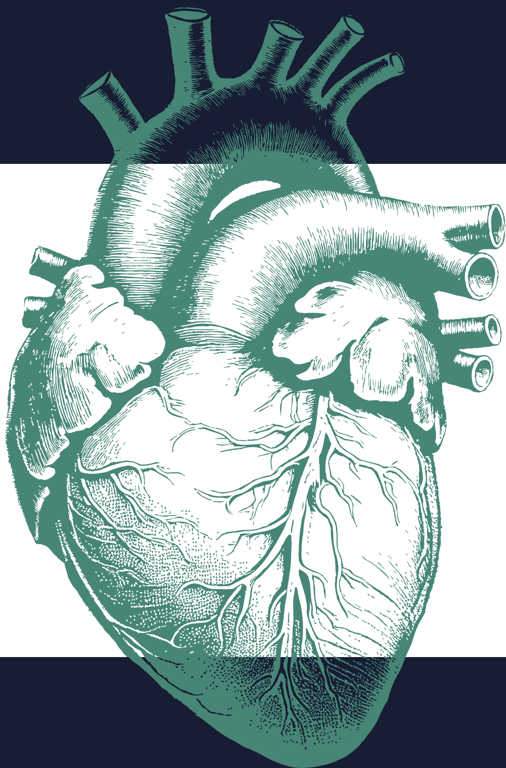
Nuevas Técnicas de Apoyo al Diagnóstico de la Enfermedad Mixomatosa de la Válvula Mitral en Perros

New Techniques to Approach the Diagnosis of Canine Myxomatous Mitral Valve Disease



Javier Engel Manchado

Doctorado de Investigación en Biomedicina
Tesis Doctoral con Mención Internacional
Marzo 2025

ULPGC Universidad de Las Palmas de Gran Canaria | Escuela de Doctorado

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JAVIER ENGEL MANCHADO

Escuela de Doctorado-Universidad de las Palmas de Gran Canaria

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Las Palmas de Gran Canaria, 10 de marzo de 2025

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NEW TECHNIQUES TO APPROACH THE DIAGNOSIS OF CANINE MYXOMATOUS MITRAL VALVE DISEASE

DOCTORANDO:

JAVIER ENGEL MANCHADO

DIRECTORES:

Dr. JOSÉ ALBERTO MONTOYA ALONSO

Dr. JOSÉ IGNACIO REDONDO GARCIA

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DOCTORADO EN INVESTIGACION EN BIOMEDICINA

TESIS DOCTORAL CON MENCION INTERNACIONAL

ESCUELA DE DOCTORADO-UNIVERSIDAD DE LAS PALMAS DE GRAN CANARIA

LAS PALMAS DE GRAN CANARIA, MARZO DE 2025

EL DOCTORANDO **EL DIRECTOR** **EL CODIRECTOR**

ULPGC Universidad de Las Palmas de Gran Canaria | Escuela de Doctorado

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INFORMA,

Que D. **Javier Carlos Engel Manchado**, Licenciado en Veterinaria, ha realizado, bajo mi dirección y asesoramiento, el presente trabajo de tesis doctoral con mención internacional titulado: NUEVAS TEÉCNICAS DE APOYO DIAGNÓSTICO DE LA ENEFERMEDAD MIXOMATOSA DE LA VÁLVULA MITRAL EN PERROS, que considero reúne las condiciones reglamentarias y de calidad científica necesarias, para su presentación y defensa, para optar al título de doctor con mención internacional por la Universidad de Las Palmas de Gran Canaria.

Y para que conste a los efectos oportunos firmo digitalmente en Las Palmas de Gran Canaria digitalmente el presente informe a la fecha incluida en la firma

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JOSÉ IGNACIO REDONDO GARCÍA, Doctor en Veterinaria y Catedrático de Anestesiología del Departamento de Medicina y Cirugía Animal de la Facultad de Veterinaria de la Universidad CEU Cardenal Herrera

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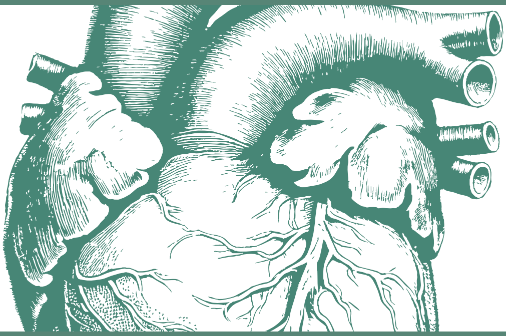

0.-
Estancias Internacionales

Royal Veterinary College
University of London

Confirmation of enrolment

I can confirm that Mr Javier Engel Manchado Ldo.Vet, MSc Cardiología, MSc Investigación Clínica y Terapéutica, Acred. AVEPA Cardiología, CertAVP (RCVS), MRCVS, was enrolled as a postgraduate student on the Certificate of Advanced Veterinary Practice (CertAVP) at the Royal Veterinary College from these dates:

A-PKS.1 Professional Key Skills	16th January 2009 – 24th October 2012
B-CKS.0 Clinical Key Skills	16th January 2009 – 8th September 2010

He successfully passed both modules.

Joanne Jarvis
CertAVP Manager
The Royal Veterinary College
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UNIVERSITY OF LIVERPOOL

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Thursday 10th August 2023

Dear Sir/Madam,

RE: Javier Engel-Manchado, Student ID 200964958

Please accept this letter as confirmation that the student named abovewas enrolled as a postgraduate studentat the University of Liverpool working towardsthe Certificate in Advanced Veterinary Practice (CertAVP), completingthe following moduleson the below dates:

B-SAP.1	Small Animal Practice	7th January – 28th April 2013
C-VC.2	Cardiovascular Diagnostics	6th January – 26th April 2020

Mr Engel-Manchado successfully passed both modules.

If you have any further queries please do not hesitate to contact me.

Yours faithfully,

L Barrett

Lucy Barrett

Veterinary Postgraduate ProgrammesSenior Administator

ROYAL (DICK) SCHOOL OF VETERINARY STUDIES
The University of Edinburgh
Easter Bush
Midlothian
EH25 9RG

Direct dial: 0131 651 7449
Website: http://www.ed.ac.uk/vet

Email: Sharon.Boyd@ed.ac.uk

Letter of attendance for Javier Engel Manchado

Date: 05 September 2023

To whom it may concern,

Javier Engel Manchado was a part-time postgraduate student on the RCVS Certificate in Advanced Veterinary Practice programme at the Royal (Dick) School of Veterinary Studies, University of Edinburgh.

Javier joined us in the 2012/2 academic year and registered for modules in Veterinary Cardiology. These are examined at Edinburgh, so his attendance in person was required during the timetabled examinations.

He passed C-VC.1 on the 29th January 2014 and C-VC.3 on the 27th January 2016. These are both 10-credit postgraduate modules at Level 11 (Scotland)/Level 7 (England and Wales). The Royal College of Veterinary Surgeons awards the Certificate and they will hold Javier's student record with regards to any other modules completed.

If you have any questions, please do not hesitate to contact me.

Regards

Sharon Boyd BA Hons (Zoo), MApplEnvSc, PgCUT, SFHEA, MSc e-Learning, CMALT
Director of CertAVP Edinburgh, Deputy Director of Postgraduate Taught Studies

Four Marks 11 March 2024

TO WHOM IT MAY CONCERN

This is to certify that Dr Javier Engel-Manchado underwent a 40-hour practical training on advanced imaging and interventional cardiology under my supervision from 26 February to 1 March 2024 at the Cardiology Department of the Ralph Veterinary Referral Centre in Marlow (Buckinghamshire) Fourth Avenue Globe Business Park, Marlow SL7 1YG

Yours faithfully

Luca Ferasin

Prof. Luca Ferasin, DVM PhD CertVC PGCert(HE) DipECVIMCA (Cardiology) GPCert(B&PS)FRCVS
European & RCVS Specialist in Veterinary Cardiology
Fellow of the Royal College of Veterinary Surgeons

Clinica Veterinaria Gran Sasso
Via Donatello, 26 – 20131 Milano
tel. 022663095 – 022665928
Fax. 022362048
P. IVA 12422130158

Milano, 08/01/2024

The undersigned Dr. Claudio Bussadori, Medical Director of the Gran Sasso Veterinary Clinic in Milan

certify that

Dr. Javier Engel-Manchado attended a practical course (40 hours) on advanced diagnostics imaging and interventional cardiology from 11 December to 17 December 2023, at the Gran Sasso Veterinary Clinic.

In fede

Claudio Bussadori

Agradecimientos

En primer lugar, me gustaría agradecer a mis dos directores el que haya llegado hasta aquí. **Alberto** fue mi primer mentor, y la persona que hizo que me gustara la cardiología veterinaria desde nuestros inicios en la Facultad de Veterinaria de la Universidad de Las Palmas de Gran Canaria. **Nacho**, es mi tutor, mentor y amigo, es la persona que se "ha empeñado" en que termine este proceso, apoyándome en los buenos y los malos momentos, aparte de ser miembro de una sociedad "secreta" llamada **"Los Perlas"**, en la que sólo entran los elegidos como él.

A mis padres, **Wolfi** y **Dely**, por haber hecho el esfuerzo de pagar mi formación en una época en la que no estábamos muy boyantes. Creo que el esfuerzo ha merecido la pena. Mi padre, allá donde esté, seguro que está contando "batallitas" de su hijo el veterinario, como hacía en vida cada vez que salíamos a comer a algún garito en el campo. Siempre me preguntaba qué nuevo curso o título había obtenido para ir a contarlo a la semana siguiente presumiendo de hijo. A mi madre, gracias por estar siempre ahí, te quiero Delita.

A mis hermanos, **Jorge** y **Sergio**, por soportarme todos estos años sabiendo que yo era el favorito, os quiero.

A mis abuelos, **Chano** y **Cielito**, por acogerme en su casa durante todos los años de la carrera, que fueron muchos, y tratarme como a un hijo. Mi abuelo Chano seguro que está orgulloso mirándome desde arriba.

A todos los tutores y pacientes y a los compañeros que participaron en todos los trabajos publicados y los que están sin publicar, gracias, sin vuestra ayuda esto no hubiera sido posible.

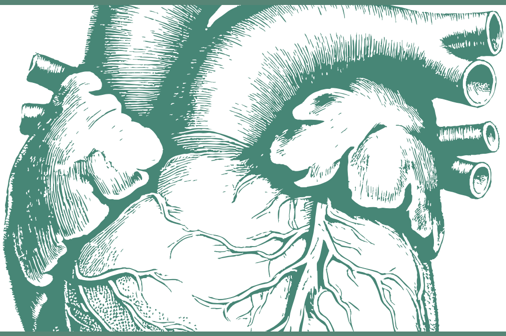
Por último, y no por ello menos importante, a **Luisi**, ***la pibita-wife***, mi compañera de vida, cuando la conocí supe que sería ella para siempre. Me ha acompañado a lo largo de todo este proceso y de muchos otros, la que me ha visto muy animado y deprimido con este proyecto, y, así y todo, ha seguido animándome. Sin ella, esto no hubiera sido posible. Gracias por todo y por muchos años más, te quiero.

Sólo me queda decir: ... ¿Y ahora qué?

The more I learn, the more I realize how much I don´t know

Albert Einstein

Índice



1.-
Abreviaturas

ACVIM: American College of Veterinary Internal Medicine

ANNs: Artificial Neuronal Nets

CARDIOBOX: Comprehensive Analysis of Results of Diagnostic Imaging Organized in a Box

CdV: Calidad de Vida.

CKCS: Cavalier King Charles Spaniel

CMD: Cardiomiopatía Dilatada

CMME: Colour M-Mode Echocardiography

ECG: Electrocardiograma

FETCH-Q™: Functional Evaluation of Cardiac Health Questionnaire

IA: Inteligencia Artificial

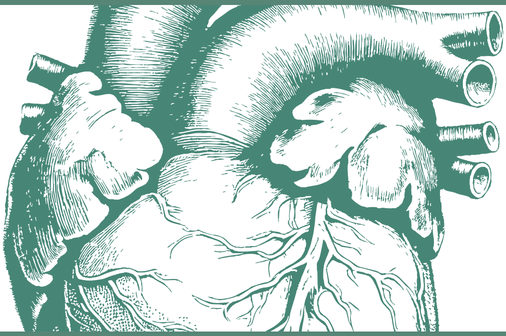
ICC: Insuficiencia Cardiaca Congestiva

ML: Machine Learning

MMVD: Myxomatous Mitral Valve Disease

STE: Speckle Tracking Echocardiography

SVM: Support Vector Machines



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Revisión Bibliográfica

2.1.- Nuevas técnicas de apoyo al diagnóstico de la enfermedad mixomatosa de la válvula mitral en perros

1. Introducción

La cardiología veterinaria ha experimentado avances significativos en las últimas décadas, reflejando la creciente importancia de la salud cardiovascular en animales de compañía. Las enfermedades cardíacas, especialmente en perros, representan una causa común de morbilidad y mortalidad, lo que subraya la necesidad de diagnósticos precisos y tratamientos efectivos.

1.1. Planteamiento del problema y relevancia de la cardiología veterinaria

La degeneración mixomatosa de la válvula mitral, también conocida como enfermedad valvular degenerativa crónica, es la afección cardíaca adquirida más frecuente en perros, representando aproximadamente el 70-80% de todas las cardiopatías caninas (Bonnett *et al.*, 2005; Egenvall *et al.*, 2005; Keene *et al.*, 2019) y la causa más común de insuficiencia cardíaca congestiva en esta especie (Borgarelli *et al.*, 2012). Esta enfermedad afecta predominantemente a razas pequeñas y de edad avanzada, como el Cavalier King Charles Spaniel, el caniche, el teckel y el beagle (Borgarelli *et al.*, 2012).

1.2. Objetivos generales y específicos de la tesis por compendio

El objetivo general de esta tesis es desarrollar y evaluar nuevas estrategias diagnósticas para la degeneración mixomatosa de la válvula mitral en perros, con el fin de mejorar la detección precoz y el manejo clínico de esta patología. Los objetivos específicos incluyen:

- **Desarrollar métodos avanzados de visualización y manejo de datos ecocardiográficos**: Implementando herramientas como el proyecto **CARDIOBOX** para facilitar la interpretación de imágenes cardíacas y mejorar la precisión diagnóstica.

- **Aplicar técnicas de aprendizaje automático en el diagnóstico y clasificación de la degeneración mixomatosa de la válvula mitral**: Integrando algoritmos de *machine learning* que analicen datos clínicos y de imagen para una clasificación más precisa de la severidad de la enfermedad.

- **Evaluar la calidad de vida en perros con enfermedad cardíaca**: Validando instrumentos como el cuestionario **FETCH-Q™** en su versión en español para medir el impacto de la enfermedad y su tratamiento en la calidad de vida de los pacientes caninos.

1.3. Organización de los artículos y su relación en el marco global de la tesis

Esta tesis por compendio se compone de tres artículos principales, cada uno alineado con los objetivos específicos mencionados:

1. **Desarrollo y validación de métodos gráficos de interpretación ecocardiográfica**: Este artículo aborda la creación del proyecto **CARDIOBOX** y su aplicación en la práctica clínica para mejorar la visualización de datos ecocardiográficos (Curra-Gagliano *et al.*, 2025).

2. **Aplicación del aprendizaje automático en la clasificación de la degeneración mixomatosa de la válvula mitral**: Se centra en la integración de técnicas de *machine learning* para analizar datos clínicos y de imagen, optimizando el proceso diagnóstico y la estratificación de riesgos (Engel-Manchado *et al.*, 2024).

3. **Validación de la versión en español del cuestionario FETCH-Q™ para la evaluación de la calidad de vida en perros con degeneración mixomatosa de la válvula mitral**: Este estudio valida la herramienta **FETCH-Q™** en la población hispanohablante, proporcionando una medida estandarizada del impacto de la enfermedad en la vida diaria de los perros afectados (Pérez *et al.*, 2020).

La interrelación de estos artículos proporciona una visión integral de las nuevas estrategias diagnósticas y de manejo de la enfermedad mitral en perros, abarcando desde innovaciones tecnológicas hasta la evaluación del bienestar animal.

