

Doppler Velocimetry of Uterine Artery in Bitches with Cystic Endometrial Hyperplasia-Pyometra Complex

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ABSTRACT

Doppler ultrasound is a useful diagnostic tool to evaluate uterine blood flow in different canine reproductive states. The aim of this study was to describe and compare uterine blood flow in bitches suffering from pyometra according to the ultrasonographic appearance of uterus. Seventy-five bitches with pyometra confirmed clinically, haematologically and ultrasonographically were included in the study. Ten healthy bitches with no haematological and ultrasonographic abnormality of uterus were also included in the study as control group. The bitches with pyometra were divided into four groups based on the sonographic characterization of uterus and its luminal contents, viz., B (few small cysts, normal endometrial surface, anechoic uterine content, n=11), C (many large cysts, irregular surface and hypertrophic endometrium, n=24), DH (many large cysts, irregular surface and hypertrophic endometrium, hyperechoic content, n=31) and DA (many large cysts, irregular surface and atrophic endometrium, hyperechoic content, n=9). The uterine horn diameter and uterine wall thickness was measured with two-dimensional ultrasonography. With the use of pulsed-wave Doppler, flow velocity waveforms of uterine artery were obtained. Parameters of blood flow velocity such as peak systolic velocity (PSV), end diastolic velocity (EDV), as well as haemodynamic parameters such as resistance index (RI), pulsatility index (PI) and systolic-diastolic ratio (S/D) were calculated electronically. Peak systolic velocity and end diastolic velocity were significantly higher in pyometra group than control with highest velocities recorded in DA group ($p < 0.05$). The RI, PI and S/D were significantly lower in pyometra group than in control ($P < 0.05$). The RI was significantly lower in group C and DA compared to groups B and DH ($p < 0.05$). However, no significant difference was reported in PI and S/D among the groups of pyometra ($p > 0.05$). It was concluded that the uterine artery blood flow velocity of bitches suffering from pyometra differs, not only from normal bitches, but also varies with the type of pyometra with varying pathological nature. Furthermore, haemodynamic parameters appear as useful markers to differentiate uterine pathologic conditions and to understand the pathological type of pyometra.

Keywords: Canine, Cystic endometrial hyperplasia, Doppler ultrasound, Pyometra.

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INTRODUCTION

Canines are prone to number of general and reproductive health disorders. The cystic endometrial hyperplasia-pyometra complex (CEH-P) is one of the most common reproductive diseases in adult intact sexually matured bitches and is of great practical importance (Kempisty *et al.*, 2013). It is characterized by accumulation of purulent material within the uterus, leading to a variety of clinical symptoms and is life-threatening in severe cases (Okano *et al.*, 1998; Johnston *et al.*, 2001). Trans-abdominal B-mode ultrasonography of the uterus provides valuable information to diagnose uterine diseases. It can be used to clearly evaluate the diameters of uterine horns, endometrial integrity, variations in the uterine wall thickness, and presence of cystic endometrial glands. Although it has been reported that the echogenicity of the uterine contents suggests cellularity, it has also been claimed that ultrasonographic differentiation of the contents is difficult (Bigliardi *et al.*, 2004; Batista *et al.*, 2016). A general classification of CEH-Pyometra complex by trans-abdominal B-mode ultrasonography was proposed by Bigliardi *et al.* (2004) and was widely used to understand the histopathological changes in the uterus with CEH-Pyometra.

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Doppler ultrasonography has become one of the best available, non-invasive and reliable technique to diagnose numerous gynaecologic lesions and to study the uterine

