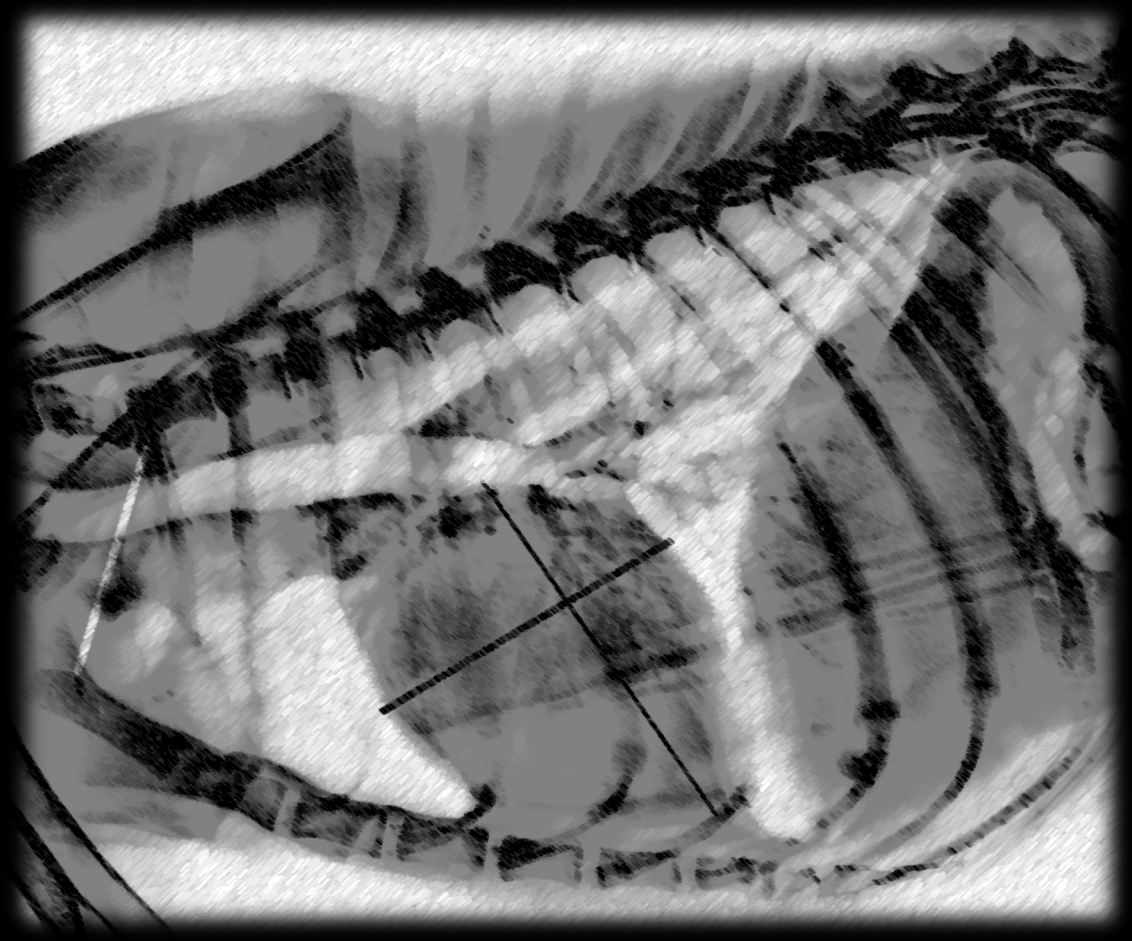

Utilidad clínica de la entrada torácica como estructura anatómica de referencia para valorar la silueta cardíaca en radiografías torácicas de la especie canina

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UTILIDAD CLÍNICA DE LA ENTRADA TORÁCICA COMO ESTRUCTURA ANATÓMICA DE REFERENCIA PARA VALORAR LA SILUETA CARDÍACA EN RADIOGRAFÍAS TORÁCICAS DE LA ESPECIE CANINA

CLINICAL UTILITY OF THE THORACIC INLET AS AN ANATOMIC REFERENCE TO ASSESS THE CARDIAC SILHOUETTE ON CANINE THORACIC RADIOGRAPHY

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ABREVIATURAS

CAP Conducto arterioso persistente
CMD Cardiomiopatía dilatada
DM Displasia de la válvula mitral
DSA Defecto del septo atrial
DSV Defecto del septo ventricular
DT Displasia de la válvula tricúspide
EA Estenosis aórtica
EE. UU. Estados Unidos
EP Estenosis pulmonar
ESA Estenosis subaórtica
EVDC Enfermedad valvular degenerativa crónica
HSVR Heart single vertebral ratio
ICC Insuficiencia cardíaca congestiva
LAS Left atrial size
MHS Manubrium heart score
MMVD Myxomatous mitral valve disease
mVLAS modified Vertebral left atrial size
M-VLAS Modified Vertebral left atrial size
RLAD Radiographic left atrial dimension
TF Tetralogía de Fallot
TI Thoracic inlet
TIHS Thoracic inlet heart score
TILAS Thoracic inlet left atrial score
VHS Vertebral heart score
VLAS Vertebral left atrial size

ÍNDICE

1.

RESUMEN

Se plantea como hipótesis que la entrada torácica puede ser utilizada como punto de referencia para valorar el tamaño de la silueta cardíaca canina en una proyección radiográfica lateral derecha del tórax. La entrada torácica es la distancia medida desde el borde craneodorsal del manubrio esternal hasta el borde craneoventral de la primera vértebra torácica. El método más conocido para medir el tamaño cardíaco en radiografías torácicas caninas, el *Vertebral heart score* (VHS), ha mostrado variación racial y, se ve afectado por alteraciones en las vértebras torácicas, y su transformación en unidades vertebrales. Se describe un nuevo método, el *Thoracic inlet heart score* (TIHS), para medir la silueta cardíaca. Los ejes corto y largo del corazón se miden siguiendo el método VHS de Buchanan y Bücheler, 1995; el resultado de esas mediciones se suma, y se divide por la longitud de la entrada torácica, obteniéndose un valor sin unidades denominado TIHS. El trabajo de investigación demuestra que este método es factible, fiable y reproducible para medir el tamaño cardíaco canino en radiografías torácicas de perros aparentemente sanos.

Por otro lado, la enfermedad valvular degenerativa crónica (EVDC) es la enfermedad cardíaca más común en el perro. La ecocardiografía y la radiografía son las dos técnicas diagnósticas de imagen recomendadas para su estadiaje. En ausencia de la ecocardiografía, el VHS y el *Vertebral left atrial size* (VLAS) dos métodos de valoración cuantitativa de la silueta cardíaca radiográfica se pueden usar para el estadiaje de la enfermedad. Se investiga la hipótesis de que el método TIHS se puede utilizar en perros con EVDC para identificar un aumento del tamaño cardíaco secundario a la enfermedad, aportando información útil al clínico que se enfrenta a un paciente con signos compatibles de la misma. El método TIHS puede identificar perros con aumento cardíaco secundario a la EVDC, y distinguir perros en distinto estadío de la enfermedad.

Con la progresión de la enfermedad, el atrio izquierdo aumenta de tamaño, habiéndose descrito varios métodos radiográficos de valoración del tamaño atrial exclusivamente, el VLAS, el *Modified-Vertebral left atrial size* (M-VLAS), y el *Radiographic left atrial dimensión* (RLAD). Estos métodos tienen en común la transformación del tamaño del atrio izquierdo en unidades vertebrales, como el método VHS. Se estudia la hipótesis que la entrada torácica puede utilizarse como punto de referencia para valorar el tamaño del atrio izquierdo, método *Thoracic inlet left atrial score* (TILAS) en una proyección radiográfica lateral derecha del tórax canino. Se mide la longitud del atrio izquierdo según el método utilizado por Malcolm y colaboradores, 2018, y se divide por la longitud de la entrada torácica, obteniéndose un valor sin unidades denominado TILAS. En una población de perros con EVDC se observa como el TILAS aumenta de un estadío al siguiente como ocurre con los métodos VLAS, M-VLAS y RLAD. El método TILAS distingue animales aparentemente sanos de animales con EVDC y remodelación cardíaca, y animales en diferente estadío de la enfermedad. Su eficacia para distinguir perros con aumento del atrio izquierdo es similar a la de los métodos VLAS y RLAD.

Palabras clave: atrio izquierdo, canina, enfermedad valvular degenerativa crónica, entrada torácica, proyección radiográfica lateral derecha, raza, remodelación cardíaca, silueta cardíaca, vertebral.

2.

SUMMARY

The present research studies the hypothesis that the thoracic inlet is a suitable reference point for the assessment of the heart size on a right lateral radiographic projection in dogs. The thoracic inlet length (TI) measured from the craniodorsal manubrium to the cranioventral first thoracic vertebrae was considered as a novel anatomic reference point to normalize the cardiac silhouette size on chest x-rays. The most known method of measuring the heart size on dogs' thoracic radiographs, the *Vertebral heart score* (VHS), has shown breed variations and is affected by vertebral malformations as well as measurements' transformation into vertebral units. A new method is described, the *Thoracic inlet heart score* (TIHS). The long and short heart axes lengths are measured as described by Buchanan and Bücheler in 1995, and their total is divided by the thoracic inlet length, the result is a unitless value named TIHS. This method is a feasible, reliable, and reproducible way of measuring a dog's heart size on thoracic radiographs of apparently healthy individuals.

On the other hand, myxomatous mitral valve disease (MMVD) is the most common acquired cardiac disease in dogs. Echocardiography and radiography are the two recommended imaging diagnostic methods for staging of the disease. In the absence of echocardiography, VHS, and Vertebral left atrial size (VLAS) are two methods of quantitative assessment of the cardiac silhouette that can be used for the staging of MMVD. The hypothesis that TIHS can be used to identify dogs with cardiac enlargement secondary to MMVD is investigated. TIHS would add useful information to the practitioner dealing with a patient showing signs of cardiac disease. The results show that TIHS method can identify dogs with cardiac enlargement secondary to MMVD, and it could differentiate dogs in different MMVD stage.

As MMVD advances, the left atrium increases in size. Several methods have been described to assess the left atrial size (LAS) exclusively, VLAS, *Modified-Vertebral left atrial size* (M-VLAS) and *Radiographic left atrial dimension* (RLAD). They share the transformation of left atrial size into vertebral units, like VHS. We hypothesize that the TI can be a reference point clinically useful to assess the LAS on dogs' right thoracic X-rays, the Thoracic inlet left atrial score method (TILAS). The LAS is measured as described by Malcolm et al, 2018, and divided by the TI, the result is a unitless value named TILAS. In a population of dogs diagnosed with MMVD TILAS increases as the disease stage worsens as do VLAS, M-VLAS and RLAD. TILAS distinguishes between control dogs and dogs with cardiac enlargement secondary to MMVD, and between dogs in different MMVD Stage. TILAS accuracy to distinguish dogs with cardiac enlargement is like VLAS and RLAD.

Keywords: thoracic inlet; canine; cardiac enlargement; cardiac silhouette; dog breed; left atrial size; myxomatous mitral valve disease; right lateral radiographic projection; vertebral.

3.
INTRODUCCIÓN

Se ha estimado que alrededor del 10% de los animales domésticos que acuden a un centro veterinario tienen algún tipo de enfermedad cardiovascular, congénita o adquirida [1,2].

3.1. Enfermedades cardiacas congénitas.

Las enfermedades cardíacas congénitas están presentes en el nacimiento y normalmente producen la muerte perinatal en la especie canina [3]. Se originan durante el desarrollo embrionario del corazón [4], por alteraciones en la formación de los septos intercamerales (Defecto del septo interventricular (DSV), Defecto del septo atrial(DSA)), de las válvulas aórtica y pulmonar (Estenosis pulmonar (EP), Estenosis aórtica(EA)), de los cojinetes endocárdicos (Displasia de la válvula mitral (DM), Displasia de la válvula tricúspide (DT)), alteraciones en la diferenciación conotruncal (Tetralogía de Fallot (TF)), en la involución de la vascularización fetal (Conducto arterioso persistente (CAP), Arco aórtico persistente, Persistencia de la vena cava craneal izquierda), o por defectos pericárdicos (Hernia peritoneo-pericardio-diafragmática) [5].

Es difícil conocer su prevalencia debido a que, algunas de ellas no producen un soplo cardíaco, pueden producir la muerte perinatal, y por la distinta distribución geográfica de las razas caninas [6]. La importancia de este último punto radica en la predisposición racial para algunas de estas patologías observada en la especie canina [4,7,8,9].

Se considera que su prevalencia es menos del 10% de las enfermedades cardíacas en perros y gatos, pero son las más comunes en los perros menores de un año [10]. No obstante, se han realizado estudios de prevalencia en distintas zonas del mundo, Italia [6], EEUU [11], Suiza [8], Polonia [12], Australia [13]. En un centro de adopción de animales de EEUU, de los 76.301 perros mestizos que fueron examinados en el mismo en un periodo de 6 años, el 0,13% presentaba una patología congénita cardíaca [11]. Estudios realizados en centros de referencia han mostrado mayores prevalencias [8,12]. En la Facultad de Medicina Veterinaria de Varsovia (Polonia), el 2,7% (301/11015), de los perros que pasaron un examen cardiovascular, incluyendo un estudio ecocardiográfico completo, en un periodo de 11 años, fueron diagnosticados de una enfermedad cardíaca congénita [12]. En la Universidad de Zurich el porcentaje fue mucho mayor, 23,5% [8], similar al de un centro veterinario privado italiano de referencia, donde el 21,7% (976/4480) de los casos que atendieron en un periodo de 13 años fue diagnosticado de patología congénita cardíaca [8]. Este mismo centro realizó un estudio posterior valorando la evolución y tendencia de estas patologías en el perro desde 1997 y hasta 2017, en su zona geográfica, y la relación con las razas caninas más habituales en ese espacio de tiempo [3], observando que la EP, el CAP, la Estenosis subaórtica (ESA) y la EA fueron más comunes en perros de raza, y el CAP y la EP en perros mestizos [3].

En EEUU la EP fue la patología congénita cardíaca más común, seguida del CAP, la EA y el DSV [11]. En Suiza la patología congénita más común fue la ESA 31,5%, seguida de la EP 23,3%, el DSV 14,4%, el CAP 13,7% y la DT 7,5% [8], resultados similares a los observados en Suecia, EA 35%, EP 20%, DSV 12%, CAP 11%, DM 8%, DT 7% y TF

0,6% [14]. En Polonia la ESA (33,9%) y la EP (18,1%) también fueron las patologías más diagnosticadas, estando en tercer lugar el CAP 16,7%, seguido de la DM 15,8%, y en menor porcentaje el DSV 6,8% y la DT 4,8% [12].

3.1.1. Diagnóstico

El diagnóstico de las patologías cardíacas congénitas comienza con la identificación de un soplo cardíaco en la auscultación, que debe ser investigado con el uso de la ecocardiografía que es la técnica de elección, pues permite identificar alteraciones en las dimensiones de las cámaras cardíacas, la localización y morfología de las lesiones, la presencia de flujos turbulentos de alta velocidad, y graduar la severidad de los defectos mediante el uso de la técnica Doppler [5]. La radiografía permite identificar cardiomegalia, dilataciones a nivel del cayado aórtico o de la arteria pulmonar, patrón pulmonar vascular, pero no permite dar un diagnóstico definitivo. Además, los estudios radiográficos son importantes para identificar signos de congestión (edema pulmonar, derrame pleural) [5].

3.2. Enfermedades cardiacas adquiridas.

3.2.1. Cardiomiopatía dilatada.

La cardiomiopatía dilatada (CMD) es la cardiomiopatía más común en el perro [15], siendo la segunda patología cardíaca adquirida más común en la especie detrás de la enfermedad valvular degenerativa [16]. Otras enfermedades cardíacas adquiridas son la cardiomiopatía hipertrófica, poco frecuente, y normalmente secundaria a otra patología: sistémica (hipertensión) o cardíaca (obstrucciones del tracto de salida), las patologías inflamatorias/infecciosas (endocarditis, miocarditis), y los tumores cardíacos [10].

La CMD idiopática es la causa más común de insuficiencia cardíaca congestiva y muerte súbita en perros de tamaño mediano y grande [15]. En algunas de estas razas la prevalencia es alta (Dóberman, Bóxer, Gran Danés, Terranova, Irish Wolfhound, Perro de agua portugués, Cocker Spaniel) [17], y estudios recientes han identificado formas heredables de CMD en razas de talla más pequeña como el Manchester Terrier toy [18], el Schnauzer standard [19] y el Welsh Springer Spaniel [20].

Un estudio realizado en un centro de referencia en EEUU a lo largo de quince años (1995-2010) observó que la incidencia de la enfermedad en los pacientes atendidos en ese periodo fue 0,4% [21]. Sin embargo, esta prevalencia alcanzaba el 58% de los perros incluidos en un estudio realizado en Europa (Alemania, Países Bajos, Austria, Suiza, Italia y países del Este de Europa) en perros de la raza Dóberman [22].

La CMD está producida por un fallo en la función sistólica seguida de la dilatación de las cámaras cardíacas y progresando a insuficiencia cardíaca congestiva, arritmia y, muerte súbita [23]. La enfermedad puede presentar una fase oculta caracterizada por la presencia

de alteraciones morfológicas en ecocardiografía y/o eléctricas en estudios electrocardiográficos y Holter-24h, en ausencia de signos clínicos, y que puede durar varios años [15]. La radiografía permite identificar la presencia de signos de insuficiencia cardíaca congestiva (ICC) (congestión venosa, edema pulmonar, derrame pleural, ascitis), cardiomegalia (generalizada, de cámaras cardíacas izquierdas y/o derechas) [24]. Aunque la identificación de una disfunción sistólica temprana con radiografías torácicas no es posible, la radiografía podría aportar una base clínica para comparar sí, y cuando, un perro desarrolla signos de ICC [25].

3.2.2. Enfermedad valvular degenerativa crónica.

La enfermedad valvular degenerativa crónica (EVDC) es la patología cardíaca más común en la especie canina [26], afectando aproximadamente al 75% de los casos de enfermedad cardíaca en perros en clínicas de Norte América [2]. Su prevalencia está relacionada con la edad y la raza, afectando más a perros de raza pequeña y de edad avanzada, menos de 20kg, como el Caniche toy y miniatura, Chihuahua, Yorkshire Terrier, Lhasa Apso, Shih-Tzu, aunque perros de raza grande pueden estar afectados, como el Pastor alemán, el Dálmata, y el Dóberman [2,10]. Estudios en las razas Cavalier King Charles Spaniel (CKCS) [27] y Dachsund [28] han mostrado evidencias del carácter hereditario de la enfermedad. En la raza CKCS la enfermedad aparece más temprano comparado con otras razas [29].

La enfermedad es 1,5 veces más común en los machos [2], y de aparición más temprana y progresión más rápida en comparación con hembras de la misma familia [30].

La válvula mitral es la única válvula afectada en el 60% de los casos; en el 30% se afectan la válvula mitral y la tricúspide, y en el 10% de los casos solo está afectada la válvula tricúspide [10]. Histológicamente, las alteraciones observadas son: el aumento en el número de fibroblastos subendoteliales, la exposición de la matriz de colágeno, la separación de fibras entre las capas, la degeneración de la capa fibrosa y el engrosamiento de la capa esponjonsa con la proliferación de miofibroblastos, dando lugar a la formación de nódulos en las valvas y cuerdas tendinosas [10]. El primer evento hemodinámico es la presencia de regurgitación mitral [31], que aumenta según la enfermedad progresa produciendo sobrecarga de volumen de las cámaras cardíacas izquierdas, remodelación del atrio y del ventrículo izquierdo e ICC [32].

El diagnóstico de la EVDC se basa primero en la detección de un soplo típico de regurgitación mitral, apical y sistólico [2], y en el uso de la ecocardiografía como método de elección para identificar la regurgitación mitral, prolapso y alteraciones morfológicas en el aparato valvular [33].

En los pacientes con EVDC se recomienda la radiografía torácica en todos los casos para valorar la relevancia hemodinámica del soplo, obtener una imagen inicial cuando el paciente es asintomático, y poder compararlo cuando el paciente presente sintomatología (tos, disnea, taquipnea) [2].

La auscultación torácica, la ecocardiografía y la radiografía son la base para el estadiaje de la enfermedad y, recomendar un tratamiento en animales asintomáticos con aumento de las dimensiones cardíacas [2]. Así, aquellos animales que presenten un soplo sistólico localizado en el ápex cardíaco con una intensidad igual o mayor a 3 sobre 6, aumento de las cámaras cardíacas medido en ecocardiografía: diámetro interno del ventrículo izquierdo normalizado al peso corporal igual o superior a 1,7, ratio atrio izquierdo aorta igual o superior a 1,6, y, aumento de la silueta cardíaca en radiografía medido con el método *Vertebral heart score* (VHS) ajustado a la raza mayor a 10,5, se clasifican en Estadio B2 y se recomienda iniciar tratamiento con pimobendan [2]. La ecocardiografía se considera el método más fiable para identificar a aquellos animales que se puedan beneficiar del tratamiento [2]. En ausencia de la ecocardiografía aquellos animales con un VHS≥11,5 o un valor comparable ajustado a la raza en aquellas razas donde hay valores VHS específicos de raza, o cuando se observa un aumento de la silueta cardiaca radiográfico en un breve tiempo pueden sustituir el valor cuantitativo de la ecocardiografía para identificar pacientes en Estadio B2 [2]. Otro método radiográfico que podría identificar animales en Estadio B2 en ausencia de ecocardiografía sería el *Vertebral left atrial size* (VLAS), un VLAS≥3 probablemente identificaría pacientes en Estadio B2 [2].

