference interval	*P* value
Hemogram					
HCT (%)*	33.25 ± 3.57	34.65 ± 4.73	35.26 ± 3.82	25–45	0.514
WBC (cells/µl)*	7120 ± 4927†	6088 ± 2728†	17,436 ± 7757	5500–19,500	<0.001
PP (g/dl)‡	7.40 (6.85–7.8)	7.30 (7.2–7.55)	8.00 (7.4–8.2)	6.0–8.0	0.072
Biochemistry					
BUN (mg/dl)‡	50 (39.98–67.63)	63.50 (46.25–72.8)	199 (63–235.9)§	40–60	0.005
Creatinine (mg/dl)‡	1.18 (1.05–1.23)	1.20 (0.99–1.43)	8.16 (1.68–11.87)§	<1.6	0.018
Phosphorous (mg/dl)‡	4.24 (3.78–4.71)	5.12 (3.62–5.69)	10.46 (5.13–11.59)§	3.3–7.8	0.024
Potassium (mEq/l)‡	4.65 (4.21–5.14)	4.75 (4.19–5.46)	5.52 (4.90–7.39)	3.7–5.4	0.048
Sodium (mEq/l)‡	152.65 (149.3–159.7)	154.40 (150.35–164)	146.50 (144.9–155.7)	146–160	0.113
Urinalysis					
USG‡	⩾1.050	1.040	1.025§	1.035–1.060	<0.001
pH*	7.1 ± 1.2	7.8 ± 1.5	6.6 ± 0.7	5.0–7.0	0.181
Protein‡	Positive (2+)	Positive (2+)	Positive (3+ or more)	Negative	0.301
Erythrocytes‡	0–5/field	>5/field	>5/field	0 – 5/field	0.002
Leukocytes‡	<5/field	>5/field	>5/field§	0 – 5/field	0.001
Bacteria‡	Negative	Negative	Positive§	Negative	0.017

*Variables with normal distribution: ANOVA (mean)
†Significantly different from OG ($P<0.05$), one-way ANOVA followed by Tukey's test
‡Variables without a normal distribution: Kruskal–Wallis test (median)
§Significantly different from CG ($P<0.05$), Kruskal–Wallis followed by Dunn's test between the groups
CG = control group; nOG = non-obstructive feline lower urinary tract disease; OG = obstructive feline lower urinary tract disease; HCT = hematocrit; WBC = white blood cells; PP = plasma protein; BUN = blood urea nitrogen; USG = urine specific gravity

in all samples. Crystals (struvite, amorphous phosphate, amorphous urate) were identified in small amounts in some samples. USG was higher in cats in the CG, while leukocytes in urine and bacteria in urine were higher in cats in the OG. Although the comparison of potassium serum levels and erythrocytes in urine showed a significant difference, Dunn's test did not determine where the difference occurred.

B-mode ultrasound

B-mode ultrasound was performed on all animals (Table 3). Bladder wall thickness in animals in the nOG and OG was significantly greater than in the CG. In the OG, all cats showed severe bladder repletion, therefore the bladder was significantly larger in the OG than in the CG and nOG. Urine echogenicity was greater in cats in the OG than those in the CG and nOG, and the sediment-dependent portion was greater in OG cats than in nOG cats. Other abnormalities identified were the presence of peritoneal fluid in cats in the OG and cystolithiasis in cats in the nOG. Renal length >4.5 cm was identified in eight cats in the OG, both in the right and left kidneys. Dilation of the renal pelvis was identified in seven cats in the OG. Renal cortex echogenicity was predominantly isoechogenic or hyperechogenic in relation to the spleen in both groups. An increase in medullary pyramid echogenicity was significantly larger in cats in the OG compared with those in the CG and nOG, and a greater loss of corticomedullary definition was observed in cats in the OG than in those in the CG.

