Original Article

Novel methods to diagnose pulmonary hypertension in dogs assessed by thoracic radiography

Kawinthip Chanroon[1] Thanat Tuntipas[1] Promsin Sukpanich[1]

Pawit Punyarit[1] Sirilak Disatian Surachetpong[2*]

Abstract

The objective of this retrospective study was to distinguish between dogs with pulmonary hypertension (PH) and non-PH by using parameters obtained from thoracic radiographs. Data of 72 dogs of small breeds aged more than 1 year old and weighing less than 10 kg were retrieved. Echocardiography was used as a gold standard to diagnose PH and separate the dogs into two groups: PH (n=15) and non-PH (n=57). Seven formulae were created from measurements on right lateral and ventrodorsal radiographic views. Five formulae from the ventrodorsal view provided an outcome that could differentiate PH and non-PH dogs. Two formulae are recommended including 1) the ratio of the area of the pulmonary artery crossing the 9th rib and the area of the 9th thoracic vertebra (areaPA/areaT9) (cut-off >0.08; sensitivity of 83% and specificity of 89.4%) and 2) the ratio of the width of the pulmonary artery crossing the 9th rib and the width of the 9th thoracic vertebra (widthPA/widthT9) (cut-off >0.3; sensitivity of 83.3% and specificity of 78.9%). Both measurement criteria provided high negative predictive values with moderate positive predictive values. In conclusion, these two new formulae can be used as a screening tool for distinguishing between PH and non-PH in dogs.

Keywords: diagnosis, dogs, heart, pulmonary hypertension, radiography

[1]6th year student academic year 2016, Faculty of Veterinary Science, Chulalongkorn University, Thailand 10330
[2]Department of Veterinary Medicine, Faculty of Veterinary Science, Chulalongkorn University, Thailand 10330
***Correspondence**: sirilakd27@gmail.com*

Introduction

Pulmonary hypertension (PH) is a condition caused by an increase in pressure within the pulmonary system more than 30 mmHg (Fleming and Ettinger, 2006). Common causes of pulmonary hypertension include 1) an increase in right ventricular cardiac output, e.g. congenital shunts, 2) an increase in pulmonary vascular resistance, and 3) an increase in venous pressure from advanced left-sided heart disease. In the past, the major cause of pulmonary hypertension in dogs was heartworm disease. However, nowadays, most dogs develop pulmonary hypertension secondary to the advanced left-sided heart disease such as degenerative mitral valve disease (DMVD) (Johnson, 1999). The prevalence of pulmonary hypertension in DMVD dogs is approximately 13-53% (Borgarelli et al., 2015; Guglielmini et al., 2010; Serres et al., 2006).

Clinical signs of dogs with PH include cough, dyspnea, weakness, and syncope. The gold standard diagnostic method of PH is the direct blood pressure measurement through cardiac catheterization (Serres et al., 2006). However, cardiac catheterization is an invasive method that requires anesthetizing the dogs; therefore, it is not routinely used for PH diagnosis in veterinary medicine. Dogs are usually diagnosed with PH through the measurement of estimated pulmonary artery pressure via echocardiography. However, performing echocardiography has some limitations including the requirement of an expensive ultrasound machine and an experienced echocardiographer; therefore, in veterinary medicine, the diagnosis of PH is limited to referral centers and veterinary teaching hospitals.

Radiography is one of the best screening methods for heart disease and congestive heart failure in dogs. However, the radiographic assessment used to test for PH in dogs nowadays, which includes changes of cardiac silhouette and vessels (i.e. a reversed D shape and an enlargement of the main pulmonary artery and branches), is subjective and non-specific (Kellum et al., 2007), and the sensitivity of the radiography used for PH diagnosis is low. Nevertheless, radiographic examination is an easy method to employ and is routinely used in all animal hospitals. Thus, the quantitative measurement method assessed by radiography to diagnose PH is essential and useful in veterinary medicine. A previous study showed a correlation between radiographic changes and severity of the pulmonary arterial hypertension diagnosed using Doppler echocardiography (Adam et al., 2017). However, only subjective parameters were studied. Another study demonstrated a correlation between caudal pulmonary artery diameter at the level of the first bifurcation to body surface area ratio (CPAD/BSA) and estimated systolic pulmonary arterial pressure in dogs (Lee et al., 2016). However, there were some overlapping results between normal and PH dogs, which limited the usefulness of this parameter when diagnosing PH in dogs.

