

## Evaluation of early renal disease in bitches with pyometra based on renal doppler measurements

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**ABSTRACT:** Pyometra is a widely detected, chronic infection of the uterus. One of the complications of this infection is renal disease. Kidney biopsy, urinary biomarkers and blood tests were done to detect pyometra-associated renal disease. To our knowledge, no reports are available describing values for renal Doppler measurements in the bitches with pyometra. Doppler ultrasonography is a relatively new method used for evaluation of the renal diseases. The aims of this study were to determine whether renal vascular resistance does increase in dogs with pyometra and to make an early diagnosis of renal disease in dogs with pyometra. Eighteen bitches diagnosed with pyometra and ten healthy bitches were evaluated. Mean values for renal resistive index (RI) and pulsatility index (PI) were  $0.65 \pm 0.02$  and  $1.73 \pm 0.09$  for dogs with pyometra;  $0.55 \pm 0.03$  and  $1.18 \pm 0.03$  for the healthy ones, respectively. Of these, four animals had increased RI values and fourteen had an increased PI level. In conclusion, renal vascular resistance determined by renal RI and PI, was increased in some dogs with pyometra. In early detection of the disease intrarenal PI values were more sensitive than intrarenal RI.

**Keywords:** renal doppler ultrasonography; pyometra; dog

Doppler ultrasonography is non-invasive, painless, and relatively easy to perform method both in humans and animals. Doppler measurements provide information about real time vascular flow. Resistive index (RI) and pulsatility index (PI) are the two major indices which are used in clinical practice and provide information about resistance within an artery (Novellas et al. 2007). These measurements can be used to evaluate changes due to hepatic disorders, renal disease (acute and chronic renal failure, congenital dysplasia, and urinary obstructions) (Novellas et al. 2007; Novellas et al. 2008), hyperadrenocorticism, diabetes mellitus, hypoadrenocorticism, cardiac disease (Chetboul et al. 2012) and anaemia (Koma et al. 2006).

One of the major importance in renal dysfunction are the bacterial infections. Pyometra is a chronic bacterial infection of the uterus and a common reproductive disease in female intact dogs and cats. Kidney biopsy findings, urinary bio-

markers and blood tests supported renal disease in dogs with pyometra (Maddens et al. 2011). For anaesthesia planning purposes and prognosis it is very important to determine early renal disease in patients with pyometra. However, early detection of renal disease is difficult with blood tests. Serum creatinine levels are important indicators of the renal disease but their blood levels do not increase until the late course of the disease (Platt et al. 1991). These authors concluded that Doppler ultrasonography allows detection of changes associated with acute renal failure according to the renal cortical vasoconstriction with elevation of renal arterial resistance. We hypothesised that using renal Doppler measurements, early detection of pyometra-associated renal disease may be made. Therefore the aim of this study was to determine and analyse changes in renal RI and PI values for making an early diagnosis of renal disease in dogs with pyometra.

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## MATERIAL AND METHODS

Eighteen bitches with pyometra and ten healthy bitches of several breeds and ages were included in the study. All animals were privately owned and presented to our clinics.

Pyometra in this study was characterised by history, clinical signs with or without vulvar discharge and ultrasound examination typical for the disease. If concurrent diseases were detected in dogs with pyometra, these dogs were excluded from the study.

Physical examination, routine blood tests (haematological and biochemical), urinary tests, urinary protein/creatinine (UPC) ratio, ultrasonographic and Doppler examinations were performed on all dogs on the presentation day.

Total cell count (Mindray BC 2800 vet, Chine), plasma concentrations of glucose, urea, creatinine, AST, ALT, total protein, albumin, calcium, phosphorus were assayed (Tokyo Boeki TMS 1024, Japan). Urine specimens had been obtained from dogs either by voluntary voiding or catheterization. Routine dipstick analysis was performed and all samples underwent microscopic examinations. UPC ratio was determined using routine methods.

