Journal of
Veterinary Clinics
www.ksvc.or.kr

Ultrasonography, Affected Age, Hematology and Clinical Signs according to Open or Closed Cervix in Dogs with Pyometra

Jun-Am Lee, Ill-Hwa Kim, Dae-Youn Hwang* and Hyun-Gu Kang[1]

Laboratory of Veterinary Theriogenology, Veterinary Medical Center and College of Veterinary Medicine,
Chungbuk National University, Cheongju 28644, Korea
*Department of Biomaterials Science, Pusan National University, Miryang 50463, Korea

Abstract : The aim of the study was to evaluate ultrasonographic findings, affected age, hematology, blood chemistry and clinical signs according to open or closed cervix in 102 bitches presented for treatment of pyometra. The prevalence of pyometra according to breed was observed in Maltese 22.5%, Yorkshire Terrier 13.7% and Shih Tzu 12.7%. The mean age of dogs was 9.6 ± 0.3 years, and open cervix pyometra was more prevalent than closed cervix pyometra. Clinical signs included anorexia, vaginal discharge, depression, polyuria/polydipsia, vomiting, and abdominal distension. The concentration of BUN and the activity of ALP in dogs with closed cervix pyometra were significantly higher than those in dogs with open cervix pyometra ($p < 0.05$). The white blood cell and neutrophils in dogs with closed cervix pyometra were significant higher than those in dogs with open cervix pyometra ($p < 0.05$). Ultrasonographic findings of the uterus with open or closed cervix pyometra showed variable patterns. The uterine wall was variable in appearance, from thick and irregular to smooth and thin. The uterine wall was thicker in open cervix pyometra than in closed cervix pyometra. The luminal cavity included smaller amount of anechoic fluid in open cervix pyometra than in closed cervix pyometra.

Key words : pyometra, dog, open or closed cervix, ultrasonography, blood profile.

Introduction

Cystic endometrial hyperplasia (CEH)-pyometra complex is a very common disease in bitches over 8 years of age (11). Pyometra typically affects mature bitches that have undergone repeated estrous cycles (20). Pyometra is classically a disease of the diestrual bitch and can be classified as open-cervix or closed-cervix pyometra according to presence or absence of vaginal discharge (4,31).

Generally, the cervical canal opens in response to estrogen and closes in response to progesterone, which are ovarian steroid hormones. Furthermore, the presence of progesterone receptors in the uterine cervix is related to the cervical patency (34). Progesterone has a role in the increased secretory activity of the endometrial glands and decreases myometrial contractility, which therefore closes the cervix (18).

Clinical signs of the bitch with closed-cervix pyometra are inappetence, depression, polydipsia, lethargy, and abdominal distension (1,5). Typically, the bitch is afebrile, and will often have an elevated white blood cell count (5,31). In contrast, the bitch with open cervix pyometra present with a vaginal discharge. Therefore, the clinical signs of closed cervix pyometra are less obvious than open cervix pyometra, and closed cervix pyometra is a medical emergency requiring rapid intervention to prevent subsequent sepsis and potential patient death (31).

The diagnosis of canine pyometra closed-cervix or open-cervix pyometra is best made with ultrasonography and radiology (2,30,36). Ultrasonographically, a fluid-filled organ with variable wall thickness and proliferative changes can be visualized (9,26). A lateral abdominal radiograph can be utilized to identify a sausage-like fluid-filled tubular organ located between the descending colon and the urinary bladder (33).

The treatment of choice for any older, systemically ill bitch, or one with closed cervix pyometra, is complete ovariohysterectomy (OHE) (10,23,37). Young bitches that present with an open cervix pyometra, normal organ function, and a compliant, reasonable owner may be treated with prostaglandins in an attempt to preserve their breeding value (15,16).

There has been many previous reports about pyometra. But, to the best of our knowledge, comparable evaluation according to open and closed of cervix in dogs with pyometra not yet been reported. Therefore, the aim of this clinical study was to evaluate ultrasonographic findings, affected age, hematology, blood chemistry, and clinical signs according to open or closed cervix pyometra in bitches presented for treatment of pyometra.