Doppler ultrasound

It was not possible to obtain an adequate wave spectrum for the right kidney and left kidney, respectively, in two cats in the CG. In total, RI and PI measurements were performed in 56 kidney units. All data obtained from this study are available in Table 1 in the supplementary material.

The mean ± SD values for the RI and PI in cats in the CG were, respectively, 0.64 ± 0.04 and 1.09 ± 0.16 for the right kidney and 0.64 ± 0.04 and 1.06 ± 0.12 for the left. For nOG cats, the RI and PI were, respectively, 0.75 ± 0.07 and 1.53 ± 0.38 for the right kidney and 0.71 ± 0.05 and 1.32 ± 0.20 for the left. In the OG cats, RI and PI were, respectively, 0.72 ± 0.10 and 1.52 ± 0.83 for the right kidney and 0.71 ± 0.11 and 1.46 ± 0.66 for the left. Cats in the CG had RI and PI values below the upper limit of normal suggested by other studies, while cats in the nOG and OG had RI and PI values above these limits (Table 1 and Figure 2). For right kidneys, the RI and PI were significantly higher in cats in the nOG compared with cats in the CG. Although significant in the Kruskal–Wallis test, the multiple comparison (Dunn's test) did not determine where the difference in RI and PI between the groups occurred (Figure 2). Positive correlation was observed for PI and RI ($r = 0.949$; $P < 0.001$) and for PI and creatinine ($r = 0.371$; $P = 0.047$).

Table 3 Characterization of the sample with respect to B-mode ultrasound changes for the control (CG), non-obstructive feline lower urinary tract disease (nOG) and obstructive feline lower urinary tract disease (OG) groups

Parameter	CG (n = 10)	nOG (n = 8)	OG (n = 11)	*P* value
Bladder				
Bladder wall thickness (cm)*	0.12 ± 0.05	0.26 ± 0.11†	0.19 ± 0.06†	0.002
Repletion*				<0.001
Low	4	8	–	
Moderate	6	–	–	
Severe	–	–	11†	
Urine echogenicity*				<0.001
Absence of content	–	5	–	
Anechoic to slightly echogenic	10	2	1	
Moderately echogenic	–	–	4	
Severely echogenic	–	1	6†	
Sediment-dependent portion*				0.002
Absence of content	–	5	–	
Absent	7	2	2	
Light	3	–	6	
Moderate	–	1	1	
Serious	–	–	2†	
Cystolithiasis*				0.066
Negative	10	5	11	
Positive	–	3	–	
Peritoneal fluid*				0.441
Negative	10	8	10	
Positive	–	–	1	
Kidneys				
Renal length (cm)‡				0.001
Right kidney	4.00 ± 0.15§	3.93 ± 0.23§	4.51 ± 0.47	
Left kidney	3.99 ± 0.17§	3.87 ± 0.24§	4.49 ± 0.43	
Renal pelvis (cm)*				<0.001
Right kidney	0.06 ± 0.03	0.08 ± 0.02	0.29 ± 0.14†	
Left kidney	0.09 ± 0.02	0.08 ± 0.03	0.28 ± 0.16†	
Cortical echogenicity relative to spleen*				0.189
Hypoechogenic	2	1	–	
Isoechogenic	4	5	4	
Hyperechogenic	4	2	7	
Medullary echogenicity relative to cortex renal*				<0.001
Anechoic to slightly echogenic	9	8	3	
Moderately echogenic	1	–	8†	
Corticomedullary definition*				0.003
Preserved	10	5	3	
Discrete loss	–	3	6	
Moderate loss	–	–	2†	
Retroperitoneal fluid*				0.441
Negative	10	8	10	
Positive	–	–	1	

Data are provided as n unless otherwise stated. Reference intervals: renal length = 3.0–4.5 cm; bladder wall = 0.13–0.17 cm; renal pelvis = 0.1–0.2 cm[40]

*Variables without normal distribution: Kruskal–Wallis test (median)

†Significantly different from CG ($P < 0.05$), Kruskal–Wallis followed by the Dunn's test between groups