Therefore, this study was conducted to create quantitative measurement methods that can distinguish dogs with and without PH. Furthermore, the optimal cut-off values for identifying PH using each method were also determined.

Materials and Methods

Dogs: This study is a retrospective, case-control design study. Cardiology reports from 2015-2017 from the Cardiology Unit of the Small Animal Veterinary Teaching Hospital, Chulalongkorn University, Thailand were reviewed. Data of dogs of small breeds with an age of more than 1 year old and a weight of less than 10 kg that had received echocardiographic examination were retrieved. All dogs had thoracic radiographs obtained within 24 hours of the echocardiographic examination. For inclusion in the study, the dogs had never received cardiovascular drugs before the first day of diagnosis. All dogs had received echocardiography in an un-sedated condition by using an ultrasound machine (Eko7, Samsung Medison, Seoul, South Korea) with 2-4 and 4-12 MHz multi-frequency phased array transducers performed by an experienced veterinarian (SS). Two-dimensional (2D) echocardiography was performed to evaluate cardiac structural abnormalities. DMVD was diagnosed with thickening of mitral valve leaflets and mitral valve regurgitation assessed by 2D and color Doppler on 2D echocardiography, respectively. Estimated systolic pulmonary artery pressure was measured on the left apical four-chamber view with continuous wave Doppler echocardiography. The pressure gradient was calculated automatically by an ultrasound machine using modified Bernoulli equation (Johnson, 1999). The estimated systolic pulmonary artery pressure was calculated from the pressure gradient between the right ventricle and right atrium plus estimated right atrial pressure 0 mmHg (Johnson, 1999). The dogs were classified into two groups: the non-PH group (systolic pulmonary arterial pressure less than 35 mmHg) and the PH group (systolic pulmonary artery pressure more than 35 mmHg).

Thoracic Radiography: Digital radiographic images of selected dogs were retrieved from 2015-2017. All radiographs were from the Imaging Unit of the Small Animal Veterinary Teaching Hospital, Chulalongkorn University, Thailand. Only good quality films were recruited to the study. Radiographs with an incorrect position, vertebral abnormalities, and abnormalities obscuring the cardiac silhouette, e.g. pleural effusion and intrathoracic mass, were excluded.

On the right lateral radiographs, the parameters including the width of the cranial pulmonary artery and vein crossing the 4th rib (cm) and the width of the 4th rib (cm) were measured. Two formulae were generated, including:

1) The ratio of the width of cranial pulmonary artery crossing the 4th rib (cm) and the width of the 4th rib (cm) (widthPA/widthR4)

2) The ratio of the width of cranial pulmonary vein crossing the 4th rib (cm) and the width of the 4th rib (cm) (widthPV/widthR4)

Measurements on ventrodorsal radiographs included the width of the caudal pulmonary vein and artery crossing the 9th rib (cm) (Fig. 1), the width of the 9th rib (cm), and the length and the width of the 9th

thoracic vertebrae.

From the measurements on VD view, five formulae were created.

1) The ratio of the area of the pulmonary artery crossing the 9th rib (cm^2) and the area of the 9th thoracic vertebrae (cm^2) (areaPA/areaT9)

2) The ratio of the area of the pulmonary vein crossing the 9th rib (cm^2) and the area of the 9th thoracic vertebra (cm^2) (areaPV/areaT9)

3) The ratio of the area of the pulmonary artery crossing the 9th rib (cm^2) and the width of the 9th thoracic vertebra (cm) (areaPA/widthT9) (cm)

4) The ratio of the width of the pulmonary artery crossing the 9th rib (cm) and the width of the 9th thoracic vertebra (cm) (widthPA/widthT9)

5) The ratio of the width of the pulmonary vein crossing the 9th rib (cm) and the width of the 9th thoracic vertebra (cm) (widthPV/widthT9)

Four investigators measured each parameter three times. All investigators were blinded to the echocardiographic results. Values from each created formula were calculated and averaged.