Materials and Methods

Study population

Clinical records were obtained from database of dogs with pyometra from the Veterinary Medical Center in Chungbuk National University between January 2005 and May 2014. A

[1]Corresponding author.
E-mail : kang6467@cbu.ac.kr

total of 109 cases of pyometra were enrolled in the present study.

Diagnosis of pyometra

An initial diagnosis of pyometra was made based on history taking, physical examination, abdominal radiographic findings (Directview CR500; Eastman Kodak Co., NY, USA), and abdominal ultrasonographic findings (ProSound Alpha 5; Hitachi Aloka Medical, Tokyo, Japan). According to the history taking and physical examination, intact female dogs having vaginal discharge combined with polyuria and polydipsia, abdominal distension, and palpable enlarged uterus were suspected to have pyometra. On survey radiograph, pyometra was diagnosed from observation of a tubular structure between the urinary bladder and descending colon at lateral abdominal view. Dogs with abnormal ultrasonographic findings, such as fluid-filled uterus or uterine horn, were diagnosed with pyometra. The status of the patient was also evaluated by laboratory findings such as serum chemistry (Hitachi 7202; Hitachi High-Technologies Co., Tokyo, Japan), electrolyte analyses (Humalyte; HUMAN Gesellschaft fur Biochemica und Diagnostica mbH, Wiesbaden, Germany), and complete blood count (CBC) (BC-5300 Vet TM; Mindray Co., Shenzhen, China).

Data collection

Data were collected from the clinical records of the selected 102 dogs. The following data were individually collected from each case of pyometra: breed, age, body weight, type of pyometra (open-cervix or closed-cervix pyometra), clinical signs on admission (vaginal discharge, anorexia, depression, lethargy vomiting, diarrhea, polydipsia and polyuria, abdominal distension, fever, and dehydration status), results of hematological and biochemical analyses on admission (concentrations of sodium, chloride, and potassium; packed cell volume [PCV]; platelet, neutrophil, monocyte, and lymphocyte counts; concentration of serum total protein, albumin, albumin-globulin ratio, BUN, creatinine, and glucose; activities of ALT and ALP), treatment (surgery or medical treatments), and duration of hospitalization.

Statistical analysis

For the statistical analysis, the bitches were separated into open or closed cervix pyometra groups. The statistical analysis of data was performed with Exel® 2014 software (Microsoft Corp, Redmond, WA, USA). The percentages of all data were estimated to the nearest tenth of decimal place. Clinical signs, blood cells and blood chemistry in two groups were compared by student t-test. Differences were judged as significant if the p value was ≤ 0.05.

Table 1. The mean age of 102 dogs with pyometra according to breed

Breeds	No. of bitches (%)	Age (Mean ± SE, range, years)
Maltese	23 (22.5)	10.2 ± 0.21 (4-15)
Yorkshire Terrier	14 (13.7)	9.0 ± 0.54 (1-16)
Shih Tzu	13 (12.7)	10.3 ± 0.23 (6-16)
Miniature Schnauzer	11 (10.8)	9.6 ± 0.35 (5-17)
Poodle	10 (9.8)	11.1 ± 0.21 (8-15)
Pekingese	7 (6.8)	7.1 ± 0.18 (5-9)
Jindo	4 (3.9)	7.8 ± 0.43 (5-17)
Mongrel	12 (11.8)	10.3 ± 0.34 (8 months-13)
Other breeds	8 (7.8)	8.5 ± 0.31 (6-15)
Total	102 (100.0)	9.6 ± 0.32 (8 months-17)

Results

Prevalence of pyometra

The prevalence of pyometra according to breed is summarized in Table 1. The highest prevalence of pyometra over 10-year-old was observed in Maltese dogs (22.5%). Yorkshire Terriers, Shih Tzus and Miniature Schnauzers also showed a higher prevalence of pyometra than other breeds.

The mean age of the 102 dogs was 9.6 ± 0.32 years (range, 8 months to 17 years); however, the mean age varied among breeds; (e.g., 7.1 years for Pekingese [n = 7] and 11.1 years for poodle [n = 10]) (Table 1).

Open cervix pyometra was more prevalent (61.8%) than closed cervix pyometra (Table 2). Among all dogs, the prevalence of pyometra without CEH was 59.8% (61/102), and 40.2% for CEH-pyometra complex (41/102). In dogs with closed-cervix pyometra, prevalence of pyometra without CEH (74.4%) was higher than that with CEH (25.6%).