‡Variables with normal distribution: ANOVA (mean)

§Significantly different from OG ($P < 0.05$), one-way ANOVA followed by Tukey's test

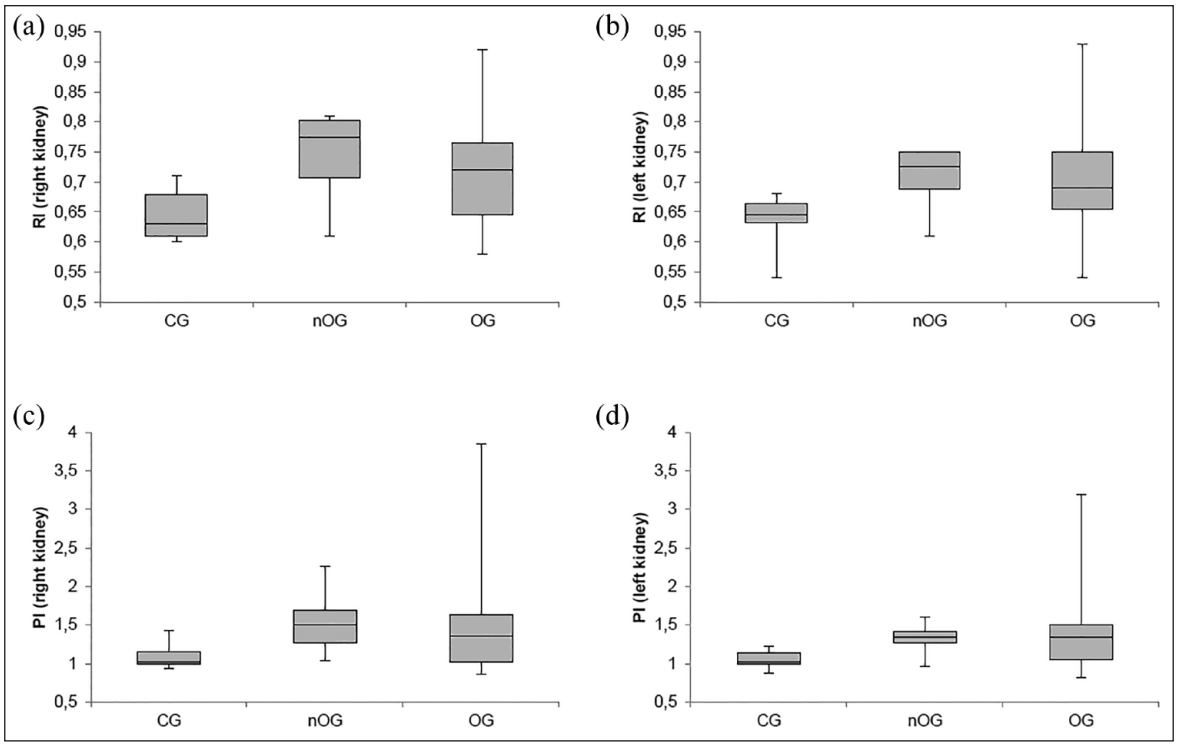

Figure 2 Boxplots of the resistivity index (RI) distribution for (a) the right and (b) the left kidney, and of the pulsatility index (PI) for (c) the right kidney and (d) left kidney for cats in the control (CG), non-obstructive feline lower urinary tract disease (nOG) and obstructive feline lower urinary tract disease (OG) groups

