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**Research article**

## A retrospective study of suspected pyometra causing systemic illness in 348 dogs

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**Abstract**

The study is a retrospective review for investigate the mortality rate, risk factors for death, and accompanying costs of treatment due to suspected pyometra in dogs from a single vet teaching hospital in Thailand during the year 2016 to 2018. There were 348 dogs with fluid filled in uterine meanwhile had systematically ill during the period of the study. Three dogs were died prior to surgery. The prevalence of urgent ovariohysterectomy was 345 cases from 35,138 of canine outpatients (0.98%). Mongrel dogs were most undergoing surgery followed by Poodles and Shih Tzus. The median age was seven years (range of 11 months to 16 years). A major risk factor for fluid filled in uterine was the use of the injectable medroxyprogesterone acetate as a contraceptive (27.20 %). The post-operative mortality rate was 9.85 % (34/345 dogs). After surgery, nine dogs were died within 12 hours, seven dogs were died between 12 hours to seven days, three dogs were died between seven days to 12 days, five dogs were died at more than 14 days, and ten dogs had unclear death time. The main contributing mortality factor was uterine rupture (adjusted OR 7.38 (95% CI =2.73,19.93)). The cost of hospital treatment per case ranged between 3,000 to 29,815 Thai baht. Ovariohysterectomy in systemically ill dog due to suspected of pyometra can be avoid by schedule spay before seven-year-old. Peri-operative complications such as pancreatitis and renal injuries can occur and cause death. Post-operative monitoring not less than 2 weeks is recommended.

**Keywords:** Canine, Mortality, Non-elective ovariohysterectomy, Systemically ill, Thailand

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## INTRODUCTION

Abnormal fluid filled in the uterine of the dog mostly is caused by five common diseases including acute metritis, cystic endometrial hyperplasia (CEH), mucometra, hydrometra and pyometra (Hagman, 2014; Macintire, 1994). Metritis is commonly present one to seven days after parturition and the other four uterine diseases occur during diestrus or one to four months after estrous (Macintire, 1994). To differentiate those four diseases; cystic endometrial hyperplasia (CEH), mucometra, hydrometra and pyometra may be difficultly in routine practice (Hagman, 2014; Pretzer, 2008). Histopathology is a standard diagnostic tool for identify the uterine diseases (Fransson et al., 1997; Fransson et al., 2004). Pyometra is suspected if the dog is in diestrus and has presenting of fluid-filled in uterine with signs of systemically ill such as inappetite, lethargy, fever, vomiting, polydipsia, diarrhea, severe dehydrate or any other life-threatening status (Hagman, 2014, 2018; Pretzer, 2008; Smith, 2006).

Complications that occur in pyometra dogs were including of peritonitis, kidney injuries, urinary tract infection, uveitis, endotoxaemia, bacteremia, septic shock, disseminated intravascular coagulation (DIC) and multiple organ dysfunction syndrome (MODS) (Hagman, 2017, 2018; Jitpean et al., 2014). In the patients with systemically illness and suspected pyometra, ovariohysterectomy is recommended to be performed as soon as possible to remove the suspected source of inflammation and infection (Hagman, 2018; Macintire, 1994; Martins-Bessa et al., 2015; Smith, 2006). However, non-elective or urgent ovariohysterectomy has high anesthetic risk and results in severe complications with a higher risk of death. The aim of this study is to investigate the mortality rate, risk factors for death, and accompanying costs of treatment in suspected pyometra dogs from a small animal teaching hospital (SATH), Chiang Mai university (CMU) during the year 2016 to 2018. It is the hope of the authors that this study can describe the complications and mortality rate of the dog that underwent an urgent ovariohysterectomy due to suspected of pyometra and to investigate the risk factors that associated death. The information that became from this study might aid Thai veterinarians and dog owners in the prevention and reduction of mortalities associated with surgery in suspected pyometra dog.

## MATERIALS and METHODS

### Study population

Data was collected from the electronic database of the SATH, CMU. The retrospective period of study was between January 1, 2016 to December 31, 2018.