Blood profiles

Blood profiles of dogs with closed or open cervix pyometra are shown in Table 3. In the electrolyte profile, the mean concentrations of sodium in closed and open cervix pyometra, chloride and potassium were found to be within the reference range. There were no abnormal findings in the serum biochemistry of dogs with closed and open cervix pyometra, including the concentrations of total protein and creatinine, and the activity of ALT; however, the concentration of BUN, glucose, and albumin, and the activity of ALP were abnormal in dogs with pyometra. In dogs with closed and open

Table 2. The incidence rate of cystic endometrial hyperplasia (CEH) according to open or closed cervix in 102 dogs with pyometra

Types	No. of bitches (%)	CEH With (%)	CEH Without (%)	Age (Mean ± SE, range, year)
Closed-cervix	39 (38.2)	10 (25.6)	29 (74.4)	9.3 ± 0.54 (1~16)
Open-cervix	63 (61.8)	31 (49.2)	32 (50.8)	9.4 ± 0.42 (1~17)
Total	102 (100.0)	41 (40.2)	61 (59.8)	9.4 ± 0.34 (1~17)

Table 3. Mean level (± SE) of electrolytes, serum chemistry, and complete blood counts in 102 dogs with pyometra

Parameters	Unit	Mean level (Mean ± SE)		Reference range
		Closed-cervix (range)	Open-cervix (range)	
Electrolytes				
Sodium	mmol/L	142.7 ± 1.6 (116-157)	145.8 ± 0.9 (123-161)	141-152
Chloride	mmol/L	107.6 ± 1.8 (77-119)	112.6 ± 0.7 (91-123)	105-115
Potassium	mmol/L	4.4 ± 0.1 (2.3-5.8)	4.4 ± 0.1 (2.0-5.6)	3.6-5.8
Serum chemistry				
Total protein	g/dL	6.5 ± 0.1** (4.2-7.9)	6.5 ± 0.1** (3.5-8.7)	5.4-3.3
Albumin	g/dL	2.3 ± 0.1* (1.3-3.7)	2.3 ± 0.1* (1.0-4.2)	2.6-3.3
A-G ratio		0.59 ± 0.04 (0.28-1.03)	0.6 ± 0.03 (0.25-0.03)	0.59-1.11
BUN	mg/dL	39.2 ± 6.8 (5-180.3)**,a	23.9 ± 2.6 (4.2-106)**,b	7.0-25.0
Creatinine	mg/dL	1.2 ± 0.2 (0.3-7.3)	1.1 ± 0.2 (0.2-7.4)	0.5-1.5
ALT	IU/L	47.2 ± 7.5 (9-244)	57.6 ± 12.0 (6.0-513)	21-102
ALP	IU/L	710.5 ± 114.3**,c (39-3,000)	505.6 ± 74.0**,d (26-3,000)	29-97
Glucose	mg/dL	144.4 ± 26.6 (47-1,027)	122.4 ± 7.8 (31-530)	65-118
CBC				
WBC	$10^3/\mu L$	28.0 ± 4.1**,e (1.1-102.7)	19.8 ± 1.7**,f (1.4-56.5)	6-17
Neutrophils	$10^3/\mu L$	22.4 ± 3.5**,g (0.5-94.8)	16.0 ± 1.5**,h (1.2-53.3)	3-11.8
Monocytes	$10^3/\mu L$	2.4 ± 0.4 (0.03-10.9)	1.6 ± 0.2 (0.01-7.9)	0.2-2
Lymphocytes	$10^3/\mu L$	2.0 ± 0.4 (0.2-12.4)	1.5 ± 0.1 (0.1-4.8)	1-4.8
PCV	%	38.9 ± 1.3 (21.8-56.1)	39.5 ± 1.2 (14.3-62.4)	37-55
Platelet	/μL	297.2 ± 33.1 (6-865)	265.5 ± 20.2 (15.7-586.0)	200-500

SE, standard error; A-G ratio, albumin-globulin ratio; BUN, blood urea nitrogen; ALT, alanine aminotransferase; ALP, alkaline phosphatase; CBC, complete blood counts; WBC, white blood cell; PCV, packed cell volume.
*Significantly lower than reference range, **significantly higher than reference range.
[a,b; c,d; e,f; g,h]$p < 0.05$.

