수의학석사 학위논문

Development and Feasibility of New Cardiac Measurement Method Using Vertebral Heart Area Ratio in Dogs

개의 척추 심장 면적비를 이용한 새로운 심장 측정 방법의 개발 및 타당성

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이 논문을 수의학석사 학위논문으로 제출함

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Abstract

Development and Feasibility of New Cardiac Measurement Method Using Vertebral Heart Area Ratio in Dogs

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Accurate determination of cardiac size is important for assessing heart function and evaluating patients with a variety of disorders. Computed tomography can visualize the heart as a 3D structure, and the quantitative evaluation of the size of the heart. However, it is difficult to use it in small animal clinical practice because measuring the heart size with CT scans need general anesthesia. The vertebral heart scale (VHS) is the most common method used to evaluate the heart size; however, VHS is a unidimensional method and has the possible limitation of relying on only two linear measurements to determine the heart size and not the entire cardiac circumference.

Thus, the development of a more objective method for determining heart size based on the entire cardiac structure may provide a useful diagnostic method for heart disease. In this study, we hypothesized that heart size could be determined using a two-dimensional vertebral heart area ratio (VHAR), which measures the heart area in relation to the fourth thoracic vertebra (T4) body area (heart area/T4 body area) in dogs. We aimed to compare the correlation between VHAR, using radiography, and cardiac volume, using CT scans, in dogs and to investigate whether the VHAR values differed between observers. This retrospective study included a total of 125 dogs. Simple linear regression analyses were performed to compare the correlation between VHS and the vertebral heart area ratio (VHAR = heart area/T4 body area) using radiography and the vertebral cardiac volume ratio (cardiac volume/T4 body volume) using CT in each dog. The mean cardiac and T4 body volumes were 116.99 ± 108.07 cm^3 and 0.92 ± 0.91 cm^3, respectively. The mean values of observers 1 and 2 were 9.9 ± 0.7 v (VHS), 42.64 ± 27.94 cm^2 (heart area), and 1.37 ± 0.96 cm^2 (T4 body area). Intraclass coefficients were the highest for the heart area, followed by the T4 body area and VHS. The VHAR showed a moderate correlation with VHS in observers 1 (r = .671) and 2 (r = .633). The vertebral cardiac volume ratio showed a more positive correlation with VHAR (r = .573) than with VHS (r = .426). These results indicated that VHAR could be used as a complement to VHS for heart size measurement, and the high degree of observer agreement for the measurements indicated the measurement reproducibility of VHAR.

Keywords: VHS, planimetry, volumetric measurement, three-dimensional (3D)

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Introduction

Accurate determination of cardiac size is important for assessing heart function and evaluating patients with a variety of disorders. Several techniques have been used to estimate the cardiac size, including the vertebral heart scale (VHS) on radiography, echocardiography, and computed tomography (CT). Computed tomography scanning is one of the best modalities for accurately determining the three-dimensional (3D) morphology of the heart (Uehara et al., 2019). Computed tomography can visualize the heart as a 3D structure, which is its original appearance, and greatly improves the quantitative evaluation of the size or function of the heart. However, it is difficult to use it in small animal clinical practice because measuring the heart size with CT scans need general anesthesia. Therefore, VHS or echocardiography, a simpler method than CT, is used to measure the size of the heart.

The VHS is the most common method used to evaluate the heart size. Measurement of VHS on radiographs is a number that indexes the heart size to the body size using the vertebral body length as the unit of measure (Buchanan & Bücheler, 1995). The VHS is a unidimensional method and has the possible limitation of relying on only two linear measurements to determine the heart size and not the entire cardiac circumference (Torad & Hassan, 2014). Thus, the development of a more objective method for determining heart size based on the entire cardiac structure may provide a useful diagnostic method for heart disease.

In this study, we hypothesized that heart size could be determined using a two-dimensional vertebral heart area ratio (VHAR), which measures the heart area in relation to the fourth thoracic vertebra (T4) body area (heart area/T4 body area) in dogs. In this study, we aimed to compare the correlation between VHAR, using radiography, and cardiac volume, using CT scans, in dogs and to investigate whether the VHAR values differed between observers.