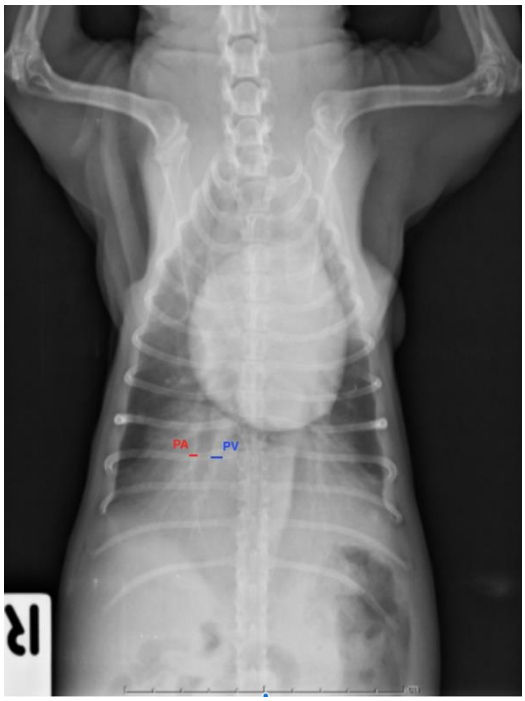


Figure 1 The measurement of the pulmonary artery (PA) (red) and vein (PV) (blue) on ventrodorsal view

Statistical analysis: Statistical analyses were performed using SPSS version 24 (IBM, Chicago, IL, USA). The general linear model and the Bonferroni pairwise comparison were used to test the independence of values from each formula between the PH group and the non-PH group. Correlations between age and weight and values from each formula were analyzed by the Pearson correlation. The Receiver Operating Characteristic (ROC) curve was performed to determine the cut-off, sensitivity, and specificity of each formula for diagnosing PH. The positive predictive value (PPV), negative predictive value (NPV), and inter- and intra- coefficients of variation (CV) were calculated. The PH group was divided into two groups: PH dogs with estimated pulmonary artery pressure >50mmHg and <50mmHg. Difference between the two groups was analyzed by student's t-test. *P-value* less than 0.05 was considered statistically significant.

Results

The radiographs of 72 dogs were retrieved. The average ± standard deviation (SD) weight of the dogs was 6.40 ± 4.40 Kg. Breeds of dogs included Poodle (19), Shih Tzu (15), mixed breed (10), Pomeranian (6), Chihuahua (5), Jack Russel (4), Yorkshire Terrier (4), Miniature Pinscher (3), Pekingese (2), Cavalier King Charles Spaniels (1), Cocker Spaniel (1), Miniature Schnauzer (1) and Pug (1). The age range was 2-19 years old. Thirty-five were females and thirty-seven were males. Fifty-seven were in the non-PH group comprising twenty-nine normal dogs and twenty-eight DMVD dogs while the PH group consisted of fifteen dogs. The characteristics of the dogs in both groups are presented in Table 1. The age and weight of dogs in the non-PH and PH groups were not significantly different (p=0.741 and p=0.478, respectively). The average estimated pulmonary artery pressure in the PH group was 70.55±33.34 mmHg.

Five of seven formulae could distinguish between the non-PH and PH groups. The five formulae included 1) areaPA/areaT9, 2) areaPV/areaT9, 3) areaPA/widthT9 (cm), 4) widthPA/widthT9 and 5) widthPV/widthT9. All were generated from the parameters measured on the ventrodorsal view. From the Bonferroni pairwise comparison results, values calculated from none of these formulae were significantly different between the normal dogs and DMVD dogs without PH. The general linear model results are summarized in Table 2. Values from only one formula, areaPA/widthT9, correlated weakly with body weight (Table 2). The cut-off value, sensitivity, and specificity of each formula are presented in Table 2.