2. Fundamentos de la enfermedad cardíaca en perros

Las enfermedades cardíacas en perros representan una de las principales causas de morbilidad en la medicina veterinaria. Se clasifican en congénitas y adquiridas, siendo estas últimas las más prevalentes, con la enfermedad mixomatosa de la válvula mitral (MMVD) como la afección más común en perros adultos (Brambilla *et al.*, 2020).

2.1. Epidemiología y prevalencia de las cardiopatías caninas

Las cardiopatías en perros tienen una prevalencia variable dependiendo de la edad de presentación, la raza y el sexo. La enfermedad mixomatosa de la válvula mitral (MMVD) es la afección cardíaca adquirida más común, representando aproximadamente el 75-80% de los casos en perros mayores de 8 años (Borgarelli *et al.*, 2012). La cardiomiopatía dilatada (CMD) es la segunda enfermedad adquirida más frecuente, afectando principalmente a razas grandes y gigantes, como el Doberman y el Gran Danés (Elsharkawy *et al.*, 2022).

Por otro lado, las cardiopatías congénitas afectan a aproximadamente el 2.8% de los perros, con la estenosis pulmonar, el conducto arterioso persistente y la estenosis aórtica como los defectos más comunes (Brambilla *et al.*, 2020). Razas como el bóxer, el bulldog francés y el pastor alemán presentan una predisposición genética a estas enfermedades (Lucina *et al.*, 2021).

2.2. Fisiopatología de las principales enfermedades cardiacas

La **enfermedad mixomatosa de la válvula mitral (MMVD)** se caracteriza por la degeneración mixomatosa de la válvula mitral, lo que provoca insuficiencia valvular progresiva y sobrecarga del volumen en el ventrículo izquierdo. Esta alteración fisiopatológica lleva a la remodelación cardíaca y, en etapas avanzadas, a insuficiencia cardíaca congestiva (ICC) (Keene *et al.*, 2019).

La **cardiomiopatía dilatada (CMD)** se caracteriza por una disfunción sistólica primaria del miocardio que conlleva una dilatación progresiva de los ventrículos y una reducción de la fracción de eyección, lo que predispone a arritmias ventriculares y muerte súbita (Elsharkawy *et al.*, 2022).

2.2.1 Clasificación de la Enfermedad Mixomatosa de la válvula mitral (MMVD)

La clasificación de la MMVD se basa en las guías del **American College of Veterinary Internal Medicine (ACVIM)**, dividiéndolas en cuatro estadios (Keene *et al.*, 2019):

- **Estadio A:** Perros en riesgo sin evidencia estructural de enfermedad.
- **Estadio B1:** Presencia de soplo cardíaco sin remodelación cardíaca.
- **Estadio B2:** Soplo cardíaco con dilatación ventricular sin signos de ICC.
- **Estadio C:** Insuficiencia cardíaca congestiva manifiesta.
- **Estadio D:** Insuficiencia cardíaca refractaria al tratamiento convencional.

2.3. Importancia clínica y pronóstico de la enfermedad cardiaca canina

El impacto clínico de las enfermedades cardíacas en perros varía según la gravedad de la afección. La enfermedad valvular mitral puede permanecer asintomática durante años, pero una vez que se desarrolla insuficiencia cardíaca congestiva, el tiempo de supervivencia promedio sin tratamiento es de aproximadamente 9 meses (Brambilla *et al.*, 2020). En el caso de la cardiomiopatía dilatada, el pronóstico es generalmente reservado, con un tiempo de supervivencia promedio de 3 a 6 meses después del diagnóstico (Elsharkawy *et al.*, 2022).

La detección temprana y el manejo adecuado son fundamentales para mejorar la calidad de vida y la supervivencia de los pacientes. Evaluaciones como la auscultación cardíaca, la ecocardiografía Doppler y los biomarcadores cardíacos (NT-proBNP y Troponina I) han demostrado ser herramientas útiles para el diagnóstico precoz (Keene *et al.*, 2019).

3. Evolución de las técnicas diagnósticas en cardiología veterinaria

Las técnicas diagnósticas en cardiología veterinaria han evolucionado significativamente en las últimas décadas. Desde métodos convencionales como la auscultación y el electrocardiograma (ECG), hasta herramientas avanzadas como la ecocardiografía Doppler y el análisis de deformación miocárdica, la precisión diagnóstica ha mejorado considerablemente (Scansen & Drees, 2020).

El diagnóstico precoz es muy importante para el manejo de la enfermedad, y está basado en diferentes pruebas como son la radiografía de tórax, el electrocardiograma, las pruebas analíticas y la ecocardiografía. Siendo la ecocardiografía la prueba más importante para confirmar la MMVD (Ljungvall *et al.*, 2017; Keene *et al.*, 2019). Sin embargo, persisten limitaciones en la accesibilidad y estandarización de algunas técnicas.

3.1. Métodos convencionales: auscultación, radiografía y ECG

Auscultación

La auscultación cardíaca es el primer paso en la evaluación cardiovascular de los perros. Se trata de un método económico y de fácil aplicación, aunque su interpretación depende de la experiencia del clínico (Pace, 2017). Mediante esta técnica, se pueden identificar soplos cardíacos indicativos de enfermedad valvular mitral, arritmias y otras alteraciones hemodinámicas.

El principal signo clínico en pacientes con MMVD es la presencia de soplo sistólico a la altura del ápex cardíaco en el hemitórax izquierdo (Côté *et al.*, 2015). En perros con fases iniciales de MMVD, el soplo suele tener una gradación baja, menos de III/VI, mientras que, en fases avanzadas de la enfermedad, la gradación suele ser elevada V-VI/VI. También puede ocurrir que perros con enfermedad en estadios muy iniciales, puedan tener un soplo no audible (Pedersen *et al.*, 1999).

Radiografía torácica

La radiografía torácica es una buena herramienta diagnóstica que está al alcance de casi todas las clínicas veterinarias (Poad *et al.*, 2020), y nos sirve para evaluar las consecuencias hemodinámicas de la MMVD (cardiomegalia, congestión/edema pulmonar), así como el aumento del atrio izquierdo (Mostafa *et al.*, 2017; Szatmári *et al.*, 2023). El estudio radiográfico del tórax también nos sirve para valorar el sistema respiratorio, ya que a veces estos pacientes vienen con patologías respiratorias concomitantes (broncomalacias, colapso traqueal/bronquial, bronquitis crónica, etc.) (Singh *et al.*, 2012; Ferasín *et al.*, 2019). Sin embargo, la radiografía tiene limitaciones para evaluar la funcionalidad cardíaca en tiempo real.

Electrocardiograma (ECG)

El electrocardiograma no es una prueba muy sensible para valorar la existencia de MMVD y la presencia de remodelación cardíaca, pero si es útil para diagnosticar la existencia de arritmias. Normalmente, estas arritmias son más frecuentes en razas grandes, aunque las razas pequeñas también las pueden presentar (Loon *et al.*, 2021).

Existe una relación estrecha entre la MMVD y la presentación de las diferentes arritmias cardíacas. Se ha observado que hay una correlación con la activación de los mecanismos compensatorios a nivel neurohormonal, debido a la remodelación cardíaca generada por la MMVD en los distintos estadios de la enfermedad (Rosa *et al.*, 2019).

El ECG es fundamental para diagnosticar arritmias y evaluar la conducción eléctrica del corazón. Un estudio reciente demostró que las alteraciones en la duración de la onda P y el intervalo QT pueden ser útiles como marcadores pronósticos en perros con insuficiencia cardíaca congestiva (Na *et al.*, 2021). A pesar de su utilidad, el ECG tiene una capacidad limitada para evaluar la morfología cardíaca.

3.2. Principios de la ecocardiografía en perros

Aunque hemos visto anteriormente, que la presencia de un soplo sistólico apical en el hemitórax izquierdo de razas predispuestas es casi diagnóstica de MMVD (Côté *et al.*, 2015). Existen pacientes con estadios iniciales de MMVD donde el soplo es casi inaudible (Häggström *et al.*, 1995; Pedersen *et al.*, 1999). Por ello, la ecocardiografía es la prueba no invasiva más importante y el "*gold standard*" para el diagnóstico definitivo de la MMVD (Chetboul *et al.*, 2012; Ljungvall *et al.*, 2017; Keene *et al.*, 2019).

La ecocardiografía ha revolucionado la cardiología veterinaria al permitir la evaluación anatómica y funcional del corazón en tiempo real. Existen diferentes modalidades de ecocardiografía utilizadas en perros:

- **Ecocardiografía modo M y bidimensional (2D):** Permite la medición de diámetros ventriculares y la evaluación de la contractilidad miocárdica (Han et al., 2018).
- **Ecocardiografía Doppler:** Esencial para evaluar flujos sanguíneos y detectar insuficiencias valvulares (Han et al., 2018).
- **Speckle Tracking (STE):** Técnica avanzada utilizada para evaluar la deformación miocárdica y detectar disfunción cardíaca temprana en perros con enfermedad valvular mitral (Coelho et al., 2015).

3.3. Limitaciones y desafíos de los métodos diagnósticos tradicionales

A pesar de los avances en el diagnóstico cardiológico veterinario, persisten varias limitaciones:

- **Variabilidad interobservador:** La interpretación de la auscultación y ecocardiografía puede variar entre clínicos con diferente experiencia, afectando la precisión del diagnóstico (Pace, 2017).
- **Costo y accesibilidad:** Mientras que la auscultación y el ECG son económicos, la ecocardiografía Doppler requiere equipos costosos y entrenamiento especializado, lo que limita su disponibilidad en muchas clínicas (Lucina et al., 2017).
- **Dificultad en la evaluación funcional:** Técnicas como la radiografía no permiten evaluar la contractilidad cardíaca en tiempo real, y el ECG no proporciona información detallada sobre la estructura cardíaca (Szatmári et al., 2023).

El desarrollo de nuevas herramientas de diagnóstico, como el análisis de *Strain* miocárdico y el uso de inteligencia artificial en la interpretación de ecocardiografías, promete mejorar la precisión y accesibilidad de la cardiología veterinaria en el futuro.

4. Nuevas propuestas en la visualización y manejo de datos ecocardiográficos

La ecocardiografía es una de las principales herramientas en cardiología veterinaria para la evaluación estructural y funcional del corazón. A pesar de su utilidad, presenta desafíos en la interpretación de imágenes, especialmente en la identificación de estructuras cardíacas y en la evaluación de la función miocárdica (Ghorbani *et al.*, 2020). En los últimos años, han surgido nuevas metodologías para mejorar la visualización y análisis de datos ecocardiográficos, incorporando inteligencia artificial y aprendizaje profundo.

4.1. El proyecto CARDIOBOX: antecedentes y justificación

El proyecto **CARDIOBOX** surge de la necesidad de mejorar la interpretación ecocardiográfica en veterinaria, utilizando métodos gráficos avanzados y modelos computacionales para estandarizar la visualización de imágenes cardíacas (Curra-Gagliano *et al.*, 2025). En la medicina humana, se han desarrollado modelos de aprendizaje automático capaces de identificar y clasificar estructuras cardíacas con una precisión superior a la de cardiólogos experimentados (Madani *et al.*, 2018). La implementación de estas tecnologías en veterinaria puede optimizar la evaluación de enfermedades como la degeneración mixomatosa de la válvula mitral y la cardiomiopatía dilatada.

Un estudio reciente demostró que la clasificación automática de vistas ecocardiográficas mediante redes neuronales convolucionales alcanzó una precisión del 97.8%, superando la evaluación manual de cardiólogos certificados (Madani *et al.*, 2018). Estas técnicas han sentado las bases para el desarrollo de herramientas como **CARDIOBOX,** con el objetivo de proporcionar una interfaz de interpretación gráfica más eficiente para la cardiología veterinaria (Curra-Gagliano *et al.*, 2025).

4.2. Diseño y validación de métodos gráficos de interpretación ecocardiográfica

El uso de herramientas computacionales en la ecocardiografía ha permitido mejorar la precisión diagnóstica mediante la optimización del procesamiento de imágenes. La introducción de modelos de aprendizaje profundo ha facilitado la identificación de estructuras cardíacas en tiempo real y la detección de patrones anómalos en estudios ecocardiográficos (Ghorbani *et al.*, 2020).

Entre los métodos más innovadores se encuentran:

- ***Speckle Tracking Echocardiography* (STE)**: Permite evaluar la deformación miocárdica y ha demostrado ser más sensible que la fracción de eyección en la detección temprana de disfunción cardíaca (Chang *et al.*, 2024).

- **Modelos de segmentación basados en *deep learning***: Se han desarrollado técnicas para la segmentación automática de estructuras cardíacas utilizando redes neuronales, mejorando la consistencia en la evaluación de la contractilidad miocárdica (Wang *et al.*, 2024).

- ***Colour M-Mode Echocardiography* (CMME)**: Un método emergente que permite evaluar diferencias de presión intraventricular sin necesidad de procedimientos invasivos, mejorando la evaluación de la función diastólica en animales (Mandour *et al.*, 2023).

4.3. Impacto de la visualización avanzada en la toma de decisiones clínicas

La incorporación de herramientas de inteligencia artificial y visualización avanzada en la ecocardiografía ha demostrado beneficios en la precisión diagnóstica y en la eficiencia del flujo de trabajo clínico. Modelos de aprendizaje profundo como ***EchoNet*** han sido capaces de predecir volúmenes ventriculares y fracción de eyección con una correlación significativa respecto a la evaluación manual (Ghorbani *et al.*, 2020).

Los principales beneficios de estas innovaciones incluyen:

- **Reducción de la variabilidad interobservador**: Los modelos automatizados han demostrado reducir errores de interpretación en comparación con la evaluación manual (Madani *et al.*, 2018).

- **Mejor estandarización del diagnóstico**: La automatización de la interpretación ecocardiográfica permite aplicar criterios diagnósticos de manera uniforme en diferentes centros veterinarios (Chang *et al.*, 2024).

- **Optimización de la toma de decisiones clínicas**: Herramientas como la ecocardiografía asistida por inteligencia artificial han mostrado ser útiles en la detección temprana de disfunción cardíaca y en la predicción de resultados clínicos (Mandour *et al.*, 2023).

En el futuro, la implementación de estos métodos en veterinaria podría mejorar significativamente la precisión diagnóstica y la personalización del tratamiento en pacientes con enfermedades cardíacas.

5. Aprendizaje automático aplicado al diagnóstico y clasificación de la enfermedad cardíaca

El uso de algoritmos de aprendizaje automático (*machine learning*, ML) en la medicina veterinaria ha crecido en los últimos años, ofreciendo herramientas avanzadas para la detección y clasificación de enfermedades cardíacas en perros. Los modelos de ML pueden analizar grandes volúmenes de datos clínicos, imágenes ecocardiográficas y señales electrocardiográficas para mejorar la precisión diagnóstica y facilitar la toma de decisiones clínicas (Vani, 2021).

5.1. Fundamentos del machine learning en veterinaria

El aprendizaje automático se basa en la capacidad de los algoritmos para identificar patrones en conjuntos de datos sin necesidad de programación explícita. Se ha utilizado en diversas aplicaciones médicas, desde la predicción de enfermedades hasta la personalización de tratamientos (Pazhanivel *et al.*, 2023). En veterinaria, ML ha mostrado gran potencial en la detección temprana de enfermedades cardíacas, optimizando el diagnóstico mediante la combinación de información clínica y de imagen.

Los algoritmos más utilizados incluyen:

- ***Support Vector Machines* (SVM)**: Se han empleado con éxito para la clasificación de enfermedades cardíacas a partir de electrocardiogramas y ecocardiografías (Pazhanivel *et al.*, 2023).
- **Redes neuronales artificiales (ANNs)**: Son utilizadas para la detección de anomalías cardíacas y predicción de riesgo cardiovascular (Hamid & Ali, 2023).
- ***Random Forest y Decision Trees***: Métodos basados en árboles de decisión que han mostrado alta precisión en la clasificación de insuficiencia cardíaca en humanos y modelos animales (Solanki *et al.*, 2023).

5.2. Aplicaciones específicas en la clasificación de la enfermedad valvular mitral

La enfermedad mixomatosa de la válvula mitral (MMVD) es la cardiopatía adquirida más frecuente en perros y representa un desafío diagnóstico debido a su progresión gradual. Recientes estudios han demostrado que ML puede mejorar la estratificación de riesgo en perros con MMVD, identificando factores clínicos y ecocardiográficos asociados con la progresión de la enfermedad (Zheng, 2024).