Materials and methods

1. Animals

This retrospective study included 184 dogs who underwent a CT scan from July 2016 to June 2021. All dogs had undergone a thoracic radiographic examination within 15 days before the CT scan for the preanesthetic examination. Among them, 59 dogs were excluded: 17 dogs with unclear heart boundaries on CT due to various diseases (right atrial mass [1], pleural effusion [6], mediastinal tumor [8], and lung mass [2]), 28 dogs with CT slices beyond 1.0-mm apart, one dog with vertebral body rotation on thoracic radiograph, and 13 dogs with a previous heart disease. A total of 125 dogs with no history of cardiopulmonary disease and no auscultable murmur were analyzed.

2. Radiographic examination

Thoracic radiographs were obtained using appropriate exposure settings depending on the patient's thoracic thickness measurements, that is, 200–300 mA and 45–75 kVp, with a focal film distance of 100 cm. All right lateral thoracic radiographs were taken using the same digital radiographic system (EVA-HF525, GEMSS, Gyeonggi-do, Korea).

3. Computed tomographic examination

The CT scans were performed using a 64-slice scanner (Aquillion 64^{TM}, Toshiba Medical Systems, Tochigi, Japan) with the following settings: 1.0-mm slice thickness, 120 kVp, 200 mAs, 512 × 512 matrix, 0.75 s/rotation, and a spiral pitch factor of 1.484. The dogs were examined in the sternal recumbency position under general anesthesia. Anesthetic protocols were as follows: acepromazine (0.02 mg/kg IV, Sedaject®, SamuMedian Co., Seoul, South Korea) was used for premedication, alfaxalone (2.0 mg/kg IV, Alfaxan® , Jurox Pty Ltd., Rutherford, NSW, Australia) for induction, and isoflurane (Ifran®, Hana Pharm., Seoul, South Korea) for maintenance. During the anesthesia, noninvasive blood pressure, heart rate, oxygen saturation, and end-tidal carbon dioxide were monitored. All CT scans were performed under apnea and achieved with hyperventilation to minimize motion artifacts. Contrast-enhanced CT scans were performed after IV administration of 2 mL/kg of non-ionic contrast medium (Omnipaque^{TM} 300, GE Healthcare, Oslo, Norway) containing 300 mg/mL of iodine using a power injector (Stellant^{TM}, Medrad Inc., PA, USA).

4. Digital image analysis

All digital images were evaluated using a DICOM viewer freeware (Horos, https://horosproject.org), and measurements were made using a circular region of interest measurement tool and electronic calipers. The evaluation of the radiography and CT scans were performed independently. Radiographic images were reviewed by three veterinary radiologists. The CT volumes of the heart and T4 body were measured by the author (JBS). The VHS, heart area, and T4 body area were measured by two observers (MSJ and JWJ, veterinary diagnostic imaging expertise). All observers were blinded to patient signalment at the time of measurements.

5. Measurements of VHS

The VHS was measured according to a previously described method (Buchanan & Bücheler, 1995). On the right lateral radiograph, the long axis of the heart was measured from the ventral border of the left main stem bronchus to the most distant ventral point of the cardiac apex. The maximum short axis was measured on a line perpendicular to the long axis at the level of the caudal vena cava. The lengths of the two axes were compared to that of the vertebrae, starting at the cranial edge of T4, and the results are presented as units of vertebral length (Figure 1A).

6. Measurements of areas of the heart and T4 body

The areas of the heart and T4 body were measured on the same image where the VHS was measured. The boundaries of the heart were measured according to the method previously described (Brown et al., 2020). The “area” measurement tool of the software program was used to trace the contour of the cardiac silhouette along the cranial cardiac border and waist, cardiac apex, caudal cardiac border and waist, cardiac base, and again at the cranial border. The area of the T4 body was measured by drawing directly along the boundary of the vertebral body (Figure 1B).