cervix pyometra, the concentration of BUN (39.2 ± 6.8 *vs* 23.9 ± 2.6 mg/dL, respectively) and glucose (144.4 ± 26.6 *vs* 122.4 ± 7.8 mg/dL, respectively), and the activity of ALP (710.5 ± 114.3 *vs* 505.6 ± 74.0 IU/L, respectively) were higher than the reference range, whereas the concentration of albumin (2.3 ± 0.1 *vs* 2.3 ± 0.1 g/dL, respectively) was lower. Furthermore, the concentration of BUN and the activity of ALP in dogs with closed cervix pyometra were significantly higher than those in dogs with open cervix pyometra ($p < 0.05$). In

the CBC of dogs with closed and open cervix pyometra, PCV and platelet counts were within the reference range, whereas the white blood cell (WBC; 28.0 ± 4.1 *vs* 19.8 ± 1.7 × $10^3/\mu L$, respectively) and neutrophils (22.4 ± 3.5 *vs* 16.0 ± 1.5 × $10^3/\mu L$, respectively) were higher than the reference range. The white blood cell and neutrophils in dogs with closed cervix pyometra were significant higher than those in dogs with open cervix pyometra ($p < 0.05$).

Clinical signs

Clinical signs of 102 dogs with pyometra were anorexia (72.5%, n = 74), vaginal discharge (62.7%, n = 64), depression (52.9%, n = 54), polyuria/polydipsia (33.3%, n = 34), vomiting (41.2%, n = 42), fever (35.8%, n = 39), abdominal distension (32.4%, n = 33), and diarrhea (23.9%, n = 26). The mean duration of clinical signs was 8.39 ± 1.37 days, with a range of 0 to 120 days. Vaginal discharge was more pronounced in dogs with open-cervix pyometra than in those with closed cervix pyometra. Also, abdominal distension was more pronounced in dogs with closed cervix pyometra than in those with open cervix pyometra.

Treatment and outcomes

Among 102 cases of dogs with pyometra at initial presentation, 6 cases were lost because of the economic burdens of clients or referral to other hospitals. Therefore, a total of 96 cases were evaluated for outcome. Surgical treatment was per-

Table 4. Classification according to the clinical signs in 102 dogs with pyometra

Parameters	Incidence (%)		Total (n = 102)
	Closed-cervix (n = 39)	Open-cervix (n = 63)	
Dehydration (≥ 8%)	23 (59.0)a	24 (38.1)b	47 (46.1)
Vaginal discharge	1 (2.6)c	63 (100.0)d	64 (62.7)
Anorexia	34 (87.2)a	40 (63.5)b	74 (72.5)
Polyurea/polydipsia	14 (35.9)	28 (44.4)	34 (33.3)
Vomiting	18 (38.5)	24 (38.1)	42 (41.2)
Depression	23 (59.0)a	31 (49.2)b	54 (52.9)
Abdominal distension	21 (53.8)s	12 (19.0)b	33 (32.4)

Within a row, values with different superscript letters (a and b; c and d) differ ($p < 0.05$).

formed in 86 patients (78.9%), and 10 patients (9.2%) died before surgery. OHE and surgical treatments such as cystotomy and mastectomy for other disorders were performed. Irrespective of surgery, fluid therapy, administration with antibiotics and analgesics, and symptomatic therapy were performed in individual patients. The mean duration of hospitalization was 2.91 ± 0.24 days, with a range of 1 to 13 days. The surgical mortality rate was 10.5% (9/86). The recovery rate of all pyometra cases was 80.2% (77/96), and that of surgery cases was 89.5% (77/86).

Ultrasonographic appearances of various types of pyometra

Ultrasonographic findings of closed-cervix pyometra included variable patterns (Fig 1). The uterine horns were markedly enlarged and contained hypoechoic material that showed movement in real time. The uterine wall was variable in appearance, from thick and irregular (30 cases) to smooth and thin (36 cases). Thickened uterine wall had cystic and focal hyperechoic structures. The thickened endometrium contained many focal hyperechoic structures that represented tortuous glandular ducts. The luminal cavity included anechoic fluid with strong distal enhancement.