Based on the sensitivity and specificity, two out of the five formulae (areaPA/areaT9 and widthPA/widthT9) were selected to evaluate the

positive predictive value (PPV), negative predictive value (NPV), and inter- and intra- coefficients of variation (CV) (Table 3).

The scatter plots of areaPA/areaT9 and widthPA/widthT9 are presented in Fig. 2. Only two dogs in the PH group had values calculated from both formulae less than the cut-off points. There was no correlation between the estimated pulmonary artery pressure and values from both formulae. When dividing the PH group into two groups (the estimated pulmonary artery pressure >50 mmHg and <50 mmHg), the values from each formula were not significantly different between the two groups (Table 4).

Table 1 Characteristics of dogs in the non-pulmonary hypertension (PH) and PH groups

Group	Number	Age (year)	Body weight (Kg)
Non-PH	57	11.5±3.7	6.1±3.3
Normal	29	9.9±3.9	5.7±2.6
DMVD	28	13.1±2.6	6.5±3.9
PH	15	11.3±1.8	7.5±3.4

Data presented as mean ± standard deviation (SD)
PH= pulmonary hypertension; DMVD= degenerative mitral valve disease

Table 2 General linear model, correlation between values from five formulae to body weight and age and cut-off value, sensitivity, and specificity of each formula

Formulae	General linear model	Pearson correlation				Receiver Operating Characteristic (ROC) curve		
		Body weight		Age				
	p-value	r	p-value	r	p-value	Cut-off value	Sensitivity	Specificity
areaPA/areaT9	<0.0001*	-0.166	0.164	-0.006	0.962	0.08	83	89.4
areaPV/areaT9	0.003*	-0.085	0.530	-0.090	0.506	0.07	75	71.7
areaPA/widthT9	<0.0001*	0.295	0.024*	0.057	0.667	0.08	75	68.1
widthPA/widthT9	<0.0001*	0.039	0.786	-0.115	0.386	0.30	83.3	78.9
widthPV/widthT9	0.013*	0.004	0.975	-0.80	0.545	0.30	76.9	80.4

*indicates statistical significance.
areaPA/areaT9= the ratio of the area of the pulmonary artery crossing the 9th rib and the area of the 9th thoracic vertebra; areaPV/areaT9= the ratio of the area of the pulmonary vein crossing the 9th rib and the area of the 9th thoracic vertebra; areaPA/widthT9= the ratio of the area of the pulmonary artery crossing the 9th rib and the width of the 9th thoracic vertebra (cm); widthPA/widthT9= the ratio of the width of the pulmonary artery crossing the 9th rib and the width of the 9th thoracic vertebra; widthPV/widthT9= the ratio of the width of the pulmonary vein crossing the 9th rib and the width of the 9th thoracic vertebra

Table 3 Positive and negative values and inter- and intra-observer coefficient of variation

Formulae	Predictive value		Coefficient of variation	
	Positive	Negative	Intra-observer	Inter-observer
areaPA/areaT9	66.66%	95.45%	9.47%	3.2%
widthPA/widthT9	47.6%	94.8%	10%	13%

areaPA/areaT9= the ratio of the area of the pulmonary artery crossing the 9th rib and the area of the 9th thoracic vertebra; widthPA/widthT9= the ratio of the width of the pulmonary artery crossing the 9th rib and the width of the 9th thoracic vertebra

Table 4 Comparison between pulmonary hypertension dogs with estimated pulmonary artery pressure >50 mmHg and <50 mmHg

	>50 mmHg	<50 mmHg	p-value
Average estimated pulmonary artery pressure	41.3±6.0 mmHg	90.06±29.2 mmHg	
areaPA/areaT9	0.11±0.03	0.09±0.04	0.521
widthPA/widthT9	0.36±0.08	0.32±0.09	0.461

