A DISSERTATION FOR THE DEGREE OF MASTER

Digital Radiographic Uterus Size for Detecting Uterine Disease Diagnosed by Ultrasound in Dogs

암컷 개에서 자궁질환 진단을 위한 디지털 방사선 영상 상 자궁 크기 평가

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Department of Veterinary Medicine

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지도교수 윤 정 희

이 논문을 수의학석사학위논문으로 제출함

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수의학과 임상수의학 (수의방사선과학) 전공

윤 수 경

윤수경의 석사학위논문을 인준함

2015 년 12 월

위 원 장 _____ 최 민 철 _____ (인)

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Abstract

Digital Radiographic Uterus Size for Detecting Uterine Disease Diagnosed by Ultrasound in Dogs

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It has been believed that the normal uterus is not seen on abdominal radiography in intact female dog. Empirically, however, the uterus can be visualized on radiographs even if the dogs do not have with uterine diseases. The objectives of this study were to prove that the normal non-gravid uterus can be seen on abdominal radiographs, to determine a quantitative index for normal uterus diameter and to evaluate its usefulness in predicting uterine disease in practice.

A total of 213 intact female dogs with abdominal radiographs and abdominal sonograms including full examination of reproductive system were included. They were classified into normal and abnormal groups (cystic endometrial hyperplasia or dilated uterus such as hydro-, muco-, and pyometra) based on the ultrasonographic findings. For each dog, the height of the body of the fifth lumbar vertebra (L5) and the maximal uterus size (U, if identified) were measured on right lateral radiographs and the maximal uterus diameter to the height of the body of the fifth lumbar vertebra (U/L5) ratio was calculated. Seventy eight dogs were into normal group and one hundred thirty five dogs were into abnormal group. Normal uterus was not infrequently identified on abdominal radiographs (twenty seven dogs, 35% in normal group), so identification of the uterus on radiographs alone was not necessarily meaning that the dog have uterine diseases. It was suggested that U/L5 ratio of 1.18 ± 0.53 (mean± 2 SD) be used as normal radiographic uterus size in intact female dogs and a value of 1.60 was recommended for clinical use as having uterine disease is very likely if the value is greater than this.

Key words: female dog, uterus size, ultrasonography, radiography

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Contents

Introduction

Cystic endometrial hyperplasia (CEH) and dilated uterus (hydro-, muco- and pyometra) were common uterine diseases in intact female dogs (Dow, 1959; Feldman and Nelson, 1996; Smith, 2006). The diagnosis of the diseases is best made with aid of the ultrasonography and findings typically include enlarged uterine horns filled with anechoic to echogenic fluid with or without thickened endometrium with cystic structures which is diagnostic for CEH (Bigliardi *et al*, 2004; Schafer-Somi, 2015; Voges and Neuwirth, 1996).

Radiography may also be used as a diagnostic tool for uterine diseases or pregnancy, but frequently inconclusive (Pretzer, 2008). The normal uterus is rarely seen radiographically in the female dog because of its small diameter and soft tissue opacity which is similar to adjacent intestinal loops (Ackerman, 1981; Kinns and Nelson, 2013; Rivers and Johnston, 1991). Compression radiography of abdomen for evaluation of the uterus has been described (Farrow, 1978; Armbrust *et al*, 2000; Woodland *et al*, 2014). It facilitates identification of the uterus by decreasing superimposition of caudal abdominal structures, although it is rarely used today. Uterine width must be at least twice that of small bowel to be reliably detected in abdominal radiographs (Muhlbauer and

Kneller, 2013). In other literature, the diameter of the anestrous, nongravid uterus on survey radiographs was estimated as approximately half of the diameter of the small bowel (Kneller, 1986). Otherwise, previous reports on normal uterus size on radiography are not available. Empirically, however, the uterus can be seen not infrequently on abdominal radiographs even if the uterus was not enlarged.