Ultrasonographic appearances of open cervix pyometra were as seen in Fig 2. The uterine horns contained hyperechoic or anechoic material that showed movement in real time. The uterine wall was thicker than that of closed cervix pyometra. Also, the uterine wall was thickened and irregular (16 cases), and contained multiple tiny anechoic cysts (Fig 2C). The luminal cavity included smaller amounts of anechoic fluid than that of closed-cervix pyometra.
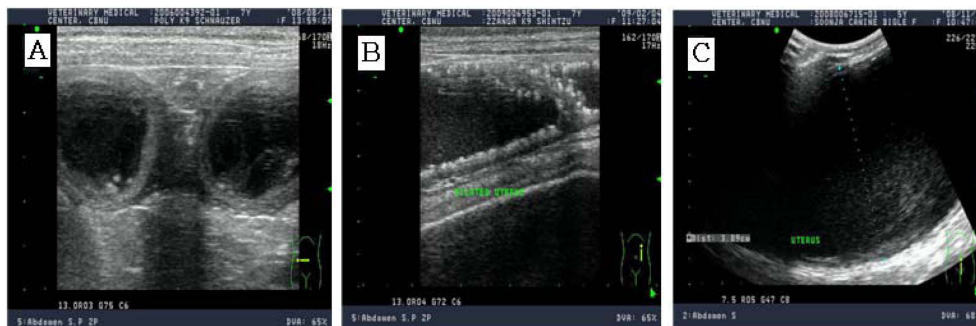

Fig 1. Ultrasonograms of the uterus in dogs with closed-cervix pyometra. A) Right and left uterine horns in a 7-year-old Schnauzer dog with cystic endometrial hyperplasia-pyometra complex, transverse image. The uterine horns contain hypoechoic material that showed movement in real time. The uterine walls are thick. Thickened uterine walls have cystic and focal hyperechoic structures. B) Left uterine horn in a 7-year-old Shih Tzu dog with cystic endometrial hyperplasia-pyometra complex, sagittal image. The uterine horns contain hypoechoic material. The uterine wall is thick. Within the thickened endometrium, there are many focal hyperechoic structures that represent tortuous glandular ducts. A 7.5-10 MHz multi-transducer was used (images A and B). C) Enlarged uterine horn in a 5-year-old Beagle dog with pyometra, transverse image. The uterine horn is markedly enlarged and contains hypoechoic material that showed movement in real time. The uterine wall is thin. The luminal cavity includes anechoic fluid with strong distal enhancement. A 5-10 MHz convex array transducer was used.
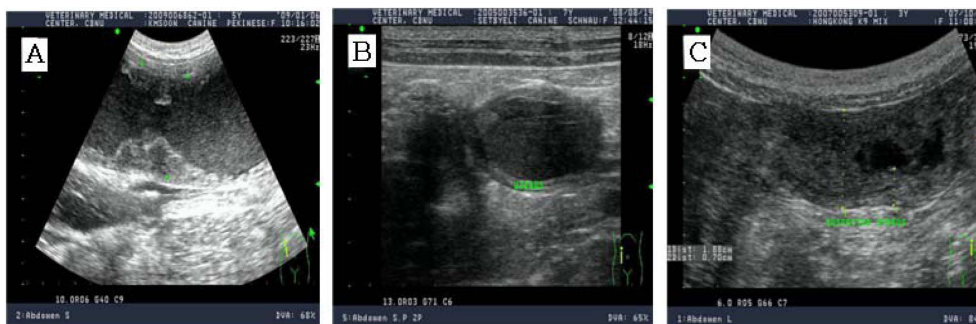

Fig 2. Ultrasonograms of uterus in dogs with open-cervix pyometra. A) Right uterine horn in a 5-year-old Pekingese dog with cystic endometrial hyperplasia-pyometra complex, sagittal image. The uterine horns contain hyperechoic material that showed movement in real time. The uterine walls are thick. Thickened uterine wall have cystic and focal hyperechoic structures. A 5-10 MHz multi-convex array transducer was used. B) Right and left uterine horns in a 7-year-old Schnauzer dog with cystic endometrial hyperplasia-pyometra complex, transverse image. The uterine horn contains hypoechoic material that showed movement in real time. The uterine wall is thick. Thickened uterine walls have cystic and focal hyperechoic structures. A 7.5-10 MHz multi-transducer was used. C) Left uterine horn in a 3-year-old mixed-breed dog with cystic endometrial hyperplasia-pyometra complex, sagittal image. The uterine wall is thickened and irregular and contains multiple tiny anechoic cysts. A small amount of anechoic fluid is present in the uterine lumen. A 5-10 MHz multi-convex array transducer was used.