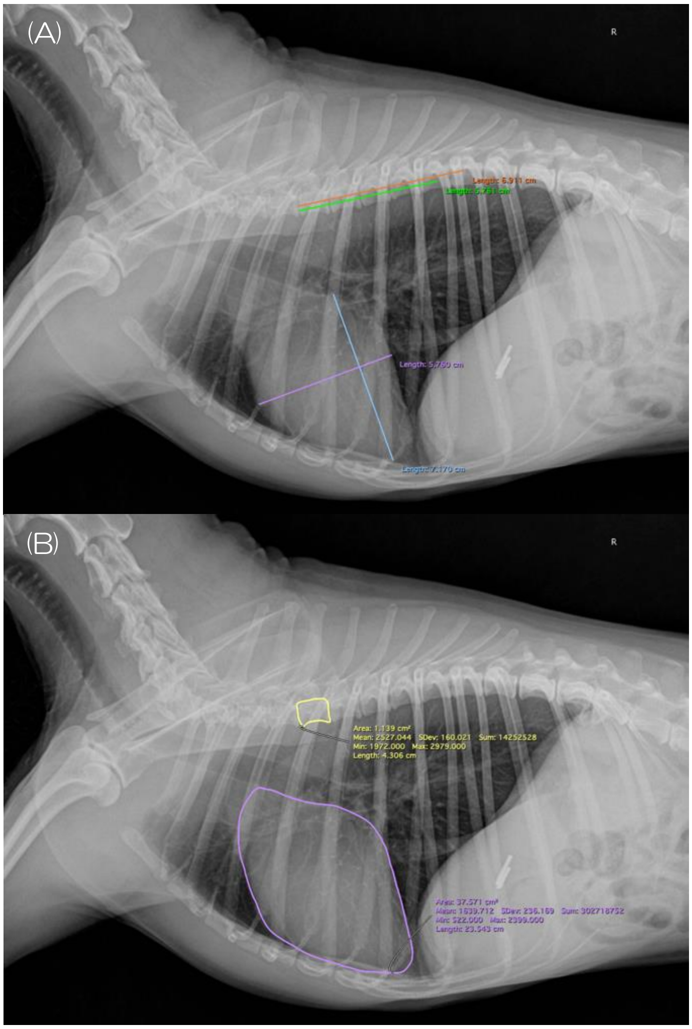

Figure 1. Right lateral thoracic radiograph showing an example of (A) vertebral heart scale (VHS) and (B) the measurement of areas of the heart and the fourth thoracic vertebra (T4) body in a fox terrier dog. The VHS was 10.0 vertebrae, the heart area was 37.57 cm^2, and the T4 body area was 1.14 cm^2. Technique: kVp, 47; mAs, 2.5. The image file was created from the original DICOM format file.

7. Measurements of the cardiac and T4 body volume

Cardiac volume was calculated as the sum of the heart area measured using a transverse section on a CT image with a window width of 330 HU and window level of 30 HU. Images with 1.0-mm slice thickness and 1.0-mm interval were used, and the boundary of the heart was drawn directly in each section. The craniocaudal border of the heart was measured from the right auricle, which is the most cranial side, to the apex, which is the most caudal side. Large blood vessels and pulmonary blood vessels connected to the heart were excluded from the measurement if they were clearly demarcated from the heart and traveled separately. If blood vessels were present within the heart border, they were included as the volume of the heart. (Figure 2A and B). The volume of the T4 body was measured on a CT image on the bone window with a window width of 1500 HU and window level of 300 HU. In each transverse section, the boundary of the T4 body was drawn directly from the most cranial part of the thoracic vertebra to the caudal part. The T4 body area of each section was automatically summed using the DICOM viewer to calculate the volume (Figure 2C and D).