- **Clasificación basada en ecocardiografía**: Se han desarrollado modelos de ML para automatizar la identificación de insuficiencia mitral y predecir la evolución clínica de los pacientes (Vani, 2021).
- **Integración de biomarcadores**: Modelos de aprendizaje automático han logrado correlacionar niveles de NT-proBNP con la gravedad de la enfermedad, mejorando la detección de insuficiencia cardíaca congestiva (Pazhanivel *et al.*, 2023).

5.3. Integración de anamnesis, examen físico y algoritmos de aprendizaje automático

El desarrollo de herramientas de diagnóstico asistido por IA ha permitido la integración de múltiples fuentes de datos en la evaluación cardiovascular. Modelos híbridos combinan información de anamnesis, signos clínicos, ECG y ecocardiografía para mejorar la precisión diagnóstica (Solanki *et al.*, 2023).

- **Sistemas de apoyo a la decisión clínica**: La implementación de modelos ML en *software* clínico ha demostrado reducir el error diagnóstico en la detección de enfermedades cardíacas (Hamid & Ali, 2023).
- **Predicción de progresión de enfermedad**: Algoritmos como *Random Forest* han sido utilizados para predecir la evolución de la MMVD, permitiendo una mejor planificación del tratamiento (Zheng, 2024).

5.4. Retos y perspectivas de la IA en el ámbito clínico veterinario

A pesar del potencial del ML en cardiología veterinaria, existen desafíos que deben abordarse antes de su implementación generalizada:

1. **Necesidad de grandes volúmenes de datos**: La eficacia de los modelos de ML depende de la disponibilidad de datos de alta calidad, lo cual sigue siendo un reto en veterinaria (Vani, 2021).

2. **Interpretabilidad de los modelos**: Algunos algoritmos, como las redes neuronales profundas, funcionan como "cajas negras", lo que dificulta su validación en entornos clínicos (Hamid & Ali, 2023).

3. **Implementación en la práctica diaria**: La integración de ML en la rutina veterinaria requiere desarrollo de *software* accesible y capacitación de los profesionales para su uso efectivo (Solanki *et al.*, 2023).

En el futuro, la combinación de ML con técnicas de imagen avanzadas y biomarcadores permitirá diagnósticos más precisos y personalizados, mejorando el pronóstico de los pacientes con enfermedades cardíacas.

6. Evaluación de la calidad de vida en perros con enfermedad cardíaca

La evaluación de la calidad de vida (CdV) en perros con enfermedad cardíaca ha cobrado una importancia creciente en la medicina veterinaria. El impacto de las cardiomiopatías en la calidad de vida no solo afecta a los pacientes, sino también a sus tutores, lo que ha motivado el desarrollo de herramientas específicas para medir el bienestar de los animales con enfermedades cardiovasculares (Freeman *et al.*, 2018).

6.1. Concepto de calidad de vida y su importancia en medicina veterinaria

La calidad de vida se define como la percepción global del bienestar de un individuo, incluyendo aspectos físicos, emocionales y sociales. En perros con enfermedad cardíaca, la presencia de signos clínicos como disnea, fatiga e intolerancia al ejercicio puede comprometer significativamente su bienestar (Freeman *et al.*, 2018). Además, se ha demostrado que el impacto de estas enfermedades no solo afecta al perro, sino también a sus tutores, quienes experimentan una disminución en su propia calidad de vida debido al estrés y la carga emocional de cuidar a un animal con una enfermedad crónica (Freeman *et al.*, 2018).

En este contexto, la evaluación de la calidad de vida ha cobrado relevancia en la toma de decisiones clínicas, ayudando a los veterinarios a establecer cuándo iniciar o ajustar tratamientos, así como a determinar el momento adecuado para considerar cuidados paliativos (Strunz *et al.*, 2017).

6.2. Instrumentos de medición: el cuestionario FETCH-Q™ y sus propiedades psicométricas

El ***Functional Evaluation of Cardiac Health Questionnaire*** **(FETCH-Q™)** es una herramienta validada para evaluar la calidad de vida en perros con enfermedad cardíaca. Este cuestionario ha sido desarrollado para medir de manera objetiva el impacto de la enfermedad en la vida del animal y la percepción del dueño sobre su bienestar (Pérez *et al.*, 2020).

En la validación del cuestionario **FETCH-Q™**, se evaluaron 228 perros con enfermedades cardiovasculares, encontrando que el instrumento presentaba alta fiabilidad y consistencia interna (**α** = 0.89), así como una correlación significativa con la gravedad de la enfermedad (**ρ** = 0.82, $p < 0.05$) (Pérez *et al.*, 2020). La versión en español del cuestionario **FETCH-Q™** también ha sido validada y ha demostrado ser una herramienta confiable para la evaluación de la calidad de vida en perros hispanohablantes (Pérez *et al.*, 2020).

Otros estudios han confirmado la utilidad del **FETCH-Q™** para evaluar la respuesta al tratamiento en perros sometidos a cirugía de la válvula mitral, demostrando mejoras significativas en la calidad de vida hasta 12 meses después del procedimiento (Pennington *et al.*, 2022).

6.3. Relevancia clínica de la evaluación de la calidad de vida en perros con cardiomiopatías

El uso de herramientas como el **FETCH-Q™** ha permitido correlacionar la calidad de vida con marcadores clínicos objetivos. En un estudio reciente, se encontró que valores elevados de NT-proBNP y una mayor puntuación en el cuestionario **FETCH-Q™** estaban significativamente asociados con un peor pronóstico y mayor riesgo de mortalidad en perros con MMVD (Strunz *et al.*, 2017).

Además, la evaluación de la calidad de vida ha demostrado ser útil en la toma de decisiones clínicas, permitiendo ajustar los tratamientos en función del bienestar percibido por el dueño y los signos clínicos observados. Se ha recomendado su uso rutinario en la práctica veterinaria para mejorar la comunicación con los tutores y optimizar la gestión de pacientes con cardiomiopatías crónicas (Freeman *et al.*, 2018).

En conclusión, la integración de herramientas de evaluación de la calidad de vida en la práctica veterinaria permite una atención más integral, centrada no solo en la supervivencia del paciente, sino también en su bienestar y el de sus cuidadores.

7. Integración de los tres ejes de investigación

La combinación de métodos avanzados de visualización ecocardiográfica, aprendizaje automático y evaluación de calidad de vida representa un enfoque integral en la cardiología veterinaria. La sinergia entre estas técnicas mejora la precisión diagnóstica y optimiza la toma de decisiones clínicas (Engel-Manchado *et al.*, 2024).

7.1. Relación entre la visualización ecocardiográfica (CARDIOBOX) y las técnicas de clasificación *(machine learning)*

El desarrollo de modelos computacionales para la interpretación de imágenes ecocardiográficas ha permitido automatizar la identificación y clasificación de anomalías cardíacas. Algoritmos de aprendizaje profundo han demostrado ser efectivos para mejorar la segmentación de estructuras cardíacas y la detección de insuficiencia valvular mitral (Lončarić *et al.*, 2021).

El proyecto **CARDIOBOX** se basa en el uso de gráficas para mejorar la interpretación de datos ecocardiográficos (Curra-Gagliano *et al.*, 2025). Los modelos de aprendizaje automático como árboles de decisión han mostrado ser capaces de clasificar con alta precisión a perros con MMVD en diferentes etapas, utilizando imágenes ecocardiográficas y datos clínicos (Engel-Manchado *et al.*, 2024). Además, la implementación de estos sistemas reduce la variabilidad interobservador y optimiza la eficiencia en la detección de enfermedad cardíaca.

7.2. Beneficios de incorporar la evaluación de la calidad de vida (FETCH-Q™) al protocolo diagnóstico y de seguimiento

El cuestionario **FETCH-Q™** ha sido validado como una herramienta fiable para medir la calidad de vida en perros con enfermedad cardíaca, permitiendo evaluar la progresión de la enfermedad y la respuesta al tratamiento (Pérez *et al.*, 2020). Recientes estudios han demostrado que la integración de estos cuestionarios con modelos de *machine learning* mejora la estratificación de riesgo en pacientes con MMVD (Engel-Manchado *et al.*, 2024).

- **Predicción de progresión de la enfermedad**: Se ha observado que los valores de calidad de vida correlacionan significativamente con la clasificación de la enfermedad mediante ecocardiografía y *machine learning* (Engel-Manchado *et al.*, 2024).

- **Toma de decisiones clínicas**: La evaluación conjunta de calidad de vida y datos ecocardiográficos facilita la personalización del tratamiento, ayudando a determinar cuándo iniciar o ajustar terapias cardiovasculares.

7.3. Sinergias potenciales para la medicina veterinaria: de la teoría a la práctica

El uso combinado de visualización ecocardiográfica avanzada *machine learning* y evaluación de calidad de vida ofrece varios beneficios en la práctica clínica veterinaria:

1. **Mayor precisión diagnóstica**: La combinación de técnicas de imagen y algoritmos de *machine learning* mejora la clasificación de enfermedades cardíacas en perros (Valanrani, 2024).

2. **Optimización del tiempo y recursos**: La automatización de la interpretación ecocardiográfica y la integración de encuestas de calidad de vida reducen la carga de trabajo de los clínicos y mejoran la eficiencia diagnóstica (Patel *et al.*, 2022; Curra-Gagliano *et al.*, 2025).

3. **Mejor seguimiento del paciente**: La correlación entre calidad de vida y parámetros ecocardiográficos permite un monitoreo más preciso de la evolución de la enfermedad y la respuesta al tratamiento (Engel-Manchado *et al.*, 2024).

En conclusión, la integración de estos tres ejes de investigación no solo mejora el diagnóstico y manejo de la MMVD en perros, sino que también allana el camino para la implementación de modelos más avanzados de atención veterinaria personalizada.

8. Perspectivas futuras y retos en investigación

El avance de la inteligencia artificial y las técnicas de imagen en la cardiología veterinaria ha abierto nuevas oportunidades para mejorar la precisión diagnóstica y el manejo clínico de las enfermedades cardíacas en perros. Sin embargo, aún existen desafíos importantes que deben abordarse para su implementación efectiva en la práctica veterinaria (Zamzmi *et al.*, 2020).

8.1. Ampliación de bases de datos y mejora de algoritmos

Uno de los principales retos en el desarrollo de modelos de aprendizaje automático es la disponibilidad de grandes volúmenes de datos de calidad. En la actualidad, la mayoría de los modelos se entrenan con conjuntos de datos relativamente pequeños y específicos de ciertas poblaciones, lo que limita su aplicabilidad en diferentes entornos clínicos (Alaa *et al.*, 2022). Para mejorar la generalización de estos modelos, es fundamental:

- **Estandarizar los protocolos de adquisición de datos**: La variabilidad en la calidad y formato de las imágenes ecocardiográficas dificulta la comparación entre estudios (Zamzmi *et al.*, 2020).
- **Ampliar el acceso a bases de datos multicéntricas**: Iniciativas como ***ETAB*** han demostrado que el uso de conjuntos de datos anotados de manera homogénea puede mejorar significativamente la precisión de los modelos de aprendizaje profundo (Alaa *et al.*, 2022).
- **Optimizar la eficiencia de los algoritmos**: El uso de técnicas de optimización computacional, como modelos de redes neuronales convolucionales, ha permitido mejorar la segmentación de estructuras cardíacas en ecocardiografía con mayor precisión (Gandhi *et al.*, 2018).

8.2. Validación clínica multicéntrica a gran escala

Para que los avances en inteligencia artificial sean clínicamente útiles, es necesario validar los modelos en estudios multicéntricos con poblaciones diversas. Actualmente, la mayoría de los modelos de aprendizaje automático han sido probados en entornos de investigación controlados, pero su desempeño en la práctica clínica real sigue siendo incierto (Krittanawong *et al.*, 2023).

- **Estandarización de métricas de validación**: Es crucial definir criterios homogéneos para evaluar el desempeño de los modelos, incluyendo sensibilidad, especificidad y valores predictivos (Zamzmi *et al.*, 2020).
- **Ensayos clínicos prospectivos**: La validación de modelos en escenarios clínicos reales permitirá evaluar su impacto en la toma de decisiones médicas y en los resultados de los pacientes (Fletcher *et al.*, 2021).
- **Integración en los flujos de trabajo clínicos**: El uso de inteligencia artificial en ecocardiografía requiere interfaces intuitivas que permitan a los clínicos aprovechar su potencial sin aumentar la carga de trabajo (Gandhi *et al.*, 2018).

8.3. Aplicación de estas metodologías en otras patologías o especies

El éxito de la inteligencia artificial en la cardiología veterinaria podría extenderse a otras especialidades médicas y a diferentes especies animales. Estudios recientes han demostrado que modelos de aprendizaje automático pueden ser útiles en el diagnóstico de enfermedades respiratorias, endocrinas y neurológicas en animales de compañía (Ben Ali *et al.*, 2021).

- **Extensión a cardiomiopatías en otras especies**: El uso de *machine learning* para la evaluación de enfermedades cardíacas en gatos y caballos representa un área de investigación emergente con gran potencial (Patrascanu *et al.*, 2024).
- **Aplicación en el monitoreo remoto de la salud**: El desarrollo de dispositivos portátiles con sensores integrados permitiría el monitoreo continuo de parámetros fisiológicos en animales con enfermedades crónicas (Fletcher *et al.*, 2021).

- **Personalización del tratamiento**: La combinación de inteligencia artificial con biomarcadores clínicos podría permitir una medicina veterinaria más personalizada y basada en datos objetivos (Ghorbani *et al.*, 2020).

En conclusión, la inteligencia artificial y las técnicas avanzadas de imagen tienen el potencial de transformar la cardiología veterinaria. Sin embargo, su implementación efectiva requiere la ampliación de bases de datos, validaciones clínicas rigurosas y su aplicación en un contexto más amplio de enfermedades y especies.

9. Consideraciones finales

Los avances en cardiología veterinaria han sido impulsados por el desarrollo de nuevas tecnologías de diagnóstico, la implementación del aprendizaje automático y el enfoque en la evaluación de la calidad de vida de los pacientes. La integración de estas innovaciones ha permitido mejorar la precisión en la detección y clasificación de la MMVD, optimizando así la toma de decisiones clínicas y los resultados terapéuticos (Ben *Ali et al.*, 2021).

9.1. Principales avances logrados por los trabajos presentados

En las últimas décadas, la cardiología veterinaria ha experimentado un crecimiento significativo gracias a la incorporación de herramientas de inteligencia artificial y técnicas avanzadas de imagen cardíaca (Yang et al., 2021). Entre los principales avances logrados se destacan:

- **Mejoras en la visualización ecocardiográfica**: La integración de aprendizaje profundo en la ecocardiografía ha permitido una segmentación más precisa de las estructuras cardíacas y una evaluación automatizada de la insuficiencia mitral (Ben Ali *et al.*, 2021).
- **Aplicación de *machine learning* en la clasificación de enfermedades cardíacas**: Algoritmos como *Support Vector Machines* (SVM) y redes neuronales han mostrado una alta precisión en la predicción de la progresión de la enfermedad valvular mitral (Zheng, 2024).
- **Evaluación objetiva de la calidad de vida en perros con cardiopatías**: Herramientas como el cuestionario **FETCH-Q™** han sido validadas para medir el impacto de la enfermedad y el tratamiento en el bienestar del paciente y de sus cuidadores (Pérez *et al.*, 2020).