The objectives of this study were to prove that a normal non-gravid uterus can be seen not infrequently on abdominal radiographs, to determine a quantitative index for normal uterus diameter and to evaluate its usefulness in predicting uterine disease in practice.

Materials and Methods

Animals

Abdominal radiographs and ultrasonograms from intact female dogs, which presented for various causes at Seoul National University Veterinary Medical Teaching Hospital from March 2011 to September 2015 were reviewed. For inclusion, dogs had to have both abdominal radiographs and ultrasonograms with no more than one day apart. Dogs had to have diagnostic quality of radiographs that included right lateral and ventrodorsal views. Dogs with poor serosal detail, or with abnormal lumbar vertebral column were excluded. A normal lumbar vertebra was defined as 7 lumbar vertebra with no transitional vertebra and no other vertebral abnormalities affecting height or length of the vertebral body. Ultrasonograms including captured images of a whole reproductive system (bilateral ovaries, uterine horns, and uterine body or cervix) were included. Patient basic information (age, sex, body weight) and all the relevant clinical data were obtained and evaluated from medical records.

Radiographic measurements

Abdominal radiographs were performed with a digital radiography system (EVA-HF 525, COMED medical system, Seongnam, Korea). kVp and mAs varied depending of the size of patients at a focal film distance of 100 cm.

First, each radiograph was evaluated whether the uterus was observed or not. Positive results, which means the uterus was observable, were only made when the uterus was visualized as a well-defined tubular soft tissue opacity structure between the descending colon and the urinary bladder (Fig. 1). If the uterus was visualized, the dog was classified into "observable" group or, if not, "unobservable" group. Second, the maximal uterus diameter (U) was measured on right lateral view in observable group. Last, the body height of fifth lumbar vertebra (L5) was measured at its narrowest point on the right lateral radiograph. Then the maximal uterus diameter to the height of the body of the fifth lumbar vertebra (U/L5) ratio was calculated. All radiographic measurements were performed three times using an electronic caliper in DICOM (Infinite PACS, Infinite Healthcare, Seoul, Korea) workstation.

FIG. 1. Right lateral abdominal radiograph of an intact female dog in this study. There was a tubular soft tissue opacity structure within the caudal abdomen consistent with the uterus (biheaded arrow), then the dog was classified into observable group. This dog had no remarkable findings in the uterus on following ultrasound exam.

Ultrasonographic uterus size

For each dog, ultrasonograms and ultrasound reports were reviewed. Measurements of right and left maximal uterine diameters on either transverse or longitudinal section which original examiner had made using an electronic caliper of ultrasound machines were scored. And then they were classified into two groups based on the ultrasonographic findings: "Normal" group was defined as no dilatation or thickening and having no cysts or mass lesions in uterine wall. "Abnormal" group included dogs with dilated uterine horns filled with anehoic to echogenic fluid (hydro-, muco-, pyometra) and/or cystic structures embedded in the uterine wall, which is diagnostic for cystic endometrial hyperplasia. Pregnancy, uterine neoplasia or congenital anomalies were excluded in this study.

Group

Based on observation of the uterus on abdominal radiographs and ultrasonographic diagnosis of uterine status, all dogs were classified into 4 groups: Normal-unobservable (group 1), Normal-observable (group 2), Abnormal-unobservable (group 3) and Abnormal-observable (group 4).

Intra- and inter-observer reliability

Sixty-five radiographs were randomly selected and were evaluated by two observers (S.Y. and J.L.). In each radiograph, identification of the uterus was recorded (yes/no) and the uterus maximal diameter, height of L5, and U/L5 ratio were measured three times by each observer independently. The mean of these measurements were compared to evaluate interobserver reliability.