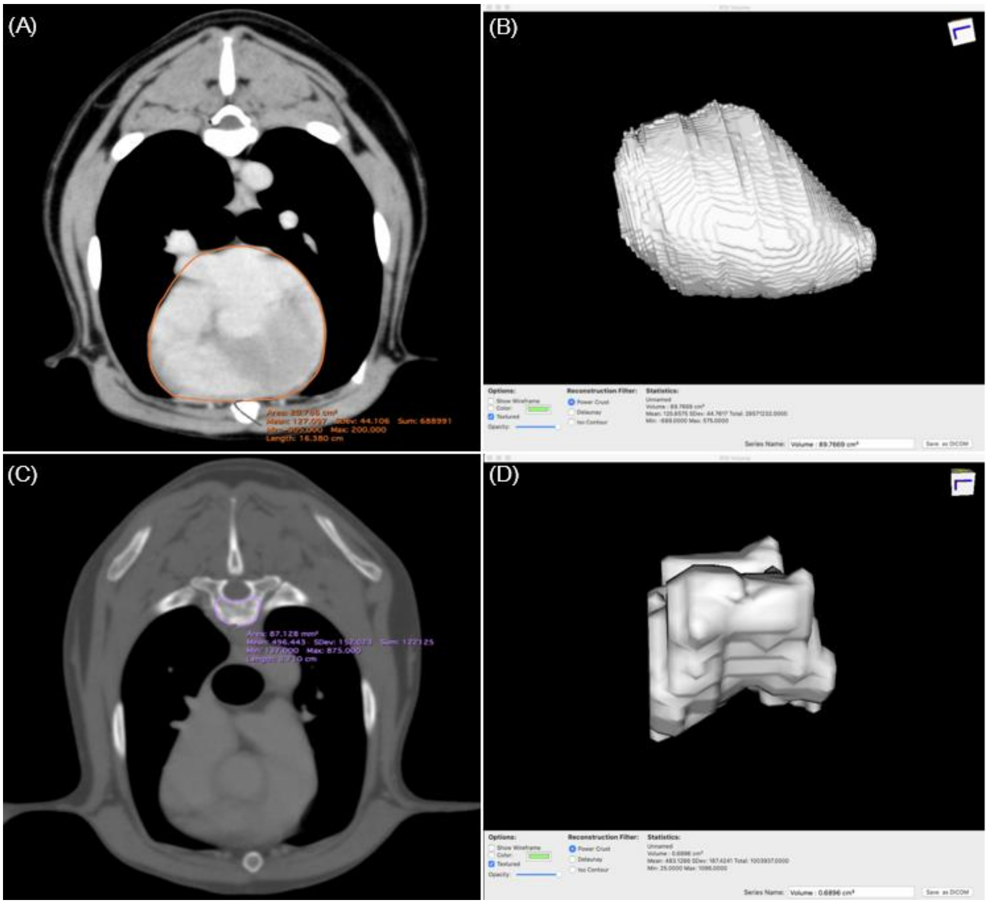

Figure 2. Image acquired by thoracic computed tomography (CT) in a dog. The contours of the heart (A, orange solid line) and T4 body (C, purple solid line) were manually outlined, generating calculated heart surface areas. The sum of the measured area of the heart and T4 body CT images were acquired using the following settings: 120 kVp, 200 mA, 1.0-mm slice thickness, and 1.0-mm interval. The sum of the measured areas of the heart and T4 body multiplied by the thickness of the slice represents the cardiac (B) and T4 body volume (D) of the three-dimensional (3D) images. Window width, 330; window level in A, 30; window width, 1,500; window level in B, 300.

8. Statistical analyses

Categorical variables were presented as numbers and percentages. Data were expressed as mean ± standard deviation. Data analyses were performed using IBM SPSS version 21.0 (SPSS Inc., IBM, Chicago, IL, USA). Correlations between VHS, VHAR and cardiac volume were analyzed by Pearson's linear regression. The intraclass correlation coefficient (ICC) was used to analyze the inter-observer reproducibility of the heart variables. Inter-observer reproducibility was deemed poor for intraclass correlation coefficient (ICC) < 0.50; moderate for ICC = 0.50-0.75; good for ICC = 0.76-0.90, and excellent for ICC > 0.90. P-value < .05 was considered as statistically significant.