### Case selection

All suspected pyometra dogs that received ovariohysterectomy after diagnosed fluid filled in uterus at the SATH, CMU were recruited in this study. Fluid accumulation in uterine had confirmed by physical examination, abdominal radiography, and/or abdominal ultrasonography. The common

presenting symptoms of systemically illness included inappetite, lethargy, fever, abdominal distension, vaginal discharge, vomiting, pyrexia, diarrhoea, polyuria and polydipsia, severe dehydrate, and/or shock. Individual case data was recorded for breed, age, body weight, physical examination parameters, clinical signs, and outcome.

### **Blood Analysis**

Hematology including hematocrit, total white blood cell count, platelet count; and blood chemistry tests including blood urea nitrogen (BUN), creatinine, total protein, and albumin were reviewed for each case.

### **Mortality**

The information of death or hospital discharge in all cases were collected from the medical record. In the cases that had no information of death in the electronic database, telephone interview with the dog owners were performed to verify the mortality case by case.

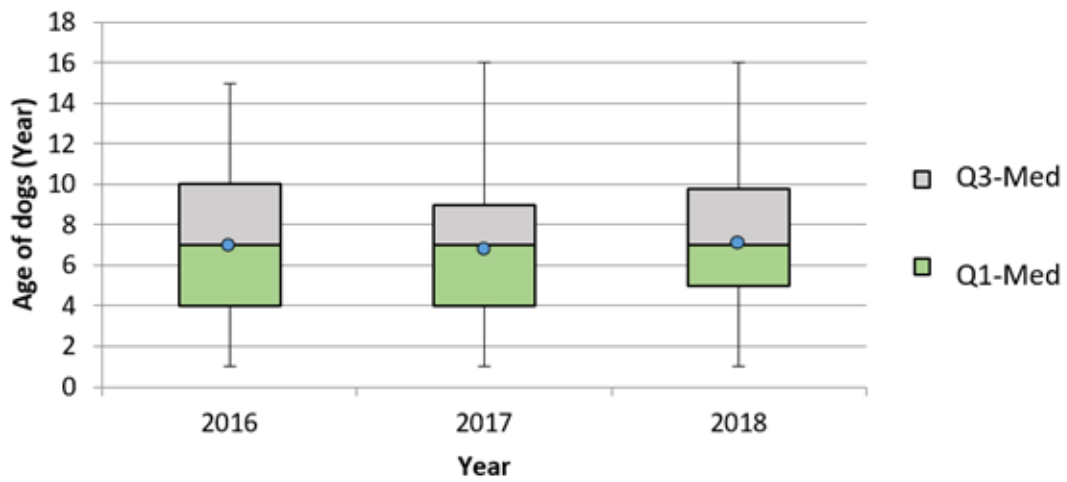
### **Statistical Analysis**

Descriptive analysis was used (e.g., mean, standard deviation, proportion, and percentage). Dog breeds were defined by categories set in the hospital database, with all Mongrel breeds grouped into a single category for data analysis. The incidence and prevalence were calculated using the denominator as the total number of female dogs presenting to SATH for treatment in each year and during the three-year period, respectively. R software program, version 3.6.0 (R Foundation for Statistical Computing) was using to analyses risk factors for death. Crude Odd ratio and adjusted Odd ratio with 95% CI were calculated with the clinical variables that were significant ( $P < 0.05$ ) based on multivariate analysis.