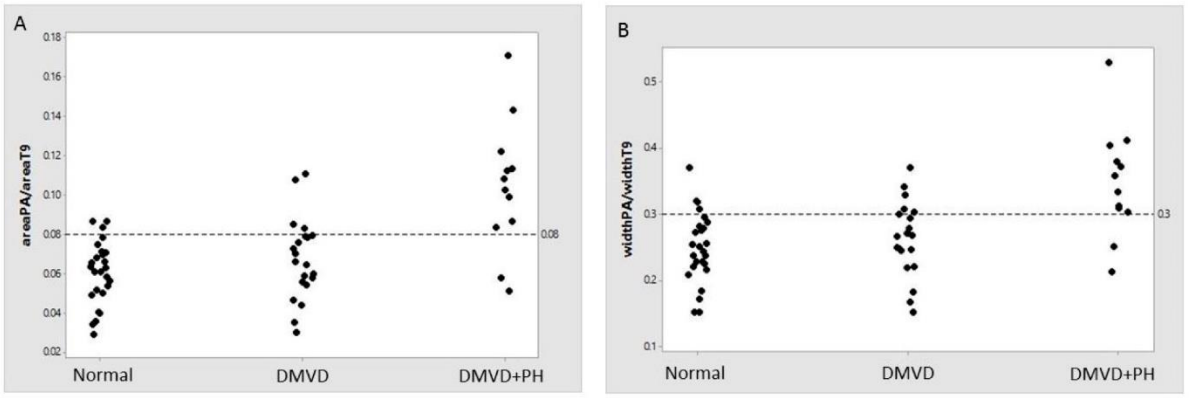
Data presented as mean ± standard deviation (SD)
areaPA/areaT9= the ratio of the area of the pulmonary artery crossing the 9th rib and the area of the 9th thoracic vertebra; widthPA/widthT9= the ratio of the width of the pulmonary artery crossing the 9th rib and the width of the 9th thoracic vertebra

Discussion

This study presents new quantitative measurement methods assessed by thoracic radiography to distinguish dogs with and without PH. Currently, many veterinarians use radiographic signs including enlargement of right-sided heart and dilatation of the main pulmonary artery and branches (Robert, 2007). However, the subjectivity of some radiographic findings can produce some limitations. A previous study investigating the effectiveness of a subjective method by comparison between the pulmonary artery and rib width for diagnosing PH found that the accuracy and the sensitivity of this method were low (Lee et al., 2016). In the present study, the width and area of the pulmonary artery and vein crossing the rib were used as major parameters for creating formulae. The width and area of the thoracic vertebra and the width of the rib were used as normalized parameters to reduce variation of each

dog.

Based on the result of this study, the size of pulmonary vessels on the right lateral view could not be used as a parameter to distinguish PH and non-PH dogs. The ventrodorsal view is the better view to reveal and measure pulmonary vessels for diagnosing PH. Because the best landmark to measure the size of the pulmonary artery and vein is at the level of the 9th rib (Robert, 2007), the width and the area of the 9th thoracic vertebrae located in the same region as the 9th rib were used as self-normalized parameters of each dog.



Formulae	Normal (n=26)	DMVD (n=21)	DMVD+PH (n=12)
areaPA/areaT9	0.06±0.01	0.07±0.02	0.1±0.03
widthPA/widthT9	0.25±0.05	0.26±0.06	0.35±0.08

Figure 2 Scatter plots of the ratio of the area of the pulmonary artery crossing the 9th rib and the area of the 9th thoracic vertebrae (areaPA/areaT9). (A) and the ratio of the width of the pulmonary artery crossing the 9th rib and the width of the 9th thoracic vertebrae (widthPA/widthT9) (B) of normal, degenerative mitral valve disease (DMVD), and DMVD with pulmonary hypertension (PH)

Because values calculated from the areaPA/widthT9 moderately correlated with the body weight, this formula is not recommended for use. The recommended formulae are the areaPA/areaT9 and the widthPA/widthT9. Both formulae provided moderate sensitivity and specificity. The negative predictive values of both formulae were high, but the positive predictive values were moderate, suggesting that these methods are suitable for use as a screening method before confirming PH with echocardiography. They are also suitable for identifying dogs without PH. Although the areaPA/areaT9 formula provides more specificity, better positive and negative predictive values, and less inter- and intra- observer CV of variations, it might take a bit longer to assess when compared to the widthPA/widthT9 because four parameters need to be measured at each evaluation.