Discussion

Canine pyometra is a commonly diagnosed disease of the reproductive system at routine clinical fields, but is potentially life-threatening disease (3,27,29). Therefore, prompt and accurate diagnosis is essential for proper treatment of dogs with pyometra.

In this study, Maltese, Yorkshire Terrier and Shih Tzu dogs showed a higher prevalence of pyometra than other breeds, Pekingese and Poodle showed a lower prevalence of pyometra than other breeds. This was inconsistent with a previous study that reported that Pekingese and Poodle had a significantly lower risk of developing pyometra than other breeds (22). A genetic predisposition for pyometra has not been evaluated, but, several studies have described a high prevalence of pyometra within certain breeds including Bullmastiff, Golden Retriever, Rottweiler and Miniature Schnauzer (14,19,25).

The mean age of the cases (9.57 years) in this study is similar to that in a study on colony-reared Beagles (13) but older than other studies (6,14,25). The higher mean age may be associated with the relatively high distribution of small and toy breeds. Distribution of canine breeds in Korea is not yet described, so further study is required. Variation in age at diagnosis of pyometra among breeds was consistent with previous study (14). However, in the present study, Pekingese dogs presented with pyometra at a younger age (7.1 years) and Poodle dogs presented at an older age (11.1 years) than other breeds, which was not discussed in previous studies (14,25). One study described that the risk of pyometra and developing age may be associated with breeds with possible genetic predispositions (7).

In the present study, the mean interval from the last known estrus to presentation was 10.3 weeks (data not shown), which was similar to previous report (2). Based on the history taking, the duration from onset of clinical signs to admission was 8.39 days, which indicated that most of the clinical signs of pyometra were nonspecific when compared with other disorders. In the authors' opinion, besides cases with vaginal discharge, most owners may not become suspicious of pyometra based only on clinical signs. The proportion of clinical signs was not different from previous studies (15,31). Dogs with closed cervix pyometra were 3.8 times more likely to have a worse prognosis than dogs with open cervix pyometra (28). This may have been due to inhibited elimination of the infectious contents of the uterine lumen due to the closed uterine cervix and the increased probability of complications such as endotoxemia, septicemia, and septic peritonitis (24,28).

Dogs with pyometra showed various abnormalities of hematological and biochemical variables (5,12,15,21). In the present study, abnormal patterns of blood profiles were similar to previous studies (12,21). The degree of electrolyte imbalance may be caused by the severity and duration of dehydration. Increased concentrations of BUN and creatinine were common complications of pyometra, and they may be also caused by dehydration associated with anorexia and vomiting (17,32). In dogs with pyometra, the mean concentration of albumin was lower than the reference range, but the concentration of total protein was within the reference range. This means that albumin was lost through the kidney and/or was under-produced by hepatic disease, but levels of acute phase proteins such as C-reactive protein and gamma-globulin, which are produced in response to chronic antigen stimulation, were increased as an acute and chronic inflammatory reaction (3,12,21). The mean activity of ALP (552.9 ± 60.4 IU/L) was increased. This indicated that toxemia originating from pyometra may inhibit synthesis of liver enzymes and damage the hepatic membrane (2,21). Leukocytosis with neutrophilia was assessed as a response of leukocytes to inflammation. However, the mean lymphocyte count was at the low end of the reference range, indicating that suppression of lymphocyte activity may be induced by toxemia (8).

The onset of clinical signs in dogs with pyometra is gradual and insidious (35). Generally, clinical signs include vomiting, abdominal distension, dehydration, anorexia and polyuria/polydipsia (1,5,35). In the present study, the occurrence order of clinical signs of pyometra in dogs were anorexia, depression and dehydration, and these clinical signs were not different between open or closed cervix pyometra. Polyurea/polydipsia and renal impairment are cited as signs of pyometra, but these signs are not consistent, being recorded in ≤ 50% of bitches with pyometra (35). In the present study, the prevalence of polyurea and polydipsia was 41.2%, which was similar to previous report (35).