Statistical analyses

Statistical tests were selected and performed by one of the authors (S.Y.) using SPSS (IBM SPSS Statistics for Windows, Version 23.0, IBM Corp.m Armonk, NY). Normality of data was assessed by Shapiro-Wilk test. Age, body weight, radiographic and ultrasonographic measurements were compared in each group using Kruskal-Wallis test and Mann-Whitney test. Correlation between radiographic and sonographic uterus size were assessed by Spearman's correlation coefficient. Receiver operating characteristic (ROC) analysis was performed and the area under the curve (AUC) was calculated to determine cutoff points which are best for overall accuracy, optimizing sensitivity (100% sensitivity), and optimizing specificity (100% specificity). Intra- and interobserver reliabilities were evaluated using the intraclass

correlation coefficient (ICC). The value of ICC was interpreted as follows: >0.75 was excellent, 0.40–0.75 was fair to good, <0.40 was poor (Fleiss, 1999). All data were presented as mean ± standard deviation (SD). For all analyses, a value of $P < 0.05$ was considered statistically significant.

Results

Animals

A total of 213 intact female dogs were included in this study. Seventy-eight dogs (36.6%) were determined to be with normal uterus based on ultrasonographic diagnosis. One hundred thirty five dogs (63.4%) were classified into abnormal group. The uterus appeared on abdominal radiographs in 27 dogs (34.6%) in normal group and 72 dogs (53.3%) in abnormal group.

Breeds were variable and most of them were small breed dogs (Table 1). Shih Tzu was overrepresented (12/27 dogs) in group 2.

The mean age of all dogs was 9.5 ± 3.3 years (range 1 – 17 years old). Ages were significantly different between group 1 and group 3, 4(P = 0.048 between group 1 and 3, P = 0.011 between group 1 and 4). The mean body weight was 5.60 ± 6.34 kg (range 1.4 – 43.0 kg) and it was not significantly different between all groups (Fig. 2).

Table 1. Breed distribution

Breeds	Groups				Total (%)
	1*	2	3	4	
Shih Tzu	7†	12	13	14	46 (21.6)
Maltese	11	4	16	14	45 (21.1)
Yorkshire Terrier	10	1	15	10	36 (16.9)
Poodle	5	1	2	6	14 (6.6)
Mixed breed	4	2	2	2	10 (4.7)
Cocker Spaniel	4	3	1	2	10 (4.7)
Miniature Schnauzer	1	0	5	4	10 (4.7)
Pomeranian	3	1	1	2	7 (3.3)
Pekingese	0	1	1	5	7 (3.3)
Chihuahua	1	0	0	5	6 (2.8)
Golden Retriever	0	0	0	4	4 (1.9)
Jindo Dog	1	1	1	0	3 (1.4)
Dachshund	1	0	1	1	3 (1.4)
Miniature Pinscher	0	0	3	0	3 (1.4)
Others	3	1	2	3	9 (4.2)
Total	51	27	63	72	213 (100.0)

*Group 1, normal-unobservable; group 2, normal-observable; group 3, abnormal-unobservable; group 4, abnormal-observable