9.2. Aportes para la práctica clínica y la investigación futura

El uso de inteligencia artificial y el análisis de datos a gran escala han revolucionado la práctica clínica en cardiología veterinaria. Las principales contribuciones incluyen:

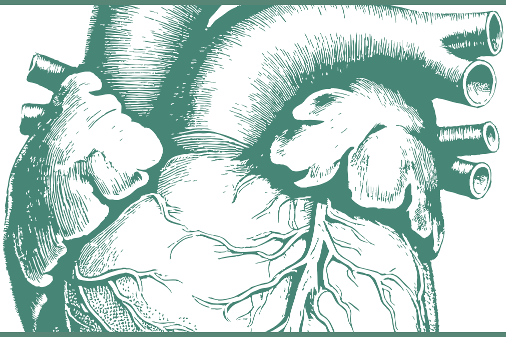
- **Mayor precisión en el diagnóstico y seguimiento**: La combinación de ecocardiografía avanzada con modelos de *machine learning* ha mejorado la detección temprana de enfermedades cardíacas, permitiendo una intervención más oportuna (Juárez-Orozco *et al.*, 2019).
- **Optimización de la estratificación de riesgo**: La integración de datos clínicos, biomarcadores y cuestionarios de calidad de vida ha permitido personalizar los tratamientos en función del estado del paciente (Cuocolo *et al.*, 2019).
- **Desarrollo de modelos predictivos**: Los avances en aprendizaje automático han abierto nuevas oportunidades para la predicción de eventos adversos en pacientes con cardiopatías, mejorando la planificación terapéutica y el pronóstico (Zheng, 2024).

9.3. Contribución a la cardiología veterinaria

Los avances en ecocardiografía, *machine learning* y evaluación de calidad de vida han transformado el diagnóstico y manejo de la MMVD en perros. Sin embargo, aún existen desafíos por resolver:

1. **Validación multicéntrica de algoritmos de IA**: La implementación de modelos de aprendizaje automático en la práctica clínica requiere estudios prospectivos que evalúen su desempeño en diferentes entornos clínicos (Ben Ali *et al.*, 2021).
2. **Estandarización de bases de datos**: La recopilación y procesamiento de datos ecocardiográficos deben ser homogéneos para garantizar la reproducibilidad de los resultados (Yang *et al.*, 2021).
3. **Aplicación en otras especies y patologías**: La expansión de estas metodologías a otras especies, como gatos y caballos, podría mejorar el diagnóstico y manejo de enfermedades cardíacas en diferentes poblaciones animales (Juárez-Orozco *et al.*, 2019).

En conclusión, la integración de tecnologías avanzadas en la cardiología veterinaria ha permitido mejorar la precisión diagnóstica y la calidad de vida de los pacientes. Sin embargo, es fundamental continuar con investigaciones que validen la aplicabilidad clínica de estos avances y su impacto en la medicina veterinaria a largo plazo.



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Objetivos/Objectives

3.1.- El objetivo de este estudio multicéntrico fue evaluar las características psicométricas de la versión española de la encuesta de calidad de vida **FETCH-Q™**, y validarla en tutores de habla hispana con perros en los distintos estadios ACVIM de la enfermedad mixomatosa de la válvula mitral (MMVD).

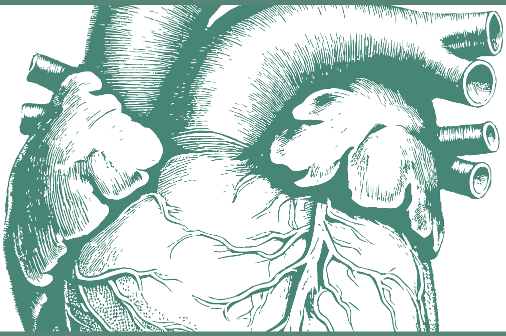
3.2- El objetivo principal de este estudio fue evaluar si con una historia clínica bien estructurada, la encuesta de calidad de vida **FETCH-Q™** y un examen físico completo, se podía llegar a clasificar la MMVD en las distintas fases ACVIM en perros utilizando técnicas de aprendizaje automático *("machine learning").*

3.3.- Los objetivos de este estudio fueron los siguientes (a) diseñar un método para la representación gráfica de resultados ecocardiográficos estandarizados y (b) validar la utilidad del método en un entorno clínico.

3.1- *This multicentre study aimed to evaluate the psychometric characteristics of the Spanish version of the* **FETCH-Q™** *quality of life survey and to validate it in Spanish-speaking tutors with dogs in the different ACVIM stages of mitral valve myxomatous disease (MMVD).*

3.2- *The main objective of this study was to evaluate whether a well-structured medical history, the* **FETCH-Q™** *quality of life survey, and a comprehensive physical examination could be used to classify MMVD at different ACVIM stages in dogs using machine learning techniques.*

3.3- *This study aimed to (a) design a method for the graphical representation of standardised echocardiographic results and (b) validate the method's usefulness in a clinical setting.*



4.-

Publicaciones científicas

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Research Article

Psychometric Properties of the Spanish Version of the Functional Evaluation of Cardiac Health Questionnaire "FETCH-Q™" for Assessing Health-related Quality of Life in Dogs with Cardiac Disease

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A B S T R A C T

To evaluate the psychometric properties of the Spanish version of the "FETCH-Q™", 228 dogs with cardiovascular diseases were included. After forward and back translation of the original questionnaire, nonexperts, ethologists and veterinary colleagues evaluated the content's validity through feedback. For criteria validity, the total score was correlated with the heart disease/failure class. For construct validity, the overall quality of life of the dog and the results obtained in each question was correlated. The reliability of the questionnaire was assessed using the Cronbach's alpha coefficient. To evaluate the test-retest validity the intra-class correlation coefficient and Wilcoxon signed-rank test were used. A good agreement with the original questionnaire was evident. For construct validity, the questionnaire obtained $r > 0.09$ to < 0.82. The criterion validity was appropriate and the correlation was rho = 0.82, with an effect size of 0.55 ($P < 0.05$). Cronbach's alpha coefficient was ($\alpha = 0.89$). The test-retest assessment revealed adequate repeatability (correlation coefficient = 0.87; $P < .001$). There was no difference in the owner responses to the questionnaire at baseline and 2 weeks later in dogs with stable cardiac disease ($P > .05$). This study supports the validity of psychometric properties of the Spanish version of the functional evaluation of cardiac health questionnaire "FETCHSV2-Q™" to assess Health-related Quality of Life in dogs with cardiovascular disease in clinical settings and research.

Introduction

Traditionally, physicians and veterinarians have acquired key information from patients and pet owners that focuses on the clinical history, including the frequency and severity of clinical signs at presentation, and on recurrence of events, such as hospitalization.[1-3] In recent decades, especially in human medicine, additional information has been sought out and collected regarding variables that are indicative of the day-to-day changes in quality of life of patients.[1,4,5] When the information comes directly from the patient, the approach is known as patient-reported outcomes for humans. When the information comes from the observation of someone different to the patient or health professional regarding animals, neonates and people with disabilities it is called observer-reported outcomes (obsRO).[6]

Playing a critical role in this approach, the health-related quality of life (HRQoL) measurement has been the most assessed obsRO in the last years in human and veterinary medicine.[7,8] The obsRO is a comprehensive approach to the standardized collection of information focused on the perspective that proxies have on the quality of life at any point in time.[9] This information is commonly obtained through a validated questionnaire[1,2,10] and the main utility is often its ability to monitor the progression of the disease and the impact of therapeutic interventions.[4,11] In human beings the obsRO can also be useful in predicting outcomes and survival time.[5,12,13]

Quality of life is a broad multidimensional concept that usually includes subjective evaluation of variables that have both positive and negative effects on life.[14,15] HRQoL refers to the impact of a disease and its clinical consequences in individual's quality of life.[16-18] HRQoL measurements are a common reference point that can then be used to measure the impact of different interventions and treatments for the same health conditions.[19] Those instruments that assess HRQoL have been developed to measure the impact of the disease, the effect of specific treatment and a range of other health-related variables on the lives of patients.[16,20] Thus, it is essential to submit any questionnaire designed to assess HRQoL to rigorous testing, mainly to determine if this sort of instruments are reliable and valid methods of measurement within the target population. Considering the above, the questionnaire must be psychometrically analyzed and should also be easy to interpret before being used in clinical settings.[21-23]

The Functional Evaluation of Cardiac Health Questionnaire "FETCH-Q™" created in 2005 by Freeman and colleagues[24] was originally developed and validated with 360 dogs belonging to English-speaking owners. The questionnaire was designed to be used as a disease-specific instrument to assess health-related quality of life in dogs with congenital and acquired heart disease. The FETCH-Q™ is a questionnaire designed to be easily completed by owners with the instruction to consider only the prior 7 days of the pet's life to solve each item. High scores on the FETCH-Q™ indicate a negative impact of the heart disease on health-related quality of life. To use this questionnaire within the Spanish-speaking community it is necessary to assess the psychometric properties as well the reliability and validity. Therefore, the aim of this cross-sectional multicenter study was to evaluate the psychometric properties of a Spanish version of the "FETCH-Q™" and validate its use with Spanish-speaking owners of dogs with cardiac disease.

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Materials and Methods

Validation of the FETCHSV2-Q™

The validation procedure of the Spanish version of the functional evaluation of cardiac health questionnaire (FETCHSV2-Q™) was achieved using an internationally accepted translation methodology recommended by Mapi Research trust, a research organization in Lyon, France. This methodology is described and detailed by Beaton and coworkers.[25]

Two professional translators translated the FETCH-Q™ from English into Spanish independently. After forward and back translation of the original questionnaire, the face and content validity of the FETCHSV2-Q™ (Functional Evaluation of Cardiac Health Spanish Version 2-Questionnaire) were evaluated by pre-evaluators including nonexperts (lay persons), ethologists and veterinary colleague's feedback seeking to include different perspectives. The structure of the questionnaire consists of eighteen items that ask about how cardiac disease negatively affects the quality of life of the pet. Both questionnaires consider only the prior 7 days of the pet's life to solve each item.

The possible score in the FETCHSV2-Q™ ranked between (0 - 85 points) was transformed to a percentage by dividing the score obtained for each patient by the maximum possible score and multiplied by 100 only for statistical purposes and data analysis. High scores on the questionnaire indicate a negative impact of heart disease on quality of life.

To demonstrate criterion validity the total FETCHSV2-Q™ score was correlated with an existing and standardized classification system, the International Small Animal Cardiac Health Council[26] using Spearman rank correlation test (rho). A total of 139 dogs was estimated to achieve a minimum effect size of 0.3 with a P-value $< .05$, a statistical power of 80%, and assuming 30% refusals and losses. For construct validity, owners at the same time were requested to evaluate the overall quality of life of their dogs by means of numerical rating from 0 to 5, being 0 nonaffected at all and 5 severely affected quality of life (see appendix) and their answers were correlated with the results obtained in the individual items to analyze the variation and assess if each measure follow the same tendency using Spearman rank correlation test. A calculation indicated that a total of 174 dogs would be needed to achieve a minimum effect size of 0.3 with a P-value $< .05$, a statistical power of 80% and assuming 30% refusals and losses for this analysis.

Study Population

Any dog diagnosed with congenital or acquired heart disease with or without documented congestive heart failure (CHF) that was examined between January 2015 and December 2016 was eligible to be included in this study. Dogs could be of any age, weight, breed or sex. The dogs were examined at seven private veterinary clinics and 2 veterinary teaching hospitals located in 4 Spanish-speaking countries (Manizales-Colombia, Medellin-Colombia, San Martin de los Andes-Argentina, Buenos Aires-Argentina, Caracas-Venezuela, Malaga-España, Vigo-España, Valencia-España). After obtaining institutional review board approval from the ethics committee of the University of Caldas on February, 2014 (act 02 February 24, 2014) reaching the requirements of the code of ethics of veterinary medicine for professional practice (Law 576, 2000), the respective review committees at each clinic approved the project and informed consent was obtaining from each owner.

Reliability Cohort

Randomly selected, 51 owners completed the questionnaire during the first visit and again 2 weeks later to perform the questionnaire's test-retest reliability.[27] Dogs included in this group were classified in the first visit as ISACHC class Ia-Ib-II and again reclassified two weeks later. The most severely affected dogs were not considered in this analysis because it was essential that the patients remained stable during this period of time.

Data Collection

The referring clinician and certified cardiologist provided routine clinical and diagnostic data for each dog that included an echocardiogram, thoracic radiographs, an electrocardiogram, cardiac biomarkers (NT-proBNP or cardiac troponin I), an assessment of the functional class of heart failure (ISACHC class) and the results of the FETCHSV2-Q™. Although each veterinary doctor had autonomy in their criteria, whenever possible the patients were diagnosed and classified according to the last version to the date of data collection with guidelines of the European society of veterinary cardiology[28] and the guidelines of the American college of veterinary internal medicine according to the disease suffered by each dog.[29] The questionnaire was completed by each owner during the consultation in a paper format and saved using a website designed to collect the data (www.scorefetchsv2.wixsite.com/inicio). All owners had to be willing to participate in the study, Spanish had to be their native language, had to have an acceptable level of education or at least international grade 6 of secondary school, had to have no history of cognitive impairment and had to have lived with the dog for at least 6 consecutive months prior to first visit to the veterinary cardiologist. If more than 30% of the FETCHSV2-Q™ questions were not properly filled in, the questionnaire was excluded from the statistical analysis.

Statistical Analysis for Reliability and Repeatability

All the statistical analyses were carried out using the statistical software R V.2.15.3. The data normality was evaluated using the Kolmogorov-Smirnov test. The reliability of the questionnaire was assessed with the Cronbach's alpha coefficient (α).[30] This coefficient reflects the cohesion of each item or question with the same objective (e.g., assess the impact of disease on quality of life). Cronbach's alpha (α) values ≥ 0.7 have been considered acceptable, a value > 0.8 have been considered good and a value > 0.9 has been considered excellent. To evaluate the test-retest repeatability of the questionnaire, the intra-class correlation coefficient and the Wilcoxon rank test were used to analyze the changes in FETCHSV2-Q™ score of patients that were followed-up two weeks later as described by Terwee.[27] The 2-way random intra-class correlation coefficient (ICC) of single measures denotes the proportion of variability in scores and an ICC $>$ 0.4, 0.6 and 0.8 indicate moderate, substantial and excellent repeatability, respectively. The ceiling and floor effect were displayed with the mean scores, standard deviation and percentage of patients with the maximum possible score and minimum possible score, respectively as described by Gonzalez.[31] A P-value $< .05$ was considered statistically significant.

Results

Records from 240 dogs were obtained and only the data of 228 dogs was used for statistical analysis since 12 dogs were considered missing data due to absence of complete information on clinical history/ISACHC classification, informed consent not provided by the owner or difficult issues uploading information to a web-designed platform. None of the dogs were removed from the statistical analysis due to incomplete questionnaires. Table 1 shows the demographic information and Fig 1 shows the distribution of dogs in the preclinical (n = 110) and congestive heart failure stages (n = 118). Most dogs were suffering from myxomatous atrioventricular valve disease (n = 149, 66%). Dilated cardiomyopathy was present in 29% of the

Table 1
Demographic Characteristics of Dogs Without Congestive Heart Failure (ISACHC Ia - Ib) and With Congestive Heart Failure (ISACHC II – IIIa – IIIb)

	Non-CHF (Mean ± SD/percentage)	CHF (Mean ± SD/percentage)	P value
Ages (years)	8.9 ± 4. 2	12.1 ± 5. 4	P = .02*
females	48.7%	20.6%	P = .3
Weight (Kg)	16.72 ± 5.9	12.28 ± 7.0	P = .06
Neutered	87%	49%	P = .001*

CHF, patients in congestive heart failure, Non-CHF, patients without congestive heart failure.
* Level of significance (P value < .05).

dogs (n = 67), most frequently affecting giant breeds and cocker spaniels. Pulmonary hypertension (n = 3) and arrhythmogenic right ventricular cardiomyopathy (n = 4) were present in 3% of overall population, all of them boxer breed dogs. Atrial septal defect (n = 2), cor triatriatum dexter (n = 1), subaortic stenosis (n = 1) and patent ductus arteriosus (n = 1) added up to 2% of the diseases of dogs included in this study.

After forward and back translation, no changes were identified in the questionnaire and a good agreement with the original questionnaire was subjectively evident. All the pre-evaluators considered that the face and content validity was appropriate and easy to understand for the owners. For construct validity, each item was correlated with the overall quality of life evaluated by the owner by means of numerical rating and the correlations (rho) ranged > 0.09 to < 0.82; the effect size ranged 0.25 (small) to 1.00 (large), ($P < .05$). The criterion validity was appropriate (Fig 2) and with an effect sizes of .55 (medium) the correlation between a set of ranges of the total score obtained in the FETCHSV2-Q™ and the classes of heart disease/failure ISACHC class was rho = 0.82 ($P < .05$).