Results

A total of 125 dogs (65 males and 55 females) were analyzed during the study period, and their clinical characteristics are summarized in Table 1. The mean age of the dogs was 10 years (range, 1–16 years), and the mean body weight was 9.71 kg (range, 1.41–55 kg). Breeds were, as follows: Maltese (n = 25), Shih-Tzu (n = 15), Poodle (n = 15), Mixed (n = 14), Cocker spaniel (n = 10), Yorkshire Terrier (n = 9), Shetland Sheepdog (n = 3), Miniature Schnauzer (n = 3), Malamute (n = 3), Pekingese (n = 3), Labrador Retriever (n = 3), Golden Retriever (n = 3), Chihuahua (n = 3), West highland White Terrier (n = 2), Spitz (n = 2), Shiba inu (n = 1), Shar-pei (n = 1), Scottish Terrier (n = 1), Pomeranian (n = 1), Papillon (n = 1), Jindo (n = 1), I.W hound (n = 1), Fox terrier (n = 1), Chow-Chow (n = 1), Beagle (n = 1), Standard Poodle (n = 1), and Welsh Corgi (n = 1).

The mean CT volumes of the cardiac and T4 body was 116.99 ± 108.07 cm^3 (range, 28.53–553.48 cm^3) and 0.92 ± 0.91 cm^3 (range 0.21–4.69 cm^3), respectively. The measurements of the VHS, heart area, and T4 body area are shown in Table 2. The mean values of observers 1 and 2 were 9.9 ± 0.7 v for the VHS, 42.64 ± 27.94 cm^2 for the heart area, and 1.37 ± 0.96 cm^2 for the T4 body area. The results of the interobserver reliability of the heart variables showed high reliability. The ICC were the highest for the heart area (ICC, 0.998), followed by the T4 body area (ICC, 0.996) and VHS (ICC, 0.971).

The VHAR showed a moderate correlation with VHS in both the measurements of observer 1 (correlation coefficient, r = .671) and observer 2 (r

= .633) (Table 3). The scatterplot indicates a positive linear relationship of moderate strength between VHAR and VHS (Figure 3A).

When evaluating the correlations between the vertebral cardiac volume ratio (cardiac volume/T4 body volume) and the other values (Table 4), the vertebral cardiac volume ratio showed a more positive correlation with VHAR ($r = .573$) than with VHS ($r = .426$). This is shown in the scatter plot with the linear regression slope in Figure 3B and 3C.

Table 1. Clinical characteristics of the study population (N = 125)

Characteristics	Number (mean ± SD)
Age (years)	10.00 ± 3.39 (range 1–16)
Body weight (kg)	9.71 ± 10.09 (range 1.41–55.0)
BSA (cm^2)	0.42 ± 0.27 (range 0.13–1.46)
Sex	Male (65), Female (55)
Breeds	Maltese (25), Shih-Tzu (15), Poodle (15), Mixed (14), Cocker spaniel (10), Yorkshire Terrier (9), Shetland Sheepdog (3), Miniature Schnauzer (3), Malamute (3), Pekingese (3), Labrador Retriever (3), Golden Retriever (3), Chihuahua (3), West highland White Terrier (2), Spitz (2), Shiba inu (1), Shar-pei (1), Scottish Terrier (1), Pomeranian (1), Papillon (1), Jindo (1), I.W hound (1), Fox terrier (1), Chow-Chow (1), Beagle (1), Standard Poodle (1), Welsh Corgi (1).

SD, standard deviation; BSA, body surface area.

Table 2. Interobserver reliability of the measurements using radiography in the dog

Measurement	Observer 1	Observer 2	ICC	95 % CI	P-value
VHS	9.8 ± 0.7	10.0 ± 0.7	0.971	0.958–0.979	<.0001
Heart area (cm^2)	42.63 ± 27.84	42.66 ± 28.09	0.998	0.998–0.999	<.0001
T4 body area (cm^2)	1.39 ± 0.95	1.35 ± 0.97	0.996	0.995–0.997	<.0001

ICC, interclass correlation coefficient; VHS, vertebral heart scale; T4, the fourth thoracic vertebra; CI, confidence interval.