†Number of dogs

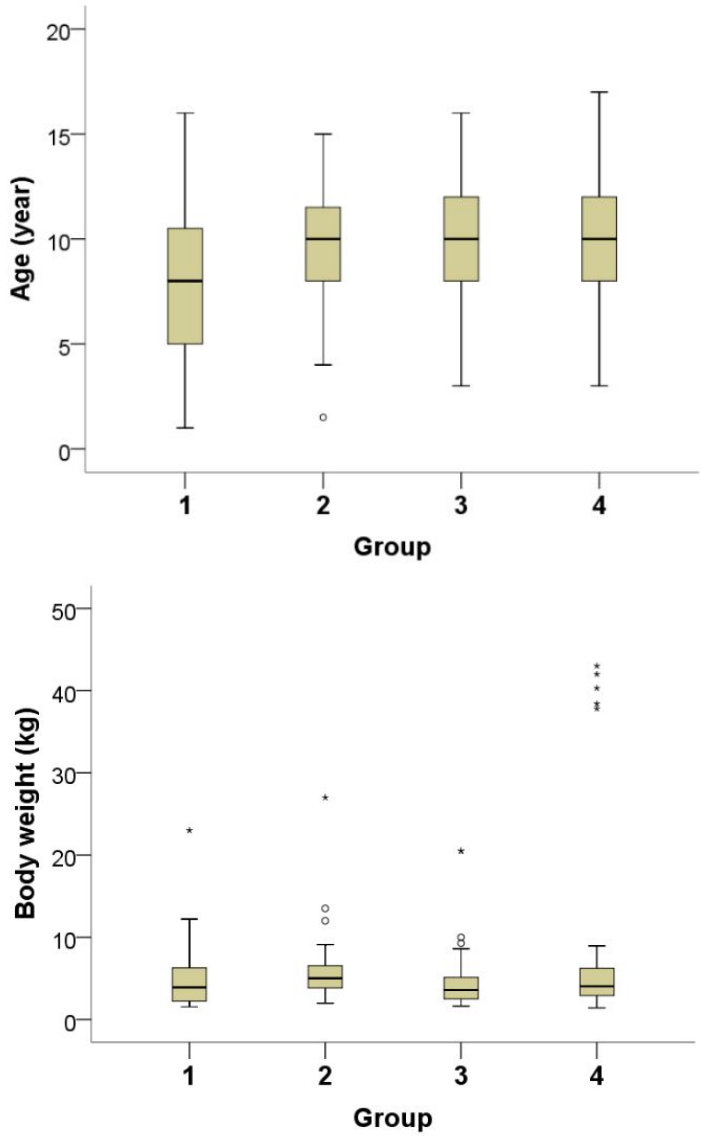

FIG. 2. Boxplots of age and body weight for each of the 4 groups. Age of group 1 was significantly younger than group 3 and 4. There was no significant difference for body weight. (Group 1, normal−unobservable; group 2, normal−observable; group 3, abnormal−unobservable; group 4, abnormal−observable)

Radiographic measurements

On radiographic measurements, the height of L5 was not significantly different between all groups. Both uterus size and U/L5 ratio were significantly higher in group 2 than in group 4 (Table 2). A U/L5 ratio in group 2 was 1.18 ± 0.27, suggesting normal range of uterus on radiographs as 1.18 ± 0.53 (mean ± 2 SD) (Gerstman and Cappucci, 1986).

Table 2. Radiographic measurements between groups

Group	L5 (mm)[‡]	Uterus (mm)	U/L5 ratio[§]	
			Mean±SD	Range
1[*] (n=51)	5.36±1.52	ND[**]	ND	ND
2 (n=27)	6.19±1.69	6.99±1.08	1.18±0.27	0.55–1.59
3 (n=63)	5.45±1.42	ND	ND	ND
4 (n=72)	5.87±2.35	19.17±15.58[†]	3.27±2.10	1.02–11.35[†]

[*]Group 1, normal–unobservable; group 2, normal–observable; group 3, abnormal–unobservable; group 4, abnormal–observable

[†]Significantly different ($P < 0.001$) between groups

[‡]The body height of the fifth lumbar vertebra

[§]The maximal uterus diameter to the body height of the fifth lumbar vertebra ratio

[**]ND, not determined

Ultrasonographic uterus size

There were significant differences ($P < 0.001$) in the uterus sizes on ultrasonographs between groups, except group 1 and 2. The uterus sizes were greater in abnormal groups compared to in the normal groups and greater in observable group than in unobservable group in abnormal groups. However, the ultrasonographic uterus sizes of group 1 and 2 were not significantly different ($P = 0.265$, Fig. 3).