haemodynamics in several species (Bollwein *et al.*, 2000; Bollwein *et al.*, 2002; Ferreira *et al.*, 2008). It was being used to characterize the blood circulation in uterine and ovarian arteries of bitches during various phases of the estrous cycle and also as a diagnostic tool for the follow-up of pregnancy and monitoring the foetal viability in bitches (Di salvo *et al.*, 2006; Miranda *et al.*, 2010; Barbosa *et al.*, 2013; Nogueira *et al.*, 2017). Evaluation of the blood flow velocities including Peak Systolic Velocity (PSV), End Diastolic Velocity (EDV) and Time Average Maximum Velocity (TAMAX) and haemodynamic indices which include Resistance Index (RI), Pulsatility Index (PI), Peak Systolic: Diastolic Velocity (S/D) served as an adjunct tool for the differential diagnosis of uterine disorders (Veiga *et al.*, 2017). Though characterization of uterine blood flow by Doppler ultrasound contribute to the precocious diagnosis of CEH and pyometra (Veiga *et al.*, 2017), there are limited studies available to demonstrate the haemodynamic changes in the vascular supply during pathology of canine uterus. The aim of this study was to determine the changes in the Doppler indices in bitches with pyometra according to the ultrasonographic classification proposed by Bigliardi *et al.* (2004) and its comparison with healthy diestrus bitches.

MATERIALS AND METHODS

The study was performed on seventy-five, 2 to 15-year-old bitches of various breeds with clinical diagnosis of pyometra. The females were evaluated for clinical signs of systemic illness, haematological and serological changes. Ten healthy non-pregnant bitches aged between 3 to 6 years with no haematological abnormality were also included in the study as control group. All the dogs under study were subjected to trans-abdominal ultrasonography by following the standard procedure using ALOKA PROSOUND α 6 machine with 3.5 to 7.5 MHz trans-abdominal curvilinear and linear probes (Alvarez-Clau and Liste, 2005). Based on the ultrasonographic appearance of the uterus the affected bitches were categorized as follows by adopting the procedure cited by Bigliardi *et al.* (2004) with slight modification.

Group A: No cysts, normal endometrial surface and anechoic uterine content.

Group B: Few small cysts, normal endometrial surface, anechoic uterine content.

Group C: Many large cysts, irregular surface and hypertrophic endometrium.

Group D: Many large cysts in the uterus, irregular surface and hypertrophic or atrophic endometrium, hyperechoic uterine content. The group D was further subdivided into groups DH and DA, based on the thickness of endometrium.

The bitches with hypertrophic endometrium as group DH and atrophic endometrium as group DA.

For Doppler velocimetry of uterine artery colourflow Doppler was first used to trace the course of the vessel (Alvarez-Clau and Liste, 2005). Colour mapping signals were visualized on both transverse and longitudinal ultrasound scan sections around the uterine body. The blood flow velocity parameters, viz., peak systolic velocity (PSV) and end diastolic velocity (EDV) and haemodynamic indices, viz., resistive index (RI), pulsatility index (PI) and peak systolic: diastolic velocity (S/D) were calculated and recorded with the help of software provided in the machine.

The ultrasonographic measurements were analyzed by one-way analysis of variance using SPSS version 20.0 (Chicago, IL, USA). Tukey's multiple comparison post hoc test was also used to find the differences between groups. All the data was presented as Mean \pm SE and $p < 0.05$ was considered significant.

RESULTS AND DISCUSSION

Ultrasound investigation was a useful and reliable method to detect uterine pathology. In bitches affected with pyometra, the distended uterine horns appeared as round or oval anechoic to hypoechoic fluid filled structures dorsal to anechoic urinary bladder. In severe distension, the uterine horns occupied the entire abdomen (Devi *et al.*, 2013; Jena *et al.*, 2014; Manokaran *et al.*, 2018). The bitches were categorized into five groups (Groups A, B, C, DH, DA) based on size of the cysts, appearance of the endometrial surface and ultrasonographic appearance of the uterine contents. In the present study, none of the affected bitches was categorized as Group A as all the bitches had cysts of variable sizes in the endometrium. In healthy control bitches, the uterus appeared as a poorly echogenic structure which was located dorsal to the urinary bladder. Uterine horn diameter was significantly ($p < 0.05$) higher in DA group followed by C, DH, B and control groups. The thickness of uterine wall of DH group was significantly ($p < 0.05$) higher compared to all the other groups (Table 1).