The Kolmogorov-Smirnov test showed a non-normal data distribution ($P < .05$). Cronbach's alpha coefficient was ($\alpha = 0.89$) showing an appropriate internal consistency of the questionnaire. The test-retest had an adequate repeatability on the intra-class correlation coefficient test (ICC = 0.87; $P < .001$). The Wilcoxon rank test showed no difference in responses at baseline and two weeks later ($P > .05$) and those patients reclassified 2 weeks later didn't change of class as well. The number of patients with the maximum score obtained (ceiling effect) was (2/228 dogs; 0.8%) and the number of patients with the minimum score obtained (floor effect) was (3/228 dogs; 1.3%).

Discussion

The growing necessity to use alternative methods to demonstrate treatment outcomes for cardiovascular diseases has been filled out with HRQoL questionnaires for different diseases where the QoL of the patient is often considered the main objective.[32] HRQoL questionnaires have become a widely used method to assess specifically the rehabilitation of chronic diseases,[33,34] demonstrating particular advantages over traditionally measured biological variables.[35] Indeed, It's clear that the evaluation of biological variables such as the presence of signs of CHF, status of ventricular function, hemodynamic stability, even

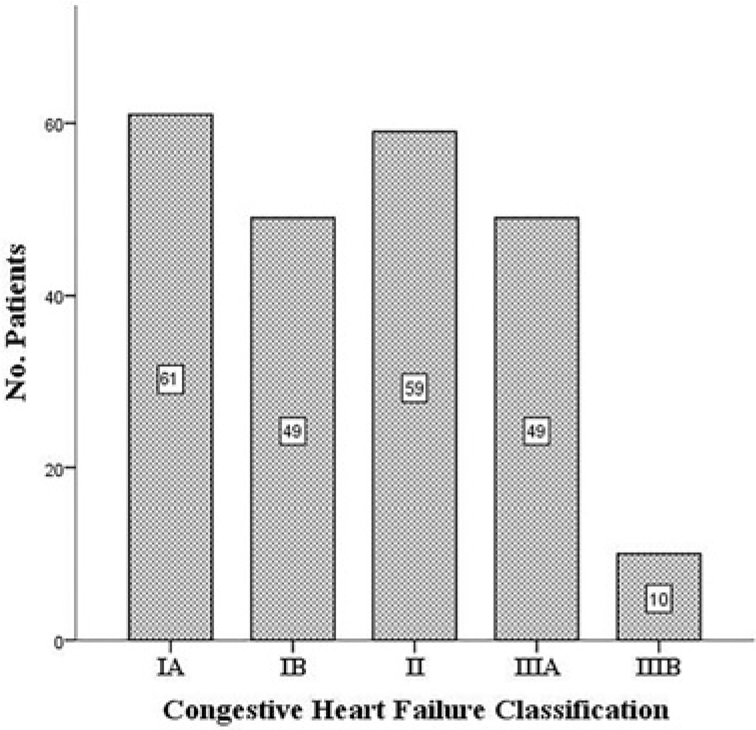

Fig 1. Distribution of patients among the different congestive heart failure class using the International Small Animal Cardiac Health Council Classification (n = 228 dogs with cardiac disease). Ia, Asymptomatic: no evidence of compensation for underlying heart disease; Ib, Asymptomatic: clinical signs of compensation for underlying heart disease (volume overload or pressure overload detected radiographically or echocardiographically); II, Mild–to–moderate heart failure with clinical signs at rest or with mild exercise; IIIa, Advanced heart failure; clinical signs of severe congestive heart failure; IIIb, Advanced heart failure; clinical signs of severe congestive heart failure.

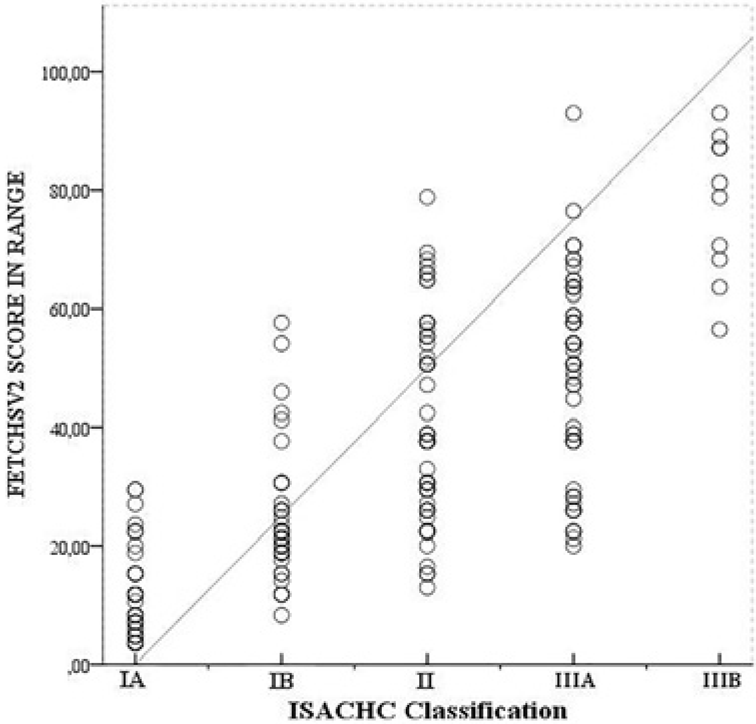

Fig 2. Correlation coefficient between International Cardiac Health Council Classification and the FETCHSV2-Q™ total score ranged to 100 (n = 228 dogs with cardiac disease). The solid line represents the linear correlation (rho = 0.82; effect size 0.55, $P < .05$). Ia, Asymptomatic: no evidence of compensation for underlying heart disease; Ib, Asymptomatic: clinical signs of compensation for underlying heart disease (volume overload or pressure overload detected radiographically or echocardiographically); II, Mild–to–moderate heart failure with clinical signs at rest or with mild exercise; IIIa, Advanced heart failure: clinical signs of severe congestive heart failure; IIIb, Advanced heart failure: clinical signs of severe congestive heart failure.

survival time are not all the essential evidence needed to provide proper management of dogs with cardiovascular disease.[16]

The assessment of HRQoL is commonly used to complement traditional measures of success such as survival time and CHF status.[1,36] Those complemental instruments have been used in areas such as drug discovery[37] and clinical practice.[4] The responsiveness of those HRQoL questionnaires documenting therapeutic success has been reported[38,39] and agencies such as the European Medicines Agency and the US Food and Drug Administration recommend the use of HRQoL questionnaires to document the effects of drugs in public health,[40] clinical practice and preventive care settings.[3]

Assessing only quantitative variables and survival time fails to address the multi-dimensionality of quality of life in an animal,[41] especially the subjective nature of some of its components.[42,43] The evaluation of some results as qualitative factors[44] that can be measurable is the complement that might be necessarily included in further research to evaluate the success of medical or surgical treatments with an overall approach.[38,45,46] Some nonclinical aspects such as emotional stress, physical discomfort, restrictions on daily life activities and loss of social-affective interaction are a sort of qualitative indicators of health-related quality of life in dogs that can then be measurable.[47,48] Thus, any HRQoL instrument that address this multidimensional approach is considered an important therapeutic benefit.[47,49,50]

Congestive heart failure morbidity not only increases the recurrence of hospitalization[51,52] and limitations during exercise (fatigue, dyspnea or syncope), it is also responsible for psychological and emotional complications in people and animals affecting their well-being.[43,53,54] In some studies, HRQoL has been shown to be a good predictor of mortality and hospitalization in human patients with CHF and this might be similar in dogs.[55] However, even after evidence, health-related quality of life is not yet a primary goal in some treatments and should be incorporate in further studies.[16]

The application of a questionnaire in a specific setting does not mean it will work in another setting.[35,56,57] Some of the most important limitations of using a questionnaire in a different setting are language and culture.[3] Oftentimes a questionnaire needs to be adapted to the context of a new population that has different sociocultural characteristics.[32,53] Specifically, the grammar, the syntax and the semantic differences upset the reliability and repeatability of the questionnaire.[32,57]

In our study precepts, if more than 30% of the FETCHSV2-Q™ items were not properly filled in, the questionnaire was excluded from the statistical analysis. The fact that none of the questionnaires were excluded demonstrates the ease and simplicity of completing the questionnaire and apparently confirms to some extent the content validity.[58] The need for a questionnaire to be simple and easy to complete has been stated in order to be a valid instrument for clinical use.[59,60]

For construct validity usually all the scores in individual items are correlated with an overall score to recognize the agreement and interaction between the items and asses if the measure, in this case each item behaves as the theory supposed the measure of the construct should behave. In this study with this sort of assessment the goal was to know the objectivity of the results of each item in the questionnaire. If an owner reacts adequately to the overall quality of life, results should be similar with almost the same tendency in each item, because the perception of how the disease impacts the quality of life of the pet is immersed in each item.

The scattered correlation of each item with the overall response of quality of life in this study suggests that some questions may not be important enough to remain in the questionnaire or that some questions were not relevant for the affected pet at the time of completing the questionnaire by each owner. Considering the variable presentation of cardiovascular diseases, some patients may not be affected by the same clinical signs, be in the same ISACHC class or have the same disease. Thus, high internal consistency between all items means there may be redundant items in the questionnaire evaluated.[1,21] However, in this study a reliability coefficient > 0.80 is excellent as it implies that 80% of the measured variances are reliable and only 20% are due to random error.

Our research describes step-by-step the rigorous psychometric evaluation to which the FETCHSV2-Q™ was submitted in a cross-cultural validation context. It proved to be a questionnaire that was apparently clear, valid, reliable, repeatable in clinical settings and useful as a measurable result for clinical research. The high internal consistency ($\alpha = 0.89$) supports the evidence that all 18 items are highly correlated with each other and suggests that the instrument is reliable for measuring the health-related quality of life in this group of dogs with different naturally occurring cardiovascular diseases. This α value was close to the results obtained during the initial validation of the FETCH-Q™ instrument[24] where authors obtained $\alpha >$ 0.90. Indeed, our research still confirms that the FETCHSV2-Q™ can be used to evaluate the clinical course of cardiovascular diseases in dogs considering the strong correlation with the ISACHC class of CHF with a moderate effect size.[59]

There are several limitations in our study that deserve consideration. First, the sample size was relatively small. However, this study was carried out at different veterinary centers in 4 countries, providing a wide range of sociocultural, economic, educational and environmental contexts that enriches the psychometric properties of the questionnaire with a heterogeneous group of dogs and possibly overcome the limitation of sample size. Second, it is unknown if the questionnaire is unidimensional or multidimensional in nature and all items in the questionnaire were treated as if they were equally important. There is a possibility that some factors perhaps are more important than others in dogs with heart disease and further research is necessary to determine these different factors by advanced statistical methods,[61] such as principal component analysis[62] or by a subjective approach.[63] Third, no sub-group analysis was done due to the number of dogs from each clinic was too small for robust statistical analysis and the entire population was considered as a total sample. The small number of critical dogs in the most severe stage of heart failure class (ISACHC IIIb) was also a limitation. Finally, the difficulty to follow-up dogs limited the collection of data to evaluate the responsiveness of the questionnaire to changes in the clinical status of the disease or the impact of the therapy over time and further research is needed.

Conclusion

The results of this study support the validity of the Spanish version of the functional evaluation of cardiac health questionnaire "FETCHSV2-Q™" to evaluate HRQoL in dogs with naturally occurring cardiovascular disease. These results justify its use in clinical settings and the authors hope it will be useful in further research that consider the good quality of life as an important goal and can be measure as complement to the quantitative results.

The management of the dog's health care can be shared through the HRQoL assessment due to the cooperation of both parties, the health professional and proxies. Participation of the owners in the health care of their own pets is indeed a critical aspect that facilitates education, communication and improves adherence to cardiologist's recommendations, especially in decision-making. Finally, further research should be developed to demonstrate responsiveness of the FETCH-Q™ or FETCHSV2-Q™ to changes in the clinical status of dogs with heart disease as well as responsiveness to changes when a therapy is established.

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Supplementary materials

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Corrigendum to <Psychometric Properties of the Spanish Version of the Functional Evaluation of Cardiac Health Questionnaire “FETCH-QTM” for Assessing Health-related Quality of Life in Dogs with Cardiac Disease>

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4.2.-

Machine Learning Techniques for Canine Myxomatous Mitral Valve Disease Classification: Integrating Anamnesis, Quality of Life Survey, and Physical Examination

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Machine Learning Techniques for Canine Myxomatous Mitral Valve Disease Classification: Integrating Anamnesis, Quality of Life Survey, and Physical Examination

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Simple Summary: Myxomatous mitral valve disease is dogs' most common acquired heart disease. The gold standard for its definitive diagnosis is echocardiography. This study aimed to develop a tool that uses a quality of life survey, structured anamnesis, and physical examination to predict the American College of Veterinary Internal Medicine classification stages. Accurately identifying a patient's stage is crucial to evaluating when treatment should be initiated and tailoring it to their ACVIM stage. The study analysed 1011 dogs from 23 hospitals, and the results showed that the majority of patients were successfully classified into the control group (healthy dogs), stage B (dogs with a heart murmur but are asymptomatic), and stage C (dogs with heart failure). However, efficient results were not obtained to differentiate between stage B1 (dogs with a heart murmur and without heart enlargement) and stage B2 (dogs with a heart murmur and heart enlargement). Further studies should be carried out to implement these techniques and improve their diagnostic value in veterinary cardiology.

Abstract: Myxomatous mitral valve disease (MMVD) is a prevalent canine cardiac disease typically diagnosed and classified using echocardiography. However, accessibility to this technique can be limited in first-opinion clinics. This study aimed to determine if machine learning techniques can classify MMVD according to the ACVIM classification (B1, B2, C, and D) through a structured anamnesis, quality of life survey, and physical examination. This report encompassed 23 veterinary hospitals and assessed 1011 dogs for MMVD using the FETCH-Q quality of life survey, clinical history, physical examination, and basic echocardiography. Employing a classification tree and a random forest analysis, the complex model accurately identified 96.9% of control group dogs, 49.8% of B1, 62.2% of B2, 77.2% of C, and 7.7% of D cases. To enhance clinical utility, a simplified model grouping B1 and B2 and C and D into categories B and CD improved accuracy rates to 90.8% for stage B, 73.4% for stages CD, and 93.8% for the control group. In conclusion, the current machine-learning technique was able to stage healthy dogs and dogs with MMVD classified into stages B and CD in the majority of dogs using quality of life surveys, medical history, and physical examinations. However, the technique faces difficulties differentiating between stages B1 and B2 and determining between advanced stages of the disease.

Keywords: anamnesis; clinical diagnosis; machine learning; predictive model; myxomatous mitral valve disease; dog

1. Introduction

Myxomatous mitral valve disease (MMVD) is the most common heart disease in dogs [1–3]. It accounts for up to 75% of all cardiovascular diseases in dogs, with an exceptionally high prevalence in senior and small dog breeds, such as Cavalier King Charles Spaniels (CKCS) [4,5]. MMVD significantly reduces life expectancy and quality of life in affected dogs [6,7]. Early diagnosis and staging of this condition are essential to determining the appropriate time to start therapy, achieving a better prognosis in most dogs [8].

The American College of Veterinary Internal Medicine (ACVIM) developed a classification system (stages A, B, C, and D) for MMVD, emphasising the importance of identifying the disease's severity and response to treatment [9]. Accurate and timely diagnosis is typically based on a combination of ancillary tests, including thoracic radiography, electrocardiography, and blood tests. Echocardiography is the most important clinical test to confirm a definitive diagnosis [9,10]. However, it is not possible to classify patients solely based on medical history and clinical signs, leading to misdiagnosis, especially when other non-cardiac illnesses present similar signs [11–13].

Although highly effective in diagnosing MMVD and its progression, echocardiography is only sometimes readily available due to the need for specialised equipment and expertise [14]. Therefore, there is a need for user-friendly tools to assist general veterinarians in classifying MMVD, especially in cases where advanced diagnostic tests are unavailable [15,16] and prompt action is crucial.

Machine learning techniques have gained recognition for their ability to analyse extensive datasets, offering flexibility, and scalability compared to traditional biostatistical methods, making them applicable to many tasks, such as risk stratification, diagnosis, classification, and survival predictions [17]. Human cardiology has successfully used these techniques to aid diagnosis and risk stratification [17,18]. However, their application in veterinary cardiology, especially for patient consultation, is still in its early stages [19–21]. A previous study demonstrated the usefulness of quality of life surveys in predicting outcomes in dogs with MMVD [22]. In addition, a recent study has shown the ability of machine learning techniques to classify patients affected by MMVD using thoracic radiographs [21].