Discussion

The purpose of our study was to compare the RI and PI in healthy cats and cats with FLUTD, with or without urinary obstruction, in order to investigate renal blood flow using a non-invasive tool. Doppler ultrasonography, used as a complementary tool to B-mode ultrasound, allows for the non-invasive assessment of the renal hemodynamics.[38] In many cases, alteration in perfusion can be the first sign that renal function has changed.[36] Nineteen cats diagnosed with FLUTD were included in the study over a period of 11 months. Doppler ultrasound was performed on all cats, without sedation or anesthesia, using only minimal manual restraint to avoid stress to the animal. Although cats in the OG received urethral obstruction relief (decompressive cystocentesis in four cats or urethral catheter in seven), which allows for the immediate relief of pressure in the urinary tract, halting the progression of kidney damage, Doppler assessment allowed us to identify changes in renal blood flow in these cats. Doppler ultrasonography proved to be an easy-to-perform and non-invasive diagnostic technique for assessing renal blood flow, a result similar to that obtained in other studies.[25]

Changes in Doppler hemodynamic indices identified by the increased vascular resistance (decreasing diastolic flow in greater proportion to systolic flow), can be a result of pathological conditions.[18] Studies involving RI and PI for the evaluation of kidney injury in cats are rare when compared with the information available for humans and dogs.[37] In addition, literature diverges as to the normal values of these indices and their clinical and diagnostic applicability.[26,31,34,37] Current reference intervals are those proposed in a study using non-sedated clinically healthy cats.[16] In our study, RI (0.64 ± 0.04 for the right kidney; 0.64 ± 0.04 for the left kidney) and PI (1.09 ± 0.16 for the right kidney; 1.06 ± 0.12 for the left kidney) values in the CG were in the range of other studies that evaluated healthy cats, showing values lower than upper limits of normal.[22,26,31,34] Although a few studies have already investigated the upper limit of RI and PI, no consensus has been reached.[37] It is possible that a reference interval will be more relevant than a single reference value, which may be the focus of future studies that include a greater number of cats.

Among the cats evaluated in this study, 58% had urethral obstruction (11/19 cats), 26% had FIC (5/19 cats) and 16% had cystolithiasis (3/19 cats). Recent studies propose a complex interrelated etiology between the different causes of FLUTD, among them the possibility of recurrent episodes of FIC as an underlying disorder or predisposing factor for the development of urolithiasis or urethral obstruction in cats.[6] As previously addressed, cats with FIC meet the same criteria used in humans for the characterization of IC/PBS.[41,42] In both species,

multiple, complex and variable abnormalities of the nervous, endocrine and immune systems, which are likely to affect more than the bladder, are present, in addition to genetic and environmental influences from birth, which may also predispose to the appearance of IC in adult life.[42,43] Many studies related to FIC have been carried out; nevertheless, evaluations regarding the involvement of other organs, such as the kidney, have not yet been reported. Additionally, it is unknown whether the changes could also be restricted to the bladder.[7] In our study, higher RI (0.75 ± 0.07 for the right kidney; 0.71 ± 0.05 for the left kidney) and PI (1.53 ± 0.38 for the right kidney; 1.32 ± 0.20 for the left kidney) in cats with non-obstructive FLUTD suggest changes in blood flow that alter renal perfusion, impairing normal function. This could suggest the onset of a kidney injury of unknown extent. To our knowledge, this is the first report of changes in renal blood flow detected by Doppler ultrasound in cats with FLUTD. Given this, some explanations for the results of the present study can be suggested, including the involvement of the sympathetic nervous system (SNS) and the role of inflammation in FIC.

Clinical signs associated with FIC may be related to stress due to the involvement of the SNS; for instance, altered bladder permeability and increased catecholamine plasma concentrations have been demonstrated in cats subjected to chronic stress.[44] Acute and chronic stress represent an important factor, not only in the development, but also in the maintenance of clinical signs related to FIC.[43] In addition, differences in the function of the hypothalamic–pituitary–adrenal axis have been reported; for example, the smaller size of the adrenal gland in cats with FIC and the consequent reduction in cortisol release in response to adrenocorticotropic hormone stimulation in cats subjected to periods of stress.[45,46] In our study, all necessary precautions to reduce stress were used. Although cortisol assessment was not performed, we monitored the cats' glucose levels and heart rates, with results within normal limits. The evaluated animals were apparently calm, which allowed the evaluation of renal indices in the vast majority. In addition, other factors could have been in play in this study, including pain, anxiety and inflammation in cats with FLUTD. Therefore, stress levels may not have been equal between groups.