The wave form of uterine artery was recorded in healthy controls and bitches with pyometra using pulsed wave doppler. In control group, the waveform showed a high resistance flow pattern, characterized by the sudden decrease in systolic peak velocity. In six bitches the waveform was characterized by systolic peak followed by diastolic flow, extending throughout the cardiac cycle with prominent early diastolic notch (Fig. 1). In one case the systolic peak was followed by a diastolic flow which was continuous with

Table 1: Uterine horn diameter and uterine wall thickness measured by ultrasonography (Mean \pm SE)

S. No.	Parameter	Control (n=10)	Group B (n=11)	Group C (n=24)	Group DH (n=31)	Group DA (n=9)
1	Uterine horn diameter (cm)	0.62 \pm 0.04 ^d	1.77 \pm 0.12 ^c	3.18 \pm 0.20 ^b	2.94 \pm 0.12 ^b	4.75 \pm 0.62 ^a
2	Uterine wall thickness (cm)	0.26 \pm 0.01 ^b	0.44 \pm 0.05 ^b	0.42 \pm 0.02 ^b	0.77 \pm 0.07 ^a	0.20 \pm 0.02 ^b

Means bearing different superscripts differed significantly in a row ($p < 0.05$)



systole but showed absence of late diastolic flow. In three bitches, systolic flow alone was recorded with characteristic monophasic high resistivity.

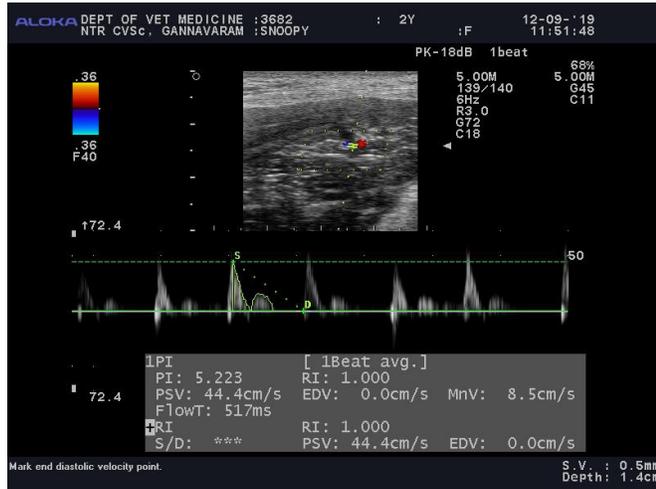


Fig. 1: Pulsed wave Doppler of uterine artery in control group

In pyometra, the blood flow was continuous with high velocity, low resistance and low pulsatility. In group B bitches, the waveform was characterized by biphasic flow with peak systole followed by diastolic flow which continued throughout the cardiac cycle. The systolic peak was followed by a sharp fall before the mid-diastolic flow (Fig. 2). However, the early diastolic notch was not as deep as identified in control bitches. In group C bitches, the biphasic waveform was characterized with short fall in peak systolic flow and was continuous with diastolic flow with high early and mid-diastolic flow (Fig. 3). In DH and DA groups, the waveform was biphasic with higher systolic and diastolic velocities. The diastolic flow was continuous with systolic flow and recorded a lowered RI and PI (Fig. 4, 5). The PSV and EDV were significantly ($p<0.05$) lower in control group when compared with all the groups of pyometra. The RI of group C and group DA was

significantly ($p<0.05$) lower than control, B and DH groups (Table 2).