The primary aim of this study was to assess the potential of a structured medical history complemented by a quality of life survey and physical examination analysed through machine learning to assist in classifying MMVD at various stages in dogs. Moreover, the purpose was to explore how owners perceive the disease in dogs with MMVD, even when they are unaware of the specific cause behind their pets' clinical signs.

2. Materials and Methods

An observational, prospective, and multicentre clinical study was conducted across twenty-three veterinary hospitals in Spain, Brazil, Argentina, Chile, and Costa Rica. All participating veterinarians had at least five years of experience in veterinary cardiology, further substantiated by postgraduate training in this specialised field (Ph.D. in cardiology research, specialised accreditation in cardiology, International School of Veterinary Postgraduate Studies (ISVPS) recognition, certificate in advanced veterinary cardiology by the RCVS, and cardiology resident by the ACVIM residency programme authorised to perform evaluations). Ethical approval was granted by the Animal Experimentation Ethics Committee of CEU Cardenal Herrera University (Spain) under reference number CEEA 22/06.

A total of 1011 client-owned dogs were evaluated; 64 healthy dogs were integrated into a control group; and 947 dogs with clinical findings of a left apical systolic murmur, which was confirmed through echocardiography, were integrated into a MMVD group. The inclusion criteria did not discriminate based on sex, breed, reproductive status, or body weight. However, dogs younger than one year old were excluded. The patients' owners were fully informed about the nature of the study, and their written consent was obtained to use their questionnaire responses and patient examination data for research purposes. The inclusion criteria for both control and MMVD groups required that the owner complete the FETCH-Q quality of life survey and that each dog be evaluated through history, physical examination, and echocardiography.

The control group were animals evaluated prior to elective surgery did not present clinical signs (absence of cardiorespiratory clinical signs, heart murmur, and systemic or organ-related diseases) and did not receive any medication. The MMVD group were dogs with the presence of a left-sided systolic heart murmur and were subsequently classified according to the ACVIM guidelines after echocardiography and radiographic examination (stage B1/B2/C/D). In particular, dogs previously treated or diagnosed with MMVD were excluded from the study, and dogs with other structural cardiovascular disorders (congenital, infectious, or degenerative) were also excluded from the study design. However, the presence of other non-cardiovascular comorbidities was not considered an exclusion factor due to the heterogeneous nature of the sample and the common occurrence of comorbidities in patients with MMVD, along with the degenerative progression of the disease.

At the time of completing the quality of life questionnaire, the owner of the patients in the group with MMVD possessed only the knowledge that their dog exhibited a heart murmur. Similarly, the sonographers conducting the echocardiography were aware that the referral was based on the presence of a heart murmur but lacked information regarding the anamnesis, physical examination, and specific stage according to the ACVIM classification.

A structured consultation comprised four distinct parts: a quality of life survey [7,22], anamnesis, a comprehensive physical examination, and an echocardiography examination, all conducted on the same day and with the same patient. The patient's medical history was meticulously documented, and the owner was asked about specific clinical signs in the previous two weeks, such as cough, dyspnoea, syncope, exercise intolerance, hypoxia/anorexia, or weight loss. Furthermore, the owner completed the Spanish version of the FETCH-Q quality of life survey [23]. A thorough physical examination encompassed the assessment of heart rate (HR), respiratory rate (RR), and rectal temperature (RT). Dogs were further categorised based on murmur grade, according to the I-VI system [24,25]. Body weight was recorded in kilograms, and the body condition score was assessed on a scale of 1 to 9 [26]. Blood pressure was measured with the following devices (SunTech Vet20, Bbraun Vet 25, and Vet30), according to ACVIM guidelines [27]. Five measurements were taken, and the values of the two extremes were discarded. With the other three values, a mean was obtained. One minute was allowed to elapse between measurements.

To standardise echocardiographic measurements, all investigators possessed extensive sonographer experience and adhered to predefined criteria [28]. Key measurements included the assessment of the left atrium and ascending aorta diameter, enabling the calculation of the left atrium/aorta ratio (LA/Ao). This ratio was determined from a 2D right parasternal short-axis view during early ventricular diastole. Additional measurements included left ventricular internal diameter in diastole (LVIDD) and normalised to body weight (LVIDDN) using the formula: LVIDDN = LVIDD (cm)/weight^0.294 (kg) [29]. The echocardiographic classification of mitral disease was conducted according to the ACVIM criteria [9], categorising patients into stages B1, B2, C, and D. Additionally, the mitral valve insufficiency (MINE score) was assessed [30]. According to the ACVIM guidelines for the classification of MMVD, thoracic radiological studies were performed for the correct diagnosis of the animals classified in stages C and D [9].

Echocardiographic data were collected using specialised veterinary cardiology equipment equipped with appropriate probes and software [Philips Affinity 50C, (Amsterdam, Netherlands); General Electric Vivid Iq, (Boston, MA, USA); Mindray Animalcare Vetus 7, (Shenzhen, China); and M8 and Canon a450, (Tokyo, Japan); with phased array probes between 2.5 and 12 MHz), and a uniform protocol was followed for image acquisition. Images were subsequently reviewed by the lead author (JEM) and a board-eligible American College of Veterinary Cardiology (YRD) member, with any substandard images being excluded from analysis.

Statistical analysis was performed using the R software (version 4.3.0, R Core Team, 2023, Vienna, Austria). Descriptive statistics summarised animal history data and were presented as mean ± SD, the number of observations, and percentages. Responses to the FETCH-Q scale were analysed using the Likert package for R [31] and represented as Likert plots. Univariate analysis was conducted to investigate differences in proportions between categories using the chi-square test [32] and a one-way ANOVA test for quantitative variables, with significance defined at $p < 0.05$.

Classification trees were developed using the rpart function of the rpart statistical package [33] to predict the stage of mitral disease as classified by the ACVIM. This was achieved using three approaches: (1) utilising the FETCH-Q survey, (2) relying on clinical signs identified during the physical examination, and (3) combining the FETCH-Q survey and physical examination findings. A minimum of 100 cases were required for a partition to be performed. The analysis was conducted in two parts: first, for the five ACVIM categories (A, B1, B2, C, and D), and second, a simplified model unifying categories B1 and B2 into classes B, C, and D into category CD. Classification trees were visualised using the rpart. plot function of the rpart.plot package [34].

Furthermore, data were analysed using the random Forest package [35], wherein 66% of the data were used as a learning sample to construct a classification tree, with a minimum of five observations per node. The remaining 33% of the data were treated as out-of-bag data for evaluating the sensitivity and specificity of the classification tree. This process was repeated 1000 times, and the weight of each ACVIM category was adjusted based on the relative percentage frequency of cases analysed. Finally, sensitivity and specificity were calculated by comparing observed results with those predicted by the classification forests, utilising the caret package for R [36].

The authors have thoroughly and comprehensively reviewed the content of the article. Additionally, the Grammarly assistant (standard version, 2023, San Francisco, CA, USA) has scrutinised the writing of the article to ensure effective presentation of information and to prevent spelling and grammatical errors in the English language.

3. Results

The study encompassed 1011 dogs, comprising 482 females and 529 males, with a median age of 12.0 years (range: 1.0 to 19.0 years) and a median body weight of 7.0 kg (range: 1.0 to 48.5 kg). The most represented breeds included crossbreeds (n = 371), Yorkshire terriers (n = 128), Chihuahuas (n = 105), Maltese (n = 59), Poodles (n = 55), and Dachshunds (n = 40), while other breeds accounted for the remaining dogs (n = 253). According to the ACVIM classification criteria, 64 dogs fell into the control group, 273 in B1, 357 in B2, 291 in C, and 26 in D. Tables 1 and 2 represent some demographic data separated by ACVIM groups.

Table 1. Demographic data (sex, age, and body weight) of the control group (healthy dogs) and the MMVD groups (ACVIM B1, B2, C, and D).

		Control Group (N = 64)	B1 (N = 273)	B2 (N = 357)	C (N = 291)	D (N = 26)
SEX	M	36 (56.3%)	139 (50.9%)	175(49%)	121 (41.6%)	11 (42.3%)
	F	28 (43.8%)	134 (49.2%)	182 (51%)	170 (58.4%)	15 (57.7%)
AGE (years) Median (Min, max)		6.0 (1.0, 16.0)	11.0 (2.0, 19.0)	12.0 (1.0, 18.0)	12.0 (5.0, 18.0)	12.8 (12.0, 17.0)
BODY WEIGHT (Kg) Median (Min, max)		13.2 (2.5, 48.5)	7 (1.0, 46.5)	7.5 (1.5, 47.5)	5.8 (1.5, 37.5)	12.8 (10.0, 17.0)

M: male; F: female.

Table 2. List of the more representative breeds in the control group (healthy dogs) and the MMVD groups (ACVIM B1, B2, C, and D).

	Control Group (N = 64)	B1 (N = 273)	B2 (N = 357)	C (N = 291)	D (N = 26)
CROSSBREED	33 (51.6%)	101 (37.0%)	132 (37.0%)	93 (32.0%)	12 (46.2%)
BEAGLE	12 (18.8%)	8 (2.9%)	11 (3.1%)	8 (2.7%)	0 (0.0%)
YORKSHIRE TERRIER	5 (7.8%)	42 (15.4%)	40 (11.2%)	38 (13.1%)	3 (11.5%)
CHIHUAHUA	2 (3.1%)	23 (8.4%)	30 (8.4%)	50 (17.2%)	0 (0.0%)
MALTESE	0 (0.0%)	19 (7.0%)	14 (3.9%)	24 (8.2%)	2 (7.7%)
POODLE	0 (0.0%)	9 (3.3%)	20 (5.6%)	24 (8.2%)	2 (7.7%)
DACHSHUND	0 (0.0%)	11 (4.0%)	19 (5.3%)	10 (3.4%)	0 (0.0%)
MINIATURE SCHNAUZER	0 (0.0%)	8 (2.9%)	9 (2.5%)	7 (2.4%)	1 (3.8%)
SHIH TZU	0 (0.0%)	11 (4.0%)	7 (2.0%)	5 (1.7%)	0 (0.0%)
COCKER SPANIEL	0 (0.0%)	3 (1.1%)	12 (3.4%)	5 (1.7%)	0 (0.0%)

Figures 1–3 illustrate the responses to the FETCH-Q questions across different ACVIM stages. It is noteworthy that, with the exception of Q06, all inquiries demonstrated statistically significant differences between groups. The observed variances imply a marked elevation in response scores with increasing severity according to the ACVIM classification, strongly suggesting a decline in quality of life.

Tables 3 and 4 provide insights into clinical signs and physical examination findings, respectively, categorised by ACVIM classification. Significant differences emerged in the proportion of various clinical indicators, including COUGH, DYSPNOEA, SYNCOPE, EXERCISE INTOLERANCE, HYPOREXIA/ANOREXIA, WEIGHT LOSS, and MURMUR GRADE. In general, clinical signs exhibited a progressive pattern of aggravation with higher ACVIM stages. Notable differences were also observed in heart rate (HR), respiratory rate (RR), and capillary refill time (CRT). However, no significant differences were noted in systolic blood pressure (SBP), diastolic blood pressure (DBP), and median arterial pressure (MAP).

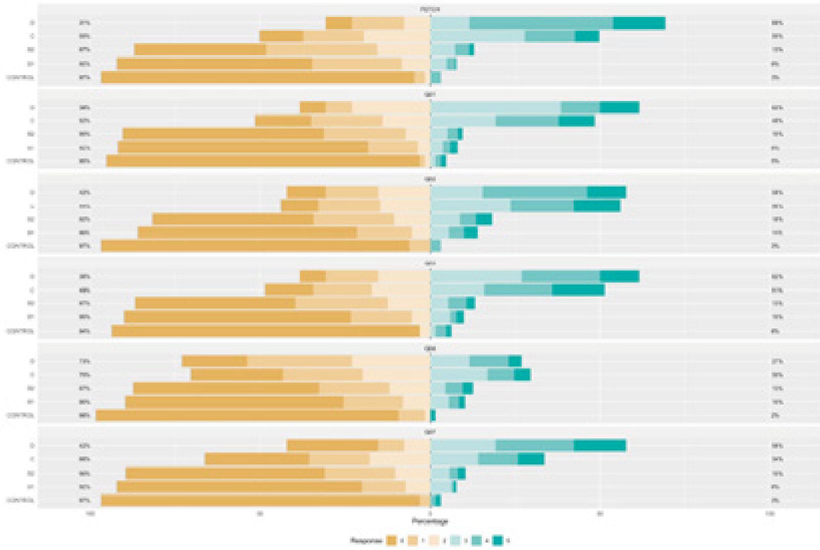

Figure 1. Likert representation of the answers for FETCH-Q and questions 1 to 7. Q1: "Does your dog have difficulty breathing?"; Q2: "Does your dog cough?"; Q3: "Does your dog often breathe very fast?"; Q4: "Does your dog snore when breathing?"; Q5: "Does your dog have difficulty in recreation? (Playing fetch, running, playing with other dogs or you, etc.)?"; Q6: "Were your dog's favourite activities limited due to exercise restrictions by the veterinarian?"; Q7: "Does your dog sit or lie down during walks? (Does not tolerate exercise)".

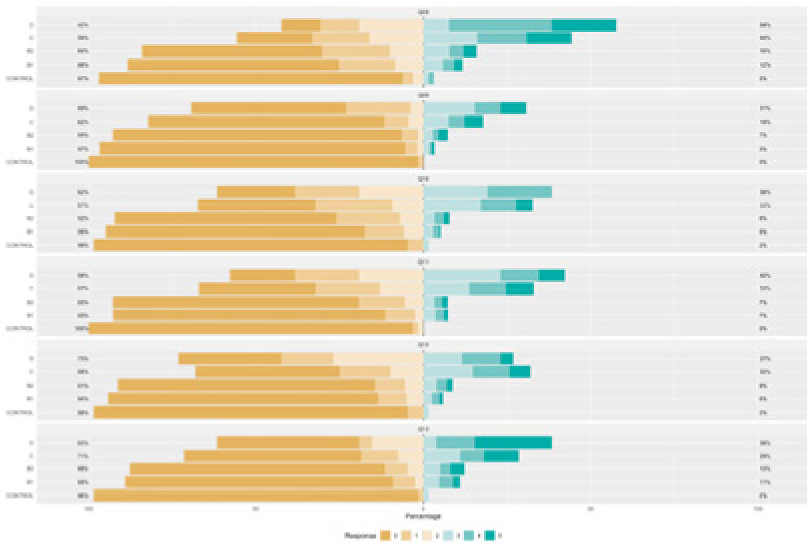

Figure 2. Likert representation of the answers for questions 8 to 13. Q8: "Does your dog have difficulty going up and down stairs?"; Q9: "Has your dog had episodes of collapse or fainting (syncope)?"; Q10: "Does your dog have difficulty getting comfortable? (At any time of the day)."; Q11: "Does your dog have difficulty sleeping through the night?"; Q12: "Is your dog eating less than he should, or has he been inappetent for the last few weeks?"; Q13: "Have you changed the type of food your dog is willing to eat?".