The increased renal RI and PI in cats with FIC could also be related to increased SNS activity, with an effect on renal perfusion. Kidneys have abundant adrenergic innervation and the SNS seems to have a potent effect on renal hemodynamics.[47,48] Increased sympathetic activity, in addition to increasing the production of norepinephrine, causes vasoconstriction, which leads to a decrease in renal blood flow.[47] Also, as inflammation clearly plays an important role in urinary tract disorders, there is a need to understand the inflammatory pathways involved in the pathophysiology of these disorders, including differentiation of local and systemic responses, which would have the potential to affect the kidneys.[49–51] Recent studies have identified structures called inflammasomes that promote the maturation and release of proinflammatory cytokines. For instance, NOD-like receptor protein 3 (NLRP3) inflammasomes, found in the bladder epithelium, have been suggested to play a fundamental part in the development of IC/PBS in humans.[52] Studies are needed to better understand a possible relation between inflammation of the urinary tract and renal function, both in humans and in cats.

A statistically significant positive correlation was achieved between the PI and creatinine levels measured in the cats. The PI is considered to be the most sensitive in differentiating abnormal waveforms as it considers the mean velocity.[16,53] This correlation can demonstrate the relationship between the degree of azotemia and the ultrasound assessment of renal hemodynamics, resulting in the possible applicability of PI in the assessment of changes in renal performance.

The small number of animals included and non-repeated measurements on the same animal at different time points are important limitations to be considered. Another limitation is the lack of a diagnosis for acute kidney injury. Renal biopsy is necessary to establish a definitive diagnosis and determine the severity of the injury;[54] however, this was not recommended for our patients. Future studies should investigate whether the change in blood flow identified through RI and PI could alter renal perfusion and damage renal function, as well as other correlations between the indices and age, weight, heart rate, blood pressure and other clinical parameters. The same operator performed all the examinations. Although intra-observer variability was not performed, other aspects were used to minimize the effects of variability on the data, such as operator experience, standardization for the evaluation of criteria and repetition of measurements. Although the patient's recumbence may influence hemodynamics, this was not evaluated in our study as patient comfort during the examination was our priority.[55] We recognize these limitations and encourage future studies to better assess the relationship of these variables with renal RI and PI in cats.

Conclusions

RI (0.75 ± 0.07 for the right and 0.71 ± 0.05 for the left kidney in the nOG; 0.72 ± 0.10 for the right and 0.71 ± 0.11 for the left kidney in the OG) and PI (1.53 ± 0.38 for the right and 1.32 ± 0.20 for the left kidney in the nOG; 1.52 ± 0.83 for the right and 1.46 ± 0.66 for the left kidney in the OG) were predominantly higher in animals with FLUTD when compared with values in healthy cats (RI 0.64 ± 0.04 and PI 1.09 ± 0.16 for the right kidney; RI 0.64 ± 0.04 and PI 1.06 ± 0.12 for the left). This difference demonstrates the increase in intrarenal vascular resistance in cats with

FLUTD. Therefore, changes in renal blood flow and the possibility of kidney injury in animals with FLUTD need to be further investigated.

Supplementary material The following file is available online:
Table 1: Data of the animals included in the study.

Conflict of interest The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding This study was financed, in part, by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior—Brasil (CAPES)—Finance Code 001.

Ethical approval The work described in this manuscript involved the use of non-experimental (owned or unowned) animals. Established internationally recognised high standards ('best practice') of veterinary clinical care for the individual patient were always followed and/or this work involved the use of cadavers. Ethical approval from a committee was therefore not specifically required for publication in *JFMS*. Although not required, where ethical approval was still obtained, it is stated in the manuscript.

