

Renal resistivity index as an aid in the diagnosis of acute kidney injury in bitches with pyometra

Índice de resistividade renal como auxiliar no diagnóstico de lesão renal aguda em cadelas com piometra

Aline de Sousa Alves¹ , Fernanda Vieira Henrique¹ , Sabrina Barros Araújo¹ , Dayanny de Sousa Alencar² , Higina Moreira Melo² , Ermano Lucena de Oliveira¹ , Rosangela Maria Nunes da Silva¹ , Almir Pereira de Souza¹ 

ABSTRACT: This study aimed to evaluate the renal function of six bitches of various breeds and ages, with open pyometra, attended in the Small Animal Medical Clinic sector of the Veterinary Hospital from Federal University of Campina Grande, through the measurement of laboratory tests: urea and creatinine serum, dosage of the urinary Protein-Creatinine Ratio (PCR), urinary gamma-glutamyltransferase (GGT) and determination of the renal resistivity index (RI). The levels of urea and creatinine were elevated in 16.6% (1/6) of the female dogs; the urinary protein-creatinine ratio was increased in 66.6% (4/6), while the urinary gamma-glutamyltransferase value was elevated in 50% (3/6). The renal resistivity index was increased in the right and left kidneys by 66.6% (4/6) of bitches, with no statistical difference between them. It was concluded that the renal resistivity index was a practical and effective method to assist in the diagnosis of acute kidney injury, along with other early markers, such as PCR and urinary GGT.

KEYWORDS: Canine; Kidneys; Urinary biochemistry; Ultrasonography.

RESUMO: Objetivou-se com esse estudo avaliar a função renal de seis cadelas com piometra aberta, de variadas raças e idades, atendidas no setor de Clínica Médica de Pequenos Animais do Hospital Veterinário da Universidade Federal de Campina Grande, através da mensuração dos exames laboratoriais: ureia e creatinina séricas, dosagem da relação proteína/creatinina (RPC) urinária, gama-glutamyltransferase (GGT) urinária e determinação do índice de resistividade (IR) renal. Os níveis de ureia e creatinina apresentaram-se elevados em 16,6% (1/6) das cadelas, a relação proteína:creatinina urinária estava aumentada em 66,6% (4/6), enquanto o valor de gama-glutamyltransferase urinária encontrou-se elevado em 50% (3/6). O índice de resistividade renal mostrou-se aumentado nos rins direito e esquerdo de 66,6% (4/6) das cadelas, não havendo diferença estatística entre ambos. Concluiu-se que o índice de resistividade renal foi um método prático e eficaz para auxiliar no diagnóstico da lesão renal aguda, juntamente com outros marcadores precoces, como RPC e GGT urinária.

PALAVRAS-CHAVE: Canino; rins; bioquímica urinária; ultrassonografia.

INTRODUCTION

Pyometra is a disease frequent among the illnesses of the female reproductive system, characterized by a bacterial infection in the endometrium that has suffered cystic hyperplasia as a result of prolonged hormonal stimulation (OLIVEIRA et al., 2019). Bacterial infection, secondary to hormonal changes, usually occurs through upward migration of bacteria present in the vagina, urinary tract and intestine to the uterus, as well as through dissemination via blood (SANCHES et al., 2015). According to the

opening or not of the cervix, it can be classified as open or closed, respectively (VOLPATO et al., 2018).

Kidney abnormalities have been reported in bitches with pyometra for factors such as: decreased ability of renal tubules to concentrate urine due to dysfunction of antidiuretic hormone receptors and endotoxemia (MARANGON et al., 2017), and as a consequence of an immunologically caused glomerulonephritis, which is aggravated by pre-renal azotemia, associated with septic shock, increasing the mortality rate in these animals (OLIVEIRA et al., 2019).

¹Universidade Federal de Campina Grande, Programa de Pós-Graduação em Ciência e Saúde Animal, Patos/PB, Brasil

²Universidade Federal de Campina Grande, Programa de Residência Multiprofissional, Patos/PB, Brasil

*Corresponding author: aline_sousa88@hotmail.com

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Kidney alterations in female dogs with pyometra should be investigated through tests that allow early detection of renal damage. Dosages of urea and creatinine serum are commonly used; however, the increase of these compounds only occurs when 75% of nephrons are affected, thus being regarded as late markers (BÄR et al., 2017; OLIVEIRA; FERREIRA; TOLENTINO, 2016). Among the means that identify early acute kidney injury are urinary gamma glutamyl transpeptidase (GGT) dosage, urinary protein/creatinine ratio (RPC), and kidney resistivity index (RI) determination (BARBOZA et al., 2016; BRAGATO et al., 2017; FREITAS et al., 2014).