## **RESULTS**

A total 348 of dog that suspected pyometra have agreed with the owner to perform ovariohysterectomy during three years of study. Unfortunately, three dogs were died prior surgery. The prevalence of ovariohysterectomy due to suspected canine pyometra in 3 years (2016 to 2018) was 0.98 percent (345/35,138). The incidence of non-elective ovariohysterectomy due to systemically illness were 120 dogs (120/11535 (1.04%)), 120 dogs (120/11881 (1.01%)), and 105 dogs (105/11722 (0.9%)) in the year 2016 to 2018, respectively. The clinical signs of suspected pyometra dogs that were recorded in the computer database included abdominal distension 84.19% (293/348), vaginal discharge 73.56% (256/348), vomiting 14.94% (52/348), pyrexia 14.08% (49/348), diarrhea 5.46% (19/348) and polyuria/polydipsia 3.73 % (13/348). All dogs had showed sign of depress and decrease appetite. Median age was 7 years, with a range of 11 months to 16 years (Figure 1). Mongrel breed dogs were most undergoing surgery (124/345, 35.94%) followed by Poodles (51/345, 14.78%) and Shih Tzus (43/345, 12.46%) (Table 1). The presence of suspected pyometra was generally uniformly distributed throughout the study period (Figure 2). An average cost of treatment in each case from 2016 to 2018 were  $4,856.97 \pm 1,938.97$ ,  $8,236.69 \pm$

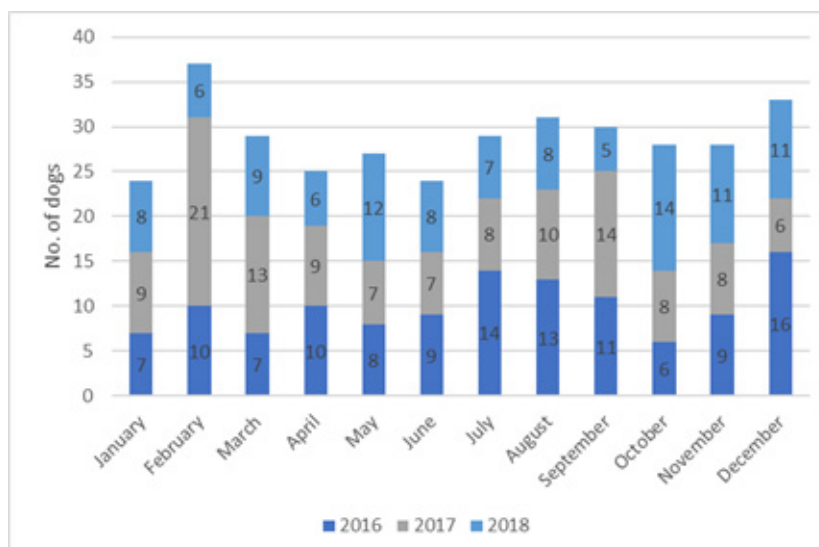
4,348.18, and 8,565.35 ± 5,038.78 Thai baht, respectively. The minimum cost of treatment was 3,000 Thai baht and the maximum cost of treatment was 29,815 Thai baht (Figure 3).



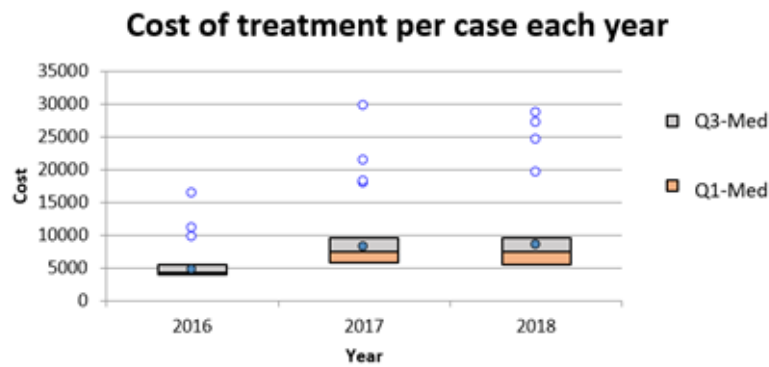
**Figure 1** Age of 348 fluid filled in uterine dogs that showed signs of systemically ill in each year (2016 to 2018). Q3-Med is the age which divide data to less than 75% and more than 25% to median of age. Q1-Med is the age which divide data to less than 25% and more than 75% to median of age.

**Table 1** The incidence of the dog breed that performed non-elective ovariohysterectomy due to systemically ill in each year (2016 to 2018) (n=345 dogs).