We failed to demonstrate the difference between two groups of PH dogs (pulmonary artery pressure >50 mmHg and < 50 mmHg). This might be because this study recruited a small number of dogs in the PH group or because the size of the pulmonary lobar artery is not associated with an increase in pulmonary arterial pressure (Adams et al., 2017). The latter possibility is supported by the results of this study, which demonstrated that the size of the pulmonary artery from the areaPA/areaT9 and the widthPA/widthT9 formulae did not correlate with the estimated pulmonary artery pressure assessed by Doppler echocardiography.

The limitation of this study is, firstly, the use of the ventrodorsal view which is not the best view for revealing the pulmonary vessels. Actually, the pulmonary vessels are clearer to observe on the dorsoventral view because the lungs are better inflated in the sternal recumbency (Robert, 2007). However, the ventrodorsal position is more popular in Thailand. Therefore, the ventrodorsal view was chosen to be studied for a more practical use. Secondly, not only pressure but also volume can cause enlargement of the pulmonary vessels that might affect the diagnosis. Lastly, these methods cannot be used in radiographs with silhouette signs obscuring the pulmonary vessels, e.g. pleural effusion or severe lung consolidation. The superimposition of pulmonary vessels makes for impossible assessment and measurement.

In conclusion, the new quantitative measurement methods created in this study can be used as a screening method for diagnosis of PH, particularly in dogs affected with DMVD.

Conflict of interest: The authors declare no conflict of interest.

Acknowledgements

This study was supported in part by the Special Project for 6th Year Student, Faculty of Veterinary Science, Chulalongkorn University. The authors would like to thank the Small Animal Hospital, Faculty of Veterinary Science, Chulalongkorn University for supporting data and facilities. Special thanks to Prof. Dr. Padet Tummarak and Assist. Prof. Dr. Chaidate Inchaisi for statistical assistance.

References

Adams DS, Marolf AJ, Valdes-Martinez A, Randal EK and Bachand AM. 2017. Associations between

thoracic radiographic changes and severity of pulmonary arterial hypertension diagnosed in 60 dogs via Doppler echocardiography: A retrospective study. Vet Radiol Ultrasound. 58(4): 454-462.

Borgarelli M, Abbott J, Braz-Ruivo L, Chiavegato D, Crosara S, Lamb K, Ljungvall I, Poggi, M, Santilli, RA and Haggstrom, J. 2015. Prevalence and prognostic importance of pulmonary hypertension in dogs with myxomatous mitral valve disease. J Vet Intern Med. 29 (2): 569-574.

Fleming E and Ettinger SJ. 2006. Pulmonary hypertension. Compend Contin Educ Vet. 28(10): 720-730.

Guglielmini C, Civitella C, Diana A, Di Tommaso M, Cipone M and Luciani A. 2010. Serum cardiac troponin I concentration in dogs with precapillary and postcapillary pulmonary hypertension. J Vet Intern Med. 24(1): 145-152.

Johnson L. 1999. Diagnosis of pulmonary hypertension. Clin Tech Small Anim Pract. 14: 231-236.

Kellum HB and Stepien RL. 2007. Sildenafil citrate therapy in 22 dogs with pulmonary hypertension. J Vet Intern Med. 21(6): 1258-1264.

Lee Y, Choi W, Lee D, Chang J, Kang JH, Choi J and Charng D. 2016. Correlation between caudal pulmonary artery diameter to body surface area ratio and echocardiography-estimated systolic pulmonary arterial pressure in dogs. J Vet Sci. 17(2): 243-251.

Pyle RL, Abbott J and MacLean H. 2004. Pulmonary hypertension and cardiovascular sequelae in 54 dogs. Int J Appl Res Vet Med. 2(2): 99-109.