Urinary GGT is an enzyme that is present in the epithelium cells of the proximal renal tubules and Henle's strap. This enzyme is not normally filtered by the glomeruli due to its high molecular weight. Its detection in urine occurs shortly after an acute epithelial tubular lesion and is thus considered as an early marker (ANDRADE et al., 2014; MENEZES et al., 2010). Normally, the kidneys cannot filter intermediate molecular weight proteins such as serum albumin and their presence in urine indicates loss of normal glomerular barrier function. The urinary protein/creatinine ratio (PCR) determination corresponds to the urinary protein loss in 24 hours and proves to be an acute indicator of kidney damage (CAVALCANTE et al., 2013).

The Resistivity Index is a value obtained through Doppler ultrasonography and represents the resistance found by the blood flow during the perfusion of a certain organ. It is acquired by the following formula: $RI = (SPV - EDV) / SPV$ (systolic peak velocity) – EDV (end diastolic velocity) / SPV (systolic peak velocity), as shown in Figure 1. This calculation is done automatically by the device (CARVALHO, 2009; RIVERS et al., 1996; SANTOS et al., 2012). Regarding the kidneys, the increase of this parameter

to values above 0.70 is related to renal perfusion changes and has been helping in the early identification of hemodynamic changes, even before the appearance of morphological changes. When vasoconstrictor substances are released after a kidney injury, the diastolic flow is reduced, resulting in a lower final diastolic velocity, which leads to an increase in the resistivity index (BRAGATO et al., 2017).

Early diagnosis of kidney injury and prevention of progression to kidney disease are essential for the survival of bitches with pyometra, enabling agile therapeutic intervention and better response to treatment (ANDRADE et al., 2014). Therefore, this study aimed to determine the development of open pyometra renal injury in bitches, with the use of acute renal markers.

MATERIAL AND METHODS

Approved by the Chamber of Ethics in Animal Experimentation (CEUA) with protocol CEP/CEUA No. 12/2018.

Six bitches of varied races and ages were evaluated. They were treated in the Small Animal Medical Clinic sector of the Veterinary Hospital from Federal University of Campina Grande with an open pyometra diagnosis, obtained after detailed anamnesis, general and special physical examination of the reproductive system, and ultrasound examination.

After diagnostic confirmation, blood samples were collected and stored in a test tube with and without ethylenediaminetetraacetic anticoagulant (EDTA) k3 at 10%, duly identified and conducted to the Clinical Pathology Laboratory, under refrigeration. Complete Blood Count (CBC) and research for hemoparasites were performed in order to identify and exclude animals with comorbidities from the selection. Serum urea and creatinine dosages were also performed.

Additionally, five mL of urine were collected by ultrasonography-guided cystocentesis for the determination of the urinary protein/creatinine ratio and urinary gamma-glutamyltransferase dosage.

An ultrasonographic evaluation of renal perfusion was performed in the right and left kidneys using the color Doppler ultrasound technique in order to obtain the renal resistivity index. The wave spectrum of the arched renal artery was achieved through three consecutive waves of good quality, without interference of artifacts, to obtain the value. The final systolic and diastolic velocity peaks were identified in each wave of the resistivity index spectrum, resulting in three values calculated by device (Figure.1). As described in the literature, the parameter of normality considered is 0.70.

For the statistical analysis, the computational program Bioestat 5.0 was used, at a 5% significance level. First, the data were submitted to the Shapiro-Willk normality test, that is, data with normal distribution are presented as mean \pm standard deviation and those with non-normal distribution are

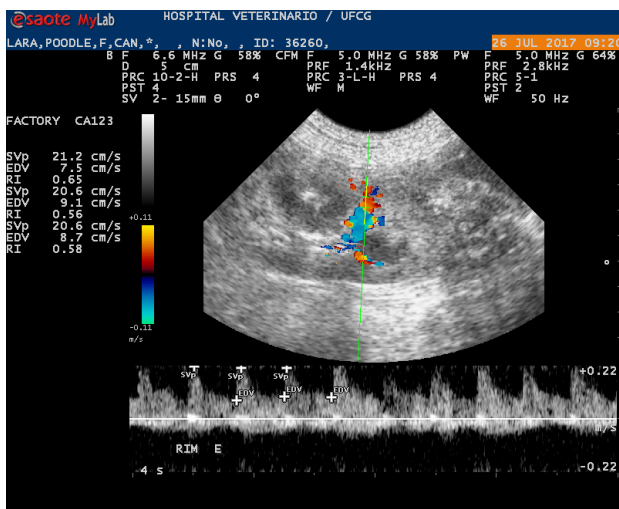


Figure 1. Spectral Doppler of the left kidney of a 2-year-old female dog, Poodle, with open pyometra. Measurement of the maximum systolic peak (SVp) and the final diastolic peak (EDV) to obtain the resistivity index of the interlobar artery in the cranial pole of the kidney.

presented as median \pm interquartile deviation. As there was no comparison between moments or groups, only the descriptive analysis of the data was performed.