Breed	2016	2017	2018
Akita	1	0	0
Bang-kaew	1	2	0
Bichon Frise	0	1	0
Chihuahua	4	3	7
Doberman Pinscher	0	1	0
French, English Bulldog	0	1	3
German shepherd	0	0	1
Golden Retriever	5	6	5
Jack-Russell Terrier	3	0	1
Labrador Retriever	4	7	6
Miniature Pinscher	1	0	2
Mongrel breeds	53	43	28
Pekingese	1	1	0
American-Pit-Bull Terrier	3	0	1
Pomeranian	3	11	9
Poodle	15	24	12
Pug	5	4	6
Rottweiler	2	0	0
Miniature Schnauzer	0	0	2
Shih-Tzu	14	12	17
Siberian Husky	2	4	2
Spritz	2	0	0
St. Bernard	0	0	1
Yorkshire Terrier	1	0	2
<b>Total</b>	<b>120</b>	<b>120</b>	<b>105</b>



**Figure 2** The number of 345 suspected pyometra dogs that were undergoing urgent ovariohysterectomy in each month during 2016 to 2018.



**Figure 3** Boxplots show cost of treatment per case in each year (2016 to 2018) (N= 348). Q3-Med is the number which divide data to less than 75% and more than 25% to median. Q1-Med is the number which divide data to less than 25% and more than 75% to median.

Three most common signs that found from blood examination were leukocytosis, hyperproteinemia, and normal BUN and creatinine (Table 2). The SNAP® 4Dx® (IDEXX Laboratories, Westbrook, ME) was performed in 53 suspected pyometra dogs. Twenty-two dogs had negative results, twenty-eight dogs had positive antibody to *Ehrlichia canis*, and *E. ewingii*, eleven dogs had positive antibody to *Anaplasma phagocytophilum* and *A. platys*, and four dogs has positive with *Dirofilaria immitis* antigen. *Hepatozoon canis* were found in blood smear of three dogs. The post-operative mortality rate was 9.85 % (34/345 dogs). The reported causes of post-operatively death in the hospital database included pancreatitis which confirmed by abnormal SNAP® cPL™ (canine pancreas-specific lipase) Test (IDEXX Laboratories, Westbrook, ME) (5 dogs), renal failure (13 dogs), severe thrombocytopenia and/or anemia (11 dogs), peritonitis from uterine rupture (3 dogs), severe leukocytosis (1 dog), and hepatic failure (1 dog). There were nine dogs that died within 12 hours post-operatively, seven dogs that died between 12 hours to seven days post-operatively, three dogs that died between one to two weeks post-operatively, four dog that died between two to 18 weeks post-operatively, one dog that died after two years post-operatively due to azotemia from renal insufficient which presented following by the disease, and 10 dogs that had died post-operatively but had undefined death times due to vague reporting times by the owners during telephone interviewing. The incidence of incomplete removal of ovaries during previous ovariohysterectomy was 0.87 % (3/345). Stump pyometra with or without ovarian remnants were noted in 2.02 % of cases (7/345). A history of using injected medroxyprogesterone acetate as contraceptives was recorded in 29.31 % of cases (102/348).

**Table 2** Preoperative blood results of the total 345 suspected pyometra dogs (2016 – 2018). There were 120, 120, and 105 suspected pyometra dogs in year 2016 to 2018, respectively.