3.3. Radiografía torácica.

Como se ha mencionado, la utilidad clínica de la radiografía torácica en el diagnóstico de las enfermedades cardíacas, congénitas y adquiridas es el poder valorar las dimensiones de la silueta cardíaca, los grandes vasos, la vasculatura pulmonar y el parénquima pulmonar [4]. Aunque, un tamaño cardíaco normal en una radiografía no descarta la presencia de una patología [34]. Modelos predictivos diagnósticos de enfermedad cardíaca en perros de raza grande han mostrado mejores resultados combinando el examen físico y la radiografía torácica comparado con el uso de la electrocardiografía, y consideran que la radiografía torácica debería ser el primer test diagnóstico de elección [35].

3.3.1. La silueta cardíaca radiográfica.

Una manera indirecta de valorar el tamaño de la silueta cardíaca es observando la posición de la tráquea y la carina. La tráquea torácica se dispone caudoventralmente en el tórax desde la entrada torácica formando un ángulo respecto a la columna vertebral, ángulo que varía según las razas caninas. El ángulo es mayor en perros de tórax profundo y menor en perros de tórax ancho. Además, la tráquea anterior a la carina presenta una curvatura ventral que normalmente se pierde en perros que presentan un aumento del tamaño de las cámaras cardíacas izquierdas [36].

Así mismo, se puede valorar la silueta cardíaca de manera semicuantitativa [36,37]. Su longitud en una proyección lateral debería ser aproximadamente el 70% de la distancia

dorsoventral de la cavidad torácica, y ocupar entre 2,5 y 3,5 espacios intercostales [36]; su anchura en una proyección dorsoventral es normalmente el 60-65% de la anchura torácica, y no debe superar 2/3 de la anchura torácica en el punto más ancho de la silueta cardíaca en una proyección ventrodorsal [37].

Para eliminar la variabilidad asociada a la valoración subjetiva de la silueta cardíaca en una radiografía, se han descrito varias técnicas de medición objetiva del tamaño cardíaco tomando como referencia distintas estructuras anatómicas torácicas [34,38,39,40].

En 1995, Buchanan y Bücheler, describen el método VHS, mediante el cual las dimensiones de la silueta cardíaca se normalizan al tamaño corporal comparándola con la longitud de la columna vertebral torácica, y se le asigna un valor en unidades vertebrales. Este método mide en una proyección lateral radiográfica del tórax los ejes cardíacos: el eje largo desde el borde ventral del bronquio izquierdo principal hasta el borde ventral del ápex cardíaco, y el eje corto perpendicular al eje largo en el lugar de mayor anchura en la región central de la silueta cardíaca. Estas medidas son trasladadas a la columna vertebral comenzando en el borde craneal de la cuarta vértebra torácica. La medida de cada eje en cuerpos vertebrales (v) aproximada a 0,1v se suman y da lugar al VHS [34].

El VHS ha sido ampliamente estudiado; Jepsen-Grant en 2013 propuso como puntos de corte para el eje largo el punto medio del borde ventral de la carina hasta el ápex, y el eje corto perpendicular al eje largo comenzando en el punto donde el borde ventral de la cava caudal y el borde caudal de la silueta cardíaca se cruzan [41].

Varios estudios han mostrado que el valor VHS es distinto en el mismo paciente medido en una proyección radiográfica derecha o izquierda [42,43], aunque el estudio original no observó esa diferencia [34].

Otros estudios indican que el valor VHS puede ser dependiente del observador [44], pero no de la experiencia del observador [45], coincidiendo en que la mayor dificultad radica en la identificación del ápex cardíaco [44,45], y la conversión de las medidas de los ejes a cuerpos vertebrales [44].

Numerosos estudios se han realizado para el cálculo del VHS en distintas razas caninas demostrando variabilidad racial [38,41,46,47,48,49,50,51,52,53,54,55,56,57,58,59,60,61,62]. Y en razas con predisposición racial a presentar malformaciones vertebrales se han observado diferencias en el VHS en función de si presentan o no esas malformaciones [41].

Como se ha mencionado, el VHS se utiliza para el estadiaje de la EVDC [2], predecir si un paciente con EVDC preclínica se encuentra en Estadio B2 [63,64], y según la velocidad de cambio del VHS predecir si el paciente desarrollará insuficiencia cardíaca congestiva [65,66]. Se considera que su principal utilidad es el seguimiento de pacientes diagnosticados con EVDC [34]

También se ha estudiado el valor predictivo del VHS en perros de raza grande para el diagnóstico de patología cardíaca adquirida, EVDC o CMD, solo o en combinación con

la presencia de un soplo cardíaco, una arritmia, y la raza del paciente, en ausencia de ecocardiografía [35]. Así, un VHS normal usando intervalos específicos de raza como referencia en perros con sintomatología compatible de ICC hace el diagnóstico de CMD improbable [25].

Otro método para valorar la silueta cardíaca es el cálculo del Ratio cardiotorácico, estudiado en la raza Pastor Alemán, y que relaciona el área que ocupa la silueta cardíaca respecto al área de la cavidad torácica [38]. El hándicap de los métodos basados en planimetría es su poca utilidad clínica [34] y la necesidad de software específico [38].

En 2017, Mostafa y colaboradores describieron un nuevo método para valorar la silueta cardíaca, el *Manubrium heart score* (MHS), normalizando las medidas de los ejes cardíacos medidas según Jepsen-Grant, a la longitud del manubrio esternal [39]. Este autor en un estudio posterior realizado con 184 perros, 83 de raza grande y 101 de raza pequeña, diagnosticados de enfermedad cardíaca (congénita o adquirida), 23/83 y 41/101, mediante ecocardiografía, concluyeron que este método podría ayudar en la identificación de aquellos perros que tuviesen una patología cardíaca [66].

Una de las principales limitaciones del VHS es su uso en animales con alteraciones vertebrales [41] por lo que un grupo de investigadores ha descrito un método para superar este problema, el *Heart single vertebra ratio* (HSVR) [40]. Este método consiste en medir los ejes cardíacos según se ha descrito para el VHS, y la longitud de varias vértebras torácicas, cuarta, quinta, sexta, séptima y octava, sumar la medida de los ejes cardíacos y, dividirlo por la medida del cuerpo vertebral de cada vértebra. El valor más consistente entre los distintos observadores del estudio se obtiene con la medida de la séptima vértebra torácica [40].

3.3.2. El atrio izquierdo radiográfico.

En los pacientes con EVDC y remodelación cardíaca el aumento de las dimensiones del atrio izquierdo es considerado un indicador fiable de la presencia de compromiso hemodinámico o de la severidad de la enfermedad [67]. Signos radiográficos sugerentes del aumento del tamaño del atrio izquierdo en una proyección radiográfica lateral son: el desplazamiento dorsal de la carina [36], y la presencia de un abultamiento con atenuación tejido blando dorsocaudal a la carina [68]; y en una proyección dorsoventral el aumento del ángulo de la bifurcación traqueal [69], aunque son poco fiables. Varios métodos de valoración del tamaño del atrio izquierdo en proyecciones radiográficas laterales del tórax se han descrito [70,71,72,73,74,75,76]. De manera indirecta, el método *Crossing li*nes [76] traza una línea desde el borde dorsal de la carina hasta el borde dorsal de la vena cava caudal en el punto de corte con el diafragma, y considera aumento del atrio izquierdo si el borde dorsal del mismo supera esa línea, pero no ha ofrecido mejores resultados que la valoración subjetiva; o los métodos *Bronchus to spine*, y *Radiographic left atrial dimensión to spine* [72], trazando una línea recta desde el borde dorsal del bronquio craneal izquierdo o desde el borde dorsal del atrio izquierdo hasta el borde ventral de la vértebra inmediatamente dorsal a la silueta cardíaca, y al atrio izquierdo, quinta y sexta

vértebra torácica respectivamente; la medida se traslada al borde craneal de la cuarta vértebra torácica y se transforma en unidades vertebrales aproximada a 0,1v, pero estos métodos han mostrado baja sensibilidad [72].

De manera directa, se han descrito varios métodos objetivos de valoración del tamaño del atrio izquierdo: VLAS [70], *Radiographic left atrial dimension* (RLAD) [71], *Left atrial width* [73], *Modified-Vertebral left atrial size* (M_VLAS) [74], y *modified vertebral left atrial size* (mVLAS) [75].

El VLAS mide la longitud que hay desde el borde ventral de la carina hasta el punto de corte entre el borde caudal de la silueta cardíaca y el borde dorsal de la vena cava caudal, el tamaño del atrio izquierdo (del inglés: *left atrial size* (LAS)), esa medida se transpone sobre la columna vertebral comenzando en el borde craneal de la cuarta vértebra torácica y se transforma en una medida en cuerpos vertebrales aproximada a 0,1v [70].

Como ha ocurrido con el VHS, se han realizado estudios raciales de valoración del VLAS [57,58,60,61]. También, se ha estudiado la utilidad clínica del VLAS para identificar perros con patología cardíaca asintomáticos y con remodelación cardíaca [45,63,64,70,73,77,78,79,80] y, perros con insuficiencia cardíaca congestiva secundaria a EVDC [81,82], observando un aumento del VLAS con la progresión de la enfermedad.

El RLAD se calcula midiendo el eje largo cardíaco desde el ápex cardíaco hasta el borde ventral del bronquio izquierdo principal, el eje corto perpendicular al largo comenzando en el punto de corte del borde dorsal de la vena cava caudal con el borde caudal de la silueta cardíaca, y trazando una línea bisectriz al ángulo formado por los ejes cardíacos hasta el borde dorsal del atrio izquierdo. Esta medida se transpone a unidades vertebrales comenzando en el borde craneal de la cuarta vértebra torácica dando una medida en cuerpos vertebrales aproximada a 0,1v [71]. Se han realizado varios estudios de raza para el RLAD [60,61], y otros estudios han valorado la capacidad del método RLAD para identificar aumento del atrio izquierdo en perros con EVDC [45,60,71,74,79].

El M-VLAS, basado en el método VLAS, valora el tamaño de la silueta cardíaca en dos dimensiones [74]. Este método mide el LAS como se ha descrito previamente, y posteriormente traza una línea perpendicular a la primera y hasta llegar a ella comenzando en el punto más dorsal del atrio izquierdo. Ambas medidas se transponen a la columna vertebral comenzando en el borde craneal de la cuarta vértebra torácica y se transforman en cuerpos vertebrales, se suman dando una medida aproximada a 0,1v. Se ha estudiado su utilidad para identificar perros con remodelación cardíaca secundaria a EVDC [74], y para identificar ICC en perros con EVDC [80].

El mVLAS es un método de valoración del atrio izquierdo en una dimensión. Se calcula trazando una línea desde el borde medio ventral de la carina hasta el punto más caudal del atrio izquierdo; la medida resultante se convierte en una medida de cuerpos vertebrales comenzando en el borde craneal de la cuarta vértebra torácica aproximada a 0,1v [75]. Los autores sugieren que este método es un indicador más específico de aumento del atrio

izquierdo que el VLAS y podría utilizarse cuando no es posible identificar la vena cava caudal, punto de referencia para el cálculo del VLAS [75].

Como se ha comentado todas estas medidas usan como estructura anatómica de referencia la columna vertebral torácica media, y como hándicap comparten la variabilidad racial, la presencia de alteraciones en la columna torácica media y, su transposición a unidades vertebrales.

La entrada torácica se ha utilizado como punto de referencia para valorar el diámetro traqueal en perros no braquicéfalos, perros braquicéfalos no bulldog, y bulldogs [83,84]. Harvey y Fink en 1982 describieron el ratio diámetro traqueal/entrada torácica para método para normalizar el diámetro traqueal. El método consiste en medir primero la entrada torácica desde el borde dorsal del manubrio esternal hasta el borde craneal de la primera vértebra torácica, y posteriormente medir el diámetro traqueal en el punto medio de la tráquea donde la línea de la entrada torácica cruza la misma, el valor obtenido al dividir la medida del diámetro traqueal por la longitud de la entrada torácica es el ratio diámetro traqueal/entrada torácica [83]. En perros normales no braquicéfalos el valor es superior a 0,20, en perros braquicéfalos no bulldog 0,16, y en bulldog 0,11 [83]. La entrada torácica no ha sido utilizada previamente como punto de referencia para valorar la silueta cardíaca.

4.

OBJETIVOS

4.1.

El primer objetivo del presente trabajo es estudiar si la entrada torácica se puede usar como estructura anatómica de referencia para normalizar el tamaño de la silueta cardíaca. El nuevo método para valorar el tamaño cardíaco utilizando la entrada torácica como estructura anatómica de referencia consistiría en medir los ejes cardíacos largo y corto, según está descrito en estudios previos, y medir la entrada torácica; dividir la suma de la medida de los ejes cardíacos por la longitud de la entrada torácica, y obtener un valor sin unidades, el *Thoracic inlet heart score* (TIHS). Se valora si existe variabilidad interracial usando este método y, si existe variabilidad intra e interoperador en su cálculo.

4.2.

El segundo objetivo es estudiar la utilidad clínica del método TIHS para identificar perros con remodelación cardíaca secundaria a la enfermedad cardíaca más común en la especie canina, la EVDC. Valorar si el método TIHS permite distinguir entre perros sanos y perros con EVDC, y perros en distinto estadío de la enfermedad.

4.3.

Como tercer objetivo se valora la utilidad de la entrada torácica como estructura anatómica de referencia para determinar el tamaño del atrio izquierdo en perros sanos y en perros con EVDC y distinguir perros en distinto estadio de la enfermedad, método *Thoracic inlet left atrial score* (TILAS). Se compara la utilidad clínica del método TILAS con métodos ya publicados y contrastados como los métodos VLAS, M-VLAS y RLAD. Se estudia la reproducibilidad de esos métodos calculados por distintos observadores en distintas poblaciones, y los resultados obtenidos.

5.

PUBLICACIONES CIENTÍFICAS

5.1.

The Thoracic Inlet Heart Size, a New Approach to Radiographic Cardiac Measurement

Marbella Fernández, D.; García, V.; Santana, A.J.; Montoya-Alonso, J.A. The Thoracic Inlet Heart Size, a New Approach to Radiographic Cardiac Measurement. *Animals 2023*, 13, pp. 389. https://doi.org/10.3390/ani13030389.

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MDPI

Article

The Thoracic Inlet Heart Size, a New Approach to Radiographic Cardiac Measurement

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Simple Summary: The present study investigates the hypothesis that the thoracic inlet is a suitable reference point for the assessment of the heart size on a right lateral radiographic projection in dogs. This is important, since the most known method of measuring the heart size on dogs' thoracic radiographs, the vertebral heart size, has shown breed variation and is affected by vertebral malformations as well as measurements' transformation into vertebral units. The shortest thoracic inlet length measured from the craniodorsal manubrium to the cranioventral first thoracic vertebrae was considered. The long and short heart axes lengths were measured as described by Buchanan and Bücheler in 1995, and their total was divided by the thoracic inlet length. We found this method to be a feasible, reliable, and reproducible way of measuring a dog's heart size on thoracic radiographs.

Abstract: In 1995, the Vertebral Heart Size (VHS) method for measuring the cardiac silhouette on thoracic radiographs was published, becoming a quantifiable and objective reference way of assessing the heart size. Since then, many studies have showed that VHS is influenced by breed variations, vertebral malformations, reference points selection, and short and long axes dimensions conversion into vertebral units. The Thoracic Inlet Heart Size (TIHS) normalizes heart size to body size using the thoracic inlet length. The lengths of the long and short axes of the heart of 144 clinically normal dogs were measured on right lateral thoracic radiographs. The sum of both measures was indexed to the thoracic inlet length. For comparison, dogs of the most represented breeds in our hospital were selected to measure their heart size using the TIHS protocol. The mean TIHS value for the population studied was 2.86 ± 0.27, and 90% of dogs had a TIHS value of less than 3.25. There was no difference in TIHS between male and female, and between small and large dogs (p-value < 0.01). There was no difference in the TIHS value between Yorkshire Terrier, Chihuahua, and Labrador retriever breeds, and between each of those three breeds and the general population. The TIHS is a simple, straightforward and accurate way to measure heart size.

Keywords: thoracic inlet; right lateral radiographic projection; cardiac size; dog breed; interobserver variability

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1. Introduction

Echocardiography is the gold standard for the evaluation of the cardiac structures when a cardiac disease is suspected based on a clinical exam finding (e.g., a heart murmur, cyanosis), clinical history information (exercise intolerance, syncope), or an abnormal cardiac silhouette on thoracic x-rays [1].

Thoracic radiography is widely available [2] and is reliable for the evaluation of generalized cardiomegaly and chamber enlargement as left atrial enlargement [3]. Different radiographic methods to determine the cardiac size have been reported: intercostal spaces, cardiothoracic ratios, Vertebral Heart Size (VHS), Vertebral Left Atrial Size (VLAS),

Radiographic Left Atrial Dimension (RLAD), and Manubrium Heart Score (MHS). The intercostal spaces method, described more than five decades ago [4], is still used today (first author Poster presentation at 27th Federation of European Companion Animal Veterinary Associations Congress, Prague 2022) but has several limitations, including variations in the cardiac axes, thorax conformation, respiratory cycle, superimposition of ribs, and imprecise reference points [5]. Determining the cardiothoracic ratio is affected by variations in the thoracic conformation among dog breeds [6], and requires specific software, limiting its use in clinical practice [7].

The VHS method, first described in 1995 [6], normalized the sum of the cardiac long and short axes to the length of the midthoracic vertebrae, with a reference value of 9.7 ± 0.5 v (v vertebral units), suggesting an upper limit for the normal heart size in most breeds of ≤10.5 v. This study considered that different breeds might have different normal upper limits, and breed-specific studies would be required to determine more precise values for individual breeds [6]. Since then, many studies have been published proposing breed-specific VHS reference values [8–26]. Additionally, potential sources of VHS variation are thoracic vertebral anomalies, interobserver differences in reference point selection, and transformation into vertebral units [27]. Radiography can be necessary when echocardiography is not available, but the clinician must be aware of the variation in dog thoracic conformations and breed differences in normal VHS [28]. VLAS [29] and RLAD [30] are two methods for detecting left atrial enlargement. Both techniques normalize the left atrial size to the vertebral body length starting at the fourth thoracic vertebrae. A VLAS value ≥ 3 in the absence of echocardiography likely identifies dogs with Stage B2 mitral valve disease [28]. RLAD has demonstrated high sensitivity and specificity for detecting left atrial enlargement [29]. As with VHS, in addition to breed-specific differences, variability between individual observers and different levels of expertise may cause considerable differences between VLAS and RLAD measurements [25].

To eliminate some of the problems associated with the VHS and cardiothoracic ratios in some dogs, the MHS was proposed [3]. The manubrium was selected because it is prominent, regularly elongated, easily identified, and can be readily measured on lateral thoracic views. However, dogs with an abnormally shaped manubrium, or when its cranial margin could not be identified, were excluded from the study. Also, no echocardiographic examinations were performed to rule out subclinical cardiac disease, nor was interbreed variation assessed.

The thoracic inlet length has been proposed as a reference point to assess tracheal diameter in brachycephalic and non-brachycephalic dogs [31–33]. Its use to normalize cardiac size could overcome some of the limitations related to the different methods described previously: vertebral malformations, conversion to vertebral units, manubrium malformations, and breed variation.

The objective of this prospective study was to establish a method to assess the heart size radiographically by measuring the cardiac long and short axes normalized by the thoracic inlet length on a thoracic right lateral radiographic view of clinically normal dogs. To determine whether sex and weight had an impact on the TIHS value, correlation of TIHS with VHS, as well as intra- and interobserver agreement were assessed. We hypothesized that TIHS is a simple, reliable, and reproducible method to assess cardiac size in a study population of healthy dogs. We also hypothesized that TIHS is not dependent on sex or body weight. We finally propose a TIHS reference value for healthy dogs.

2. Material and Methods

2.1. Animals

The study design was a prospective observational investigation. Dogs admitted to Anicura Albea Small Animal Hospital from March 2021 to September 2022 were studied. The selected population included client-owned dogs older than 1 year of age, with no history or concurrent clinical or radiographic signs of cardiovascular or respiratory diseases. Informed consent was obtained from the owners. Patient data including breed, sex, age, and

body weight were recorded. Any patients with a heart murmur, or rhythm abnormalities other than respiratory sinusal arrhythmia on auscultation, were excluded. Dogs that had a positive response to a heartworm antigen test were excluded. A basic ultrasound exam was performed on every patient. A Vivid iq portable ultrasound machine (General Electric Medical Systems, Jiangsu, PR China) was used to acquire the images that were analyzed on an Echopack DICOM viewing system. Visual assessment and measurement of standard-echocardiographic parameters in two-dimensional (2D-) Mode, M-Mode, and Doppler Mode were carried out on the right parasternal long-axis four chamber and five chamber views, right parasternal short-axis view, and left apical and cranial views. From the right parasternal short-axis view, the left ventricle internal diameter at end diastole index to body weight (LVIdN), and left atrium aortic valve ratio (LA/Ao), were calculated. Dogs with cardiac disease based on echocardiography (including valvular abnormalities, cardiac chamber enlargement, LVIdN $\geq$ 1.7 and/or LA/Ao $\geq$ 1.6, or heartworm detected on the pulmonary artery or heart chambers) were excluded.