Table 3. Correlation analysis using Pearson's correlation coefficient between VHAR and VHS

Categories	Observer 1	Observer 2	Average of observers 1 and 2
Coefficient (r)	0.671	0.633	0.685
P-value	<.0001	<.0001	<.0001

VHAR, vertebral heart area ratio (heart area/the fourth thoracic vertebra (T4) body area); VHS, vertebral heart scale.

Table 4. Correlation of VHS and VHAR to vertebral cardiac volume ratio

Categories	Observer 1		Observer 2		Average of observers 1 and 2	
	VHS	**VHAR**	**VHS**	**VHAR**	**VHS**	**VHAR**
Coefficient (r)	0.419	0.578	0.428	0.518	0.426	0.573
P-value	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001

VHS, vertebral heart scale; VHAR, vertebral heart area ratio (heart area/the fourth thoracic vertebra (T4) body area)

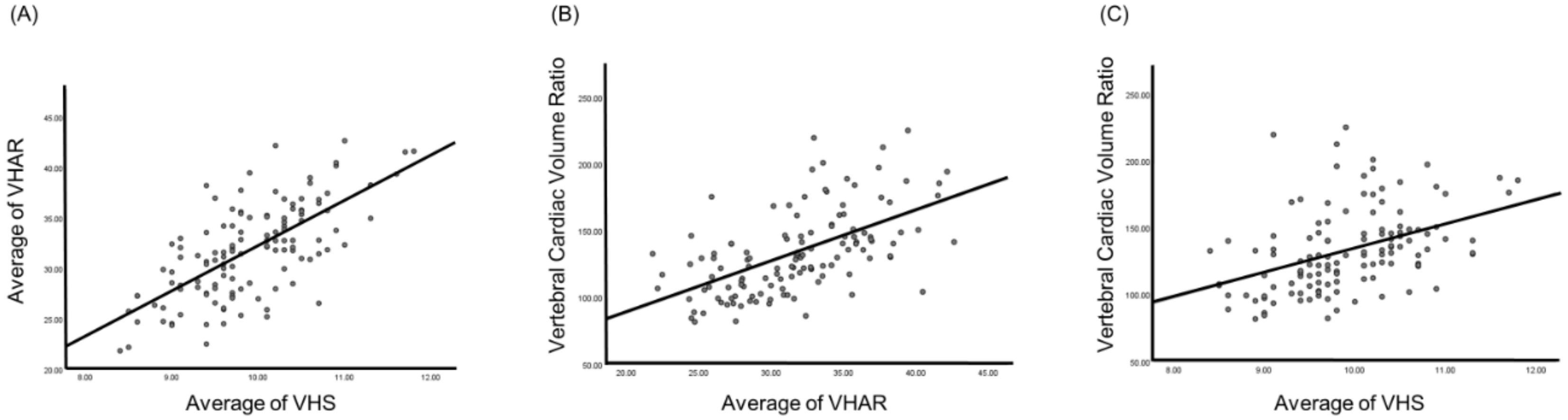

Figure 3. Scatter plots with best-fit lines comparing the average of the vertebral heart scale (VHS), average of the vertebral heart area ratio (VHAR = heart area/T4 body area), and vertebral cardiac volume ratio (cardiac volume/T4 body volume). (A) Average of VHS versus average VHAR (R^2 = .469, $P < .0001$); (B) Average of VHAR versus vertebral cardiac volume ratio (R^2 = .328, $P < .0001$); (C) Average of VHS versus vertebral cardiac volume ratio (R^2 = .182, $P < .0001$).