Blood Results	2016 (N= 120) (n (%))	2017 (N =120) (n (%))	2018 (N= 105) (n (%))	Total (N=345) (n (%))
<b>White Blood Cell Count</b>				
Leukopenia (WBC < 6x10 <sup>3</sup> /μL)	5 (4.17)	2 (1.67)	3 (2.86)	10 (2.90)
Normal (WBC ≥ 6x10 <sup>3</sup> to ≤ 16x10 <sup>3</sup> /μL)	22 (18.33)	23 (19.17)	20 (19.05)	65 (18.84)
Leukocytosis (WBC >16x10 <sup>3</sup> /μL)	93 (77.50)	95 (79.17)	82 (78.10)	270 (78.26)
<b>Band neutrophil</b>				
<10% band neutrophil	64 (53.33)	57 (47.5)	42 (40)	163 (47.25)
≥10% band neutrophil	56 (46.66)	62 (51.67)	64 (60.96)	182 (52.75)
<b>Hematocrit</b>				
Anemia (PCV < 35%)	58 (48.33)	48 (40.00)	46 (43.81)	152 (44.06)
Normal (PCV ≥ 35 to ≤ 57%)	62 (51.67)	72 (60.00)	59 (56.19)	193 (55.94)
<b>Platelet</b>				
High (>621x 10 <sup>3</sup> /μL)	2 (1.67)	1 (0.83)	2 (1.90)	5 (1.45)
Normal (≥211x10 <sup>3</sup> to ≤621x10 <sup>3</sup> /μL)	74 (61.67)	70 (58.33)	74 (70.48)	318 (92.17)
Low (<211x 10 <sup>3</sup> /μL)	44 (36.67)	49 (40.83)	29 (27.61)	122 (35.36)
<b>BUN</b>				
Increase (>28 mg/dl)	30 (25.00)	38 (31.17)	28 (26.67)	96 (27.83)
Normal (≥ 8 to ≤ 28 mg/dl)	90 (75.00)	82(68.33)	77(73.33)	249 (72.17)
<b>Creatinine</b>				
Increase (>1.7 mg/dl)	19 (15.83)	27(22.50)	19 (18.10)	65 (18.84)
Normal creatinine (≥ 0.5 to ≤ 28 mg/dl)	101 (84.17)	93(77.50)	86 (81.90)	280 (81.16)
Azotemia (increase BUN & creatinine)	15 (12.5)	26 (21.67)	17 (16.20)	58 (16.81)
Normal BUN & creatinine	105 (87.5)	94(78.33)	88 (83.81)	287 (83.19)
<b>Alkaline phosphatase (ALP)</b>				
High (≥114U/L)	63 (52.50)	70 (58.33)	68 (64.76)	201 (58.26)
Normal (>1 to <114 U/L)	57 (47.50)	49 (41.66)	38 (35.23)	144 (41.74)
<b>Total Protein</b>				
Hyperproteinemia (> 5.4 g/dl)	78 (65.00)	76(63.33)	72 (68.57)	226 (65.51)
Normal (≥ 5.4 to ≤ 7.5 g/dl)	22 (18.33)	28 (23.33)	19 (42.86)	69 (20)
Hypoproteinemia (< 7.5 g/dl)	20 (16.67)	16 (13.335)	14 (13.33)	50 (14.49)
<b>Albumin</b>				
Hyperalbuminemia (> 3.1 g/dl)	5 (4.17)	9(7.50)	4 (3.81)	18 (5.22)
Normal (≥ 2.3 to ≤ 3.1 g/dl)	53 (44.17)	58 (48.33)	56 (53.33)	167 (48.40)
Hypoalbuminemia (< 2.3 g/dl)	62 (51.67)	53 (44.17)	45 (18.10)	160 (46.38)

The calculation of risk factor with death was based on logistic regression model. The clinical variables (ages, body weight, azotemia, uterine rupture, the presenting of vaginal discharge and the amount of total white blood cell count before surgery) that were significant ( $P < 0.05$ ) based on univariate analysis were selected to perform multivariate analysis. Finally, the only one factor that related with suspected pyometra death was uterine rupture. The fluid filled in uterus dog that presented with uterine rupture had 7.38 times risk to death than dog without uterine rupture (adjusted odd ratio 7.38 (95% CI = 2.73, 19.93)) as shown in the Table 3.

**Table 3** The relationship between clinical factors including ages, body weight, azotemia, uterine rupture, the presenting of vaginal discharge and WBC with death in 345 suspected pyometra dogs. Crude odd ratio (OR) and adjusted odd ratio (OR) were calculated with 95% CI.