Ultrasonography and Doppler measurements (Terason 2000, Samsung, China) were made by the same person before the treatment and surgery. A multiconvex prob with 5 or 7 MHz was used. Renal Doppler measurements were obtained from the renal artery, interlobar, or arcuate arteries. After hair clipping an acoustic gel was applied to the skin. A morphometric examination was performed.

Colour Doppler was used to visualise the intrarenal vasculature. Sample volume was positioned in the middle of the renal vessels and the insonation angle did not exceed 60° after correction. The Doppler examination required more than 10 min in most of the dogs because of the movement or tachypnoea.

Parameters of blood flow velocity such as systolic peak velocity (SPV), end diastolic peak (EDV), and time average maximum velocity (TAMAX), as well as hemodynamic parameters such as resistive index (RI) and systolic-diastolic ratio (S/D) were calculated electronically by the ultrasound machine. Pulsatility index (PI) was calculated manually depending on the formula below (Novellas et al. 2007):

$$PI = (\text{peak systolic velocity} - \text{end diastolic velocity}) / (\text{time average maximum velocity})$$

A commercial software package (SPSS10.0) was used to analyze data. Independent samples *t*-test was applied to compare renal RI and PI values in bitches with pyometra and healthy dogs. Correlation analyses were made to determine a significant correlation between UPC and renal RI and PI values. Level of significance was set at  $P < 0.05$ . The statistic methods were based on the recommendations of Ekiz et al. (2014).

## RESULTS

A total of 18 dogs were included in the study for detailed information on their blood analysis, urinary tests, ultrasonography and Doppler examinations. Bitches among different breeds (five Terriers, two German Shepherds, two Rottweilers, two Golden Retriever, one Chow-chow, one Boxer, one Pekingese, and four crossbreds) were evaluated. The ages of the dogs were between two to 17 years, mean age was 8.7 years.

Mean values for renal RI and PI were  $0.65 \pm 0.02$  and  $1.73 \pm 0.09$  for dogs with pyometra;  $0.55 \pm 0.03$  and  $1.18 \pm 0.03$  for healthy dogs, respectively (Table 1). The cut-off upper values for normal RI and PI were 0.72 and 1.52, respectively (Novellas et al. 2007). Based on these levels, four dogs had increased intrarenal RI levels and 14 dogs had increased PI levels. The four dogs with increased RI levels also had increased PI levels. RI and PI levels for each dog are given in Table 2.

All dogs had leukocytosis and four of them had normocytic-normochromic anaemia. Nine dogs had decreased HCT ( $< 37\%$ ) and four dogs had reduced PLT ( $< 200 \times 10^9/l$ ). In blood biochemistry panel serum glucose, AST, ALT, and total protein within normal levels and one dog had hypoalbuminemia ( $< 2.6 \text{ g/l}$ ). 5 dogs had increased both urea (median 11.5 mmol/l) and creatinine (median 106.8  $\mu\text{mol/l}$ ) levels.

Table 1. Mean resistive index (RI), pulsatility index (PI) levels of renal vasculature in dogs with pyometra and healthy dogs

	RI	PI
Bitches with pyometra	$0.65 \pm 0.02^*$	$1.73 \pm 0.09^*$
Healthy	$0.55 \pm 0.03$	$1.18 \pm 0.03$

\* $P < 0.05$

Table 2. Mean resistive index (RI), pulsatility index (PI) levels, blood urea and creatinine, urinary protein/creatinin (UPC) in dogs with pyometra

Dog	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
RI	0.57	0.71	0.60	0.79	0.65	0.57	0.57	0.51	0.71	0.62	0.60	0.69	0.61	0.65	0.70	0.78	0.80	1
PI	1.01	1.68	1.62	1.59	1.81	1.78	1.92	1.68	2.20	2.34	2.10	0.9	1.61	1.73	1.65	2.13	1.26	2.59
Urea (mmol/l)	11.4	7.8	5	27.4	9.2	4.6	4.6	7.1	26	5.3	3.9	8.2	34	3.6	21.4	4.3	12.8	7.8
Creatinin ( $\mu$ mol/l)	79.6	61.9	53	185.6	141.4	70.7	79.6	79.6	168	88.4	44.2	70.7	238.7	53	185.6	53	70.7	79.6
UPC	0.4	1	0.7	1.9	0.5	0.3	0.8	1.14	1.1	0.02	0.8	0.7	1.2	0.17	0.97	0.08	0.4	0.3