Ultrasonography is the best tool for diagnosis of canine pyometra (2,30,36). Ultrasonographic findings of the uterus with pyometra showed variable patterns, such as hypoechoic or hyperechoic fluid in the uterine lumen, a thickened uterine wall, or a uterine wall with CEH (9,26,33). In the present study, the luminal cavity of open-cervix pyometra included a smaller amount of anechoic fluid than that of closed-cervix pyometra. This is due to continuous leakage of uterine fluid.

These results indicate that bitches with closed cervix pyometra are in a more serious state than those with open cervix pyometra. Therefore, these patients must undergo hematological and blood biochemical examination, as the bitches with pyometra may have liver damage, dehydration and electrolyte imbalance. Also, treatment of the liver and correction of electrolyte balance be undertaken before surgical/medical treatment of pyometra based on the patient's examination results. In particular, pyometric bitches with abdominal distention must treated as a medical emergency requiring rapid intervention to prevent uterine rupture (31).

References

1. Asheim A. Pathogenesis of renal damage and polydipsia in dogs with pyometra. J Am Vet Med Assoc 1965; 147: 736-745.
2. Bigliardi E, Parmigiani E, Cavirani S, Luppi A, Bonati L, Corradi A. Ultrasonography and cystic hyperplasia-pyometra complex in the bitch. Reprod Domest Anim 2004; 39: 136-

140.

3. Borresen B. Pyometra in the dog. II.-A pathophysiological investigation. II. Anamnestic, clinical and reproductive aspects. Nord Vet Med 1979; 31: 251-257.

4. Debosschere H, Ducatelle R, Vermeirsch H, Van Den Broeck W, Coryn M. Cystic endometrial hyperplasia-pyometra complex in the bitch: should the two entities be disconnected. Theriogenology 2001; 55: 1509-1519.

5. DeSchepper J, DeCock I, Capiau E. Urinary gamma-glutamyl transferase and the degree of renal dysfunction in 75 bitches with pyometra. Res Vet Sci 1989; 46: 396-400.

6. Dow C. The cystic hyperplasia-pyometra complex in the bitch. J Comp Pathol 1959; 69: 237.

7. Egenvall A, Hagman R, Bonnett BN, Hedhammar A, Olson P, Lagerstedt AS. Breed risk of pyometra in insured dogs in Sweden. J Vet Intern Med 2001; 15: 530-538.

8. Faldyna M, Laznicka A, Toman M. Immunosuppression in bitches with pyometra. J Small Anim Pract 2001; 42: 5-10.

9. Fayrer-Hosken RA, Mahaffey M, Miller-Liebl D, Caudle AB. Early diagnosis of canine pyometra using ultrasonography. Vet Radiol 1991; 32: 287-289.

10. Feldman EC, Nelson RW. Diagnosis and treatment alternatives for pyometra in dogs and cats. Curr Vet Ther Small Anim Pract 1989; 10: 1305-1310.

11. Fieni F, Martal J, Marnet PG, Siliart B, Bernard F, Riou M. Hormonal variations in bitches after early or mid pregnancy termination with aglepristone (Ru 534). J Reprod Fertil 2001; 57(Suppl): 243-248.

12. Fransson B, Lagerstedt AS, Hellmen E, Jonsson P. Bacteriological findings, blood chemistry profile and plasma endotoxin levels in bitches with pyometra or other uterine diseases. Zentralbl Veterinarmed A 1997; 44: 417-426.

13. Fukuda S. Incidence of pyometra in colony-raised beagle dogs. Exp Anim 2001; 50: 325-329.

14. Gibson A, Dean R, Yates D, Stavisky J. A retrospective study of pyometra at five RSPCA hospitals in the UK: 1728 cases from 2006 to 2011. Vet Rec 2013; 173: 396.

15. Gilbert RO, Nothling JO, Oettle EE. A retrospective study of 40 cases of canine pyometra-metritis treated with prostaglandin F-2 alpha and broad-spectrum antibacterial drugs. J Reprod Fertil 1989; 39(Suppl): 225-229.