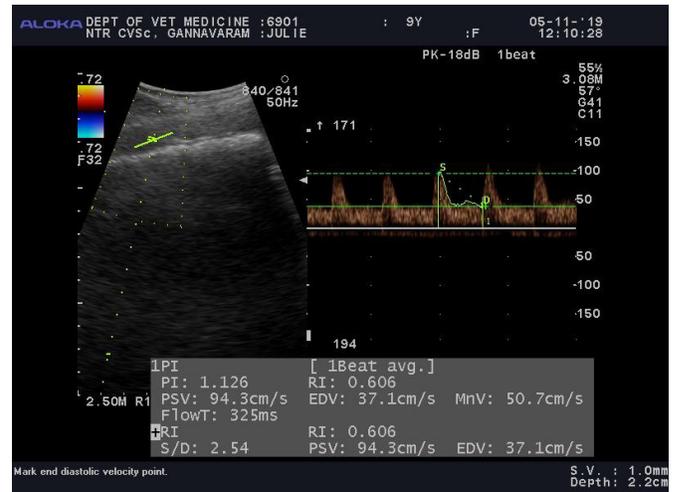


Fig. 2: Pulsed wave Doppler of uterine artery in group B

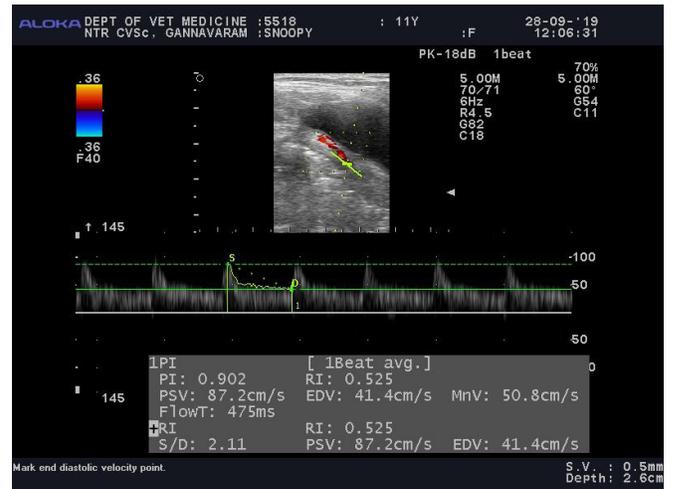


Fig. 3: Pulsed wave Doppler of uterine artery in group C

Table 2: Haemodynamic changes in the uterine artery as measured by Doppler ultrasonography in healthy controls and pyometra affected bitches (Mean \pm SE)

S. No.	Parameter	Control (n=10)	Group B (n=11)	Group C (n=24)	Group DH (n=31)	Group DA (n=9)
1	PSV (cm/s)	36.87 \pm 2.3 ^{9c}	89.46 \pm 4.7 ^{5b}	100.68 \pm 4.2 ^{0b}	106.21 \pm 3.0 ^{9ab}	125.00 \pm 7.37 ^a
2	EDV (cm/s)	2.51 \pm 0.9 ^{1d}	34.89 \pm 2.1 ^{5c}	46.44 \pm 2.5 ^{1b}	43.83 \pm 1.4 ^{9bc}	62.84 \pm 4.49 ^a
3	RI	0.92 \pm 0.0 ^{3a}	0.61 \pm 0.00 ^{5b}	0.54 \pm 0.0 ^{1c}	0.59 \pm 0.00 ^{6b}	0.49 \pm 0.02 ^c
4	PI	3.55 \pm 0.93 ^a	1.20 \pm 0.0 ^{3b}	0.97 \pm 0.03 ^b	1.07 \pm 0.02 ^b	0.84 \pm 0.07 ^b
5	S/D	11.06 \pm 2.62 ^a	2.57 \pm 0.03 ^b	2.20 \pm 0.05 ^b	2.44 \pm 0.04 ^b	2.07 \pm 0.13 ^b

Peak systolic velocity (PSV) , End diastolic velocity (EDV) Resistive index (RI), pulsatility index (PI) Peak Systolic: diastolic velocity (S/D)
Means bearing different superscripts differed significantly ($p<0.05$) in a row.