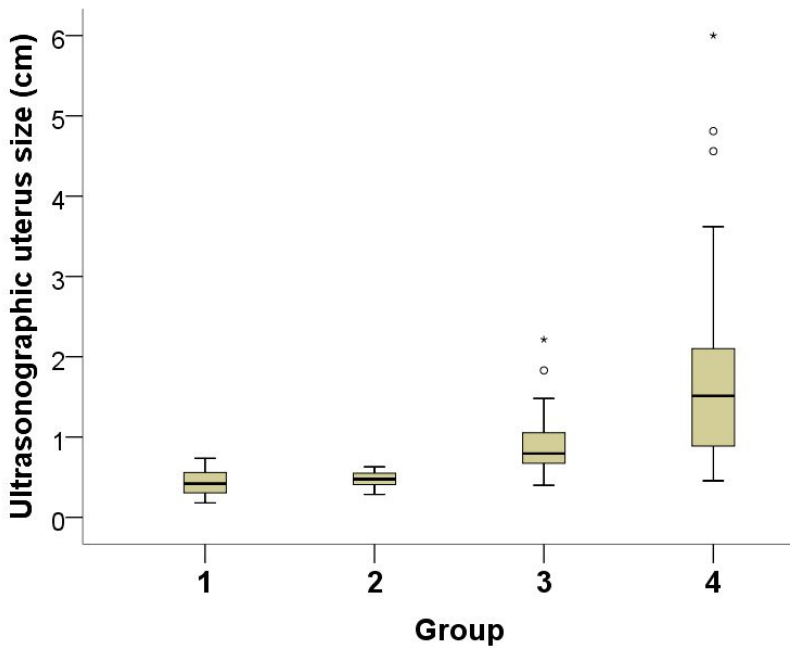

FIG. 3. Boxplots of averaged uterus sizes (cm) on ultrasonographs. Uterus size was significantly greater in abnormal groups (group 3 and 4) than in normal groups (group 1 and 2). It was also greater in group 4 than in group 3. However, there was no significant difference between group 1 and 2. (Group 1, normal−unobservable; group 2, normal−observable; group 3, abnormal−unobservable; group 4, abnormal−observable)

Correlation between radiographic and ultrasonographic uterus size

There was a strong positive linear relationship between radiographic and ultrasonographic uterus size (Fig. 4). Spearman's correlation coefficient was 0.851 ($P < 0.001$).

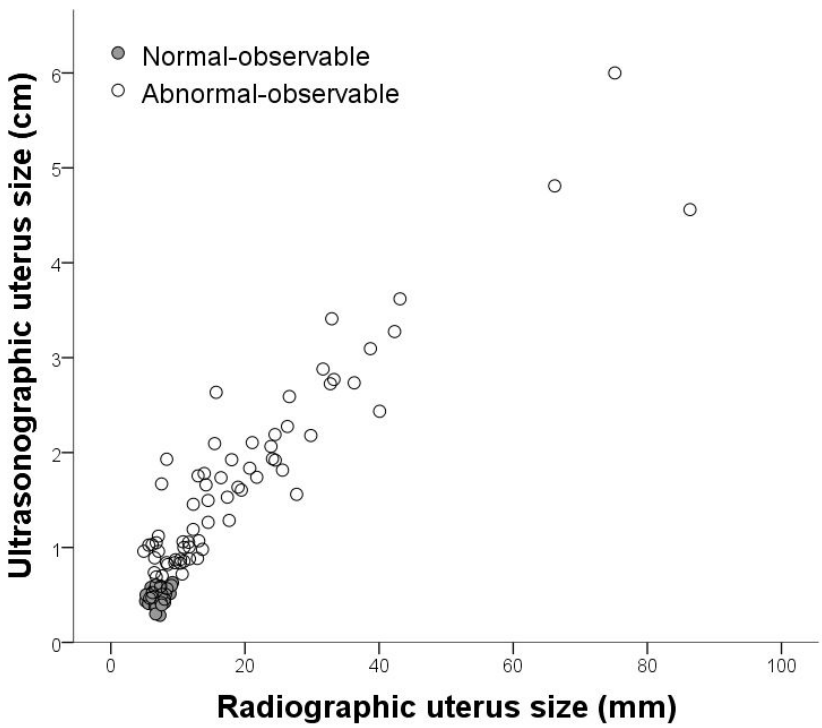

FIG. 4. Correlation between radiographic (mm) and ultrasonographic (cm) uterus size. It showed strong positive correlation between radiographic and ultrsonographic uterus size.