2.2. *Radiography*

Digital radiographs were acquired using the same digital radiographic unit (Intech's Veterinary Digital DR System Model Futura 10, La Cartuja Baja, Zaragoza, Spain) and retrieved with an image archiving communication system (IntechForView 12.5.1.1, La Cartuja Baja, Zaragoza, Spain). A right lateral projection was acquired for each dog as it is the usual projection taken at our hospital. Most dogs also had a ventrodorsal and left lateral projection acquired. kVP and mAs were selected for each dog based on a radiographic technique chart. Subjects with pulmonary, airway, and/or cardiovascular abnormalities, as well as those with a history of neck or chest surgery, were excluded from the investigation. The investigated thoracic radiographic views were assumed to be taken at the time of peak inspiration, and without sedation or anesthesia. The thoracic limbs were pulled as cranially as possible, to minimize superimposition with the cranial thorax. Dogs with thoracic vertebral malformations were not excluded from the study. Right lateral thoracic radiographs on which the cranial portion of the manubrium could not be identified, or the cardiac silhouette was not clearly defined, or the image was blurred due to motion artifact, were excluded.

The VHS was obtained as described by Buchanan et al. [5] and modified according to Jepsen-Grant et al. [14]. Briefly, the long axis of the cardiac silhouette was measured, starting from the central and ventral border of the carina to the most distant point of the cardiac apex. The short axis was drawn at a 90° angle to the long axis and at the level of the ventral intersection of the caudal vena cava and the cardiac silhouette. The measurements of the two axes were indexed to thoracic vertebral bodies starting at the cranial edge of T4 and summed. The VHS was measured to the nearest 0.1 vertebra.

Based on the VHS, a method to measure the cardiac silhouette indexed to the thoracic inlet is presented. The length of the long and short axes of the cardiac silhouette, measured as described previously for the VHS, were summed and divided by the corresponding thoracic inlet length (TI). The TI is the distance extending from the cranio-ventral aspect of the first thoracic vertebra to the craniodorsal manubrium at its highest point, the point of the minimum length of the thoracic inlet. A unitless value, the Thoracic Inlet Heart Score (TIHS), is obtained (Figure 1).

Both VHS and TIHS were measured from the right lateral projection on images in DICOM format using a digital caliper in a commercial viewing system (IntechForView 12.5.1.1, La Cartuja Baja, Zaragoza, Spain). Three measurements were made for each method and the average was used for statistical analysis.

Echocardiography and lateral radiographs were made within 24 h by the first author (DM), a PhD student with over 20 years of clinical experience and echocardiography expertise, who measured the VHS and TIHS values on every patient. This investigator was not blinded to the clinical data and echocardiographic measurements at this time.

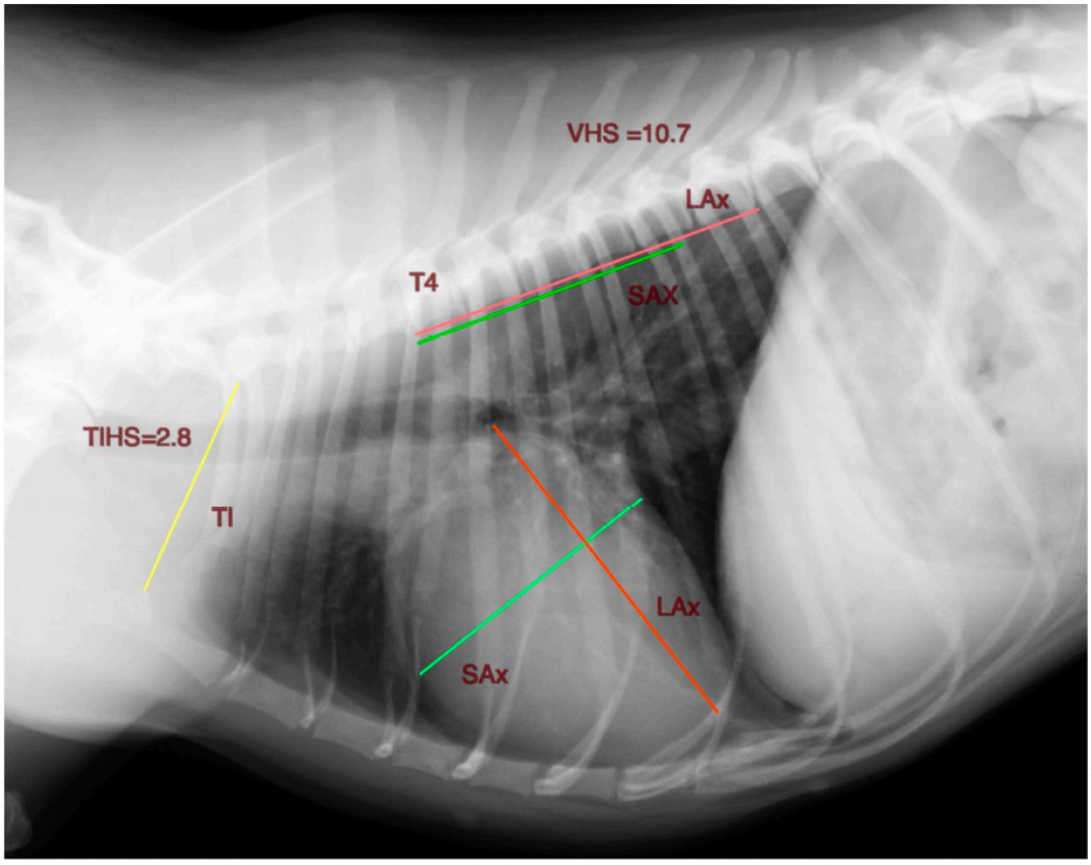

Figure 1. Right lateral thoracic radiographic projection of a clinically normal 9 years old chihuahua illustrating the thoracic inlet heart size measurement method (THIS). The long axis (LAx) and short axis (SAx) of the heart and the thoracic inlet (TI) are measured. The sum of the LAx and SAX is divided by the TI to obtain the thoracic inlet heart size. VHS Vertebral Heart Size.

To assess the intra and interobserver variability, two observers (DM and VG, a general practitioner with less than five years of clinical practice) assessed the radiographs of 16 randomly selected dogs independently. The same radiograph was evaluated two times at least one week apart. VG was blinded to the clinical status of each dog and the measurements determined by the other investigator. The interobserver coefficient of variation (CV) was measured by pairing the first measurements of both observers.

2.3. *Statistical Analysis*

Descriptive variables (age, body weight) were reported as the median and the range (minimum and maximum values). To determine the influence of body weight on the TIHS and VHS, the dogs were divided into four groups (≤10 kg, 10.01–20 kg, 20.01–30 kg, ≥30.01 kg). The variables of interest (TIHS and VHS) were reported as the median, the standard deviation, and the range. A 95% confidence interval (CI) was calculated for the selected measurements, TIHS and VHS. A paired Student's t test was performed to identify differences in the TIHS values between male and female subjects, between different body weights, and differences in VHS values depending on both sex and body weight. Differences with a p-value < 0.01 were considered significant. Pearson's correlation was performed to assess the relationship between the TIHS and VHS values, $p < 0.05$. In addition, the correlations of the TIHS with the cardiac long axis (LAx), and cardiac short axis (SAx) were assessed. The correlation of the TI length with the fourth thoracic vertebra length (T4) was assessed, as well as the correlation between TI and body weight, TI and LAx, TI and SAx, TI and the sum of LAx and SAx, body weight and LAx, and body weight

and SAx. The correlation of VHS and LAx and SAx was also assessed. The correlation was considered weak, moderate, strong, or perfect, when the value of the correlation was 0.1–0.3, 0.4–0.6, 0.7–0.9 or 1, respectively.

For the intraobserver and interobserver variability, a Kappa agreement (K [95% confidence interval]) was interpreted as: slight agreement (0.01–0.2), fair (0.21–0.40), moderate (0.41–0.60), substantial (0.61–0.80), and almost perfect agreement (0.81–0.99). All statistical analyses were performed using commercially available software (SAS/STAT software, version 16.5, Microsoft Excel 2021).

3. Results

One hundred and forty-four dogs over 1 year of age took part in the study. Breeds represented were 62 mixed-breed, four each of the breeds Chihuahua, French Bulldog, Golden Retriever, Labrador Retriever, and Yorkshire Terrier; three each of the breeds American Pitbull, American Staffordshire, and German Shepherd Dog; two each of the following: Bull Terrier, Canarian hound, Pug, Scottish Terrier, and West Highland White Terrier; and one each of the following: American Bulldog, Beagle, Bichon, Border Collie, Boston Terrier, Boxer, Cavalier King Charles Spaniel, Check Wolf, Chow-Chow, Dachshund, Dalmatian, Garafian Shepherd, Jack Russell Terrier, Lobo Herreño, Malinois, Pekingese, Pomeranian, Pinscher Miniature, Rottweiler, Schnauzer Miniature, and Spanish Water Dog. For the general population statistical study, 22 dogs were excluded, so as not to include more than four dogs of the same breed (9 Yorkshire Terriers, 8 Chihuahuas, 4 Labrador Retrievers, and 1 French Bulldog). Dogs were included in order of entrance to the study, once four dogs of the same breed had been studied the rest were excluded. Eventually, data from 122 dogs (61 males and 61 females), with a median age of 4 years and 2 months (range 1–16 years) and mean body weight of 8.39 kg (1.8–48.5 kg) were statistically analyzed. For the body weights: 52/122 (42.6%) dogs weighed less than 10 kg, 26/122 (21.3%) weighed between 10.1 kg and 20 kg, 28/122 (22.9%) weighed between 20.1 kg and 30 kg, and 16/122 (13.1%) weighed over 30 kg.

Normally distributed, the TIHS value for the overall population was 2.86 ± 0.27 (Table 1). The TIHS value did not differ depending on sex or body weight, p=0.96 and $p > 0.01$, respectively. The VHS value for the overall population was 10.12 ± 0.92. The VHS values did not show significant differences depending on sex, $p = 0.49$. The VHS value was lower for the ≤ 10kg group (9.77 ± 0.68) compared to the general population (10.12 ± 0.92) and the other groups (10.01–20 kg was 10.42 ± 1.20; 20.1–30 kg was 10.32 ± 1.01; and ≥30 kg was 10.60 ± 1.12), $p < 0.01$ (Figure 2). The TIHS value was less than 3.25 in 90% of the dogs. The VHS value was ≤ 10.5v in 72% of the dogs, and ≤ 11.5v in 92% of the dogs.

Only one dog presented vertebral malformations, a male 10-year French bulldog weighing 13.6 kg. Excluding French bulldogs, the TIHS and VHS values were 2.87 ± 0.27 and 10.05 ± 0.83, respectively.

TIHS and VHS values were calculated for the four most represented breeds in our hospital: Yorkshire Terrier (13), Chihuahua (12), Labrador Retriever (8), and French Bulldog (5) (Table 2). The Yorkshire Terrier TIHS value showed no differences with the general population, $p = 0.10$. On the contrary, the VHS value for the Yorkshire Terrier breed dogs was significantly different to that of the general population and Labrador Retrievers, $p < 0.01$. The Chihuahua TIHS and VHS values showed no differences compared to the general population, $p = 0.30$ and $p = 0.09$, respectively. The Labrador Retriever TIHS and VHS values showed no differences compared to the general population, $p = 0.013$ and $p = 0.23$, respectively. The French Bulldog TIHS value was significantly shorter compared to the general population, Yorkshire Terrier, and Labrador Retriever, $p < 0.01$. The French Bulldog VHS value was significantly higher than the VHS for the general population, Yorkshire Terrier, Chihuahua, and Labrador Retriever, $p < 0.01$ (Figure 3).

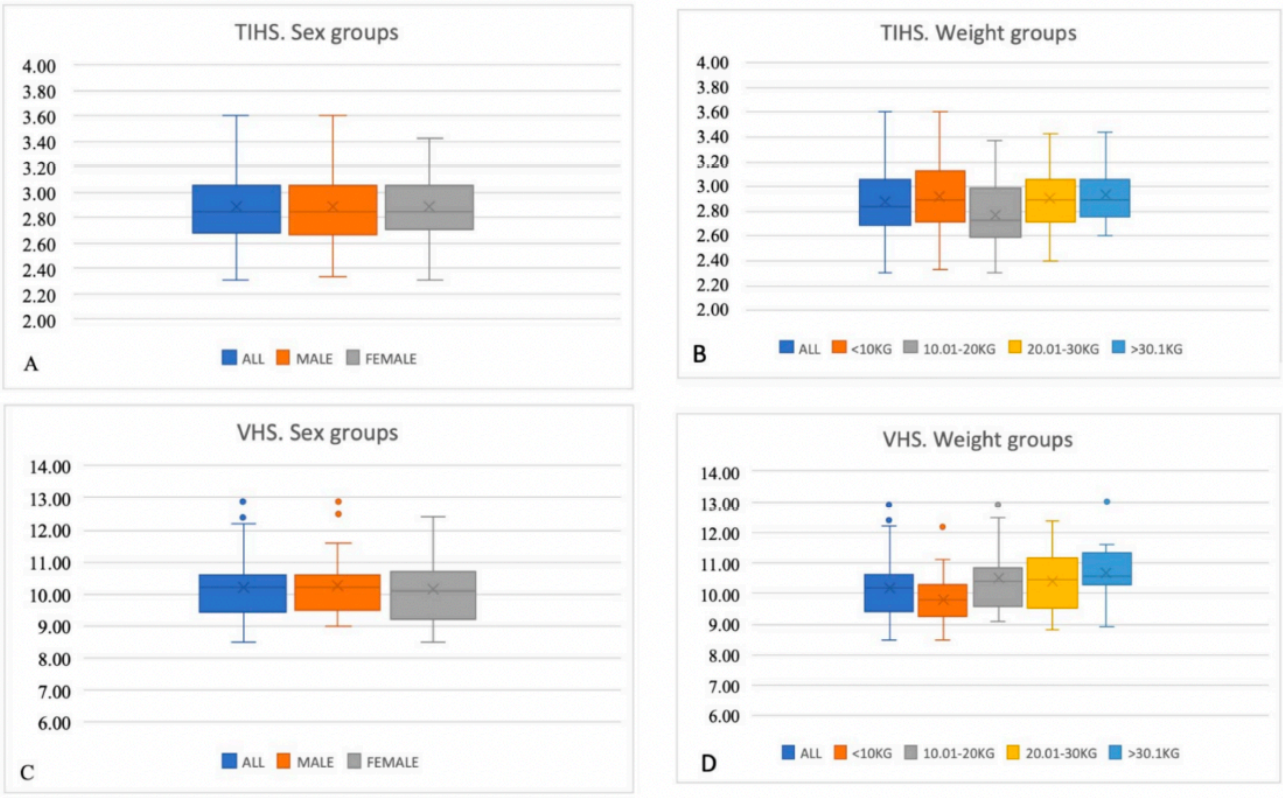

Figure 2. Box plots illustrating TIHS (**A**,**B**) and VHS (**C**,**D**) for the general population, sex groups (male and female), and body weight groups (≤10 kg, 10.01–20 kg, 20.01–30 kg, and ≥30.01 kg). Dots represent outliers.

Figure 3. Box plots illustrating TIHS (**A**) and VHS (**B**) for the general population and four most represented dog breeds. Dots represent outliers.

There was a correlation between TI and T4: $r > 0.9$, $p < 0.05$. There was also a correlation between TI and LAx, SAx, and the sum of LAx and SAx: $r > 0.9$, $p < 0.05$. There was a correlation between T4 and LAx and SAx: $r > 0.9$, $p < 0.05$. There was a strong correlation between TI and body weight: $r > 0.7$, $p < 0.05$; and between T4 and body weight: $r > 0.7$, $p < 0.05$. The correlation between body weight and LAx and SAx was $r > 0.7$ and $p < 0.05$. There was not a correlation between TIHS and LAx and SAx: $r < 0.3$, $p < 0.05$. There was not a correlation between VHS and TI: $r < 0.3$, $p < 0.05$. There was not a correlation between VHS and LAx and SAx: $r < 0.3$, $p < 0.05$. TIHS and VHS showed no correlation: $r < 0.24$, $p < 0.05$.

Table 1. Mean (SD), range, and 95% Confidence Interval (CI) for measurements of the cardiac size on a right lateral thoracic radiographic projection obtained from 122 normal dogs. $p < 0.01$. n number of dogs. TIHS Thoracic Inlet Heart Size. VHS Vertebral Heart Size. * Difference statistically significant in VHS value between ≤10 kg group the general population, and the other groups.

		TIHS				VHS			
	n **( )**	**(Mean ± SD)**	**Range**	**CI 95%**	***p*** **Value**	**(Mean ± SD)**	**Range**	**CI 95%**	***p*** **Value**
General population	122	2.86 ± 0.27	2.31–3.60	2.81–2.91		10.12 ± 0.92	8.5–13.0	9.95–10.29	
Sex	Male (61)	2.86 ± 0.26	2.33–3.60	2.77–2.95		10.18 ± 0.92	9.0–13.0	9.88–10.48	
	Female (61)	2.85 ± 0.27	2.31–3.43	2.76–2.94	0.96	10.05 ± 0.95	8.5–12.40	9.74–10.36	0.49
Weight	≤10 kg (52)	2.89 ± 0.27	2.33–3.60	2.77–2.99	0.41 (GP) 0.03 (10.01–20) 0.77 (20.01–30) 0.77 (>30)	9.77 ± 0.68	8.5–12.20	9.66–10.22	0.007 (GP) * 0.0011 (10.01–20) * 0.0017 (20.01–30) * 0.0001 (>30) *
	10.01–20 kg (26)	2.75 ± 0.27	2.31–3.37	2.60–2.90	0.48 (GP) 0.07 (20.01–30) 0.07 (>30)	10.42 ± 1.20	9.1–13.0	9.81–11.03	0.31 (GP) 0.71 (20.01–30) 0.64 (>30)
	20.01–30 kg (28)	2.88 ± 0.24	2.40–3.43	2.76–3.00	0.73 (GP) 0.59 (>30)	10.32 ± 1.01	8.80–12.40	9.83–10.81	0.05 (GP) 0.33 (>30)
	≥30.1 kg (16)	2.92 ± 0.24	2.61–3.44	2.76–3.10	0.40 (GP)	10.60 ± 1.12	8.90–13.00	9.88–11.32	0.05 (GP)

Table 2. Mean (SD), range, and 95% Confidence Interval (CI) for measurements of the cardiac size on right lateral thoracic radiographic projection obtained from 48 normal dogs of four different breeds. $p < 0.01$.

		TIHS				VHS			
Breeed	***n***	**(Mean ± SD)**	**Range**	**CI 95%**	***p*** **Value**	**(Mean ± SD)**	**Range**	**CI 95%**	***p*** **Value**
Yorkshire terrier	13	3.01 ± 0.31	2.64–3.34	2.79–3.23	0.10 (GP) 0.70 (Chihuahua) 0.73 (Labrador Retriever)	9.28 ± 0.74	9.0–10.5	8.75–9.81	0.002 (GP) ** 0.07 (Chihuahua) 0.003 (Labrador Retriever) **
Chihuahua	12	2.96 ± 0.33	2.73–3.60	2.71–3.19	0.30 (GP) 0.45 (Labrador Retriever) 0.011 (French Bulldog)	9.82 ± 0.60	9.10–10.90	9.38–10.26	0.09
Labrador retriever	8	3.05 ± 0.16	2.87–3.36	2.91–3.19	0.013 (GP)	10.54 ± 0.63	10.57–11.94	9.97–11.11	0.23
French Bulldog	5	2.66 ± 0.13	2.55–2.86	2.41–2.81	0.0028 (GP) * 0.0027 (Yorkshire Terrier) * 0.0007 (Labrador Retriever) *	12.29 ± 0.45	12.00–13.00	11.77–12.81	0.0012 (GP) ** 0.0000 (Yorkshire Terrier) ** 0.0000 (Chihuahua) ** 0.0002 (Labrador Retriever) **

GP: General Population. n: number of dogs. THIS: Thoracic Inlet Heart Size. VHS: Vertebral Heart Size. * Difference statistically significant in TIHS value between French Bulldog breed dogs and the general population, Yorkshire Terrier and Labrador Retriever. ** Difference statistically significant in VHS value between Yorkshire Terrier and the general population, and Labrador Retriever; and in VHS value between French Bulldogs and the general population, Yorkshire Terrier, Chihuahua and Labrador Retriever dogs.

Intraobserver variability showed almost perfect agreement for TIHS and VHS values, 0.93 and 0.99, respectively. Interobserver variability showed substantial agreement for this values, 0.77, and almost perfect agreement for VHS values, 0.85 (Figure 4).