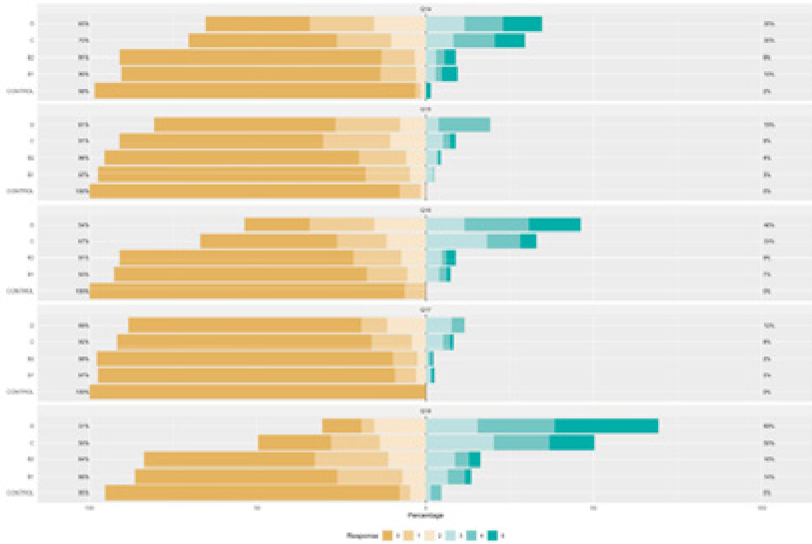

Figure 3. Likert representation of the answers for questions 14 to 18. Q14: "Increased urinary accidents in the house? (Urinating inside the house or where he should not)?"; Q15: "Has your dog had vomiting episodes?"; Q16: "? Has your dog had any limitations in spending time with you and the family (cannot get on the bed or sofa, avoids moving around, avoids bed or sofa, avoids moving)"; Q17: "Has your dog become irritable or unwilling to be touched? (Behaviour change)"; Q18: "Is your dog less active and vital?".

Table 3. Correlation between the clinical signs reported during history and the ACVIM classification.

		Control Group (N = 64)	B1 (N = 273)	B2 (N = 357)	C (N = 291)	D (N = 26)
Cough	Yes	4 (6.3%) [a]	55 (20.1%) [b]	94 (26.3%) [b]	169 (58.1%) [c]	17 (65.4%) [c]
	No	60 (93,8%)	218 (79.9%)	263 (73.7%)	122 (41.9%)	9 (34.6%)
Dyspnoea	Yes	3 (4.7%) [a]	15 (5.5%) [a]	27 (7.6%) [a]	171 (58.8%) [b]	16 (61.5%) [b]
	No	61 (95.3%)	258 (94.5%)	330 (92.4%)	120 (41.2%)	10 (38.5%)
Syncope	Yes	1 (1.6%) [ab]	7 (2.6%) [a]	30 (8.4%) [b]	48 (16.5%) [c]	7 (26.9%) [c]
	No	63 (98.4%)	266 (97.4%)	327 (91.6%)	243 (83.5%)	19 (73.1%)
Exercise Intolerance	Yes	1 (1.6%) [a]	13 (4.8%) [a]	36 (10.1%) [b]	100 (34.4%) [c]	14 (53.8%) [c]
	No	63 (98.4%)	260 (95.2%)	321 (89.9%)	191 (65.6%)	12 (46.2%)
Anorexia	Yes	0 (0%) [a]	10 (3.7%) [a]	15 (4.2%) [a]	42 (14.4%) [b]	9 (34.6%) [c]
	No	64 (100%)	263 (96.3%)	342 (95.8%)	249 (85.6%)	17 (65.4%)
Body weight loss	Yes	0 (0%) [a]	5 (1.8%) [a]	6 (1.7%) [a]	19 (6.5%) [b]	8 (30.8%) [c]
	No	64 (100%)	268 (98.2%)	351 (98.3%)	272 (93.5%)	18 (69.2%)

Data are presented as frequency tables. Classes with different letters are statistically different ($p < 0.05$).

Table 4. Correlation between the physical examination and the ACVIM classification.

		Control Group (N = 64)	B1 (N = 273)	B2 (N = 357)	C (N = 291)	D (N = 26)
Murmur	Yes	0 (0%) ^{a}	273 (100%) ^{b}	357 (100%) ^{b}	291 (100%) ^{b}	26 (100%) ^{b}
	No	64 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Murmur grade	No	64(100%) ^{a}	0 (0%) ^{b}	0 (0%) ^{c}	0 (0%) ^{d}	0 (0%) ^{e}
	1	0 (0%)	18 (6.6%)	3 (0.8%)	0 (0%)	0 (0%)
	2	0 (0%)	71 (26%)	28 (7.8%)	4 (1.4%)	1 (3.8%)
	3	0 (0%)	124 (45.4%)	123 (34.5%)	30 (10.3%)	1 (3.8%)
	4	0 (0%)	56 (20.5%)	143 (40.1%)	97 (33.3%)	5 (19.2%)
	5	0 (0%)	4 (1.5%)	52 (14.6%)	141 (48.5%)	12 (46.2%)
	6	0 (0%)	0 (0%)	8 (2.2%)	19 (6.5%)	7 (26.9%)
CRT	>2 s	0 (0%) ^{a}	2 (0.7%) ^{a}	1 (0.3%) ^{a}	5 (1.7%) ^{a}	3 (11.5%) ^{b}
	<2 s	64 (100%)	271 (99.3%)	356 (99.7%)	286 (98.3%)	23 (88.5%)
HR	bpm	107 [60, 176] ^{a}	120 [60, 220] ^{b}	124 [55, 230] ^{b}	142 [60.0, 290] ^{c}	150 [85.0, 260] ^{c}
RR	bpm	24.0 [12, 60.0] ^{a}	24.0 [15, 100] ^{a}	24.0 [12, 90.0] ^{a}	44.0 [16.0, 180] ^{b}	40.0 [24.0, 210] ^{b}
SAP	mm Hg	136 [101, 187] ^{a}	134 [73, 206] ^{a}	130 [79, 224] ^{a}	140 [75, 210] ^{a}	135 [95, 154] ^{a}
DAP	mm Hg	84.0 [48, 158] ^{a}	88.0 [48, 142] ^{a}	87.0 [51, 150] ^{a}	89.0 [36, 129] ^{a}	92.0 [60, 113] ^{a}
MAP	mm Hg	95.0 [65, 163] ^{a}	98.0 [59, 147] ^{a}	95.0 [70, 166] ^{a}	98.0 [57, 148] ^{a}	107 [71, 120] ^{a}
RT	°C	38.0 [37.0, 40.0] ^{a}	38.1 [35.4, 40.5] ^{a}	38.2 [36.7, 39.7] ^{a}	38.2 [35.0, 39.5] ^{a}	38.1 [36.6, 39.3] ^{a}

Data are presented as frequency tables and medians [minimum, maximum]. Classes with different letters are statistically different ($p < 0.05$). CRT: capillary refill time. HR: heart rate. RR: respiratory rate. SAP: systolic arterial pressure. DAP: diastolic arterial pressure. MAP: mean arterial pressure. RT: rectal temperature.

Figures 4 and 5 present the classification tree and the variable importance plot derived from the random forest analysis for the FETCH-Q survey, respectively.

Similarly, Figures 6 and 7 depict the classification tree and variable importance plot obtained from the random forest analysis for the anamnesis and the physical examination.

Figures 8 and 9 extend this analysis to include the FETCH-Q, the anamnesis, and the physical examination.

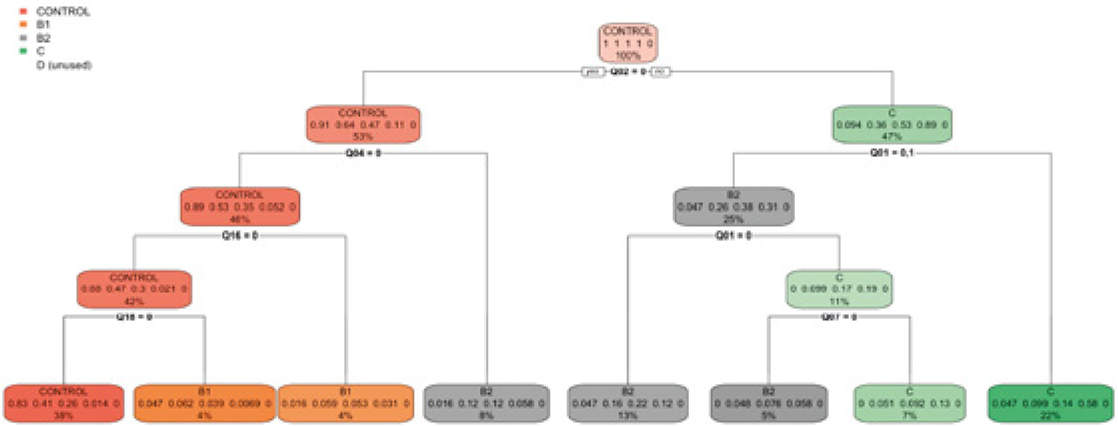

Figure 4. Classification tree for the model using the FETCH-Q. It represents the different selection criteria or 'decision nodes' used to predict the most correct classification of the total number of dogs (represented at the tree's root as 100%). As the data are classified into subsets, the percentage value represents the probability of a dog belonging to that data subset. ACVIM class D was unused due to the few dogs recorded. Q1: "Does your dog have difficulty breathing?"; Q2: "Does your dog cough?"; Q4: "Does your dog snore when breathing?"; Q7: "Does your dog sit or lie down during walks? (Does not tolerate exercise)."; Q18: "Is your dog less active and vital?".

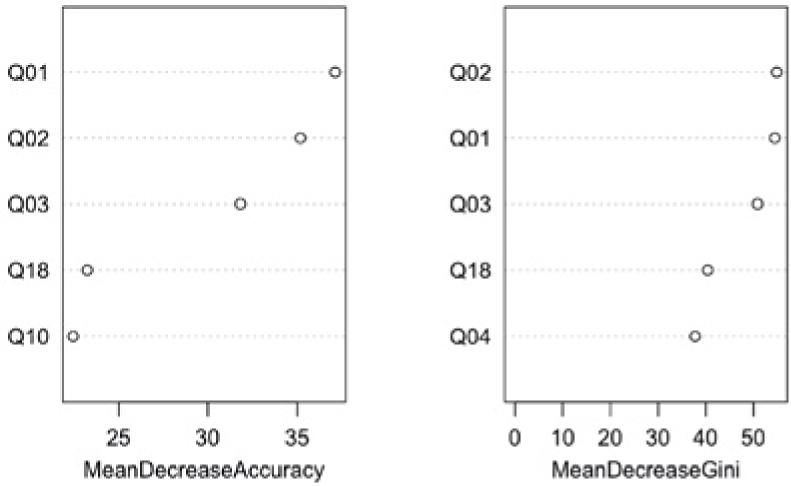

Figure 5. Variable importance plot of the first five variables for the model created using the FETCH-Q. The random forest algorithm measures the importance of each variable in classifying the data. The Mean Decrease Accuracy plot and Mean Decrease in the Gini coefficient help identify the variables that contribute most to the homogeneity of nodes and leaves in the forest. Variables are ranked in order of importance based on how much accuracy is lost when excluded. Q1: "Does your dog have difficulty breathing?"; Q2: "Does your dog cough?"; Q3: "Does your dog often breathe very fast?"; Q10: "Does your dog have difficulty getting comfortable? (At any time of the day)?"; Q18: "Is your dog less active and vital?".

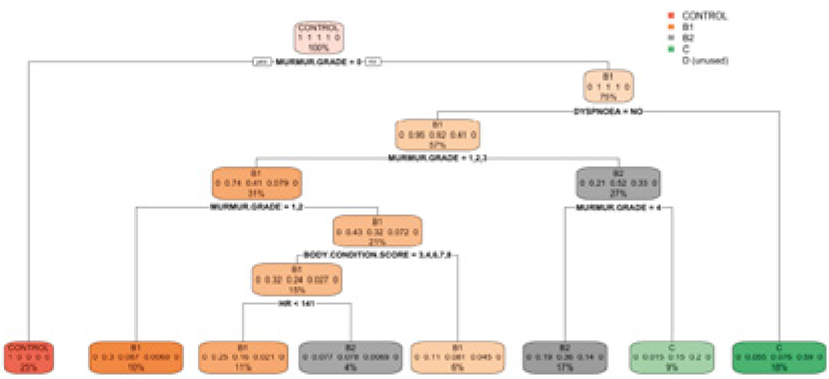

Figure 6. Classification tree for the anamnesis and the physical examination model. The classification tree represents the different selection criteria or 'decision nodes' used to predict the most correct classification of the total number of dogs (described at the tree's root as 100%). As the data are classified into subsets, the percentage value represents the probability of a dog belonging to that data subset. ACVIM class D was unused due to the few dogs collected.

Table 5 summarises the model's ability to correctly categorise dogs based on ACVIM classification in the three analyses. Notably, combining the FETCH-Q scale and physical examination significantly improved classification accuracy compared to using each component individually. In the combined model, the overall accuracy reached 0.64 (95% CI: 0.609–0.669; $p < 0.0001$; Kappa's Cohen: 0.489), whereas individual models yielded accuracies of 0.484 (95% CI: 0.453–0.515; $p < 0.0001$; Kappa's Cohen: 0.263) for the FETCH-Q scale-only model and 0.599 (95% CI: 0.568–0.630; $p < 0.0001$; Kappa's Cohen: 0.435) for the clinical signs-only model. In the complex model, 96.9% of the control group category, 49.8% of B1, 62.2% of B2, 77.2% of C, and 7.7% of D were correctly classified. Notably, B1 dogs were often confused with B2 (83.2% of B1 dogs misclassified as B2), and B2 dogs were mistaken for B1 and C (57.0% of B2 dogs misclassified as B1 and 43.0% as C). Dogs in category C were frequently misclassified as B2 (86.3%), and D tended to be confused with C (87.5%).

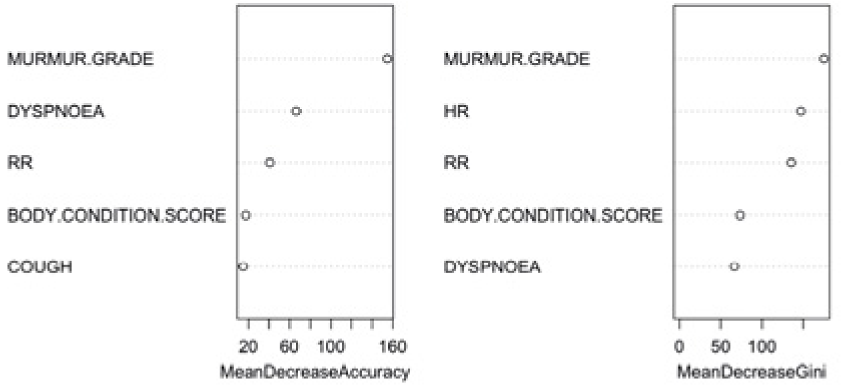

Figure 7. Variable importance plot of the first five variables for the model created using anamnesis and physical examination. The random forest algorithm measures the importance of each variable in classifying the data. The Mean Decrease Accuracy plot and Mean Decrease in the Gini coefficient help identify the variables that contribute most to the homogeneity of nodes and leaves in the forest. Variables are ranked in order of importance based on how much accuracy is lost when excluded. RR: respiratory rate; HR: heart rate.

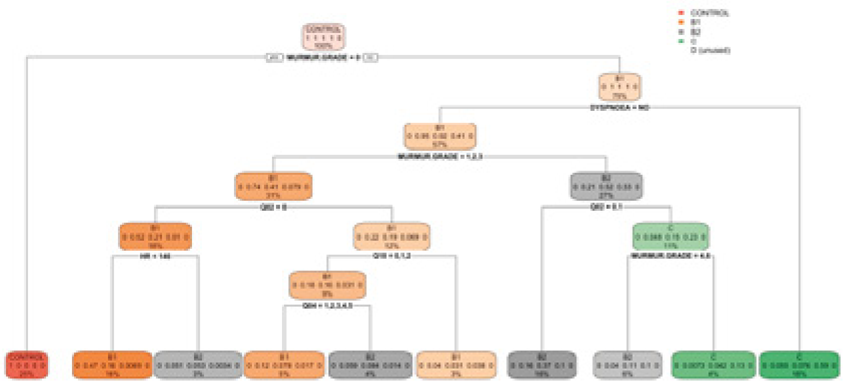

Figure 8. Classification tree for the model using the FETCH-Q, the structured anamnesis, and the physical examination. The classification tree represents the different selection criteria or 'decision nodes' used to predict the most correct classification of the total number of dogs (represented at the tree's root as 100%). As the data are classified into subsets, the percentage value represents the probability of a dog belonging to that data subset. ACVIM class D was unused due to the few dogs collected. Q2: "Does your dog cough?"; Q4: "Does your dog snore when breathing?"; Q18: "Is your dog less active and vital?".