RESULTS AND DISCUSSION

There was an increase in the serum levels of urea and creatinine in the blood of 16.6% (1/6) of the bitches in this experiment (Table 1). Evangelista et al. (2010) similarly found in their study that the levels of urea and creatinine serum were increased by 30% (6/20) of the female dogs with open pyometra analyzed. This finding is a result of renal dysfunctions that occur concomitantly with the infectious process (SANTOS et al., 2012); however, they only occur when 66 to 75% of the nephrons are afunctional, making them late markers and ineffective in the acute detection of the lesion (FREITAS, 2014).

The urinary gamma-glutamyltransferase (GGT) measurement was increased in 50% (3/6) of animals, considering the normal values proposed by Schepper et al. (1989), from 13 to 92UI/L (Table 2). In a similar study, Andrade (2014) observed an increase in urinary GGT levels in 70% (7/10) of the analyzed dogs, without a concomitant increase in serum creatinine, indicating that the measurement of this enzyme in urine is effective in the early detection of tubular lesions in bitches with pyometra.

The increased urinary protein/creatinine ratio was present in 66.6% (4/6) of the female dogs, in accordance with what was observed by Maddens et al. (2011), when they identified that the urinary protein/creatinine ratio was significantly higher (41/47) in bitches with pyometra, compared to healthy dogs and that increased values of this urinary biomarker were associated with renal structural lesions and glomerular and tubular dysfunction.

Santos et al. (2012), likewise, detected alterations in the protein/creatinine ratio in 19/30 of bitches with pyometra.

Table 1. Median and interquartile deviation of serum urea and creatinine levels of six bitches with open pyometra assisted at the veterinary hospital from Federal University of Campina Grande.

Parameters	Median and interquartile deviation	Reference*
Urea (mg/dL)	20.4 \pm 7.4	21-60
Creatinine (mg/dL)	0.6 \pm 0.1	0.5-1.5

*Thrall (2007).

Table 2. Mean and standard deviation of urinary parameters of urinary protein-creatinine and gamma-glutamyltransferase ratio of female dogs with open pyometra attended at the veterinary hospital from Federal University of Campina Grande

Parameters	MO	Reference*
PU:CU	0.6 \pm 0.4	< 0.5
GGT (UI/L)	112 \pm 58	13 a 92

*Osborne et al. (1995); Thrall (2007).

Thus, they conclude that the evaluation of this parameter is a good marker of early diagnosis and prognosis of kidney diseases and its determination is essential in monitoring possible glomerulopathies.

The Kidney Resistivity Index was increased (> 0.7) in both kidneys of (66.6%) 4/6 bitches in this experiment (Table 3), corroborating the suggestion made by Santos et al. (2011) in their study that the determination of RI through dopplerfluxometry is an ally in the early investigation of kidney damage of bitches with pyometra. There was no statistical difference between right and left kidney RI values (Chart 4), which is in line with that found by Chang et al. (2010), Morrow et al. (1996), Novellas et al. (2007) and Rivers et al. (1997).

Santos et al. (2012) observed that the animals with higher values of protein/creatinine ratio presented higher reduction of renal perfusion, with higher resistivity indexes, where 7/30 presented both values increased, suggesting a relationship between these variables and the severity of the renal injury. This is in line with what was observed in this study, where four bitches presented both values increased.

It is important to routinely use these tests together in the early identification of kidney injuries in bitches with pyometra and, although they have not been used for further evaluation in this experiment, they also help in determining the progression of kidney injury in these patients, enabling the veterinarian to avoid the installation of more serious changes that can cause the death of the animal (BARBOZA et al., 2016; MADDENS et al., 2011).

CONCLUSIONS

The measurement of the renal resistivity index, when accessible, associated with the values of urinary GGT and urinary RPC, allow the early identification of kidney lesions in bitches with pyometra, when compared to the presence of azotemia, allowing the veterinarian to better evaluate the progression of the kidney lesion and avoid more serious complications that can lead to the death of the animal.

Table 3. Individual values and mean \pm standard deviation of the Kidney Resistivity Indices obtained from the right and left kidneys of bitches with open pyometra assisted at the veterinary hospital from Federal University of Campina Grande

Animals	Resistivity Index (Right kidney)	Resistivity Index (Left Kidney)
Animal 1	0.62	0.64
Animal 2	0.71	0.74
Animal 3	0.73	0.76
Animal 4	0.81	0.77
Animal 5	0.7	0.69
Animal 6	0.74	0.71
Mean \pm SD	0.7 \pm 0.05	0.7 \pm 0.05

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