Informed consent Informed consent (verbal or written) was obtained from the owner or legal custodian of all animal(s) described in this work (experimental or non-experimental animals, including cadavers) for all procedure(s) undertaken (prospective or retrospective studies). No animals or people are identifiable within this publication and therefore additional informed consent for publication was not required.

ORCID iD Gabriela CL Evangelista https://orcid.org/0000-0001-9699-7172
Emily CC Reis https://orcid.org/0000-0002-9794-6972

References

1 Hostutler RA, Chew DJ and Dibartola SP. **Recent concepts in feline lower urinary tract disease.** *Vet Clin North Am Small Anim Pract* 2005; 35: 147–170.
2 Little SE. **The lower urinary tract.** In: Little SE. The cat – clinical medicine and management. St Louis, MO: Elsevier, 2012, pp 980–1013.
3 Gunn-Moore DA. **Feline lower urinary tract disease.** *J Feline Med Surg* 2003; 5: 133-138.
4 Buffington CAT. **Lower urinary tract disease in cats – new problems, new paradigms.** *J Nutr* 1994; 124 Suppl 12: 2643S–2651S.
5 Osborne CA, John MK and Jody PL. **Feline lower urinary tract disorders: definition of terms and concepts.** *Vet Clin North Am Small Anim Pract* 1996; 26: 169–179.
6 Lund HS and Eggertsdóttir AV. **Recurrent episodes of feline lower urinary tract disease with different causes: possible clinical implications.** *J Feline Med Surg* 2019; 21: 590–594.
7 Buffington CAT. **Idiopathic cystitis in domestic cats – beyond the lower urinary tract.** *J Vet Intern Med* 2011; 25: 784–796.
8 Chancellor MBA. **Multidisciplinary consensus meeting on IC/PBS. In: Chancellor MBA. Outcome of the consensus meeting on interstitial cystitis/painful bladder syndrome, 10 February 2007, Washington (DC).** *Rev Urol* 2007; 9: 81–83.
9 Westropp JL and Buffington CAT. **In vivo models of interstitial cystitis.** *J Urol* 2002; 167: 694–702.
10 Reche A Jr and Hagiwara MK. **Semelhança entre a doença idiopática do trato urinário inferior dos felinos e a cistite intersticial humana.** *Cienc Rural* 2004; 34: 315–321.
11 Treutlein G, Dorsch R, Euler KN, et al. **Novel potential interacting partners of fibronectin in spontaneous animal model of interstitial cystitis.** *PLoS One* 2012; 7: e51391. DOI: 10.1371/journal.pone.0051391.
12 Griffin S. **Feline abdominal ultrasonography: what's normal? What's abnormal? The kidneys and perinephric space.** *J Feline Med Surg* 2020; 22: 409–427.
13 Granata A, Zanoli L, Clementi S, et al. **Resistive intrarenal index: myth or reality?** *Br J Radiol* 2014; 87. DOI: 10.1259/bjr.20140004.
14 Boddi M, Natucci F and Ciani E. **The internist and the renal resistive index: truths and doubts.** *Intern Emerg Med* 2015; 10: 893–905.
15 Bragato N, Borges NC and Fioravanti MCS. **B-mode and Doppler ultrasound of chronic kidney disease in dogs and cats.** *Vet Res Commun* 2017; 41: 307–315.
16 Novellas R, Espada Y and De Gopegui RR. **Doppler ultrasonographic estimation of renal and ocular resistive and pulsatility indices in normal dogs and cats.** *Vet Radiol Ultrasound* 2007; 48: 69–73.
17 Radermacher J, Ellis S and Haller H. **Renal resistance index and progression of renal disease.** *Hypertension* 2002; 39: 699–703.
18 Platt JF, Rubin JM, Ellis JH, et al. **Duplex Doppler US of the kidney: differentiation of obstructive from nonobstructive dilatation.** *Radiology* 1989; 171: 515–517.
19 Haitsma Mulier JLG, Rozemeijer S, Röttgering JG, et al. **Renal resistive index as an early predictor and discriminator of acute kidney injury in critically ill patients; a prospective observational cohort study.** *PLoS One* 2018; 13: e0197967. DOI: 10.1371/journal.pone.0197967.
20 Nyland TG, Fisher PE, Doverspike M, et al. **Diagnosis of urinary tract obstruction in dogs using duplex Doppler ultrasonography.** *Vet Radiol Ultrasound* 1993; 34: 348–352.
21 Morrow KL, Salman MD, Lappin MR, et al. **Comparison of the resistive index to clinical parameters in dogs with renal disease.** *Vet Radiol Ultrasound* 1996; 37: 193–199.
22 Novellas R, De Gopegui RR and Espada Y. **Assessment of renal vascular resistance and blood pressure in dogs and cats with renal disease.** *Vet Rec* 2010; 166: 618–623.
23 Macrì F, Pugliese M, Di Pietro S, et al. **Doppler ultrasonographic estimation of renal resistive index in horse: comparison between left and right kidneys.** *J Equine Vet Sci* 2015; 35: 111–115.
24 Siwinska N, Zak A, Slowikowska M, et al. **Renal resistive index as a potential indicator of acute kidney injury in horses.** *J Equine Vet Sci* 2021; 103. DOI: 10.1016/j.jevs.2021.103662.
25 Matos I, Azevedo P and Carreira LM. **Pilot study to evaluate the potential use of the renal resistive index as a preliminary diagnostic tool for chronic kidney disease in cats.** *J Feline Med Surg* 2017; 20: 940–947.