Discussion

In this study, the VHAR showed a significant positive correlation with VHS and vertebral cardiac volume ratio. Considering the correlation of determination, VHAR better reflects cardiac volume than VHS. This positive correlation indicates that VHAR can be considered as an additional tool for determining cardiac volume. The VHS is a traditional method for evaluating heart size on radiographs in dogs. A previous study on canine cardiomegaly showed that VHS was an important indicator for evaluating canine cardiomegaly and was correlated with echocardiography (Nakayama et al., 2001). However, it couldn't evaluate the entire area of the heart, and the size of the heart could be incorrectly assessed as normal despite the dilation of a specific heart chamber (Buchanan & Bücheler, 1995; Torad & Hassan, 2014). Although previous reports have shown that VHS measurements are not affected by the examiner's experience (Hansson et al., 2005), VHS measurements have the disadvantage of having difficulty in determining the reference point of the cardiac axis (Hansson et al., 2005; Spasojević-Kosić et al., 2007).

Computed tomography is one of the most accurate methods for measuring heart size (Uehara et al., 2019; Watanabe et al., 1981). The estimation of cardiac volume using CT is performed by adding the volumes of all voxels in all sections containing the organ to be measured. This technique allows volumetric measurement of irregularly shaped organs to be measured with high accuracy (Ahlberg et al., 1989). Previous studies have shown that the measurement of the cast volume, the right and left ventricles, and cardiac phantom of dogs using CT correlated well with the physically measured volume (Guthaner et al., 1985; Hoffman & Ritman, 1985; Miller et al., 1977). In a recent study that examined the accuracy and feasibility of CT in the quantification of ventricular volume based on semi-automated 3D threshold-based segmentation in pig hearts, the left and right ventricular volumes of pig hearts measured by CT showed a high correlation with the casting mold ($r = .845$, $P = .008$; $r = .933$, $P = .001$, respectively) (Xu et al., 2019). In this study, the volumes of the heart and T4 body were measured based on CT images of dogs. In human medicine, this method of measuring the volumes of the heart and T4 body represents similar results to the actual volumes of the heart and T4 body (Odaci et al., 2003; Watanabe et al., 1981).

In human medicine, comparative measurements on radiograph are useful (Friedberg, 1966; Meschan, 1966) to detect enlargement of the cardiac silhouette. Although similar techniques have been studied in dogs in the 1980s and 1990s, the previous reports (Hamlin, 1957, 1968; RL, 1960) showed that planimetry and cardiothoracic ratios were considered difficult to use clinically (Hamlin, 1968; Holmes et al., 1985; Schulze & Nöldner, 1957; Toombs & Ogburn, 1985) because extensive statistical analysis of all breeds, ages, and body composition was required (RL, 1960). In recent years, the digitalization of radiographs has improved the quality of images, making measurements more accurate and easier. However, there have only been a few studies on the evaluation of heart size using cardiac silhouettes on radiographs. In this study, we investigated whether heart size could be quantified by the ratio of the area of the heart divided by the area of the T4 body. In the case of geometrically similar objects, the area could be expected as the square of the length and volume as the cube of the length (Cornell et al., 2004). Because the first nine thoracic vertebrae in dogs are similar in size (Evans & De Lahunta, 2013), the T4 body was used as a representative value. Therefore, in this study, the ratio was obtained by dividing the area and volume of the heart by the area and volume of the T4 body, respectively, and the correlation between the VHS and the two ratios was compared.

The results of this study showed that the VHAR was significantly positively correlated with the vertebral cardiac volume ratio and correlated with existing VHS. Compared with that of VHS, VHAR showed a higher correlation with the vertebral cardiac volume ratio. These results indicate that VHAR can be a more accurate quantitative value for predicting cardiac volume than VHS. In addition, a high degree of observer agreement between the observers for the measurements indicated the reproducibility of these measurements. It is not difficult to measure the heart area on radiographs, and it does not take much time compared to the VHS measurement. Thus, VHAR, a tool for measuring heart size based on the entire cardiac silhouette, can provide a useful method for evaluating changes in heart size.