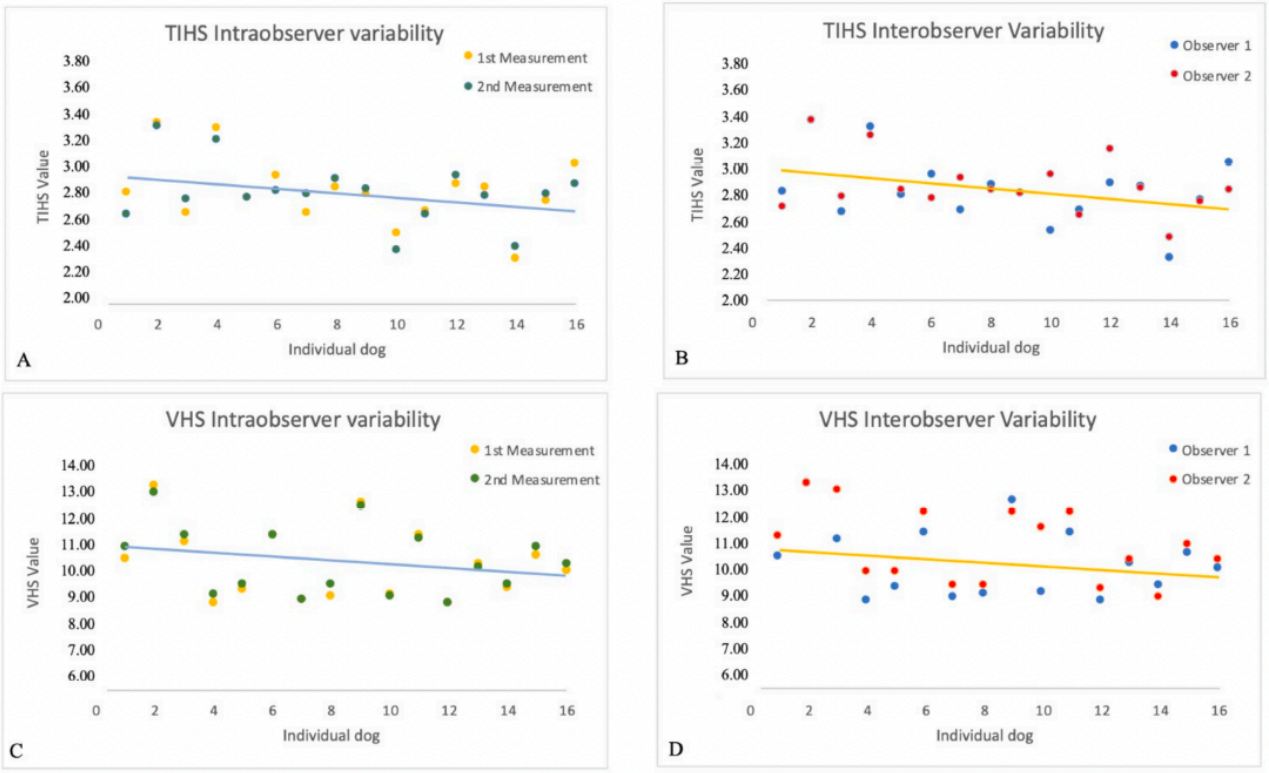

Figure 4. Scatterplots for intra- and interobserver variability on TIHS (**A**,**B**) and VHS (**C**,**D**) values measured on right lateral thoracic radiographs from 16 randomly selected dogs. The solid line represents the tendency line for the variable measured.

4. Discussion

This study was carried out to describe a radiographic method to assess the heart size normalized to the thoracic inlet length. It shows that TIHS is a simple, straightforward, reliable, and reproducible way to measure a dog's cardiac silhouette on a thoracic right lateral radiographic projection. The TI length defined in the present study was the distance extending from the craniodorsal manubrium at its highest point to the cranioventral aspect of the first thoracic vertebrae, resulting in the shortest distance. The same thoracic inlet distance reference points have been used in a recent study comparing the radiographic tracheal diameter at different levels on non-brachycephalic small breed dogs [33].

In 2000, Buchanan [6] found a strong correlation between the sum of the long- and short-axes heart dimensions and a 10 vertebrae reference length in 100 normal dogs of various types, $r = 0.98$, suggesting that those structures were related in a proportional way and considering it a useful reference to evaluate the cardiac silhouette. They also found a good correlation between heart size and the length of three or four sternebrae ($r = 0.94$ and $r = 0.95$, respectively, $p < 0.0001$), considering it not to be advantageous over vertebral correlations, except in dogs with hemivertebrae or other vertebral abnormalities.

More recently, the manubrium length has been proposed a possible reference value to normalize the measurements of width and height of the cardiac silhouette in small- and large-breed dogs [3]. Although anomalies of the manubrium are uncommon [34], it can adopt different shapes: elongated, bullet-shape, rectangular, and camel head-neck-shape [3]. Dogs with an abnormally shaped manubrium, or where its cranial margin could not be

identified, were excluded from that study, and a strong correlation was found between the manubrium length and SAx and LAx [3].

The present study included radiographs of dogs where the manubrium could be clearly identified. It showed a strong correlation between TI and LAx and SAx, and Lax + SAx, $r = 0.96, 0.96, 0.97$, respectively. It also showed a strong correlation between the TI and T4 length, and between TI and body weight, indicating a proportion in body structures that is stable enough not to cause high variations that would make the technique unreliable.

We observed that 42/122 (34.4%) of dogs studied had a manubrium shape considered as bullet shape or camel head-neck shape, as mentioned before (3). The craniodorsal edge of these manubria seemed to be subjectively wider than the rest of the bone. However, the TIHS value for those dogs was 2.86 ± 0.25 (2.31–3.44), compared to the TIHS value of those with rectangular-shaped manubria: 2.86 ± 0.27 (2.31–3.60), without statistically significant difference, $p = 0.97$.

Also, some dogs had a sternum with a prominent curvature with respect to the thoracic spine. Those dogs (32/122, 26.2%) had a THIS value of 2.91 ± 0.31 (2.44–3.60). On the other hand, dogs with a regular curvature (90/122, 73.8%) had a THIS value of 2.84 ± 0.25 (2.31–3.39). This difference was not statistically significant, $p = 0.16$. Even though no statistical difference was found with respect to sternum inclination or manubrium shape in our population, further studies might be needed to assess how different sternal angulation with respect to the thoracic spine, or different manubria shapes between breeds or individually, affect the TI length.

This study showed a moderate correlation between the VHS value and the sum of LAx and SAx, $r = 0.31$. On the contrary, a weak correlation and no correlation between VHS and the sum of LAx and SAx in large- and small-breed dogs, respectively, was observed by Mostafa et al. [3]. They suggested that this could be related to the relative variations in the vertebral size and shape among dog breeds, and variations in the intervertebral disk space. In a recent study carried out on pugs, 9/12 did not show typical vertebral body malformation, but irregularly shaped vertebrae, trapezoid vertebral bodies that even caused kyphosis and lordosis in three of them [25]. Our study did not exclude dogs with vertebral malformations; however, only one dog presented thoracic vertebral malformations, a French bulldog with VHS 12.5 v.

Another potential reason for the weak correlation between VHS and Lax + SAx could be the transformation of the short and long axes dimensions into VHS units, and in the selection of anatomic reference points.

Correlations between the VHS and MHS values were identified for large-breed dogs but not for small-breed dogs, suggesting that for evaluation of cardiac dimensions in large-breed dogs, VHS may be more convenient, but overall-MHS could be considered for further evaluation in both clinically normal and ill dogs, regardless of breed size [3]. Our study found a weak correlation between the VHS and TIHS values. This could suggest that both methods are not interchangeable.

The VHS value in the present study, 10.12 ± 0.92 (95% CI, 9.95–10.29), was higher than that found by Buchanan et al. [5], 9.7 ± 0.5, and Greco et al., 9.8 ± 0.6 [35], and in agreement with the results of more recent studies, 10.3 ± 0.8 (95% CI, 10.1–10.5) [3], 10.7 ± 0.65v) [36]. Besides, in the present study, only 72% of dogs had a VHS ≤ 10.5 v compared to 95% in the Buchanan study [5]. These differences could be related to the sample size and the number of dogs of each breed included in the different studies, although the present study and Buchanan did not include more than four dogs of the same breed. Another reason could be the reference point selected for the cardiac long axis, the ventral border of the left main stem bronchus to the most distant ventral contour of the cardiac apex [5] compared to the ventral border of the carina for the long axis in the present study. Also, an adjustable caliper was used by Buchanan et al., compared to a digital caliper in the present study.

A study by Hannson et al. [27] showed that the VHS method is dependent on an individual selection of reference points, mainly for the long axis; the reference point at

the heart base, because of greater complexity and variability of the topographic anatomy compared with other reference points, and difficulty in defining the apex because of superimposition of ribs, skin folds, or cranial parts of the liver, and the transformation of the long and short axes dimensions into VHS units. The VHS is an indicator of heart size in relation to body length expressed as total units of vertebral length to the nearest 0.1 vertebra [5]. The TIHS shares the same reference point but lacks the transformation to vertebral body length. The TIHS method relies on the length of a single reference segment, the TI, which strongly correlated with the cardiac axes, T4 length and body weight. The TIHS could be measured in dogs with mid thoracic vertebral malformations, as it does not need to be transposed onto vertebral bodies. However, malformation in the cranioventral aspect of T1 might render its use unreliable. Also, it is a unitless value that reduces bias, as cardiac axes measures do not need to be transformed into vertebral units. We proposed the thoracic inlet length as an appropriate reference value to normalize the short and long heart axes measured on a thoracic right lateral radiographic projection in dogs.

The present study only measured the TIHS and VHS values on right lateral projections. The original VHS study showed no differences on radiographic projections [5]. Some studies have observed differences between the right and left projections [18,35], suggesting that the increased VHS values in right lateral recumbency may be due to a greater distance of the heart from the radiographic cassette in comparison to left lateral recumbency [35]. As determining the existence of differences between right and left projections was not an objective of this study, we suggest the use of the same projection consistently as recommended by Buchanan and Bucheler [5].

This study only included dogs older than 12 months, in agreement with other studies [8,10,12,14,17,37]. A study on growing dogs of different breeds showed no significant differences in relative heart size at 3, 6, and 12 months, 10.0 ± 0.5, 9.8 ± 0.4, and 9.9 ± 0.6 v [38]. No significant correlation was found between age and vertebral heart scale on 61 healthy Norwich terriers [20]. However, another study suggested that there could be an increase in the VHS value with age, due to the deposition of epicardial fat as dogs age, if this occurs in dogs as it has been shown to in humans [18]. If there is a difference in TIHS with aging, this needs to be investigated.

Considering body weight, our results did not find differences on TIHS values between different groups ($p > 0.01$). Many other studies also did not find differences on VHS depending on body weight [6,11,12,15,17–19,21–24,39]. However, we found that the VHS value for the ≤ 10 kg group was lower than that of the general population and heavier groups. This is in agreement with Mostafa et al., who found that large dogs (≥16 kg) had a higher VHS (10.7 ± 0.5) than small-breed dogs (≤12 kg) (10.3 ± 0.8), $p < 0.001$ [3].

Neither were differences found in the TIHS value between males and females, nor in the VHS value, in agreement with some other studies [5,10–13,16,19–22,24,25,39]. However, two different studies have found a higher VHS in females than in males: a multibreed study that showed a female Yorkshire Terrier VHS of 10.2 ± 0.7, versus a value for males of 9.6 ± 0.4, $p < 0.05$ [14]; and a study on Dachshund, where the female VHS was 10.8 versus the male VHS of 9.99, $p = 0.0002$ [18]. In this later study, the authors hypothesized that this occurred because their female population was older, and older animals may deposit more epicardial fat [18].

The first VHS study was carried out on 100 dogs with no more than four individuals of the same breed and suggested VHS ≤ 10.5 as a clinically useful limit for normal heart size in most breeds [5]. It also implied that larger numbers of dogs of each breed would be required to determine more precisely normal values for different breeds [5]. With that premise, breed-specific VHS values have been published in the last two decades [7–25] (Table 3).

Table 3. Breed-specific VHS obtained in different studies since the original Vertebral Heart Size study was published by Buchanan and Bücheler in 1995.

Breed	Number	VHS	Study
American Pitbull Terrier	24	10.9 ± 0.4 (10.5–11.8)	[26]
Australian cattle dog	20	10.5 ± 0.5 (9.8–11.3)	[19]
Beagle	19	10.3 ± 0.4 (9.2–11.2)	[13]
Belgian Malinois	19	9.58 ± 0.53 (8.52–10.35)	[16]
Boston Terrier	19	11.4 ± 1.2 14.2 ± 1.6 (Vertebral anomalies)	[14]
Boxer	22	11.3 ± 0.8 (10.3–12.6)	[8]
Brittany Spaniel	28	10.6 ± 0.2	[23]
Bulldog	30	12.1±1.5 13.4 ± 1.6 (Vertebral anomalies)	[14]
Cavalier King Charles Spaniel	20	10.6 ± 0.5 (9.9–11.7)	[8]
Chihuahua	30	10.0 ± 0.6 (8.9–11.0)	[21]
Dachsund	29 51	9.7 ± 0.5 10.3 (9.25–11.55)	[14]
Doberman	20	10.0 ± 0.6 (9–10.8)	[8]
German Shepherd Dog	21 100	9.9 ± 0.7 (8.7–11.2) 9.8 ± 0.5 (9.2–10.3)	[8] [7]
Greyhound	42	10.5 ± 0.1	[12]
Indian Spitz	20	10.21 ± 0.23	[17]
Labrador	19 24 20	10.8 ± 0.6 (9.7–11.7) 10.39 ± 0.5 10.22 ± 0.20	[8] [15] [17]
Lhasa apso	18	9.6 ± 0.8	[14]
Maltese	81	9.53 ± 0.4	[22]
Norwich Terrier	61	10.6 ± 0.60	[20]
Poodle	30	10.12 ± 0.51 (9.2–11.1)	[9]
Pomeranian	18	10.5 ± 0.9	[14]
Pug	30 32	10.7 ± 0.9 11.25 ± 0.62 (10.1–12.8)	[14] [25]
Rottweiler	38	9.8 ± 0.1	[12]
Shih-Tzu	30	9.5 ± 0.6	[14]
Turkish Shepherd Dog	120	9.7 ± 0.67 (8.4–10.9)	[11]
Whippet	44	11.03 ± 0.5 (10.1–11.8)	[10]
Yorkshire Terrier	12 30	9.7 ± 0.5 (9.0–10.5) 9.98 ± 0.6	[8] [14]

The present study compared VHS and TIHS values for the four most popular breeds in our hospital: Yorkshire Terrier, Chihuahua, Labrador Retriever and French Bulldog. We found differences in the TIHS values between French Bulldogs and the general population, Yorkshire Terriers, and Labrador Retrievers, $p < 0.01$. French Bulldogs have a higher VHS compared to other breeds (14), as has been shown in this study. Considering these results, a larger sample of dogs for each breed would be necessary to ascertain whether different breeds have different this values.

Intraobserver variability showed almost perfect agreement for both TIHS and VHS, 0.93 and 0.99, respectively, which is in line with previous VHS studies [25,36]. Interobserver variability showed substantial agreement for TIHS, 0.77, and almost perfect agreement for VHS, 0.85. A difference of almost 1 vertebral unit has been observed between observers measuring VHS [27]. However, a more recent study measuring VHS, VLAS, and RLAD in pugs showed that the VHS was the score with the fewest interobserver differences: merely differing between 0.06 to 0.18 v [25], which agrees with several studies showing an interobserver agreement between 0.89 and 0.99 [12,18,20,25,36,40].

A better interobserver agreement for VHS values in our study could be explained because VHS is a well-established and reproducible radiographic score [25], and is commonly

used [8,27]. In a study that investigated the reproducibility of several radiographic measurements, and the ease of determining the exact position of their radiographic reference points, the VHS value was independent of the observers' experience, the cranial contour of the cardiac silhouette being the easiest landmark to locate, with the hardest being the cardiac apex [36]. TIHS is a method that requires the measurement of TI, a segment not usually measured, and it might take some time to identify the reference points.

This study has some limitations. The main observer was not blinded to the dogs' clinical status and echocardiography values, which could have caused a radiographic measurement bias. Radiographs where the manubrium was clearly visible were included in the study, although in some patients the manubrium dorsal border was blurry and that could hamper the caliper positioning. The same is true for the cranioventral aspect of the first thoracic vertebrae; in some animals, the superimposition of the first rib with the cranioventral aspect of the vertebra could have misled the authors in the identification of the reference point.

As mentioned, there was a small interobserver variability while measuring TIHS. We think that this could be related to measuring the TI rather than the LAx and SAx axes, as these two measures were the same for VHS and, the interobserver variability for VHS was less than that for TIHS. As happened with measuring the LAx and SAx to determine the VHS, practitioners need to become familiar with measuring the TI length to calculate TIHS. A study comparing the results of more observers would be desirable.

Although radiographs were intended to be taken during peak inspiration, this is not always possible in awake animals. Moreover, whether there is a change in the thoracic inlet length depending on the respiratory cycle has not been studied, nor how this could affect the TIHS value.

Though the study included more than 120 animals, as preferable for creating valid reference values in veterinary medicine according to recent guidelines [41], and the number of dogs included for measurements in the present study is higher than those of others studies investigating ranges for VHS [5,11,12,19,20,22], the TIHS value showed here could differ with a larger study. Also, studies on selected breeds might show breed-specific TIHS values, as happens with VHS.

The THIS value results from this study come from a dog population considered to have a normal heart based on history, clinical signs, examination findings, radiography, and echocardiography. Some heart diseases such as aortic stenosis, pulmonic stenosis, mild atrial or ventricular septal defects, early myxomatous mitral valve disease, arrythmias, and endocarditis, do not necessarily change the cardiac size. Studies assessing the usefulness of the TIHS method to discriminate between dogs with and without heart disease are warranted.

5. Conclusions

The TIHS method is a feasible, simple, and reliable method to measure the radiographic cardiac silhouette in dogs. With a mean value of 2.86 and a confidence interval of 2.81–2.91 (95%), a TIHS value $\leq$ 3.2 is suggested as a clinically useful upper limit for the normal heart size for a healthy dog in a general population.

Author Contributions: D.M.F. designed the study and wrote the manuscript. D.M.F. and V.G. acquired the data. D.M.F., V.G., A.J.S. and J.A.M.-A. analyzed and interpreted the data. All authors participated in the discussion of the results. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement: The study was carried out in accordance with the current Spanish and European legislation on animal protection. Ethical review and approval were not required for the animals in this study.

Informed Consent Statement: Informed consent was obtained from the owners for the participation of their animals in this study.

Data Available Statement: The data presented in this study are available on request from the corresponding author.

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5.2.

The thoracic inlet length as a reference point to radiographically assess cardiac enlargement in dogs with myxomatous mitral valve disease.

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The Thoracic Inlet Length as a Reference Point to Radiographically Assess Cardiac Enlargement in Dogs with Myxomatous Mitral Valve Disease

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Simple Summary: The present study investigates the hypothesis that the thoracic inlet heart score (TIHS), a recently described method to assess the cardiac silhouette on dogs' chest radiographs, can be used to identify dogs with cardiac enlargement secondary to myxomatous mitral valve disease (MMVD). This method uses the thoracic inlet length as a reference point. Degenerative mitral valve disease is the most common acquired cardiac disease in dogs and radiographic studies are important in its diagnosis and follow up. The VHS and VLAS are recommended radiographic measurements to use in the staging of the disease. The TIHS method is simple to perform and provides practitioners with another tool when evaluating dogs with clinical signs compatible with cardiac disease. Comparing the results obtained from clinically healthy dogs and dogs in different MMVD Stage, we found that this method identified dogs with cardiac enlargement secondary to MMVD, and it could differentiate dogs in different MMVD stage.

Abstract: The diagnostic value of the vertebral heart size (VHS) in dogs with mitral valve degeneration (MVD) is compromised when middle thoracic vertebral anomalies are present. The objective of this study was to assess the use of the thoracic inlet heart score (TIHS) to identify left heart enlargement (LHE) secondary to MVD. The cardiac silhouette of 50 clinically healthy dogs and 106 MVD dogs in different stages was assessed on a right lateral chest radiograph. The TIHS and VHS value were calculated for each patient and compared. The TIHS was significantly different between the control dogs and the dogs with MMVD, increasing with disease stage, control 2.91 ± 0.23, Stage B1 2.98 ± 0.36, B2 3.25 ± 0.34, and C 3.53 ± 0.36, $p < 0.05$. A THIS ≥3.3 showed 69% sensitivity and 81% specificity to identify LHE. The TIHS showed moderate correlation with the VHS, LA/Ao, and LVIDDN 0.59, 0.42, and 0.62, respectively. The intraobserver and interobserver agreement were almost perfect, 0.96, and substantial, 0.73. The TIHS method can be used to identify LHE secondary to MMVD on dogs' thoracic radiographs.

Keywords: thoracic inlet; canine; myxomatous mitral valve disease; cardiac enlargement

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1. Introduction

Myxomatous mitral valve disease (MMVD), the most common cardiac disease in dogs [1], is diagnosed based on clinical, radiographic, and echocardiographic findings. MMVD causes left heart chambers enlargement. Echocardiography is the gold standard diagnostic tool for the identification of mitral valve thickening and/or valve prolapse

and regurgitation that characterize the disease. It is also used for staging the disease in conjuction with auscultation and radiography [1]. Radiography can also assist the small animal practitioner in the identification of patients with cardiac enlargement when echocardiography is not available. Radiography is also crucial for the diagnosis of congestive heart failure in dogs with symptoms associated with the disease (tachypnea, dyspnea, and/or cough) [2].

Different radiographic methods to assess the dog heart size have been described: intercostal spaces [3], VHS [4], cardiothoracic ratio [5], MHS [6], HSVR [7], TIHS [8], and more specific for the left atrium Tracheal-bifurcation angle [9], VLAS [10], RLAD [11], Br-Spine [12], MVLAS [13], m-VLAS [14]. The diagnostic value of some of these methods, VHS [2,15–20], MHS [21], VLAS [10,16,18–20,22,23], RLAD [11,16,20,23], MVLAS [13], m-VLAS [14], Br-Spine [12], Tracheal-bifurcation angle [9] to discriminate between dogs suffering mitral valve disease with and without cardiac enlargement has been studied.