26 Mitchell SK, Toal RL, Daniel GB, et al. **Evaluation of renal hemodynamics in awake and isoflurane-anesthetized cats with pulsed-wave Doppler and quantitative renal scintigraphy.** *Vet Radiol Ultrasound* 1998; 39: 451–458.

27 Pollard R, Nyland TG, Bernsteen L, et al. **Ultrasonographic evaluation of renal autografts in normal cats.** *Vet Radiol Ultrasound* 1999; 40: 380–385.

28 Halling KB, Graham JP, Newell SP, et al. **Sonographic and scintigraphic evaluation of acute renal allograft rejection in cats.** *Vet Radiol Ultrasound* 2003; 44: 707–713.

29 Carvalho CF, Cerri GG and Chammas MC. **Parâmetros Doppler velocimétricos das artérias renais e da aorta abdominal em gatos da raça persa** [article in Portuguese]**.** *Cienc Rural* 2009; 39: 1105–1110.

30 Carvalho CF and Chammas MC. **Normal Doppler velocimetry of renal vasculature in Persian cats.** *J Feline Med Surg* 2011; 13: 399–404.

31 Gonul R, Koenhemsi L, Bayrakal A, et al. **Renal-pulsed wave Doppler ultrasonographic findings of normal Turkish Angora cats.** *Pak Vet J* 2011; 31: 369–370.

32 Tipisca V, Murino C, Cortese L, et al. **Resistive index for kidney evaluation in normal and diseased cats.** *J Feline Med Surg* 2015; 18: 471–475.

33 Ostrowska J, Kielbowicz Z, Zaleska-Dorobisz U, et al. **Resistive index (RI) obtained in renal interlobar arteries of normal dogs and cats by means of Doppler ultrasonography.** *Pak Vet J* 2016; 36: 45–48.

34 Azizi F, Masouleh MN, Rafie SM, et al. **Effects of medetomidine on intra-renal arteries resistive and pulsatility indices in clinically normal adult domestic shorthair cats.** *Vet Res Forum* 2018; 9: 137–143.

35 Mello FPS, Torres VN, Cunha RF, et al. **Sedation effect of midazolam, ketamine, and butorphanol on spectral Doppler ultrasound values in femoral and large abdominal arteries in cats.** *Semin Cienc Agrar* 2019; 40: 3493–3500.