Seven of the 18 dogs had urine UPC < 1.015, six dogs had proteinuria according to the dipstick test. Eight dogs had UPC < 0.5, six dogs had  $0.5 \leq$  UPC < 1, and four dogs had UPC > 1. Correlation analysis did not demonstrate a statistically significant correlation between UPC and renal RI values ( $r = 0.218$ ) and between UPC and renal PI values ( $r = -0.187$ ).

Echogenicity of kidneys were normal in ultrasonographic examination.

## DISCUSSION

This study tries to describe the changes of the renal vascular resistance, evaluated by means of renal RI and PI in dogs with pyometra. Early clinical detection of renal disease is difficult to determine by the classical tests because the serum creatinine does not increase until late in the course (Platt et al. 1992). Five of the 18 dogs (28%) had increased serum levels of both urea and creatinine in our study (Table 2).

Proposed normal upper limit values differ slightly from 0.70 to 0.73 in previous studies for renal RI in dogs (Rivers et al. 1997; Novellas et al. 2007). Novellas et al. (2007) concluded that baseline values were 0.52–0.72 for intrarenal RI and 1.52 for intrarenal PI in the healthy dogs. These values were used as normal limits for renal RI in our study. According to these four dogs in the current study had increased RI levels and 15 dogs with elevated levels of PI. However, in some cases RI was near or just at the upper limit value (0.70 in one animal and 0.71 in two animals) (Table 2). Although RI is more widely used than the PI, PI is more sensitive than RI, because it considers the mean velocity within one cycle. Therefore PI was recommended for use as an indicator for renal vascular resistance in humans (Novellas et al. 2007; Novellas et al. 2008).

Glomerulosclerosis, tubular atrophy, and interstitial nephritis were common lesions in the dogs with pyometra in most of the studies (Maddens et al. 2011). Rivers et al. (1997) concluded that increased RI level is likely compatible with tubulointerstitial rather than glomerular disease. Although it is difficult to describe the difference between these pathological findings by using Doppler ultrasonography; perhaps this suggests another reason that we had one increased RI level in our study. Future studies have to be done by using both renal histomorphology and Doppler ultrasonography in the dogs with pyometra.

Among five dogs with increased serum creatinine and urea, one had increased RI and all had increased PI levels (Table 2). These increased levels of renal RI and PI with azotemia are compatible with other results (Rivers et al. 1997). Anaemia is another important factor in the discussion of renal Doppler values. An elevation in the mean intrarenal RI and PI has been determined in the dogs with anaemia (Koma et al. 2006). There were four dogs with normocytic-normochromic anaemia in our study, however, none of these dogs had higher RI values.

Proteinuria is one of the earliest signs of acute renal disease. UPC is used to detect protein in the urine recently. UPC ratio of < 0.5 was considered normal, 0.5–1.0 was considered questionable, and > 1 was considered increased (IRIS 2013). There were four dogs with UPC > 1. Of these, two had increased RI and PI levels and the other two had high levels of PI (Table 2). However, proteinuria has not been related to increased renal RI values in humans and dogs (Rivers et al. 1997). Our analyses did not demonstrate a statistically significant correlation between UPC and renal RI values and between UPC and renal PI values.

Elevations in RI have been found in young and elderly humans. This is one of the major limita-

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tions of the renal Doppler (Terry et al. 1992; Rivers et al. 1997). In the present study, one of the dogs with increased RI and PI was seventeen years old. Age might be the cause of these differences. Future studies should elucidate age-induced differences.

In conclusion, renal vascular resistance which is evaluated by renal RI and PI, does increase in some dogs with pyometra. In early detection of the disease intrarenal PI values are more sensitive than intrarenal RI. Authors propose that these findings may be helpful for understanding the renal disease in pyometra. This theory may warrant future investigations with the diseased animals.

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