The VHS described in 1995 [3] normalizes the sum of the cardiac long and short axes to the length of the midthoracic vertebrae, with a reference value of 9.7 ± 0.5; an upper limit for normal heart size in most breeds of ≤10.5 v was proposed. The same study monitored one dog with mitral regurgitation during a 3.5-year period and observed that the VHS increased with time. The authors concluded that the major uses of the VHS would be to identify cardiomegaly and to monitor its progression over time in a case-basis [3]. That study also considered that different breeds might have different normal upper limits. Since then, many breed-specific VHS reference values have been published [24–40].

ACVIM consensus guidelines for the diagnosis and treatment of MMVD [1] proposed a VHS ≥11.5 or a breed-adjusted VHS or evidence of increasing interval change in radiographic cardiac enlargement patterns in the absence of echocardiography as a predictor of Stage B2 dogs.

However, the VHS is affected by the presence of middle thoracic vertebral anomalies, interobserver differences in reference point selection, and transformation into vertebral units [41]. The thoracic inlet length has been used previously as a reference point to assess tracheal diameter in brachycephalic and non-brachycephalic dogs [42–44]. Its use to normalize cardiac size could overcome some of the limitations related to the presence of vertebral malformations and conversion to vertebral units. Thus, a method to assess cardiac size using the thoracic inlet length as a reference point has been described recently, namely the thoracic inlet heart size (TIHS) [8]. For a general population of healthy dogs, its mean value was 2.86 ± 0.27, and a value <3.2 was proposed as an upper limit for clinically healthy dogs. The TIHS was not different between healthy chihuahua and Yorkshire terrier, two dog breeds commonly affected by MMVD. We hypothesized that the TIHS could discriminate between MMVD dogs with cardiac remodeling from dogs without it, and healthy dogs.

The objective of this study was to determine if the TIHS method could discriminate between clinically healthy dogs and dogs with different stages of MMVD. Also, we studied the TIHS variability in dogs of the chihuahua breed diagnosed with MMVD in different stages. Correlation of the TIHS with the VHS, as well as intra- and interobserver agreement, was assessed. We finally suggested a TIHS reference value for dogs with cardiac remodeling.

2. Materials and Methods

2.1. Animals

The study design was a retrospective observational investigation conducted at Anicura Albea Small Animal Hospital. Therefore, no institutional animal care and use approval were required. Records of client-owned dogs admitted at the hospital from March 2021 to June 2022 were reviewed. Dogs were included in the study if they had had a full clinical examination, at least two thoracic orthogonal radiographic projections (one right lateral and one ventrodorsal/dorsoventral), and an echocardiography performed within 24 h. Two groups were created, a group of control dogs that included dogs older than 1 year of age with no history or concurrent clinical or radiographic signs of cardiovascular or

respiratory diseases admitted for a previous study; and a MMVD group that included dogs with an apical systolic heart murmur on auscultation, and a confirmed diagnosed of mitral valve disease consisting of thickening and/or prolapse of the atrioventricular valves and a regurgitant jet on echocardiography. Descriptive data (body weight, age, sex, and breed) were registered. In the control group, dogs with respiratory sinusal arrythmia were included in the study; the presence of other arrythmia or a heart murmur excluded the dog from taking part in the study. Subjects with pulmonary abnormalities, or a history of neck or chest surgery, were not included in the study. Any dog positive to a heartworm antigen test was excluded.

2.2. Echocardiography

Every patient had had an echocardiographic exam performed by a veterinary practitioner of our hospital with over 15 years of clinical experience and echocardiography expertise. Examination was carried out without sedation from right and left parasternal position in two-dimensional (2D-) Mode, M-Mode and Doppler Mode, and simultaneous single-lead electrocardiogram, and were performed with a Vivid iq portable ultrasound machine (General Electric Medical Systems, Jiangsu, PR China). From the right parasternal short-axis view, the left ventricle internal diameter at end diastole index to body weight (LVIDDN), measured in accordance with Cornell et al. [45], and left atrium aortic valve ratio (LA/Ao), measured in accordance with Hanson et al. [46], were calculated on an Echopack DICOM viewing system. Dogs with MMVD were classified in different stages based on the echocardiographic criteria recommended by ACVIM guidelines [1]. Dogs in Stage B1 had LVIDDN <1.7 and/or LA/Ao <1.6. Dogs with an increased left atrium, LA:Ao ≥1.6, and left ventricle, LVIDDN ≥1.7, were considered to have LHE. These dogs were included in Stage B2 if asymptomatic, or in Stage C if they had signs of congestive heart failure (tachycardia, respiratory distress, orthopnea, respiratory crackles, and wheezes) current or past.

2.3. Radiography

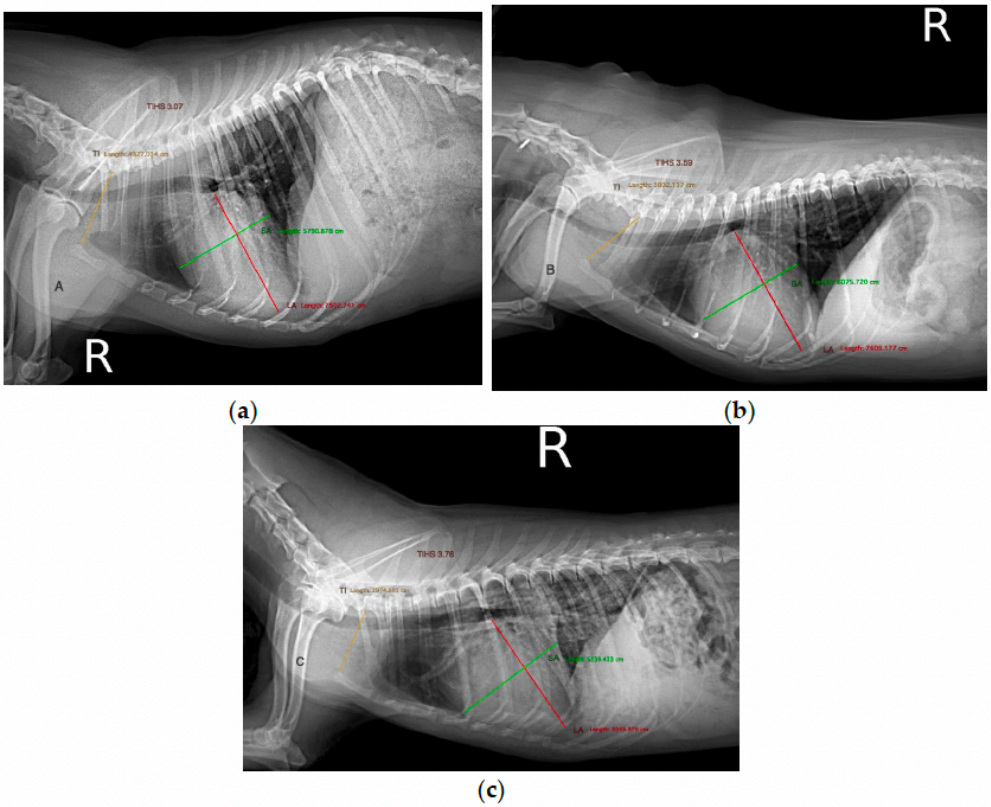
For cardiac measurements, radiographs from the hospital archiving system were retrieved with a digital viewer (IntechForView 12.5.1.1, La Cartuja Baja, Zaragoza, Spain). To be included in the study, the thoracic radiographs had to have been taken in inspiration and with the front limbs extended cranially so the sternal manubrium could be identified. Having vertebral malformations did not exclude the patient from the study. Radiographs with motion artifacts, cardiac silhouette not well defined, or the whole manubrium not included in the image were not included in the study.

Only the right lateral projection was used for the TIHS and VHS measurement. Three measurements, using a digital caliper, were taken and the mean calculated for later analysis.

The VHS was obtained as described by Buchanan et al. [3] and modified according to Jepsen-Grant et al. [47]. The VHS is the sum of the measurements of the long and short cardiac silhouette axes indexed to thoracic vertebral bodies starting at the cranial edge of T4, measured to the nearest 0.1 vertebra (v).

The TIHS was measured following Marbella et al. [8]. First, the lengths of the long axis (LA) and short axis (SA) of the cardiac silhouette were measured, the LA from the central and ventral border of the carina to the cardiac apex, and the SA, perpendicular to the LA, from the cranial border of the cardiac silhouette to the intersection of the ventral border of caudal vena cava with the caudal border of the cardiac silhouette. Second, the thoracic inlet length (TI) was the shortest distance measured from the cranioventral aspect of the first thoracic vertebra to the craniodorsal manubrium. Third, the cardiac axes measurements were added and divided by the TI.

Radiographic measurements were made by DM. At this time, this investigator was not masked to the clinical data of all the patients and their echocardiographic measurements (Figure 1).



(**a**) (**b**) (**c**)

Figure 1. Thoracic inlet heart score measure in three dogs diagnosed with myxomatous mitral valve disease in different stages. (**a**) Stage B1, (**b**) Stage B2, (**c**) Stage C. LA heart long axis, SA heart short axis, TI thoracic inlet length. THIS = (SA + LA)/TI.

Echocardiographic diagnose and radiographies had to have been performed within the same 24 h.

Intra- and interobserver variability was studied comparing the radiographic measurements of 23 dogs, 15 control and 8 MMVD, randomly selected, performed by two observers (DM and VG). For the intraobserver, variability measurements were taken two times at least one week apart. Observers were blinded to the results of one another. VG did not know what group the patient was included in. The first results of both observers were used to calculate the interobserver coefficient of variation (CV).

2.4. Statistical Analysis

The continuous variables providing descriptive information (body weight and age) were presented as median and range (minimum and maximum). For the TIHS and VHS, median, standard deviation, range, and a 95% confidence interval (CI) were calculated on each group. To identify differences in the TIHS depending on sex and body weight (<10 kg, ≥10 kg), differences in the TIHS and VHS between the control dogs versus the dogs with different MMVD stage, and between the different MMVD stages, a paired Student's *t* test was performed. Also, a Student's *t* test was performed to compare the TIHS and VHS values of chihuahua dogs included in the different groups studied. Differences with $p < 0.05$ were considered significant. The optimal clinical cutoff value for the radiographic scores was determined based on the highest Youden index ([sensitivity + specificity] − 1).

The correlation between the TIHS and VHS was studied with Pearson's correlation test. It was considered weak when its value was between 0.1–0.3, moderate between 0.4–0.6, strong 0.7–0.9, or perfect 1.

For the intraobserver and interobserver variability an intraclass correlation coefficient >0.9 was considered almost perfect, 0.9–0.7 was considered good, 0.7–0.5 was considered

moderate, and <0.5 was considered poor. All statistical analyses were performed using commercially available software (SAS/STAT software, version 16.5, Microsoft Excel 2021).

3. Results

A total of 156 dogs were included in the study. The control group had 50 dogs, 28 male and 22 female of different breeds (25 Cross breed, 3 Labrador retriever, 2 each of the breed Golden retriever, Pitbull, and Yorkshire terrier (YT), 1 each of the breed Beagle, Bichon, Border Collie, Bull Terrier, Cavalier King Charles Spaniel (CKCS), Chihuahua, Dachshund, Jack Russell Terrier, Pekingese, Waterdog, Pomeranian, Pug, Schnauzer miniature, Scottish Terrier, Shih-Tzu, Staffordshire, and West Highland White Terrier) with a median age of 4.8 years (range 1–15 years), and mean body weight 7.4 kg (2.10–38.70). Hundred and six dogs of different breeds were diagnosed with MMVD, 58 male and 48 female, with a median age of 11.3 years (5.5–18.9) and mean body weight 5.1 kg (2–26), these being significantly older and lighter than the control dogs, $p < 0.001$ and $p < 0.01$, respectively. Thirty-six dogs were in Stage B1 (15 Cross breed, 5 Chihuahua, 4 YT, 2 each of the breed Cocker Spaniel, Pinscher, and Ratonero, 1 each of the breed French Bulldog, Bull Terrier, Dachshund, Spanish Galgo, Canarian hound, and Pug), 30 in Stage B2 (16 Cross breed, 6 Chihuahua, 4 YT, 2 Spanish Galgo, 1 each of the breed Pekingese, Pinscher), and 40 in Stage C (15 Cross breed, 9 Chihuahua, 6 Bichon, 2 each of the breed CKCS and YT, 1 each of the breed Beagle, Poodle toy, Dalmatian, Pinscher, Shih-Tzu, and Spitz) 23 male, 17 female. There was no difference for age or weight between the different MMVD stages (Table 1).

Table 1. Mean and range values of descriptive variables (age and weight) of the studied dogs in the different groups. Mean and standard deviation for radiographic and echocardiographic measurements.

n	Control 50	Stage B1 36	Stage B2 30	Stage C 40
Age (years)	4.8 (1–15.3) [a]	11.6 (5.5–15.9)	11.3 (7.4–18.9)	11.4 (7.9–17.6)
Weight (kg)	7.40 [b] (2.10–38.70)	5.38 (2.60–26.0)	5.18 (2.0–19.60)	4.73 (2.80–14.80)
Male/Female	28/22	18/18	17/13	23/17
TI	29.15 ± 15.11 [c]	25.91 ± 9.50	26.25 ± 9.55	24.13 ± 7.39
SAx	39.24 ± 20.60	36.51 ± 12.53	39.84 ± 13.73	40.44 ± 11.03
LAx	45.38 ± 26.81	42.09 ± 16.96	46.23 ± 17.64	45.64 ± 12.13
SAx + LAx	87.68 ± 50.97	78.75 ± 29.30	86.24 ± 31.16	86.25 ± 22.84
LA/Ao	1.20 ± 0.18	1.36 ± 0.17	1.80 ± 0.22 [d]	2.08 ± 0.36 [d]
LVIDDN	1.57 ± 0.20	1.57 ± 0.21	1.94 ± 0.24 [d]	2.08 ± 0.29 [d]

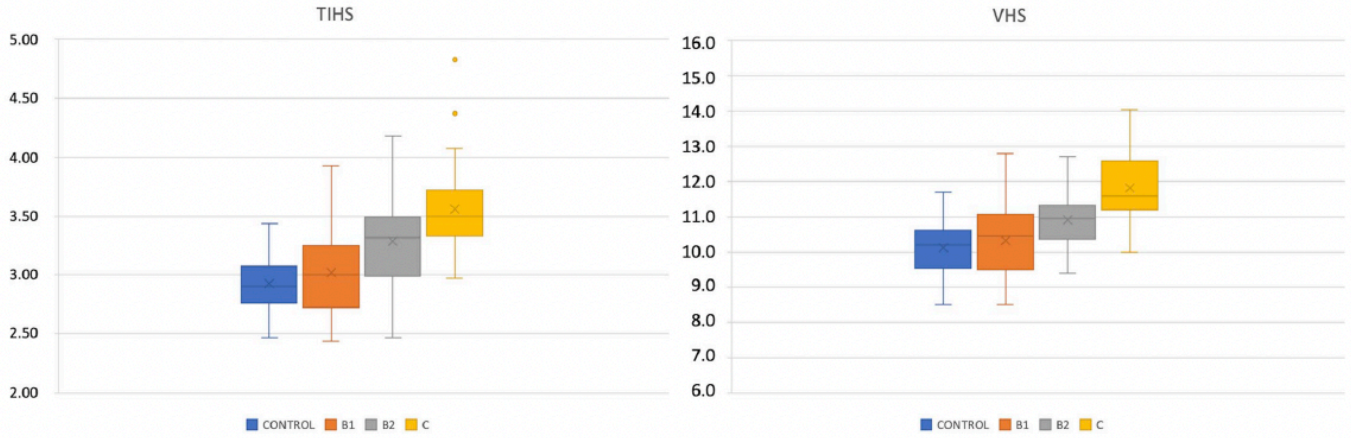
[a] Difference statistically significant between control and MMVD groups. [b] Difference statistically significant for weight between control and MMVD groups. [c] Difference statistically significant for TI between control and MMVD Stage C. [d] Difference statistically significant for left atrium and left ventricle compared to the previous group. $p < 0.05$. LA/Ao ratio left atrium aorta. LVIDDN left ventricular internal diameter in diastole normalized to body weight, LA long axis, n number of dogs, SA short axis, TI thoracic Inlet.

Normally distributed, the TIHS value for the control group was 2.91 ± 0.23 (2.47–3.44), not different from MMVD Stage B1 2.98 ± 0.36 (2.44–3.65), $p = 0.12$. The TIHS for Stage B2 3.25 ± 0.34 (2.47–4.18) and Stage C 3.53 ± 0.36 (3.20–4.83) increased compared to the control group and Stage B1, $p < 0.0001$ (Table 2). There was a statistically significant difference between Stage B1 and Stage B2 and C, $p = 0.002$ and $p < 0.0001$, respectively. The TIHS was significantly different between Stage B2 and Stage C $p = 0.002$ (Figure 2). There was no difference for the TIHS between the sex or body weight in any group, $p > 0.05$ (Table 3).

Table 2. Radiographic cardiac size measurements in the control dogs and dogs diagnosed with myxomatous mitral valve disease (MMVD) in different stages.

n	Control 50	Stage B1 36	Stage B2 30	Stage C 40	*p*
TIHS (CI)	2.91 ± 0.23 (2.84–2.98)	2.98 ± 0.36 [a] (2.87–3.11)	3.25 ± 0.34 [a] (3.09–3.39)	3.53 ± 0.36 [a] (3.42–3.64)	<0.01
VHS (CI)	10.07 ± 0.73 (9.86–10.28)	10.24 ± 0.95 [b] (9.93–10.55)	10.83 ± 0.86 [b] (10.49–11.25)	11.74 ± 0.96 [b] (11.43–12.05)	0.016

[a] Difference statistically significant for TIHS between control group and MMVD Stage B2 and C, and MMVD groups compared with the previous stage (Stage B1 and Stage B2 and C, and Stage B2 and C). [b] Difference statistically significant for VHS between control group and MMVD Stage B2 and C, and MMVD groups compared with the previous stage (Stage B1 and Stage B2 and C, and Stage B2 and C). $p < 0.05$. CI confidence interval 95%, n number of dogs, TIHS thoracic inlet heart score. VHS vertebral heart score.



(**a**) (**b**)

Figure 2. Box plots illustrating TIHS (**a**) and VHS (**b**) for dogs included in the study according to their clinical status. MMVD stages B1, B2, and C.

Table 3. TIHS value according to sex and body weight in the different groups. There was no difference statistically significant in any group, $p < 0.05$. n number of dogs.

THIS (n)	Male	Female	*p*	<10 kg	≥10 kg	*p*
CONTROL	2.88 ± 0.23 (28)	2.94 ± 0.23 (22)	0.33	2.88 ± 0.24 (27)	2.94 ± 0.22 (23)	0.41
Stage B1	3.01 ± 0.35 (18)	2.95 ± 0.38 (18)	0.62	3.04 ± 0.35 (26)	2.84 ± 0.0.35 (10)	0.13
Stage B2	3.25 ± 0.38 (17)	3.26 ± 0.29 (13)	0.91	3.26 ± 0.37 (25)	3.22 ± 0.18 (5)	0.51
Stage C	3.53 ± 0.37 (23)	3.53 ± 0.35 (17)	0.99	3.53 ± 0.37 (36)	3.50 ± 0.21 (4)	0.78

Chihuahua dogs, 32 patients, were the most represented breed in our hospital. Twelve were in the control group and 20 in MMVD group: 5 Stage B1, 6 Stage B2, and 9 Stage C. There was no difference for the TIHS nor for the VHS between the chihuahua dogs and the rest of the population neither on the control group nor on either of the MMVD groups $p > 0.05$. The TIHS for the chihuahua breed did not show differences between the control group 2.96 ± 0.33 (2.33–3.60) and Stage B1 2.92 ± 0.11 (2.81–3.06). The TIHS value increased with MMVD stage, B2 3.40 ± 0.28 (2.99–3.83) and C 3.61 ± 0.44 (2.97–4.37). The difference was statistically significant between the control group and Stage B2 ($p = 0.015$) and C ($p = 0.0008$). There was also a difference statistically significant between Stage B1 and B2 and C, $p = 0.0052$ and $p = 0.0034$, respectively (Table 4).

Table 4. Echocardiographic measurements of the left atrium and the left ventricle internal diameter in diastole, and radiographic cardiac size measurements in a population of chihuahua dogs.

Chihuahua n	Control 12	Stage B1 5	Stage B2 6	Stage C 9	*p*
LA/Ao	1.31 ± 0.01 [a]	1.33 ± 0.15 [a]	1.86 ± 0.18	2.07 ± 0.52	≤0.001
LVIDDN	1.37 ± 0.06 [b]	1.50 ± 0.24 [b]	1.87 ± 0.31	2.12 ± 0.28	≤0.001
TIHS (CI)	2.96 ± 0.33 [c] (2.77–3.15)	2.92 ± 0.11 [c] (2.87–3.11)	3.40 ± 0.28 (3.10–3.70)	3.61 ± 0.44 (3.27–3.95)	≤0.01
VHS (CI)	9.82 ± 0.60 [d] (9.44–10.2)	10.33 ± 0.65 [d] (9.76–10.90)	11.26 ± 0.71 (10.52–12.0)	12.08 ± 1.06 (11.27–12.89)	≤0.001

[a] Difference statistically significant between dogs with (B2 and C) and without (control and B1) cardiac enlargement. [b] Difference statistically significant between dogs without cardiac enlargement and Stage C. [c] Difference statistically significant for TIHS between dogs with and without cardiac enlargement. [d] Difference statistically significant for VHS between control group and Stage B2 and Stage C, and Stage B1 compared to Stage C. $p < 0.05$. LA/Ao ratio left atrium aorta, LVIDDN left ventricular internal diameter in diastole normalized to body weight, n number of dogs, TIHS thoracic inlet heart score, VHS vertebral heart score.