Factors	Death	Alive	Crude OR (95%CI)	Adjusted OR (95%CI)	P (Wald's test)	P (LR-test)
<b>Age:</b> <7 and >7 years			0.49 (0.21,1.16)	0.45 (0.18,1.16)	0.098	0.087
>7	24	163				
<7	10	148				
<b>Body weight:</b>						
Giant breed (34-54.5 kg)	1	7	Referent group	Referent group		
Large breed (25-38.5 kg)	5	33	0.58 (0.05,6.57)	0.42 (0.03,5.48)	0.507	NA
Medium breed (16-29.5 kg)	3	47	0.43 (0.04,4.82)	0.2 (0.02,2.71)	0.228	NA
Small breed (3-15.9 kg)	25	177	0.75 (0.09,6.55)	0.4 (0.04,4.17)	0.447	NA
Toy breed (0.9-4 kg)	0	47	0 (0, Inf)	0 (0, Inf)	0.99	NA
<b>Azotemia: non azotemia</b>			1.95 (0.78,4.88)	1.78 (0.62,5.16)	0.286	0.3
Azotemia	7	45				
Non azotemia	20	241				
<b>Uterine rupture, leak, Abdominal lavage: not rupture</b>			6.24 (2.64,14.76)	7.38 (2.73,19.93)	< 0.001	< 0.001
Rupture	12	35				
not rupture	22	276				
<b>Type:</b>						
open pyometra: close pyometra			0.55 (0.24,1.26)	0.63 (0.24,1.61)	0.332	0.341
Open pyometra	22	231				
Close pyometra	12	73				
<b>White blood cell:</b>						
Decrease (Leucopenia)	2	9	Referent group	Referent group		
Normal	5	49	0.32 (0.05,2.08)	0.55 (0.07,4.6)	0.581	Na
Increase (leukocytosis)	23	239	0.32 (0.06,1.63)	0.4 (0.06,2.64)	0.344	Na



## DISCUSSION

This study found that the only statistically significant factor that contributed to suspected pyometra related death was uterine rupture. The other factors, such as age, body weight, azotemia, initial white blood cell count, and the presenting of vaginal discharge, did not significantly contribute to mortality outcomes. The post-operative mortality rate of 9.85 % (34/345 dogs) was confirmed from the record in the computer database and telephone interviews with the dog owners. Post-operative complications accounted for most of the deaths, with most complications occurring within the first 14 days. Based on this study, the authors suggest close and constant post-operative monitoring of suspected pyometra cases for at least 2 weeks.

The most common hematological abnormality in fluid-filled uterine with systemically ill dogs was leukocytosis. The incidence of anemia and normal hematocrit in suspected pyometra dogs was equally presented which was similarly to the previous studies that reported, dogs with pyometra can have lower or normal red blood cell counts. (De Schepper et al., 1987). The anemia was happened in some case according to the chronic stage of disease or the systemic inflammatory response (Fransson and Ragle, 2003). In this study, the concurrent diseases e.g., Anaplasmosis, Ehrlichiosis, Hepatozoonosis, and Dirofilaria which caused worsen the severity of disease and showed more abnormality in blood results could be detected. Latent or persistent infection caused by external parasites and mosquitos are commonly found in the dog in Thailand. The Thai vet should therefore perform additional tests in the dog that has showing more severe symptoms or severe abnormal blood result. In this study, 61 out of 348 fluid-filled in uterine dogs had azotemia. From continue monitoring those azotemia dogs in the computer database, eight of them eventually died, 38 dogs recovered to normal BUN and creatinine levels, and 15 dogs progressed to chronic renal insufficiency.

There was neither an increase nor decrease in suspected canine pyometra cases over the three-year study period (2016 to 2018). The annual number of suspected pyometra dogs was approximately 105 to 120 per year (2016 to 2018). One possible reason for the low cases of suspected pyometra in this study is that SATH, CMU is a university teaching hospital that functions primarily as a referral tertiary hospital and therefore does not account for pyometra cases that have already been treated by primary care veterinarians.