16. Gobello C, Castex G, Klima L, Rodríguez R, Corrada Y. A study of two protocols combining aglepristone and cloprostenol to treat open cervix pyometra in the bitch. Theriogenology 2003; 60: 901-908.

17. Hagman R. Diagnostic and prognostic markers for uterine diseases in dogs. Reprod Domest Anim 2014; 49(Suppl 2): 16-20.

18. Hardy RM, Osborne CA. Canine pyometra: pathogenesis, physiology, diagnosis and treatment of uterine and extra-uterine lesions. J Am Anim Hosp Assoc 1974; 10: 245-268.

19. Jitpean S, Hagman R, Strom Holst B, Hoglund OV, Pettersson A, Egenvall A. Breed variations in the incidence of pyometra and mammary tumours in Swedish dogs. Reprod Domest Anim 2012; 47(Suppl 6): 347-350.

20. Johnston SD, Kustritz MVR, Olson PNS. Disorders of the canine uterus and uterine tubes (oviducts). In: Canine and Feline Theriogenology. Philadelphia: Saunders. 2001: 206-224.

21. Kaymaz M, Bastan A, Erunal N, Aslan S, Findik M. The use of laboratory findings in the diagnosis of CEH-pyometra complex in the bitch. Turk J Vet Anim Sci 1999; 23: 127-133.

22. Krook L, Larsson S, Rooney JR. The interrelationship of diabetes mellitus, obesity, and pyometra in the dog. Am J Vet Res 1960; 21: 120-127.

23. MacIntire DK. Reproductive emergencies. Presentation to participants at Western Veterinary Conference, 2004.

24. Nelson RW, Feldman EC, Stabenfeldt GH. Treatment of canine pyometra and endometritis with prostaglandin F2 alpha. J Am Vet Med Assoc 1982; 181: 899-903.

25. Niskanen M, Thrusfield MV. Associations between age, parity, hormonal therapy and breed, and pyometra in Finnish dogs. Vet Rec 1998; 143: 493-498.

26. Nyland TG, Mattoon JS. Ovaries and uterus. In: Small Animal Diagnostic Ultrasound 2nd ed. Philadelphia: Saunders. 2002: 231-249.

27. Okano S, Tagawa M, Takase K. Relationship of the blood endotoxin concentration and prognosis in dogs with pyometra. J Vet Med Sci 1998; 60: 1265-1267.

28. Pretzer SD. Clinical presentation of canine pyometra and mucometra: a review. Theriogenology 2008; 70: 359-363.

29. Purvis D, Kirby R. Systemic inflammatory response syndrome: septic shock. Vet Clin North Am Small Anim Pract 1994; 24: 1225-1247.

30. Renton JP, Boyd JS, Harvey MJA. Observations on the treatment and diagnosis of open pyometra in the bitch (Canis familiaris). J Reprod Fertil 1993; 47(Suppl): 465-469.

31. Smith FO. Canine pyometra. Theriogenology 2006; 66: 610-612.

32. Stone EA, Littman MP, Robertson JL, Bovee KC. Renal dysfunction in dogs with pyometra. J Am Vet Med Assoc 1988; 193: 457-464.

33. Troxel M, Cornetta A, Pastor K, Hartzband L, Besancon M. Severe hematometra in a dog with cystic endometrial hyperplasia/ pyometra complex. J Am Anim Hosp Assoc 2002; 38: 85-89.

34. Vermeirsch H, Simoens P, Hellemans A, Coryn M, Lauwers H. Immunohistochemical detection of progesterone receptors in the canine uterus and their relation to sex steroid hormone levels. Theriogenology 2000; 53: 773-788.

35. Verstegen J, Dhaliwal G, Verstegen-Onclin K. Mucometra, cystic endometrial hyperplasia, and pyometra in the bitch: advances in treatment and assessment of future reproductive success. Theriogenology 2000; 70: 364-374

36. Voges AK, Neuwirth L. Ultrasound diagnosis-cystic uterine hyperplasia. Vet Radiol Ultrasound 1996; 37: 131-132.

37. Wheaton LG, Johnson AL, Parker AJ, Kneller SK. Results and complications of surgical treatment of pyometra: a review of 80 cases. J Am Anim Hosp Assoc 1989; 25: 563-568.