For the entire studied population, a TIHS value of 3.3 had a sensitivity of 69% and specificity of 88% to discriminate between dogs with and without cardiac enlargement, Youden Index 0.57 (Table 5). The same value had a sensitivity of 69% and specificity of 81% to detect cardiac remodeling (stage B2 and C) in dogs with MMVD, YI 0.50. At the same time, a VHS value of 11.5 v showed a sensitivity of 37% and specificity of 97% to discriminate between MMVD dogs with and without cardiac remodeling, YI 0.34 (Table 6). The area under the curve for the THIS and VHS was good, 0.82 and 0.83, respectively (Figure 3). There was a moderate correlation between the TIHS and VHS, 0.59 (Figure 3).

Table 5. Statistical values for different TIHS and VHS cutoff to differentiate between B1 and B2 dogs. AUC area under the curve. NPV negative predictive value, PPV positive predictive value, Se sensitivity, Sp specificity.

Radiographic Method	AUC (95% CI)	Se	Sp	Youden Index	PPV	NPV	Cutoff
TIHS	0.75	0.53	0.75	0.28	0.64	0.66	≥3.25
		0.53	0.81	0.33	0.70	0.67	≥3.30
		0.43	0.81	0.24	0.65	0.63	≥3.35
VHS (v)	0.74	0.50	0.66	0.16	0.65	0.63	≥11.0
		0.20	0.94	0.14	0.75	0.59	≥11.5
		0.13	0.97	0.10	0.80	0.57	≥12.0

Table 6. Diagnostic accuracy for different TIHS and VHS cutoff values to differentiate between MMVD dogs with (B2 and C) and without cardiac enlargement (B1). AUC area under the curve. NPV negative predictive value, PPV positive predictive value, Se sensitivity, Sp specificity.

Radiographic Method	AUC (95% CI)	Se	Sp	Youden Index	PPV	NPV	Cutoff
TIHS	0.82	0.70	0.75	0.45	0.84	0.56	≥3.25
		0.69	0.81	0.50	0.87	0.57	≥3.30
		0.60	0.81	0.41	0.86	0.51	≥3.35
VHS (v)	0.83	0.73	0.66	0.40	0.81	0.56	≥11.0
		0.37	0.94	0.31	0.93	0.44	≥11.5
		0.21	0.97	0.26	0.95	0.41	≥12.0

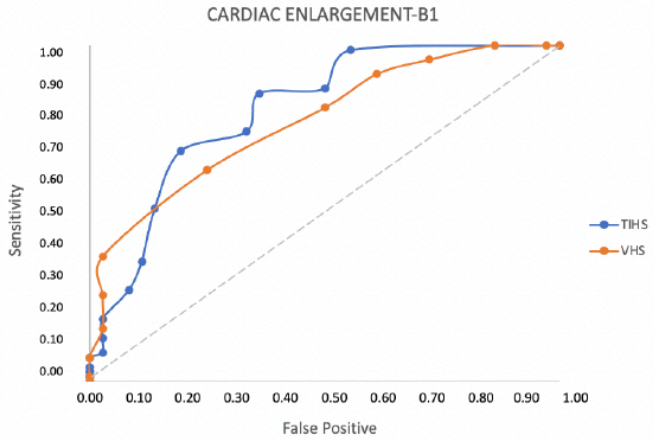


Figure 3. Comparison of the receiver operating characteristics curves for thoracic inlet heart score (TIHS) and vertebral heart score (VHS) for detecting cardiac enlargement in 106 dogs with myxomatous mitral valve disease.

The intraobserver variability was almost perfect for the TIHS in the 23 dogs compared, also considering only the 15 control dogs and the 8 MMVD dogs, 0.97, 0.93, and 0.96, respectively. The same accounts for VHS of 0.98, 0.99, and 0.96. Interobserver variability was good for TIHS of 0.78 and VHS of 0.87 for the 23 dogs compared, 0.77 and 0.84, considering only the 15 control dogs. And it was good for the VHS, 0.84, but poor for TIHS of 0.43, in the MMVD (Figure 4).

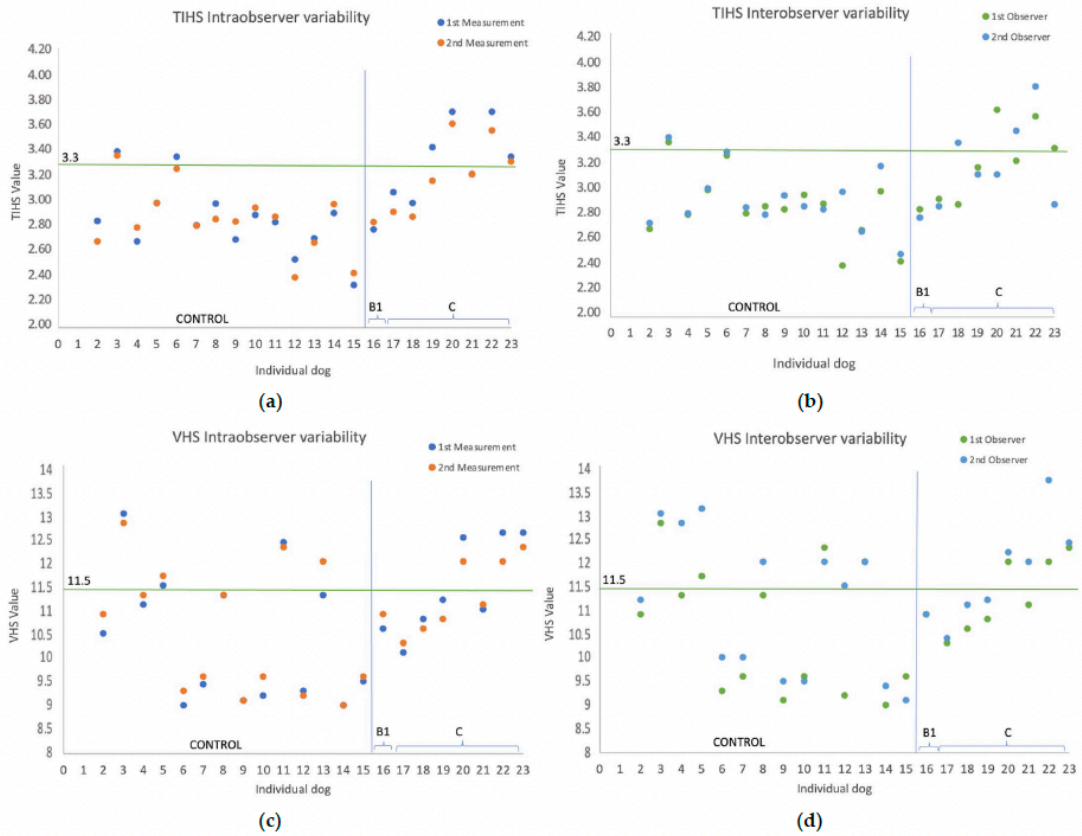


Figure 4. Scatterplots for intra- and interobserver variability on TIHS (**a**,**b**) and VHS (**c**,**d**) values measured on right lateral radiographic projections from 23 randomly selected dogs, 15 control and 8 MMVD. The horizontal line represents the cutoff value. The vertical line separates control dogs from MMVD dogs.

4. Discussion

The TIHS method can be used to identify dogs with cardiac enlargement secondary to MMVD. A TIHS cutoff of 3.3 detected 69% of the dogs with cardiac enlargement and 81% of the dogs that did not have cardiac enlargement. A previous study showed that 90% of clinically healthy dogs had a TIHS < 3.2 [8]. In this study, 86% (43/50) of normal dogs had a TIHS < 3.2, and that percentage decreased in the dogs with MMVD as the disease worsened, 66% (24/36) Stage B1, 46% (14/30) B2, and 10% (4/40) Stage C.

For the overall population, the control group was heavier than any MMVD group and its TI was longer compared to Stage C dogs, $p = 0.003$. Only 4 dogs in Stage C weighted more than 10 kg compared to 23 dogs in control group. The TI, SA, LA length, and SA + LA were longer for dogs ≥10 kg compared to dogs <10 kg independently of the group, the heavier the dog the longer the heart axes and thoracic inlet length. Comparing different groups, SA and LA and their sum were higher for dogs in Stage B2 and C versus normal dogs, independently of the weight. On the contrary, there was no difference for the TI between the different groups depending on the weight. In dogs <10 kg, the TIHS increased significantly from the control group to Stage C, in every group respect to the previous; control vs. Stage B1 ($p < 0.04$), B2 ($p < 0.0001$) and C ($p < 0.0001$), Stage B1 vs. B2 ($p < 0.02$) and C ($p < 0.0001$), and Stage B2 vs. C ($p < 0.007$). The difference in the TIHS was statistically significantly for dogs ≥10 kg between the control group and Stage B2 ($p < 0.01$) and C ($p < 0.0001$), and Stage B1 and C ($p < 0.005$). According to our results, the difference observed in the TIHS value between groups was due to the increase in heart short and long axes length secondary to mitral valve disease as the disease progresses.

The TIHS value increased with the disease stage as did the VHS. This could be expected as the cardiac axes measurement in both methods are the same. The increase in the VHS observed in this study is in accordance with previous studies in dogs with MMVD [2,20] and it is associated with the stage of the disease [2]. One study assessed the increase in the VHS before the onset of congestive heart failure [48]. In the present study, the TIHS increased with disease stage. It seems that the TIHS could be used to monitor the disease progression in a patient, but a longitudinal study would be ideal to confirm this point.

A VHS ≥ 11.5 v, a value that could be considered evidence of cardiomegaly [1], showed lower sensitivity 0.37 and YI 0.31 compared to a TIHS ≥ 3.3, Se 0.69, and YI 0.50, though its specificity was higher, 0.94 vs. 0.81. Previous studies evaluating radiographic predictors for detection of left heart enlargement in dogs with MMVD have proposed different VHS cutoffs [16–18,20]. In their study, Levicar et al. found that a VHS > 11 v had an 82% sensitivity and 71% specificity, AUC 0.82, to discriminate between B1 and B2 dogs [20]. Duler et al. indicated in their research that a VHS > 11.1 v had a 65.5% sensitivity and 80% specificity, AUC 0.78, to detect Stage B2 [18]. In our population, a VHS >11 v showed a lower sensitivity 40% but similar specificity 75%, AUC 0.74, to discriminate between Stage B1 and B2 dogs. The maximum specificity was a VHS >12 v, 97%. Other studies have found similar specificity for a cutoff >12 v [17,18]. The differences observed between different studies might be related to breed variability within the studied populations.

In the present study, a VHS ≥11.5 v would not identify cardiac enlargement in 63% (44/70) compared to 31% (22/70) for a TIHS ≥ 3.3, of the dogs diagnosed with cardiac enlargement on echocardiography. A lower VHS, ≥11 v, showed higher sensitivity 0.73, than a TIHS ≥ 3.3, 0.68. It did not identify cardiac enlargement in fewer dogs that did have it compared to a TIHS ≥3.3, 29% (19/70) and 31% (22/70), respectively. However, it diagnosed left heart enlargement in more dogs that did not have it than a TIHS ≥3.3, 33% (12/36) compared to 19% (7/36). A high specificity, meaning few false positive, is important because discriminating between B1 and B2 is associated with the prescription of lifelong treatment. On the other hand, a low sensitivity would deny treatment to some dogs that might benefit from it.

Although the population size was small, we evaluated the TIHS in Chihuahuas. Dogs of this breed are frequently diagnosed with MMVD [2,36,49]. A cutoff TIHS ≥3.3 discriminated between chihuahua dogs in Stage B1 and B2 with higher specificity than a

VHS ≥11.5, 83% and 62%, respectively. Whether there are breed differences in the TIHS value needs further study.

The correlation between the TIHS and VHS was moderate 0.60. Correlation between the TIHS and echocardiographic measurements, LVIDDN and LA/Ao, was also moderate, 0.62 and 0.42, respectively. Correlation between the VHS and LVIDDN and LA/Ao was moderate, 0.56 and 0.47, respectively. These results vary compared to other studies, being higher to the results of Stepien et al.'s study [17] but lower than the results by Lam et al. [13] and Duler et al. [18]. Not surprisingly, correlation was higher for the left ventricle. As shown on angiocardiographic views, the heart axes combined include the right and heart chambers [3]. CT images have shown that this is especially true for the short axis, but the left atrium is not specifically included [50]. More specific methods to assesses the left atrium radiographically like VLAS, M-VLAS, RLAD have shown higher positive correlation with echocardiographic values than the VHS [11,13,18,23], though others have not [39]. Comparison of those methods with the TIHS was not a goal of this research, and it would need further study.

Interobserver agreement for the 23 dogs compared was better for the VHS than the TIHS, 0.87 and 0.78, respectively. The interobserver agreement in the VHS for the MMVD dogs, 0.85, was lower compared to previous studies with MMVD dogs, ranging between 0.96 [51] and 0.92 [52]. The agreement between observers in the TIHS for the control group was 0.77. Interestingly, the interobserver variability showed poor agreement for the MMVD dogs when compared, 0.43. However, there was no statistically significant difference in the TI, LA, and SA measurements between observers. The identification of reference points in dogs with MMVD could be hampered by the presence of congestive heart failure (6/7 dogs with MMVD compared were in Stage C). The TIHS method being a ratio can change with a small difference in some of the magnitudes that take part in its calculation when measured by different observers. Previous studies have concluded that the VHS was independent of the observer's experience [51,52] but dependent of individual observer. This could be the case for the TIHS too, as it is an adaptation of the VHS method. As with the VHS, the ideal clinical scenario would be that the same practitioner did the follow up in a particular case [52].

This study has some limitations. Although echocardiographic exams were not performed by the same operator, standardized methods were used to obtain echocardiographic measurements and staging of dogs with MMVD. Thus, the heart chambers' measurements could be subjected to interobserver variability. The main observer was not blinded to the dog's clinical status and echocardiographic results, which could have caused radiographic measurement bias. The recommendation for the treatment of MMVD dogs included in this study followed ACVIM guidelines, adapted for every case. Thus, diuretic dosages could be different between dogs for the diuretic drug used (furosemide or torasemide), or the administration of spironolactone or amlodipine. Treatment changes the VHS in the first 6 months of treatment [53]. The TIHS being a variant of the VHS could be affected in a similar way, and this needs further study. Our study population of the control dogs and the dogs with MMVD were not homogenous and included different a number of dogs of different breeds, reflecting a general population of dogs attending a veterinary hospital. The effect of breed variability on the echocardiographic [54,55] and radiographic measurements has been studied [24–40]. This needs to be considered when conducting radiographic follow up of dogs with MMVD. Dog breeds can have different thorax conformation, and how this affects the TIHS needs further study. Radiographs were intended to be taken during peak inspiration, but this is not always possible in awake animals. Caudal thorax diameter varies with the respiratory cycle, and whether respiration changes the thoracic inlet length has not been studied, nor how this could affect the TIHS value. In this population, this method has shown a low interobserver agreement for MMVD dogs. Further studies with larger populations and more observers are desirable.

5. Conclusions

The TIHS is a simple method to measure the cardiac silhouette in dogs with and without myxomatous mitral valve disease. A TIHS value >3.3 would suggest cardiac enlargement in a dog with a heart murmur secondary to mitral valve disease, recommending an echocardiography. The TIHS can help clinicians in the staging of MMVD in a general population of dogs, including dogs with midthoracic vertebral anomalies, or when the thoracic vertebral bodies cannot be identified, and of chihuahua dogs, a breed commonly affected by the disease. It could also be used to monitor progression of the disease in a dog already diagnosed.

Author Contributions: D.M.F. designed the study and wrote the manuscript. D.M.F. and V.G. acquired the data. D.M.F., V.G., A.J.S. and J.A.M.-A. analyzed and interpreted the data. All authors participated in the discussion of the results. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement: The study was carried out in accordance with the current Spanish and European legislation on animal protection. Ethical review and approval were not required for the animals in this study.

Informed Consent Statement: Informed consent was not needed as this was a retrospective observational study carried out with records from the hospital database.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

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5.3.

Radiographic Left Atrial Size Measurement of Dogs in Different Mitral Valve Disease Stages with Four Different Methods

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Radiographic Left Atrial Size Measurement of Dogs in Different Mitral Valve Disease Stages with Four Different Methods

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Simple Summary: Echocardiography and radiography are the two diagnostic imaging methods recommended for the staging of mitral valve disease (MVD) in dogs. In the absence of echocardiography, the vertebral heart size and the vertebral left atrial size (VLAS) can be used for staging. Other methods to assess the left atrial size (LAS) on dogs' radiographs are the modified-vertebral left atrial size (M-VLAS) and the radiographic left atrial dimension (RLAD). They have the transformation of LAS into vertebral units in common. The thoracic inlet (TI) was proposed as a reference point to assess the cardiac silhouette of dogs with MVD. We hypothesized that the TI can be a reference point clinically useful to assess the LAS on dogs' right thoracic X-rays and differentiate different MVD stages. The LAS was measured in a general population of healthy dogs using the TI as a reference with the TILAS method. A group of control dogs from that population was matched to dogs in different MVD stages for LAS comparison using different methods: TILAS, VLAS, M-VLAS, and RLAD. The TILAS was significantly different between control dogs and MVD dogs, increasing with the disease stage, as did VLAS, M-VLAS, and RLAD. The TILAS accuracy to distinguished dogs with cardiac enlargement was like VLAS and RLAD.

Abstract: The left atrial size increases (LAS) in patients with mitral valve disease (MVD) as the disease progresses. The vertebral left atrial size (VLAS), the modified-vertebral left atrial size (M-VLAS), and the radiographic left atrial dimension (RLAD) are methods reported to assess LAS on dogs' radiographs. All these methods transform the LAS into vertebral units. The thoracic inlet (TI) has been used as a reliable reference point to measure the cardiac silhouette of dogs with MVD in different stages. The objective of this study was to assess the clinical utility of measuring a dog LAS on right thoracic X-rays using the TI as a reference and determine whether it could differentiate dogs in different MVD stages. LAS was divided by the TI to obtain the thoracic inlet left atrial score (TILAS). This was a retrospective observational study including 135 apparently healthy dogs performed to assess their LAS with four different methods: VLAS, M-VLAS, RLAD, and TILAS. Thirty-six dogs from the general population were selected and compared to 100 dogs in different MVD stages. The TILAS was significantly different between the control dogs and MVD dogs, increasing with the disease stage: control dogs 0.51 ± 0.08, B1 0.57 ± 0.14, B2 0.75 ± 0.13, and C 0.84 ± 0.18. VLAS, M-VLAS, and RLAD also increased as the disease progressed, as shown in previous studies. The TILAS accuracy to distinguish MVD dogs with cardiac enlargement was comparable to VLAS, M-VLAS, and RLAD (AUC 0.91 vs. 0.93, 0.90, and 0.94 respectively). A TILAS > 0.8 can identify dogs with cardiac enlargement secondary to MVD.

Keywords: thoracic inlet; left atrial size; vertebral; radiographic; cardiac enlargement

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1. Introduction

Thoracic radiography could be considered the most used imaging diagnostic technique for the assessment of dogs with cardiorespiratory symptoms. Radiographic studies of the thorax provide the practitioner with very useful information on the cardiac silhouette, pulmonary vasculature, pleural space, the airways, and the lung parenchyma in a fast and simple way. The size of the cardiac silhouette can be assessed subjectively with thoracic X-rays, and it can also be estimated objectively using different methods described in the literature, such as the vertebral heart score (VHS) [1], manubrium heart score (MHS) [2], heart to single vertebra ratio (HSVR) [3], and thoracic inlet heart score (TIHS) [4]. Many cardiac diseases in dogs, congenital and acquired, can cause heart chamber enlargement, and the progression of the disease can be followed using thoracic radiography [4–8]. The most common cardiac disease in dogs is degenerative mitral valve disease (MVD) [9]. Radiography and echocardiography are two imaging diagnostic techniques used for the staging of the disease, alongside thoracic auscultation [10]. However, in the absence of echocardiography, radiography criteria alone can aid the practitioner in the staging process [10]. Left atrial enlargement is one of the main features of the disease. Left atrium enlargement is caused by volume overload secondary to mitral valve regurgitation, and it impairs pulmonary vein drainage, increases pulmonary vein and capillary wedge pressures, and eventually causes pulmonary edema. The left atrium on a lateral radiographic projection of the thorax is located on the caudodorsal aspect of the cardiac silhouette between the tracheal bifurcation and the caudal vena cava. Its size can be assessed subjectively; a bulging on the cardiac silhouette at the left atrium anatomic location can indicate left atrial enlargement. Different investigators have studied how to quantify the size of the left atrium radiographically; indirectly: the crossing lines method [11] and the bronchus to spine and radiographic left atrial dimension (RLAD) to spine methods [12], and objectively: RLAD [13], the vertebral left atrial size (VLAS) [6], the left atrial width [14], the modified-vertebral left atrial size (M-VLAS) [15], and the modified vertebral left atrial size (mVLAS) [16]. Several studies have been carried out to assess the clinical utility of those different methods of detecting left atrial enlargement in dogs with cardiac disease, such as A clinical utility of a single method to identify cardiac chamber remodeling diagnosed on echocardiography [6,7,13,15] compared to other methods [15,17–19], proposing different cutoff values and aiding the practitioner in the diagnosis of congestive heart failure in dogs with different cardiovascular diseases [8,20,21]. Other authors have studied the existence of breed variability for the VLAS [22–26], M-VLAS [24], and RLAD [22,24] methods, reporting breed-specific reference values. These methods give the left atrium size a numerical value expressed in vertebral units, using the thoracic spine as a reference point.