36 Rivers BJ, Walter PA, Polzin DJ, et al. **Duplex Doppler estimation of intrarenal Pourcelot resistive index in dogs and cats with renal disease.** *J Vet Intern Med* 1997; 11: 250–260.

37 Evangelista GCL, Viana AGA, Neves MM, et al. **Resistivity and pulsatility indexes in feline kidney disease: a systematic review.** *Vet Radiol Ultrasound* 2022; 63: 306–318.

38 Di Nicolò P and Granata A. **Renal intraparenchymal resistive index: the ultrasonographic answer to many clinical questions.** *J Nephrol* 2019; 32: 527–538.

39 Nevins JR, Mai W and Thomas E. **Associations between ultrasound and clinical findings in 87 cats with urethral obstruction.** *Vet Radiol Ultrasound* 2015; 56: 439–447.

40 Novellas R, Domínguez E, Espada Y, et al. Diagnóstico ecográfico en el gato. España: Grupo Asís Biomedia, 2021.

41 Kullmann FA, McDonnell BM, Wolf-Johnston AS, et al. **Inflammation and tissue remodeling in the bladder and urethra in feline interstitial cystitis.** *Front Syst Neurosci* 2018; 12: 13. DOI: 10.3389/fnsys.2018.00013.

42 Buffington CAT. **Developmental influences on medically unexplained symptoms.** *Psychother Psychosom* 2009; 78: 139–144.

43 Westropp JL, Delgado M and Buffington CAT. **Chronic lower urinary tract signs in cats: current understanding of pathophysiology and management.** *Vet Clin North Am Small Anim Pract* 2019; 49: 187–209.

44 Reche A Jr and Buffington CAT. **Increased tyrosine hydroxylase immunoreactivity in the locus coeruleus of cats with interstitial cystitis.** *J Urol* 1998; 159: 1045–1048.

45 Westropp JL, Kass PH and Buffington CAT. **Evaluation of the effects of stress in cats with idiopathic cystitis.** *Am J Vet Res* 2006; 67: 731–736.

46 Westropp JL, Welk KA and Buffington CAT. **Small adrenal glands in cats with feline interstitial cystitis.** *J Urol* 2003; 170: 2494–2497.

47 Johns EJ, Kopp UC and Dibona GF. **Neural control of renal function.** *Compr Physiol* 2011; 1: 731–767.

48 Larsen R, Thorp A and Schlaich M. **Regulation of the sympathetic nervous system by the kidney.** *Curr Opin Nephrol Hypertens* 2014; 23: 61–68.

49 Purves JT and Hughes FM Jr. **Inflammasomes in the urinary tract: a disease-based review.** *Am J Physiol Renal Physiol* 2016; 311: F653–F662.

50 Fan J, Xie K, Wang L, et al. **Roles of inflammasomes in inflammatory kidney diseases.** *Mediators Inflamm* 2019; 2019. DOI: 10.1155/2019/2923072.

51 Xia M, Abais JM, Koka S, et al. **Characterization and activation of NLRP3 inflammasomes in the renal medulla in mice.** *Kidney Blood Press Res* 2016; 41: 208–221.

52 Tudrej KB, Piecha T and Kozłowska-Wojciechowska M. **Role of NLRP3 inflammasome in the development of bladder pain syndrome interstitial cystitis.** *Ther Adv Urol* 2019; 11. DOI: 10.1177/1756287218818030.

53 Nelson TR and Pretorius DH. **The Doppler signal: where does it come from and what does it mean?** *AJR Am J Roentgenol* 1988; 151: 439–447.

54 Vaden SL. **Renal biopsy of dogs and cats.** *Clin Tech Small Anim Pract* 2005; 20: 11–22.

55 Selk Ghaffari M and Arman Gherekhloo A. **Effect of body position on intraocular pressure in clinically normal cats.** *J Feline Med Surg* 2018; 20: 749–751.