Receiver operating curve (ROC) analysis

In ROC analysis, AUC was 0.915 (95% confidence interval, 0.862 to 0.968). The value of U/L5 ratio for optimizing sensitivity, specificity, and overall accuracy for detection of uterine disease were determined. A U/L5 ratio of > 1.40 showed best accuracy (sensitivity 83%, specificity 85%) when screening for uterine disease, whereas the ratio of > 1.60 was highly specific (specificity 100%) for the presence of uterine diseases and the ratio of < 1.01 was highly sensitive (100% sensitivity) for the absence of uterine disease.

Intra- and interobserver reliability

Intraobserver and interobserver ICCs of all measurement were excellent (ICCs > 0.8, $P < 0.001$).

Discussion

In clinical circumstances, radiography has usually been used as an important screening examination for abdominal conditions. There have been many studies about quantitative estimation of abdominal organs in radiography in normal dogs and cats (Finco *et al*, 1971; Graham *et al*, 1998; Lee and Leowijuk, 1982; Van Bree, 1989), but about uterus, It has been said that that a normal uterus was not seen radiographically. Contrary to popular belief, however, it is found that the uterus that the normal uterus could not be infrequently observed (34.6%) on abdominal radiographs in intact female dogs even though the dog has no uterine diseases. In a previous study in queen, sensitivity of digital radiography for correctly identifying reproductive status was 28% (Woodland *et al*, 2014), which is slightly lower than this results. It might be a difference between species or observers. In veterinary medicine, the transposition from analog radiographic imaging to digital radiographic imaging has been occurred quickly. Contrast enhancement, which is the best feature of digital radiography with respect to analog radiography, makes anatomic structures more observable and distinguishable (Korner *et al*, 2007). Therefore, visualization of the uterus may be easier in digital radiographic system although comparison study was not performed in this study.

It was not surprising that abnormal groups (group 3 and 4) were older than group 1 because uterine disease are more prevalent in older dogs. However, there is no statistically significant difference between group 2 and abnormal groups. In terms of breed distribution, Shih Tzu was overrepresented in group 2. It was assumed that breed, or in other words, body conformation might affect identification of the uterus although number of group 2 was less than the other groups, thus these results might not perfectly reflect actual tendency and further study should be conducted.

There were strong correlation between radiographic and ultrasonographic uterus size and significant difference between normal and abnormal groups, representing abdominal radiography can be used as a valuable diagnostic tool to determine uterine dilatation. However, radiography should not be used to exclude uterine diseases because the uterus was absolutely not seen in 47% of abnormal groups. This suggestion is also supported by the comparison of U/L5 ratio on normal and abnormal groups. In this study, I recommended a U/L5 ratio of 1.18 ± 0.53 (mean ± 2 SD) as normal reference range on radiography in the dog. Although the ratio was significantly lower in abnormal groups, the ranges were overlapped in some degree and two pyometra cases were actually included in the suggested normal range. Therefore, further sophisticated diagnostic tests such as ultrasound may be recommended to overcome this overlapped range to identify the

presence of uterine diseases.

In ROC analysis, the best cutoff value of U/L5 ratio for detecting uterine diseases was determined to be 1.40 (sensitivity 83%, specificity 85%). In practical situation, however, this value would be worth little as alluded to in the previous paragraph. Rather than, if U/L5 ratio is over 1.60, which is highly specific to uterine disease, it is very likely that the dog has uterine disease (Sleeper *et al*, 2013; Finck *et al*, 2014). In this case, ultrasound can be used to differentiate uterine diseases.