In the previous studies reported the mean age of pyometra dogs were between 5.5 to 10 years (Fukuda, 2001; Petchoo et al., 2008; Whitehead, 2008) which is similar to the findings of suspected pyometra dogs of this study (average 7 years). In this study, mongrel dogs were most commonly affected followed by Poodles and Shih Tzus. This differed from previous studies conducted in other countries such as Sweden and the UK where the most common breeds of pyometra dogs included Bullmastiffs, Golden Retrievers, Dogue de Bordeaux, Rottweilers and Cavalier King Charles Spaniels (Gibson, et al. 2013; Jitpean et al., 2012). The pyometra populations reported in different studies may be due to country variation in breed population.

The most commonly signs of sick dogs that were recorded in the electronic database during the study period included abdominal distension, vaginal discharge, vomiting, pyrexia, diarrhea and polyuria/polydipsia. Those

clinical signs were only the obvious clinical signs that the veterinarian was found, or the owner had mentioned during the physical examination. Therefore, the proportion of the clinical signs in this study was unable to represent the truly percentage of clinical signs that should be found in pyometra dogs. A previous report in Thailand also described the major clinical signs of canine pyometra as abdominal distension and vaginal discharge (Petchoo, et al., 2008). Pyometra, pus accumulation in uterine, should confirmed and differentiated from the other uterine diseases such as metritis, cystic endometrial hyperplasia (CEH), mucometra, and hydrometra by histopathology and microbiology examination (Fransson et al., 1997; 2004). However, in SATH, CMU, performing histopathology are not routine practice. The decision to perform surgery was depended on the severity of clinical signs. In systemically ill female dog that had fluid filled in uterine, the surgery will be performed as soon as possible after the dog stable. The limitation of this study is a retrospective study which making definitive diagnosis of fluid filled in uterine was unavailable.

This study found some cases with incomplete ovariohysterectomy surgery (0.87 %) and stump pyometra with/without ovarian remnant (2.02%). Previous studies reported the incidence of incomplete ovariohysterectomy to vary between 0 to 0.5% (Muraro and White, 2014; Okkens, et al. 1997; Pope and Knowles, 2014). A major risk factor for uterine diseases in this study was the use of the injectable medroxyprogesterone acetate as a contraceptive (27.20 %) which caused the same negative effect of using contraceptive drug in the dog as the previous study (Vasetska, 2017).

Various reasons were cited by the dog owners for having an unneutered female dog. These reasons included personal belief that ovariohysterectomy is unnecessary, unwarranted perceived high costs and concerns about hospitalization for the procedure, and general unawareness of uterine diseases risks. There is a need to raise more pet owner awareness about the prevention of uterine diseases via ovariohysterectomy, as well as the financial and welfare consequences of uterine diseases and other reproductive-related problems.

## CONCLUSION

Mortalities associated with suspected canine pyometra could occur in all time peri-operatively. In this study, post-operative complications accounted for the majority of mortalities, with most occurring within the first 14 days post-operatively. The most significant contributing factor to fluid filled in uterine-related mortalities was uterine rupture. To improve outcomes, intensive and extensive pre- and post-operative plans are needed. Based on this study, the authors suggest close and constant post-operative monitoring of suspected pyometra cases for at least 2 weeks. Finally, there is a need to raise more pet owner awareness about the prevention of canine uterine diseases by schedule ovariohysterectomy especially before dog 7-year-old and avoiding of using contraceptive drugs.

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## AUTHORS CONTRIBUTION

**Surapa Rungphattanachaikul;** Data curation, Formal analysis, Investigation, and writing—original draft preparation

**Areerath Akatvipat;** Conceptualization, Methodology, Data interpretation, supervision, project administration and writing—review and editing.

**Michael Pheng Chuan Chia;** writing—review and editing.

**Kannika Na Lampang;** study design, supervision, and formal analysis application of statistical

**Nattawooti Sthitmatee;** Methodology and supervision

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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