Robert JB. 2007. Heart and pulmonary vessels. In: Textbook of veterinary diagnostic radiology. 5th ed. Thrall DE. (ed.). Philadelphia: Saunders Elsevier. p. 576-582.

Serres FJ, Chetboul V, Tissier R, Carlos Sampedrano C, Gouni V, Nicolle AP and Pouchelon JL. 2006. Doppler echocardiography-derived evidence of pulmonary arterial hypertension in dogs with degenerative mitral valve disease: 86 cases (2001-2005). J Am Vet Med Assoc. 229(11): 1772-1778.

บทคัดย่อ

วิธีการใหม่ในการวินิจฉัยภาวะความดันเลือดในปอดสูงในสุนัขด้วยภาพถ่ายรังสีทรวงอก

กวินทิพย์ จันรุณ[1] ธนัท ตันติภาสน์[1] พร้อมสิน สุขพานิช[1] ภาวิต ปุญญฤทธิ์[1] สิริลักษณ์ ดิษเสถียร สุรเชษฐพงษ์[2*]

วัตถุประสงค์ของการศึกษาแบบย้อนหลังนี้เพื่อจำแนกสุนัขที่มีและไม่มีภาวะความดันเลือดในปอดสูงโดยใช้ค่าที่วัดได้จากภาพถ่ายรังสี ทำการรวบรวมข้อมูลของสุนัขจำนวน 72 ตัว พันธุ์เล็ก อายุมากกว่า 1 ปี น้ำหนักน้อยกว่า 10 กิโลกรัม ใช้การตรวจด้วยวิธีคลื่นเสียงสะท้อนความถี่สูงเป็นวิธีมาตรฐานในการวินิจฉัยภาวะความดันเลือดในปอดสูง และแบ่งสุนัขออกเป็น 2 กลุ่ม ได้แก่ กลุ่มที่มีภาวะความดันเลือดในปอดสูง (n=15) และกลุ่มที่ไม่มีภาวะความดันเลือดในปอดสูง (n=57) ทำการสร้างสมการทางคณิตศาสตร์ 7 สมการ ซึ่งได้จากการวัดค่าต่าง ๆ บนภาพถ่ายรังสีในท่านอนตะแคงขวาและท่านอนหงาย การศึกษาพบว่า 5 สมการจากท่านอนหงายสามารถใช้จำแนกสุนัขที่มีและไม่มีภาวะความดันเลือดในปอดสูง สองสมการที่แนะนำ ได้แก่ 1) สัดส่วนของพื้นที่หน้าตัดหลอดเลือดพัลโมนารีอาเทอรี่ที่ตัดกับกระดูกซี่โครงซี่ที่ 9 และพื้นที่ของกระดูกสันหลังชิ้นที่ 9 (areaPA/areaT9) (ค่าตัด >0.08 ความไว 83% และความจำเพาะ 89.4%) และ 2) สัดส่วนความกว้างของหลอดเลือดพัลโมนารีอาเทอรี่ที่ตัดกับกระดูกซี่โครงซี่ที่ 9 และความกว้างของกระดูกสันหลังชิ้นที่ 9 (widthPA/widthT9) (ค่าตัด 0.3 ความไว 83.3% และความจำเพาะ 78.9%) ทั้งสองวิธีการวัดให้ค่าคาดการณ์เชิงลบสูงและค่าคาดการณ์เชิงบวกปานกลาง โดยสรุป ทั้งสองสมการใหม่สามารถใช้เป็นอุปกรณ์เบื้องต้นในการจำแนกสุนัขที่มีและไม่มีภาวะความดันเลือดในปอดสูง

คำสำคัญ: การวินิจฉัย สุนัข หัวใจ ภาวะความดันเลือดในปอดสูง ภาพถ่ายรังสี

[1]นิสิตชั้นปีที่ 6 ปีการศึกษา 2559 คณะสัตวแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย กรุงเทพฯ 10330

[2]ภาควิชาอายุรศาสตร์ คณะสัตวแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย กรุงเทพฯ 10330

****ผู้รับผิดชอบบทความ** E-mail: sirilakd27@gmail.com*