The thoracic inlet (TI) has proved to be a useful reference point in the assessment of the trachea diameter in brachycephalic and non-brachycephalic dogs [27]. More recently, it has been described how the size of the cardiac silhouette increases in dogs with MVD as the disease stage worsens, using the TI as a reference point, using the thoracic inlet heart score (TIHS) [4].

The objective of the present study was to assess the clinical utility of the TI as a reference point to detect left heart enlargement in dogs with MVD using the thoracic inlet left atrial score method (TILAS). The second objective was to compare the accuracy of the TILAS detecting cardiac enlargement in dogs with MVD with three different methods: VLAS, M-VLAS, and RLAD.

2. Material and Methods

This retrospective observational case–control study was carried out with records of dogs attending Anicura Albea Small Animal Hospital from March 2021 to September 2022. The dogs had to have a full clinical examination, an echocardiographic exam, thoracic X-rays, and right lateral and ventrodorsal/dorsoventral projection performed within 24 h. Dogs with an apical systolic heart murmur and echocardiographic signs of mitral valve disease, mitral valve morphological changes (thickening and/or prolapse), and regurgita-

tion were diagnosed with MVD and were given a MVD stage based on the left atrium to aorta ratio (LA/Ao) and the left ventricle internal diameter in diastole normalized to body weight (LVIDDN), which was measured on echocardiography, and radiographic cardiac silhouette size was based on the VHS method, following the ACVIM guidelines [10]. Dogs were classified in Stage B1 if they did not present left atrial and left ventricle enlargement and had a LA/Ao ratio < 1.6, and/or LVIDDN < 1.7. Dogs with echocardiographic and radiographic left heart chamber enlargement with a LA/Ao ratio ≥ 1.6, LVIDDN ≥ 1.7, and VHS > 10.5 or adjusted by breed, were classified in Stage B2. Dogs with past or current signs of congestive heart failure secondary to MVD were classified in Stage C. Dogs with tricuspid valve regurgitation secondary to degenerative valve disease were included in this study.

A group from the general population of healthy dogs attending the hospital was studied. These dogs did not have a heart murmur on clinical examination, no clinical signs of cardiorespiratory disease, and no findings on thoracic X-rays or the echocardiographic examination. From this general population, a smaller group of dogs weighing less than 20 kg was used as a matched control group for comparison with dogs diagnosed with MVD. They were included in the control group in order of entrance to the study, and no more than four dogs of the same breed were included.

Thoracic right lateral projections intended to be taken in full inspiration were used for measurement. All the radiographs were reviewed and measured using commercial digital viewing software (IntechForView 12.4.1.1, La Cartuja Baja, Zaragoza, Spain). Dogs whose radiographs were malpositioned or rotated, dogs whose cardiac silhouette borders could not be clearly identified, dogs whose thoracic inlet was not included, dogs who showed vertebral malformation and/or vertebral body remodeling, or dogs in which the reference points could not be identified were excluded. The left atrial size was measured for every patient three times using a digital caliper, and the average was calculated by the same observer (DM) using the methods described below.

The thoracic inlet left atrial score (TILAS) was calculated as follows: the left atrial size (LAS), the distance from the mid-point of the ventral border of the carina to the point where the caudal border of the cardiac silhouette crosses the dorsal border of the caudal vena cava was measured and divided by the shortest distance of the TI measured from the cranioventral point of the first thoracic vertebra to the most dorsocranial point of the manubrium. The LAS was divided by the TI, obtaining a TILAS value (Figure 1).

The vertebral left atrial size (VLAS) was obtained by measuring the LAS as described previously, transposed to the thoracic spine starting at the cranial edge of the fourth thoracic vertebra, and transformed into vertebral units, approximately 0.1 v (Figure 2).

The modified left atrial size (M-VLAS) was obtained by measuring the LAS as described previously and then drawing a second line from the most dorsal border of the left atrium up to the first line and perpendicular to it. These two measurements were transformed into vertebral units starting at the cranial edge of the fourth thoracic vertebrae and summed to obtain the M-VLAS, approximately 0.1 v (Figure 3).

The radiographic left atrial dimension (RLAD) was calculated by measuring the cardiac axes. The long axis was measured from the ventral border of the left main stem bronchus to the cardiac apex, and the short axis was measured at the level of the dorsal border of the caudal vena cava perpendicular to the long axis. Then, a line was drawn bisecting the 90° angle formed by the cardiac axes from the point where the long and short cardiac axes crossed to the dorsal border of the left atrium. That distance was transformed into vertebral units starting at the cranial edge of the fourth thoracic vertebrae, approximately 0.1 v (Figure 4).

To study the effect of weight on the studied variables, the general population was divided into four groups, <10 kg, ≥10–20 kg, ≥20–30 kg, and ≥30 kg. We also compared the different methods depending on the sex. A Shapiro–Wilk test was used to assess if the data were normally distributed. Nonnormally distributed variables giving descriptive information (age and body weight) were presented as the median and range (maximum and

minimum) and compared using the Mann–Whitney U test. Normally distributed variables were presented as the median and standard deviation. A 95% confidence interval was also calculated. For normally distributed data, an ANOVA test was performed to compare multiple groups. For the comparison between groups, an unpaired 2-tailed Student's *t*-test was used. A $p < 0.05$ was considered significant.

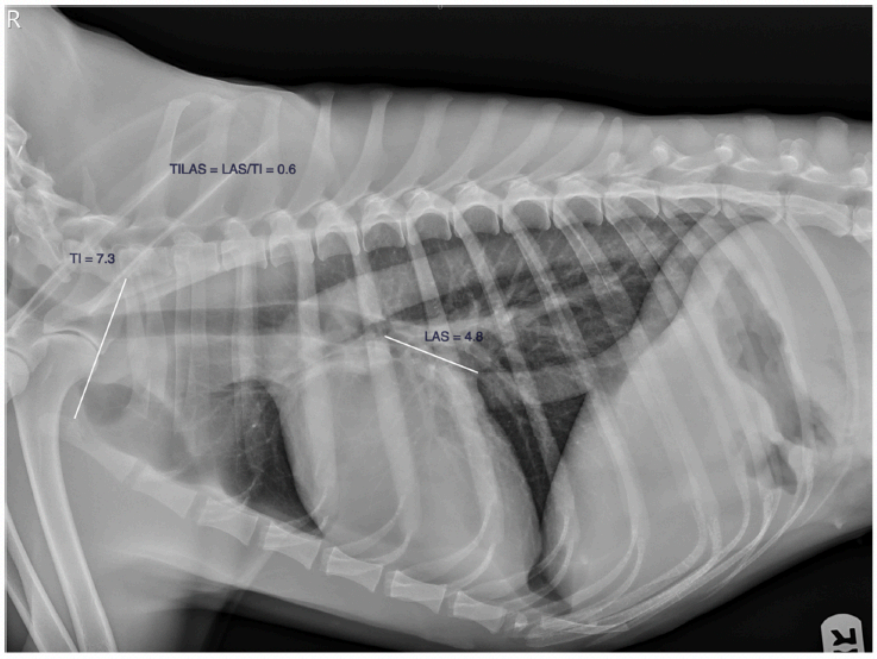

Figure 1. The thoracic inlet left atrial score method, the TILAS. The TILAS is the result of dividing the LAS by the TI. White lines depict the left atrial size and thoracic inlet length measurements.

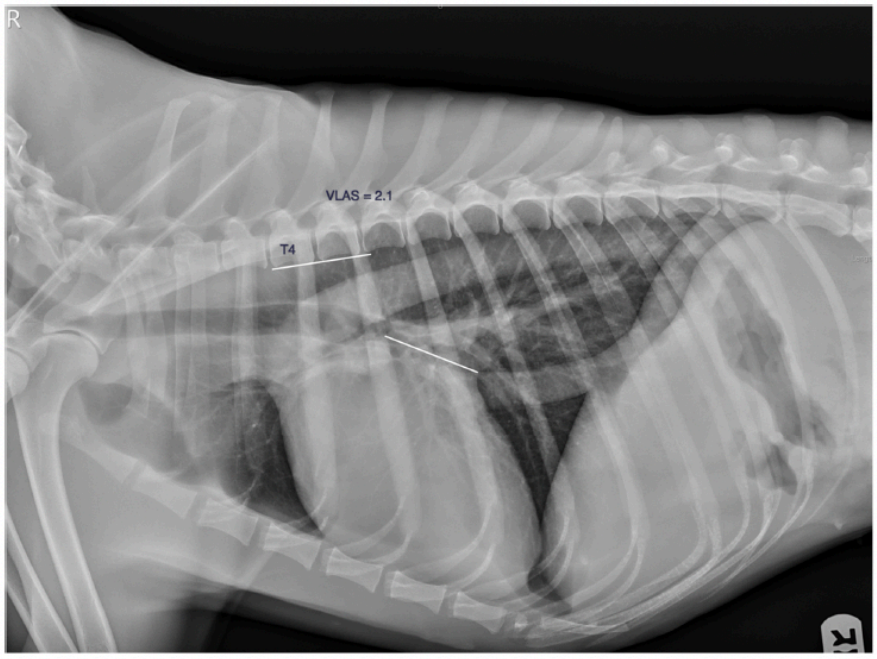

Figure 2. The vertebral left atrial size, the VLAS. The LAS is transposed to the thoracic spine starting at the cranial edge of the fourth thoracic vertebra and transformed into vertebral units, approximately 0.1 v.

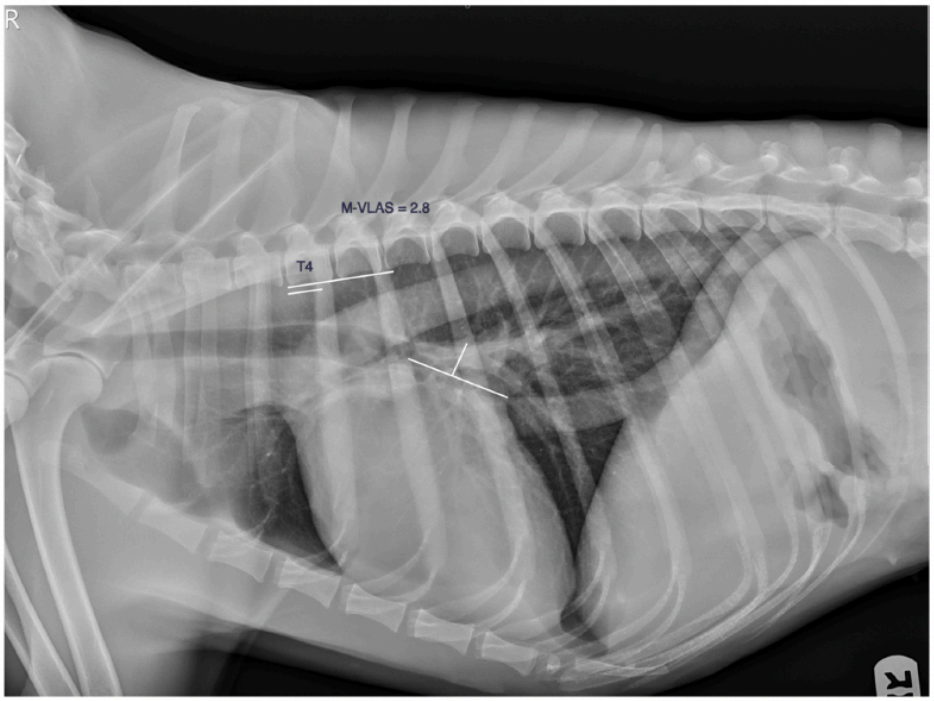

Figure 3. The modified left atrial size, the M-VLAS. The two lines resulting from measuring the left atrium are transformed into vertebral units starting at the cranial edge of the fourth thoracic vertebrae and summed to obtain the M-VLAS, approximately 0.1 v.

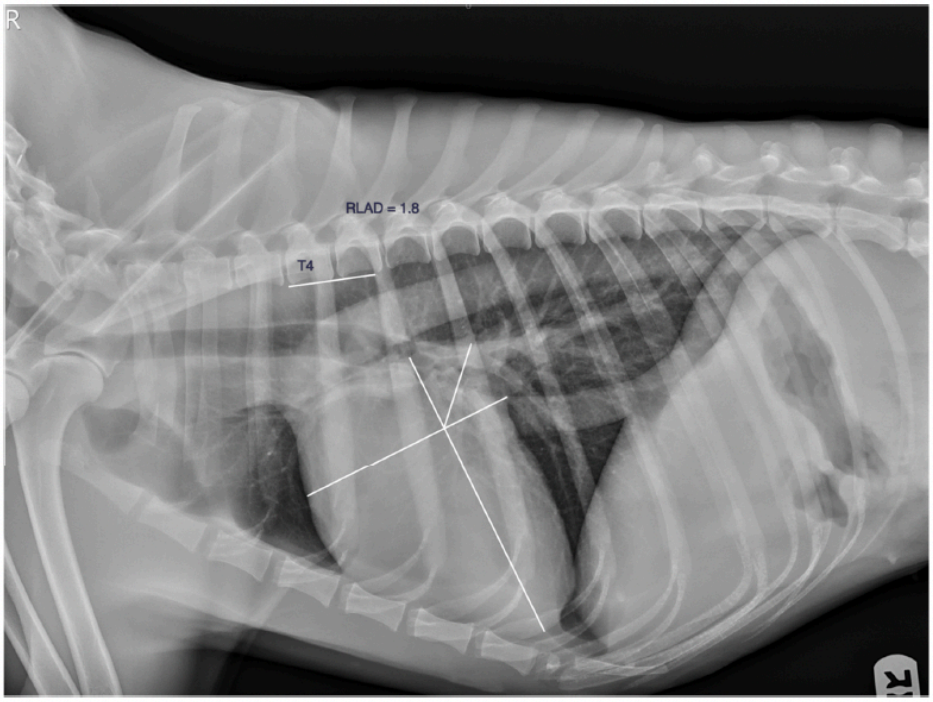

Figure 4. The radiographic left atrial dimension, the RLAD. A line that bisects the 90° angle formed by the cardiac axes from the point where they crossed to the dorsal border of the left atrium is drawn and transformed into vertebral units starting at the cranial edge of the fourth thoracic vertebrae, approximately 0.1 v.

Sensitivity, specificity, false negative, and false positive percentages to detect cardiac enlargement were calculated for the four methods. To assess the accuracy of the studied variables detecting cardiac enlargement, the receiver operator curve and the area under the curve (AUC) were calculated. Clinical optimum cutoff values to identify cardiac enlargement in dogs with MVD were calculated using the Youden index (sensitivity + specificity) − 1. Statistical analyses were performed with SAS/STAT software, version 16.5, and Microsoft Excel 2021.

3. Results

One hundred and thirty-six dogs of different breeds were selected: seventy-three males and sixty-three females. One male French bulldog with a mid-thoracic hemivertebra was excluded. A total of 135 dogs were included in the general population study: 58 crossbreeds, 16 Yorkshire Terriers, nine Chihuahuas, seven Labrador Retrievers, four French bulldogs and Golden retrievers, three Pitbull Terriers, two American Staffordshires, Bull Terriers, German shepherds, Pugs, Scottish Terriers, and West Highland White Terriers, and one Beagle, Border Collie, Boston Terrier, Boxer, Canarian Hound, Cavalier King Charles Spaniel (CKCS), Czechoslovakian Wolfdog, Chow Chow, Dachshund, Dalmatian, Garafiano, Jack Russell Terrier, Lobo Herreño, Malinois, Maltese, Miniature Schnauzer, Pekingese, Pinscher, Pomeranian, Rottweiler, Spanish Water Dog, and Staffordshire Terrier. The medium weight was 14.02 kg (1.80–44.40 kg), and the medium age was 7.5 years (1–16 y). Comparing different sexes, there were no differences in age, weight, or TILAS, VLAS, M-VLAS, and RLAD values $p > 0.05$ (Table 1). Multivariable analysis for the different body weight groups showed a difference that was statistically significant for TILAS $p = 0.005$, VLAS $p = 0.01$, M-VLAS, and RLAD, $p = 0.001$. A direct comparison showed that the TILAS value was higher for dogs less than 10 kg compared to dogs between 10 and less than 20 kg, $p = 0.005$. The VLAS was higher for dogs heavier than 30 kg compared to dogs less than 10 kg and dogs between 10 and less than 20 kg, $p = 0.013$ and $p = 0.004$, respectively. The RLAD was higher in dogs heavier than 30 kg compared to dogs less than 10 kg and dogs between 10 and less than 20 kg, $p = 0.001$ and $p = 0.009$ respectively. The M-VLAS was higher for dogs heavier than 30 kg compared to the rest of the groups $p < 0.001$ and higher in dogs between 20 and 30 kg compared to lighter dogs, $p < 0.001$.

Table 1. The general population of dogs included in this study. Values for age and weight are represented as the median and range (minimum and maximum). VLAS, M-VLAS, RLAD, and TILAS are represented by the median and standard deviation. * Statistically significant difference depending on weight, $p < 0.05$. M-VLAS, modified vertebral left atrial size; RLAD, radiographic left atrial dimension; TILAS, thoracic inlet left atrial score; VLAS, vertebral left atrial size.

	n	Age (y)	Weight (Kg)	VLAS (v)	M-VLAS (v)	RLAD (v)	TILAS
General	135	7.5 (1–16)	14.02 (1.8–44.4)	1.86 ± 0.28	2.62 ± 0.47	1.82 ± 0.40	0.52 ± 0.15
Male	72	7.8 (1–16)	13.41 (1.8–44.4)	1.86 ± 0.26	2.63 ± 0.45	1.81 ± 0.37	0.52 ± 0.10
Female	63	7.2 (1–14.3)	14.56 (2.1–34.6)	1.86 ± 0.30	2.61 ± 0.49	1.83 ± 0.44	0.53 ± 0.19
<10 kg	68	8.4 (1–15.3)	5.2 (1.8–9.9)	* 1.84 ± 0.28	* 2.57 ± 0.42	* 1.71 ± 0.34	* 0.53 ± 0.09
≥10–<20 kg	26	2.8 (1–16)	13.75 (10.2–18.2)	* 1.77 ± 0.26	2.54 ± 0.36	* 1.80 ± 0.41	* 0.47 ± 0.09
≥20–<30 kg	25	6.5 (1–14.3)	24.35 (20.1–29.8)	1.87 ± 0.27	* 2.65 ± 0.44	* 1.91 ± 0.40	0.54 ± 0.28
≥30 kg	16	6.1 (2–11.4)	34.15 (30–44.4)	* 2.10 ± 0.36	* 2.88 ± 0.73	* 2.19 ± 0.46	0.54 ± 0.13

One hundred dogs of different breeds diagnosed with MVD were included in the study: thirty-five in Stage B1, seventeen in Stage B2, and forty in Stage C. The Stage B1 group included dogs of the following breeds: fifteen crossbreeds, five Chihuahuas, four Yorkshire Terriers, two Cocker Spaniels, Pinschers, and Ratoneros, and one Canarian hound, Dachshund, French Bulldog, Pug, and Spanish Galgo.

Stage B2 group included nine crossbreed dogs, three Chihuahua, three Yorkshire terrier, and one Pinscher and Spanish galgo.

Stage C group included fifteen crossbreed, nine Chihuahua, six Maltese, two CKCS and Yorkshire Terrier, and one Beagle, Dalmatian, Pinscher, Poodle, Shih-Tzu, and Spitz.

Four dogs with left atrial enlargement (LAE) and ten with left ventricle enlargement (LVE) diagnosed on echocardiography were included in Stage B1.

Thirty-six dogs from the general population with a weight < 20 kg were used as a matched control group for comparison. Dogs included in this group were twenty-two crossbreeds, two Yorkshire Terriers, and one Beagle, Bull Terrier, CKCS, Chihuahua, Dachshund, Jack Russell Terrier, Miniature Schnauzer, Pekingese, Pomeranian, Pug, Spanish Water Dog, and West Highland White Terrier. The control dogs were younger than the MVD groups, $p = 0.0002$. There was no difference according to age between the MVD groups, $p > 0.05$. There was no difference in weight between the control dogs and MVD groups, $p > 0.05$ (Table 2). In all group comparisons, TILAS and VLAS were lower for the control dogs compared to Stage B2 and C dogs, and between Stage B1 and Stages B2 and C, $p < 0.000001$ and $p < 0.0001$, respectively. M-VLAS and RLAD values were different between the control group and the MVD groups, and they increased from one MVD group to the next as the disease worsened, $p < 0.002$. Between groups comparison VLAS, M-VLAS, RLAD, and TILAS values were different between the control group and the MVD groups, increasing from one group to the next as the disease stage worsened, $p < 0.05$.

Table 2. Control and MVD groups. Values for age and weight are represented as the median and range (minimum and maximum). VLAS, M-VLAS, RLAD, and TILAS are represented by the median, standard deviation, and 95% confidence interval. * Statistically significant differences between the control group and the MVD groups and between the different MVD groups, $p < 0.05$. M-VLAS, modified vertebral left atrial size; RLAD, radiographic left atrial dimension; TILAS, thoracic inlet left atrial score; VLAS, vertebral left atrial size.