There were several limitations in this study. The most important one is the diagnosis of the uterine diseases was only based on ultrasonographic findings. Histological, cytological and bacteriological evaluation in uterus were not performed or not considered. Although it is well known that ultrasound has high diagnostic accuracy for detecting pyometra-CEH complex (De Bosschere *et al*, 2001; Pretzer, 2008), it was found that 38% (10/26 dogs) infertile but sonographically normal bitches were positive for endometritis via cytological and bacteriological evaluations (Fontaine *et al*, 2009). Second, normal group included critically ill patients (cancer, immune-mediated diseases, cardiorespiratory diseases, etc.), therefore, normal group in this study might include dogs with subclinical uterine diseases. Third, uterine morphology changes depending on the stage of estrus cycle

or previous pregnancy (Davidson and Baker, 2009; England and Yeager, 1993; Kim *et al*, 2009; Pharr and Post, 1992; Schalafer, 2012). The uterine diameter is slightly increased (about 1–3 mm) during proestrus and estrous (Yeager and Concannon, 1995). However, it is thought that it might have minor effect on the identification of the uterus on radiographs. Finally, group 2 (normal–observable group) was relatively small population for determining cutoff points.

In conclusion, the normal uterus was not infrequently identified on abdominal radiographs therefore identification of uterus alone was not necessarily meaning that the dog has uterine diseases. I used U/L5 ratio on radiograph as quantitative index to determine normal reference range and optimal values for detecting uterine diseases. In this study, It was suggested that 1.18 ± 0.53 (mean ± 2 SD) be used as normal radiographic uterus size in intact female dogs and a value of 1.60 is recommended for clinical use as uterine disease is highly likely if the value is greater than this.

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국문초록

암컷 개에서 자궁질환 진단을 위한 디지털 방사선 영상 상 자궁 크기 평가

지도교수: 윤 정 희

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수의학과 임상수의학 (수의방사선과학) 전공

중성화하지 않은 암컷 개의 복부 방사선 영상에서 임신이나 자궁질환이 아닌 정상 자궁은 정상적으로 관찰되지 않는다고 알려져 왔다. 그러나 경험적으로 자궁질환을 가지지 않은 정상적인 개에서도 방사선 영상에서 자궁이 드물지 않게 관찰이 된다. 이 연구의 목적은 정상 개의 자궁이 복부 방사선 영상에서 관찰될 수 있음을 증명하는 것이며 또한 방사선 영상에서 정상자궁을 자궁질환과 감별할 수 있는 정량화된 지표를 설정하는 것이다. 총 213 마리의 중성화하지 않은 개가 본 연구에 포함되었으며, 모든 개는 복부 방사선 촬영 및 복부 초음파 검사를 실시하였다.

초음파 진단을 기준으로 정상적인 자궁을 가진 군과 자궁질환 (CEH, hydro-, muco-, and pyometra)을 가진 비정상 군으로 분류하였으며, 각 개체의 복부 방사선 영상에서 요추 5번의 높이와, 자궁이 확인될 경우, 자궁의 최대 직경을 측정하였다. 그 결과, 78 마리의 개가 정상 군으로, 135 마리의 개가 비정상 군으로 분류되었으며, 정상군에서는 27 마리의 개 (35%) 의 복부방사선 영상에서 자궁이 관찰되었다. 즉, 복부방사선 영상에서 자궁이 관찰되는 것이 반드시 자궁질환을 의미하지 않는다는 것이 확인되었다. 방사선 영상에서 자궁 최대 직경 대 요추 5번의 높이의 비 1.18 ± 0.53 (mean ± 2 SD)을 정상 자궁 크기로 제시할 수 있으며 또한 이 값이 1.60 이상일 경우 초음파 진단 상 자궁질환일 확률이 매우 높으므로 이 값의 임상적 활용이 추천된다.

주요어: female dog, uterus size, ultrasonography, radiography

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