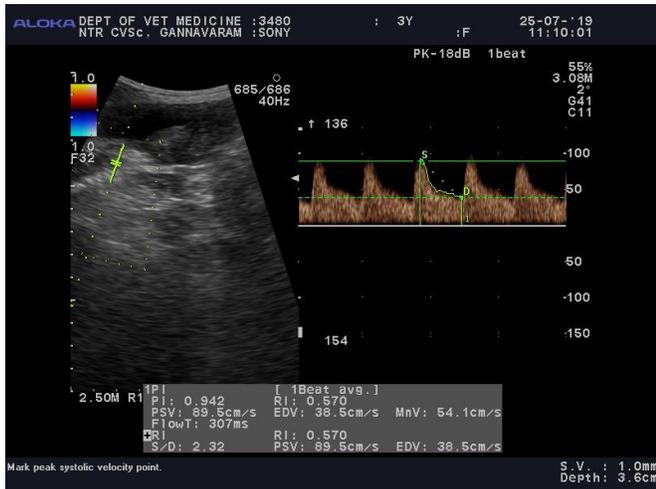


Fig. 4: Pulsed wave Doppler of uterine artery in group DH

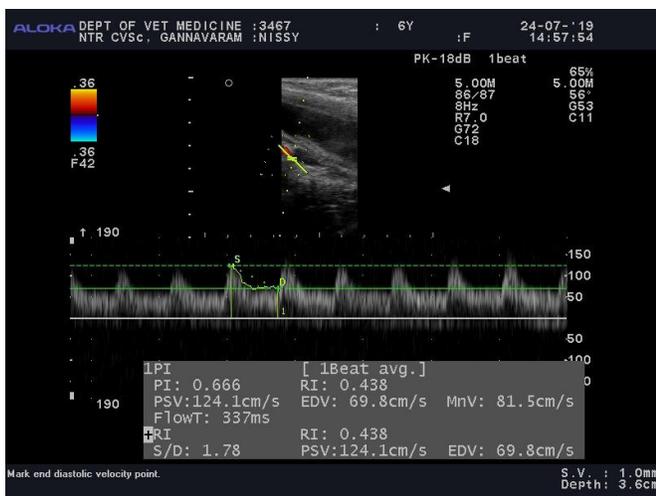


Fig. 5: Pulsed wave Doppler of uterine artery in group DA

In Veterinary Medicine, despite the characterization of the reproductive system by well established ultrasonography, little attention was given to the evaluation of uterine vascular supply (Alvarez-Clau and Liste, 2005). There are limited studies available to demonstrate the haemodynamic changes of the vascular supply during pathology of canine uterus (Batista *et al.*, 2016; Veiga *et al.*, 2017). However, no similar studies were placed on record which reported doppler velocimetry of the uterine arteries in pyometra based on the sonographic appearance. Evaluation of the uterine inflammatory response, by elucidating the information on blood flow velocity of the uterine arteries in pyometra, might contribute for the better understanding of the mechanisms involved in pathophysiology of canine pyometra. In women and cows, uterine pathologic conditions may cause an increase in blood flow that can be detected by Doppler ultrasound.

The normal bitches presented a significantly higher resistance Doppler waveform of the uterine arteries whereas the bitches with Pyometra reported a low resistance Doppler waveform having high velocity and low pulsatility. The results were similar to the earlier reports (Veiga *et al.*, 2012; Batista *et*

al., 2016; Veiga *et al.*, 2017). It was believed that in pyometra such a wave morphology of the uterine artery was related to endometrial neovascularization due to inflammation, which culminated in greater tissue perfusion. In pyometra the blood flow velocities were significantly ($p < 0.05$) highest in DA group and least in B group. The RI was significantly lower in DA group (0.49 ± 0.02) than other groups. Though, PI and S/D were lower in group DA and group C no significant difference was noticed among the groups of pyometra ($p > 0.05$). The differences in these parameters between sonographic groups of pyometra might be due to the difference in severity of inflammatory process and variations in uterine distension (Veiga *et al.*, 2017).

In the present study, the uterine horn thickness showed little variation between control and pyometra groups, except for DH group. In contrast, the blood flow velocities and haemodynamic indices differed between groups, although the same was not observed for the thickness of the uterine horns. It was suggested that the thickness of the endometrium was not directly related to the presence of inflammatory process. The present finding was in accordance with the reports of Veiga *et al.* (2017) who reported that colour Doppler ultrasound was an adjunct tool for the differential diagnosis of uterine disorders like CEH-mucometra by assessing the haemodynamic changes of uterine arteries.

CONCLUSION

Our study demonstrated that Doppler ultrasound is a non-invasive and accurate diagnostic tool to reflect haemodynamic changes in uterine pathology and also helps in differentiation of the pathological process of pyometra.

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