	Control (36)	Stage B1 (35)	Stage B2 (17)	Stage C (40)
Age (years)	8.3 (1.1–15.4)	12.1 (5.5–15.9)	12.7 (7.4–19)	11.4 (7.9–17.7)
Weight (kg)	7.60 (2.1–18.2)	7.78 (2.6–24.1)	7.38 (2–19.1)	6.3 (2.7–25)
VLAS (v)	* 1.79 ± 0.29 (1.69–1.89)	2.00 ± 0.32 (1.89–2.11)	2.57 ± 0.35 (2.39–2.75)	2.88 ± 0.55 (2.60–3.06)
M–VLAS (v)	* 2.47 ± 0.44 (2.32–2.62)	2.78 ± 0.52 (2.60–2.96)	3.54 ± 0.80 (3.13–3.95)	4.26 ± 0.90 (3.97–4.55)
RLAD (v)	* 1.63 ± 0.35 (1.51–1.75)	1.89 ± 0.39 (1.76–2.02)	2.48 ± 0.43 (2.26–2.70)	3.00 ± 0.49 (2.84–3.16)
TILAS	* 0.51 ± 0.08 (0.48–0.54)	0.57 ± 0.14 (0.52–0.62)	0.75 ± 0.13 (0.69–0.81)	0.84 ± 0.18 (0.78–0.90)

The optimum cutoff value for the TILAS to identify dogs with cardiac enlargement between the MVD dogs in Stages B1, B2, and C was 0.8. The TILAS accuracy according to the area under the curve results was comparable to the M-VLAS, 0.91 vs. 0.91, and slightly lower than VLAS and RLAD, 0.93 and 0.94, respectively. A RLAD cutoff > 2.3 showed the highest Youden index, 0.72, used to identify B2 dogs with a specificity of 91% (Table 3).

Table 3. The optimal cutoff value of the four different radiographic methods used to identify dogs with cardiac enlargement among dogs with MVD, Stages B1, B2, and C. AUC, area under the curve; FN, false negative; FP, false positive; Se, sensitivity; Sp, specificity; YI, Youden index (Se + Sp) − 1.

MVD Dogs (C-B2/B1)	Cutoff	Se (%)	Sp (%)	FP (%)	FN (%)	YI (Se + Sp) − 1	AUC
TILAS	0.8	77	83	17	23	0.60	0.91
VLAS (v)	2.5	69	97	3	31	0.66	0.93
M-VLAS (v)	3.6	71	97	3	29	0.68	0.90
RLAD (v)	2.3	81	91	9	19	0.72	0.94

The optimum cutoff value for the TILAS used to identify dogs with cardiac enlargement when comparing dogs with cardiac enlargement (C and B2) and dogs without cardiac enlargement (B1 and control dogs) was 0.8. The TILAS accuracy according to the AUC was comparable to VLAS and M-VLAS, 0.94 vs. 0.95 and 0.93, respectively, and slightly less than the RLAD, 0.97. TILAS and VLAS sensitivity and specificity were identical, 79% and 92%. A RLAD cutoff >2.3 showed the best combination of sensitivity and specificity to identify cardiac enlargement: 82% sensitivity and 94% specificity (Table 4).

Table 4. Optimal cutoff value of the four different radiographic methods used to identify dogs with cardiac enlargement (Stages B2 and C) between the control and B1 groups and B2 and C groups.

Control Dogs and MVD Dogs	Cutoff	Se (%)	Sp (%)	FP (%)	FN (%)	YI (Se + Sp) − 1	AUC
TILAS	0.8	79	92	8	21	0.70	0.94
VLAS (v)	2.4	79	92	8	21	0.70	0.95
M-VLAS (v)	3.3	82	90	10	18	0.73	0.93
RLAD (v)	2.3	82	94	6	18	0.77	0.97

4. Discussion

The thoracic inlet is a useful reference point used to assess the left atrial size on canine thoracic radiographs. The median TILAS value for the general population of healthy dogs was 0.52 ± 0.15. The TILAS value was not affected by sex, but it was lower for dogs between 10 and less than 20 kg compared to dogs less than 10kg, 0.47 ± 0.09 and 0.53 ± 0.09, respectively, $p = 0.005$.

The VLAS for the general population was 1.86 ± 0.28, like the results of different studies previously published for healthy adult dogs, such as Vezzosi et al. [28] in eighty dogs of different breeds, 1.9 (1.3–2.2), Bagardi et al. [24] in thirty CKCS, 1.79 ± 0.3, Puccinelli et al. [26] in thirty Chihuahuas, 1.8 ± 0.2, and the control dogs compared to dogs with MVD were studied by Lam et al. [15], with six control dogs, 1.83 ± 0.29. However, this was slightly shorter than the results of breed-specific studies like Baisan et al. [25] in 81 Maltese, 2 (1.8–2.1 v), and Wiegel et al. [22] in 30 Pugs, 1.96 ± 0.38 (1.1–2.8). In several other studies that compared control dogs with dogs with cardiovascular disease, Malcolm et al. [6] used 15 control dogs, 2.1 (1.8–2.3), Levicar et al. [19] used 50 control dogs, 2.07 ± 0.31, and Wesselowski et al. [23] used 271 control dogs, 2.0 (1.8–2.1). No difference in sex was observed for the VLAS, which is in agreement with the literature [24–26,28].

The VLAS seems to be affected by the dog breed, as shown by the results of different studies: CKCS [24], Maltese [25], Chihuahuas [26], Pugs [22], Boxers, 1.9 ± 0.4 (1.7–2.1), Labrador Retrievers, 2.1 ± 0.3 (1.9–2.3), and Doberman Pinschers, 2.0 ± 0.3 (1.8–2.1) [23]. The breed difference could be related to the difference in the thoracic vertebral length of those breeds relative to their body size [3,29] and their cardiac silhouette shape on thoracic radiographs. The TILAS is a ratio between the left atrial size and the thoracic inlet length. Whether the thoracic inlet length is affected by the dog breed and how it could affect the TILAS method needs further study.

The VLAS values were significantly different for different body weight groups as opposed to previous studies [28]. Different dog breeds with different body weights have shown different VLAS [22,23,25]. That difference could be breed related rather than weight related; however, it might need further study.

The M-VLAS for the general population was 2.62 ± 0.47, and no effect of sex was detected. However, heavier dogs showed higher M-VLAS. Our values were like the value obtained by Lam et al. in six control dogs [15], 2.60 ± 0.30, but higher than the result of Bagardi et al. in thirty CKCS, 2.23 ± 0.44 [24]; this latter study did not observe an effect of body weight or sex on the results.

The RLAD for the general population was lower compared to the original study by Salguero et al. [13], 1.82 ± 0.40 versus 1.97 ± 0.57. Breed-specific studies have observed

different RLAD values: CKCS, 1.2 ± 0.34 [24], and Pugs, 1.59 ± 0.34 [22]. In the present study, the RLAD was not affected by sex, but it increased with body weight. This has not been observed previously [24]. However, the RLAD seems to be affected by breed and body weight. A comparison of different breeds and larger groups with different body weights would be desirable.

This study shows that using the TI as a reference point, left heart chamber enlargement in dogs with MVD can be detected. The TILAS value increased with the disease stage, as did VLAS, M-VLAS, and RLAD. The increase in VLAS and RLAD with the progression of the disease was observed in other studies [17–19]. The TILAS could be used for the follow-up of dogs with MVD. The TILAS accuracy detecting MVD dogs with cardiac enlargement, 0.91, was comparable to the M-VLAS, 0.90, and slightly less than the VLAS, 0.93, and the RLAD, 0.94. The RLAD accuracy was reported to be better than the VLAS in some reports, 0.99 vs. 0.90 [18] and 0.85 vs. 0.81 [19], while others have reported similar accuracy detecting left atrial enlargement, 0.95, 0.97, and 0.93 for VLAS, M-VLAS, and RLAD, respectively [15], and 0.82 and 0.81 for VLAS and RLAD [17]. The RLAD in the present study was the most sensitive method of the four, 81%, identifying cardiac enlargement, versus 77% for TILAS, 69% for VLAS, and 71% for M-VLAS. These higher sensitivity results for the RLAD detecting left atrial enlargement in dogs with MVD than the VLAS agree with previous studies [15,18,19]. On the other hand, VLAS and M-VLAS were the most specific tests, 97%, followed by the RLAD at 91%, and the TILAS was the least specific at 83%.

A TILAS cutoff > 0.8 shows the best combination of sensitivity and specificity to discriminate between dogs with cardiac enlargement secondary to MVD in our population of MVD dogs and control dogs. A VLAS cutoff > 2.5 best identified MVD dogs with cardiac enlargement, which is in agreement with previously published results [6,7,14,30]. However, other authors have reported lower cutoffs, >2.2 [23], >2.3 [30–33], and >2.4 [8,15,18]. Considering the M-VLAS, a cutoff > 3.6 showed the optimal clinical utility, a result in line with the literature [15]. Regarding the RLAD method, the optimal cutoff for identifying cardiac enlargement was 2.3, a value higher than others already reported, 1.8 [18], 1.7 [15], and 2 [31]. A VLAS of ≥3 has been proposed as likely for identifying Stage 2 dogs [10] in the absence of echocardiography; in the present study, a VLAS >2.8 showed 100% specificity, minimizing false positive dogs that would be otherwise treated without the need of treatment, which is in agreement with other studies [23,30].

A direct comparison of studies is difficult due to different population sizes, breeds included in the different groups, the criteria used to classify the dogs in different disease stages, the fact that it is based only on echocardiography or echocardiographic and radiographic parameters, and the clinical feature studied, left atrial enlargement, left heart chamber enlargement, and stage of the disease the patient is on or the presence or absence of clinical signs related to having a cardiac disease (Table 5). Most of the studies revised for this work report similar cutoff values, but diagnostic accuracy was not always the same, and neither was the sensitivity or the specificity. Making a clinical decision on a cutoff value requires deciding what is more important from a clinical point of view. Relying on a higher sensitivity means fewer false negative results and treating those dogs that would benefit from treatment after echocardiographic confirmation. On the contrary, if echocardiography is not an option, higher specificity means fewer false positive individuals, preventing treating dogs that would not benefit from it. However, treating a patient should not be based exclusively on a single cutoff value but rather on combined information, clinical signs, and diagnostic imaging.

Table 5. Clinical useful cutoff values previously published for VLAS, M-VLAS, and RLAD in different populations of dogs with cardiovascular diseases in different stages and clinical status. The B2 cutoff value used to identify Stage B2 MVD diagnosed with radiography and echocardiography according to ACVIM guidelines. CHF, cutoff value to identify dogs with congestive heart failure; LAE, cutoff value to identify left atrial enlargement diagnosed on echocardiography; LHE, cutoff value to identify left heart chamber enlargement (Stages B2 and C) diagnosed with echocardiography. * Normal healthy dogs versus all preclinical dilated cardiomyopathy and MVD dogs. The VLAS for preclinical MVD 2.4 (2.1–2.6) and clinical MVD 2.9 (2.6–3.1). ** Only Cavalier King Charles Spaniel dogs with preclinical MVD. AUC, area under the curve; LVE, left ventricle enlargement. MVD, mitral valve disease. B2 MVD Stage B2; C MVD Stage C; D MVD Stage D; Se, sensitivity; Sp, specificity.

Radiographic LAS Method	Study	n	MVD Stage	Cutoff	Sensitivity (%)	Specificity (%)	AUC
VLAS	Malcolm, 2018 [6]	103	26 B2 22 C–D	≥2.5 (LAE)	67	84	0.84
	Poad, 2019 [32]	70	34 B2	>2.3 (B2)	71.8	74.4	0.767
	Duler, 2020 [30]	183	32 B2 33 C–D	>2.3 (LAE)	90.3	73.6	0.89
				>2.5 (B2)	69	85.7	0.84
	Lam, 2021 [15]	64	21 B2 21 C	≥2.4 (LAE)	80.5	96.6	0.95
	Bagardi, 2021 [17]	74	16 B2 24 C 3 D	≥2.43 (LAE)	66	88	0.82
	Stepien, 2020 [14]	56	30 B2	≥2.5 (B2)	70	84	0.79
	MIkawa, 2020 [7]	97	19 B2 14 C–D	≥2.5 (LHE)	86	84	0.87
	Vezzosi, 2021 [18]	111	32 B2 32 C–D	≥2.4 (B2)	66	100	0.90
				≥2.2 (LAE)	90	80	0.93
	Levicar 2022 [19]	200	50 B2 50 C–D	>2.3 (B2)	72	78	0.81
	* Wesselowski, 2022 [23]	455	39 B1–B2 20 C–D	≥2.2 (LAE, LVE or both)	64.4	75.2	0.722
	Lee, 2022 [8]	41	17 CHF	>2.45 (CHF)	93.3	47.6	0.71
	** Wesselowski, 2023 [33]	226	45 B2	>2.3 (LHE)	51.1	92.3	0.783
	Ross, 2023 [20]	114	57 CHF	>2.3 (CHF)	93	82.5	0.92
	Vereb 2023 [21]	869	234 B2	>2.5 (CHF)	62	80	0.76
	Present study	136	25 B2 40 C	≥2.5 (LHE)	69	97	0.93
RLAD	Salguero, 2017 [13]	77	15B2 28 C	≥1.8 (LAE)	93.5	96.8	0.9691
	Levicar 2022 [19]	200	50 B2 50 C–D	≥2.0 (B2)	75	83	0.85
	Bagardi, 2021 [17]	74	16 B2 24 C 3 D	≥1.9 (LAE)	71	82	0.81
	Lam, 2021 [15]	64	21 B2 21 C	≥1.7 (LAE)	100	72.4	0.93
	Vezzosi, 2021 [18]	111	32 B2 32 C–D	≥1.8 (B2)	100	93	0.99
				≥1.8 (LAE)	90	95	0.98
	Present study	136	25 B2 40 C	≥2.3 (LHE)	81	91	0.94
M-VLAS	Lam, 2021 [15]	64	21 B2 21 C	≥3.4	92.7	93.1	0.97
	Vereb, 2023 [21]	869	234 B2	>3.5 (CHF)	62	80	0.75
	Present study	136	25 B2 40 C	≥3.6 (LHE)	71	97	0.90
TILAS	Present study	136	25 B2 40 C	≥0.8 (LHE)	77	83	0.91

This study has some limitations. This was a retrospective study; the echocardiography scans were performed following standardized methods and current guidelines for the staging of the patients, although not by the same operator. Interobserver variability could have affected the stage the dogs were classified. Dogs included in Stage B2 had been previously diagnosed and were already on treatment with pimobendan or were diagnosed and recommended to be treated at the time of the echocardiographic examination. Dogs in Stage C were treated with pimobendan and diuretics (furosemide, torasemide), and

some were also treated with angiotensin-converting enzyme inhibitors and spironolactone. It has been observed that treatment affects the VHS measurement in the first six months of treatment [34]; if this is the case for the variables studied in this paper, further study is needed.

It has been mentioned previously that different breeds can have different cardiac chamber sizes on radiographs. It has also been observed that echocardiographic measurements can be different, depending on the dog breed, and different indexing values for the left ventricle internal diameter and cutoff values for the left atrium to aorta ratio to those in the ACVIM guidelines have been proposed [35,36]. In this study, none of the four dogs in Stage B1 that had LAE on echocardiography (LA/Ao $\geq$ 1.6) showed LAE with any of the four radiographic methods. However, five of the ten dogs with LVE (LVIDDN $\geq$ 1.7) on echocardiography showed LAE on the X-rays. We followed the recommended guidelines for the staging of the MVD disease published in 2019 [10]. Whether the results of the present study would be different considering different reference values for the staging of dogs would require further study.

A single observer does not represent all individuals, and although we did not study interobserver variability, we assessed the left atrial size with previously published methods in a clinical setting with a different population and compared our results with previously published studies, obtaining comparable results. Whether this would be the case for the TILAS method studied by other investigators needs further study.

Thoracic radiographs were intended to be taken in full inspiration, although this is not always possible in non-sedated patients. Radiographic methods are limited by the identification of the reference point, the carina, the cardiac silhouette borders, and particularly the dorsal border of the left atrium; selecting a different spot on the reference point can cause a significant variation in the results.

5. Conclusions

The TILAS method is a simple way to assess the left atrial size in dogs' thoracic radiographs. A TILAS cutoff < 0.6 means that the patient is less likely to have cardiac enlargement. A cutoff > 0.8 can be used to identify dogs that might need echocardiography for further evaluation. A cutoff > 1 can be used to identify dogs with cardiac enlargement in the absence of echocardiography.

VLAS, M-VLAS, and RLAD are reproducible methods to assess the left atrial size by a different observer in a different population.

Different reference points can be used to assess the progression of cardiac enlargement on MVD dog X-rays, considering that the only structure that changes its size with time is the cardiac silhouette.

Author Contributions: D.M.F. designed the study and wrote the manuscript. D.M.F. acquired the data. D.M.F. and J.A.M.-A. analyzed and interpreted the data. All authors participated in the discussion of the results. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement: This study was carried out in accordance with the current Spanish and European legislation on animal protection. Ethical review and approval were not required for the animals in this study.

Informed Consent Statement: This was a retrospective observational study carried out with records from the hospital database, and no informed consent was needed.

Data Availability Statement: Data are contained within the article.

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6.
CONCLUSIÓN

La entrada torácica puede ser utilizada para valorar la silueta cardíaca global y el atrio izquierdo en particular en la especie canina siguiendo el método TIHS y el método TILAS. El método TIHS es un método simple y fiable para medir la silueta cardíaca en radiografías caninas. Se puede utilizar en perros con alteraciones en las vértebras torácicas centrales. Para su cálculo no requiere de transposición a unidades vertebrales. En la población estudiada de perros sanos el valor medio fue 2,86, con un intervalo de confianza de 2,81-2,91 (95%), y se sugiere un valor 3,2 como límite superior de tamaño cardíaco normal en perros sanos en una población general. TIHS es un método simple de cálculo para medir la silueta cardíaca en perros con EVDC. Un valor superior a 3,3 sugeriría aumento cardíaco en perros con un soplo secundario a EVDC y recomendándose un estudio ecocardiográfico. Puede ayudar al clínico veterinario en el estadiaje de la EVDC incluyendo a perros con alteraciones en las vértebras torácicas centrales, o cuando los cuerpos vertebrales no se pueden identificar, como puede ocurrir en caso de edema pulmonar. También podría utilizarse para monitorizar la progresión de la EVDC en perros diagnosticados de la misma.

El método TILAS es simple de obtener para valorar el tamaño del atrio izquierdo. Un paciente con un valor TILAS<0,6 indicaría que el aumento del atrio izquierdo es poco probable. Un valor TILAS>0,8 identificaría perros que se beneficiarían de un estudio ecocardiográfico. Un valor superior a 1 identificaría perros con aumento del atrio izquierdo en ausencia de una ecocardiografía.

Los métodos VLAS, M-VLAS y RLAD son métodos para valorar el tamaño del atrio izquierdo reproducibles por distintos observadores en distintas poblaciones.

Distintos puntos de referencia pueden ser utilizados para valorar la progresión del aumento cardíaco radiográficos en perros con EVDC, considerando que la única estructura que cambia de tamaño con el tiempo es la silueta cardíaca.

7.
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8.

DIVULGACIÓN CIENTÍFICA

Divulgación del trabajo de investigación a nivel nacional e internacional.

Presentaciones en Congresos Veterinarios.

1. Marbella Fernández, D.; Perdigón, M.J. Caracterización clínica de pacientes caninos con signos cardiorrespiratorios en centros de primera opinión. Póster. *Southern European Veterinary Congress-Congreso Nacional AVEPA*. **2021**, Sevilla, Spain, 19-22 Octubre.

2. Marbella, D.; Santana, A.J.; Saavedra, D.; Perdigón, M.J. Measuring the canine heart on x-rays; known and used methods by first opinion veterinary surgeons. Poster. *FECAVA Congress*. **2022**, Prague, Czech Republic, June 8-11.

3. Marbella Fernández, D. Utilidad diagnóstica del ratio entrada torácica-corazón en perros con enfermedad valvular degenerativa. *XXII Congreso de Especialidades Veterinarias de AVEPA*, 2023, Bilbao, Spain, 21-22 Abril.

4. Marbella Fernández, D.; García, V.; Santana, A.J.; Montoya-Alonso, J.A. The thoracic inlet heart size, an alternative approach to measure the canine heart on thoracic radiographs. Oral communication. *IVRA/EDVI Joint Scientific Conference.* **2023**, University College Dublin, Ireland, June 18-23.

Publicaciones internacionales (Q1)

1. Marbella Fernández, D.; García, V.; Santana, A.J.; Montoya-Alonso, J.A. The Thoracic Inlet Heart Size, a New Approach to Radiographic Cardiac Measurement. *Animals.* **2023**, 13(3), 389.

2. Marbella, D.; Saavedra, D.; Perdigón, M.J.; Santana, A.J.; Montoya-Alonso, A.J. Thoracic inlet heart size, an alternative approach to measure the canine heart on thoracic radiographs. Abstracts from the 2023 IVRA EVDI Joint Scientific Conference Dublin, Ireland, June 18-23, 2023. Rademacher, N.; Hester McAllister H. 2023. *Vet. Radiol. Ultrasound*. **2023**, 64, 6.

3. Marbella Fernández, D.; García, V.; Santana, A.J.; Montoya-Alonso, J.A. The Thoracic Inlet as a Reference Point to Radiographically Assess Cardiac Enlargement in Dogs with Myxomatous Mitral Valve Disease. *Animals.* **2023**, 13(16), 2666.

4. Marbella Fernández, D.; Montoya-Alonso, J.A. Radiographic Left Atrial Size Measurement of Dogs in Different Mitral Valve Disease Stages with Four Different Methods. *Animals.* **2023**, 13(24), 3835.