This study had several limitations. First, it was a retrospective study with a relatively small number of patients. Second, it was possible that patients with actual heart disease were included because echocardiography was not performed. Third, accurate cardiac assessment of cycle CT volume was limited by non-ECG-gated CT scans. However, this study is the first to investigate the relationship between cardiac volume, VHS, and VHAR. To the best of our knowledge, no published reports have compared the VHS and heart area with the CT cardiac volume. Although it was impossible to measure the actual volume of the heart in live dogs, the CT scans provided measurements that were close to the actual volume of the heart.

Conclusion

The heart area/T4 body area ratio (VHAR) not only showed a correlation with the existing VHS but also showed a higher correlation with the cardiac volume measured by CT than with VHS. The measurements of the vertebral heart area ratio on radiographs better reflect the actual size of the heart than measurements of VHS. These results indicated that VHAR could be used as a complement to VHS for heart size measurement. In the future, further studies on the effectiveness of VHAR for cardiomegaly in patients with heart disease are warranted.

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국문초록

개의 척추 심장 면적비를 이용한 새로운 심장 측정 방법의 개발 및 타당성

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심장 크기의 정확한 측정은 심장 기능을 평가하고 다양한 장애가 있는 환자를 평가하는 데 중요하다. 컴퓨터 단층 촬영은 심장을 3차원 구조로 시각화하고 심장 크기를 정량적으로 평가할 수 있다. 그러나 소동물 임상에서 CT 검사로 심장 크기를 측정하려면 전신 마취가 필요하기 때문에 적용하기가 어렵다. 척추 심장 척도(이하 VHS)는 심장 크기를 평가하는 데 사용되는 가장 일반적인 방법이다. 그러나 VHS는 1차원 방법이며 전체 심장 둘레가 아닌 심장 크기를 결정하기 위해 두 개의 선형 측정에만 의존한다는 한계가 있다. 따라서, 전체 심장 구조를 기반으로 심장 크

기를 결정하는 보다 객관적인 방법의 개발은 심장 질환에 대한 유용한 진단 방법을 제공할 수 있다. 이 연구에서 우리는 개의 심장 면적을 흉추 4번 추체의 면적으로 나눈 2차원 심장 면적비 (이하 VHAR)를 사용하여 심장 크기를 결정할 수 있다는 가설을 세웠다. 우리는 개에서 방사선 촬영을 사용한 VHAR과 컴퓨터 단층 촬영을 사용한 심장 부피 간의 상관 관계를 비교하고, 관찰자 간에 VHAR 값이 다른지 여부를 조사하는 것을 목표로 했다. 이 후향적 연구에서는 총 125마리의 개를 대상으로 하였으며, VHS, VHAR 및 심장 부피 비율 간의 상관 관계를 비교하기 위해 단순 선형 회귀 분석을 수행하였다. 평균 심장 및 흉추 4번 추체의 부피는 각각 116.99 ± 108.07 cm^3 및 0.92 ± 0.91 cm^3 였다. 관찰자 1과 관찰자 2의 평균값은 9.9 ± 0.7 v (VHS), 42.64 ± 27.94 cm^2 (심장 면적) 및 1.37 ± 0.96 cm^2 (흉추 4번 추체 면적)였다. 급내 상관 계수는 심장 면적에서 가장 높았고 흉추 4번 추체 면적과 VHS가 그 뒤를 이었다. VHAR은 관찰자 1 (r = .671)과 관찰자 2 (r = .633)에서 VHS와 중등도의 상관관계를 보였다. 심장 부피비는 VHS (r=.426)보다 VHAR (r=.573)과 더 양의 상관관계를 보였다. 이러한 결과는 VHAR이 심장 크기 측정을 위한 VHS의 보완책으로 사용될 수 있음을 나타내며, 측정에 대한 높은 관찰자 동의는 VHAR의 측정 재현성을 나타낸다.

주요어: 척추 심장 척도 (VHS), 평면도 (planimetry), 부피 측정, 3차원 (3D)

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