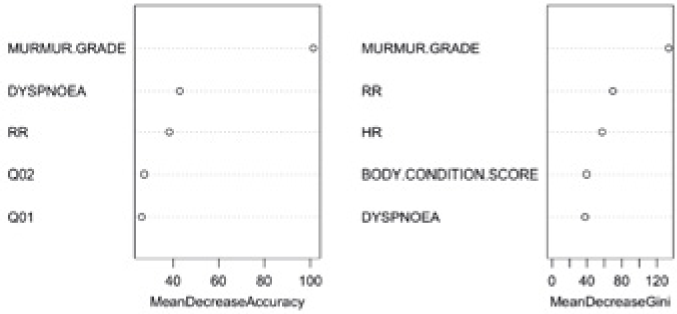

Figure 9. Variable importance plot of the first ten variables for the model created using the FETCH-Q, the structured anamnesis, and the physical examination. The random forest algorithm measures the importance of each variable in classifying the data. The Mean Decrease Accuracy plot and Mean Decrease in the Gini coefficient help identify the variables that contribute most to the homogeneity of nodes and leaves in the forest. Variables are ranked in order of importance based on how much accuracy is lost when excluded. RR: respiratory rate; HR: heart rate. Q1: "Does your dog have difficulty breathing?"; Q2: "Does your dog cough?".

Table 5. Classification matrixes of the complex models (echo-based classification). They illustrate the accuracy of the models in correctly classifying dogs based on the ACVIM classification criteria. Each row corresponds to an ACVIM class and displays the number of dogs classified into various categories by the model. The 'class error' represents the percentage of misclassified dogs when utilising the model.

			FETCH-Q model			
	Control group	**B1**	**B2**	**C**	**D**	**Class error**
Control group	2	56	3	3	0	97%
B1	2	143	84	44	0	48%
B2	0	126	138	93	0	61%
C	0	14	72	204	0	30%
D	0	0	3	21	2	92%
			Physical examination model			
	Control group	**B1**	**B2**	**C**	**D**	**Class error**
Control group	64	0	0	0	0	0%
B1	0	149	111	13	0	45%
B2	0	106	189	62	0	47%
C	0	20	68	201	2	31%
D	0	3	5	15	3	88%
			FETCH-Q plus physical examination model			
	Control group	**B1**	**B2**	**C**	**D**	**Class error**
Control group	62	1	0	1	0	3%
B1	0	136	114	23	0	50%
B2	0	77	222	58	0	38%
C	0	9	57	224	0	23%
D	0	1	2	21	2	92%

In the simplified model, which grouped categories B1 and B2 as B and C and D as CD, an improvement in classification accuracy was evident. Specifically, 93.8% of the control group, 90.8% of B, and 73.4% of CD were correctly classified, with 9.2% of B misclassified as CD and 27.0% of CD misclassified as B (Table 6). The accuracy of this model reached 85.5% (95% CI: 0.832–0.877; $p < 0.0001$; Kappa's Cohen: 0.710). The regression tree and variable importance plot for the simplified model are detailed in Figures 10 and 11.

Table 6. Classification matrix of the simplified model (echo-based classification). Categories B1 and B2 are grouped into category B, and categories C and D are grouped into category CD. The 'class error' represents the percentage of misclassified dogs when utilising the model.

Simplified Model				
	Control Group	B	CD	Class Error
Control group	60	3	1	6%
B	0	572	58	9%
CD	0	84	232	27%

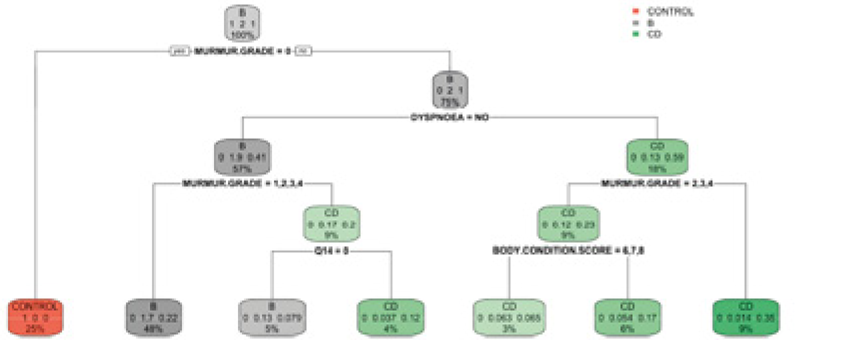

Figure 10. Classification tree for the simplified model using the FETCH-Q, the structured anamnesis, and the physical examination. The classification tree represents the different selection criteria or 'decision nodes' used to predict the most correct classification of the total number of dogs (represented at the tree's root as 100%). As the data are classified into subsets, the percentage value represents the probability of a dog belonging to that data subset. Q14: "Increased urinary accidents in the house? (Urinating inside the house or where he should not)?".

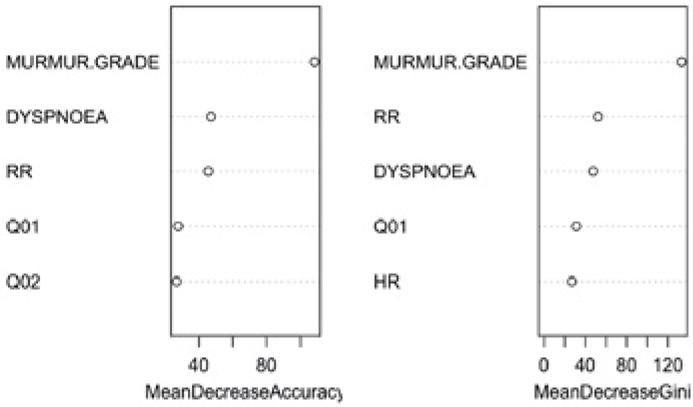

Figure 11. Variable importance plot of the first ten variables for the simplified model created using the FETCH-Q, the structured anamnesis, and the physical examination. The random forest algorithm measures the importance of each variable in classifying the data. The Mean Decrease Accuracy plot and Mean Decrease in the Gini coefficient help identify the variables that contribute most to the homogeneity of nodes and leaves in the forest. Variables are ranked in order of importance based on how much accuracy is lost when excluded. RR: respiratory rate; HR: heart rate; Q1: "Does your dog have difficulty breathing?"; Q2: "Does your dog cough?".

4. Discussion

Traditionally, suspicion of MMVD in dogs has been described by veterinarians based on the presence of a heart murmur and/or cardiorespiratory signs. Echocardiography is the definitive diagnostic method and the preferred technique for categorising the severity of the disease. The developed project has demonstrated adequate results to differentiate between healthy animals and those with MMVD using machine-learning algorithms, which use clinical history, a quality of life survey, and a physical examination. The information obtained can aid in the initial assessment of dogs with MMVD before confirmation by echocardiographic study. Furthermore, the technique allowed for capturing the owner's perspective on disease progression, contributing to a comprehensive understanding of the disease [16].

The complex model correctly classified control dogs and stage C patients, achieving 96.9% and 77.2% accuracy, respectively. However, it needed support to accurately identify the B groups, with only 49.8% of B1 and 62.2% of B2 patients correctly classified. Notably, a significant proportion of misclassified B1 patients were categorised as B2 (83.2%), while misclassified B2 patients were often mistaken for B1 (57.0%) or C dogs (43.0%). It can be challenging to distinguish between B1 and B2 stages, as asymptomatic dogs with murmurs characterise both, and to differentiate between advanced B2 and C stages, where dogs adapt to cardiac enlargement to compensate for volume overload before developing congestive heart failure [9]. In such cases, echocardiographic and radiographic diagnostics are often necessary for differentiation [9,37]. The complexity of distinguishing between classes may have led to classification difficulties for the machine learning algorithm. A simplified model achieved a higher accuracy (90.8%) in classifying B dogs without distinguishing between B1 and B2. However, the ability to determine between stages B1 and B2 is essential in MMVD. Patients definitively diagnosed as B2 according to the ACVIM consensus guidelines [9] should begin chronic oral treatment with pimobendan in order to prolong the preclinical period and delay the onset of clinical signs [6].

The algorithm also had difficulty distinguishing between stages C and D in the complex model, with 87.5% of D dogs being misclassified as C. It is challenging to differentiate between stages C and D of cardiac disease in dogs, as clinical signs largely overlap. These clinical signs include tachypnoea, dyspnoea, hyporexia/anorexia, weight loss, and cough [9]. In the simplified model, both categories were grouped.

In general, while anamnesis and physical examination contribute to staging, especially for the control group and C dogs, that information could not distinguish B1 from B2 or C from D dogs. However, the simplified model could differentiate effectively between the control group, B, and C-D dogs.

The simplified model could differentiate between the control group, B, and CD patients in the majority of dogs. With further development of the technique, this information could prove advantageous for general veterinarians who may be deficient in advanced cardiology expertise, as it may help them evaluate a patient with MMVD and determine the need for urgent referral to a cardiology centre. Furthermore, this tool could improve the cardiovascular evaluation of patients with MMVD without the risks of anaesthesia and sedation necessary for accurate ACVIM classification based on thoracic radiography [9] and, in certain geographic regions, could reduce radiation exposure to human operators.

An alternative set of simple tests has been suggested for diagnosing dogs with preclinical stage MMVD (B2), including biomarker-based diagnostics and tailored therapeutic management to avoid sedation for radiography [38]. Echocardiography, considered the "gold standard", requires specialised training [9] and has limited accessibility in first-opinion practice. Although in this study, physical examination and history helped to classify a dog with MMVD, according to the ACVIM guidelines. It would be a mistake to start treatment without prior echocardiography. The importance of early detection should be prioritised for referral to a specialist for dogs suffering from MMVD. This is a fundamental part of the developed study because machine learning techniques do not intend to replace echocardiography and the ACVIM guidelines for diagnosis in dogs but may be useful as an additional tool in the disease classification, when further developed and studied.

Diagnostic methods based on artificial intelligence have recently been implemented in canine MMVD [21]. In the research developed by Valente et al. (2023) [21], the ability of machine learning techniques to assess the severity of MMVD from canine thoracic radiographs was investigated. Radiological studies of 1242 dogs in different phases of the disease were retrospectively analysed. The results in the study of the lateral radiological views showed an AUC of 0.87, 0.77, and 0.88 for stages B1, B2, and C+ D, respectively. The high accuracy of the algorithm in predicting the MMVD stage suggests that it could be a helpful support tool in the interpretation of canine thoracic radiographs. The previous artificial intelligence study determined that stage B1, C, and D dogs were better than stage B2 dogs. As in the conducted study, the worst classification results were obtained for the stage B2 dogs. The echocardiographic study and the radiological study of dogs in phase B2 are complex, with a great clinical variety among patients compared to animals classified as B1, C, or D.

As MMVD advances, FETCH-Q scores typically rise, and owners' responses to questions during the anamnesis process also increase as clinical signs emerge or worsen in patients. These findings are consistent with previous studies [7,22]. The FETCH-Q survey contributes to dog classification to varying degrees. FETCH-Q question responses differ across the five ACVIM classes. The owner's perception of their dog's quality of life aligns with their assessment within the ACVIM classification, supporting our hypothesis. The responses obtained from the completion of a structured anamnesis through simple and objective questions by dog owners have been shown to be a critical factor in assessing cardiac diseases in primary veterinary care. The evaluation of the quality of life in dogs with MMVD is essential, and tools like the FETCH-Q scale can be beneficial. However, a conclusive diagnosis should consistently rely on support from imaging tests, particularly thoracic radiography and echocardiography [7,22].

The significance of an entire medical history is well known in human medicine. An adequate physical examination starts with a systematic patient history, which can improve diagnostic precision [39]. However, new technologies, online consultations, and artificial intelligence have disrupted this field [40,41].

Variances in clinical signs and physical examination outcomes across the groups were observed. As the ACVIM stage increased, the clinical signs became more severe. Hyporexia/anorexia and declining body condition were negative markers. These signs can indicate possible congestive heart failure [6,12,42]. Also, there was a correlation between poor outcomes and dyspnoea, cough, syncope, worsening body condition, and anorexia, as indicated by previous studies [11,38,42–44].

The physical examination remains fundamental in the ACVIM classification, distinguishing the control group from B dogs based on the presence or absence of a heart murmur [9]. A left apical systolic murmur is the initial clinical finding in MMVD patients [45,46]. The findings align with previous research, suggesting that murmur intensity beyond III/VI often coincides with advanced stages of heart disease and may indicate an increased risk of adverse outcomes [38,42,47].

The algorithm uses various physical examination variables to differentiate between stages, including heart rate, respiratory rate, and capillary refill time. Heart rate variations reflect how the sinus node responds to stimulation from the autonomic nervous system, which regulates heart rate through sympathetic tone. As MMVD severity increases, heart rate gradually rises, a trend confirmed by various studies [48–50], an observation confirmed in this study. Physical activity and environmental stress can temporarily increase heart rate [51].

Resting respiratory rate (RRR) is an easily measurable clinical parameter for clinicians and pet owners, highlighting its importance. Healthy dogs typically exhibit a RRR below 40 breaths per minute (bpm) in a clinical scenario [52–54] and below 30 bpm at home [53]. Our findings are consistent with previous studies indicating an increase in respiratory rate from stage B2 to stage C [50,53]. Capillary refill time (CRT) is a simple tool to assess peripheral perfusion, circulatory stability, and hydration status [54,55]. Our study found that CRT increased as MMVD progressed, which may indicate deteriorating haemodynamic [56]. In human medicine, it is commonly used to assess critically ill patients with cardiopulmonary pathologies [55]. CRT's usefulness may be affected by inter-observer variability, and it is recommended to be used in conjunction with other diagnostic tests [56–58].

There were no significant differences in systolic blood pressure measurements between groups. Systemic hypertension can cause irreversible damage to organs, while systemic hypotension can result in circulatory shock due to inadequate tissue perfusion [59,60]. A decrease in systolic blood pressure with MMVD progression has been documented [6,60]. While the current study employed the same blood pressure measurement protocol, the absence of significant findings between groups could be attributed to the individual variability among dogs, the level of excitement or relaxation exhibited by patients, the ease of patient handling, and the relaxed and comfortable environmental conditions where measurements were conducted.

While the study conducted provides valuable insights, it also carries limitations. First, dogs were studied only once. Other studies follow up and observe variations over time [6,12], making their data more robust by following a repeated measures model. Second, despite the efforts made to establish consistent diagnostic criteria, the multicentre approach of the study resulted in some subjectivity in collecting data from the physical and echocardiographic examinations. Experienced veterinarians performed the echocardiographic measurements, which an ACVIM board-eligible professional reviewed. However, inter-observer variability in measurements may result in differences in specific measurements, which could affect the ACVIM classification of a dog [60,61] and, consequently, the accuracy of the machine learning algorithms. Third, the study included a diverse dog population with different breeds, ages, and sizes, which was essential for developing classification trees using machine learning techniques. Although many breeds are included in this study, it is worth noting the absence of dogs from breeds with a high predisposition to the development of MMVD, such as the CKCS [4], which could affect the results obtained. This may be due to the limited presence of CKCS in the countries where the study was conducted, which may be a limiting factor of this study. The inclusion of this breed in future studies may improve the results of our hypothesis. Concurrent diseases were not excluded, which mirrors the reality of geriatric patients with multiple comorbidities. Fourthly, owners' subjective assessments may have been influenced by concomitant pathologies, his personal opinions and emotional state, and the dog's clinical signs, making it challenging to differentiate cardiac-related signs. Similar observations have been seen in human patients with congenital heart disease and high anxiety levels [62] and in patients who withhold medical information due to embarrassment or ignorance [63,64]. The efficacy of machine learning techniques relies on proper pre-processing of data, precise training of models, and refinement of systems [65]. These factors pose significant challenges that require additional efforts to overcome. As such, exploring and implementing strategies that address these challenges are crucial to enhancing the accuracy and reliability of machine learning processes.

5. Conclusions

Machine learning techniques, based on a quality of life survey, clinical history, and physical examination, can be helpful additional tools when approaching dogs with MMVD in the first-opinion scenario. In most cases, the proposed model could classify healthy dogs and patients in stages B and C, according to the ACVIM classification for MMVD. However, it still faces difficulties differentiating between stages B1 and B2 and determining the advanced stages of the disease, C and D. Furthermore, the FETCH-Q survey showed that owners were aware of their dogs' deterioration as MMVD progressed. To validate the algorithms, conducting clinical prospective studies on patients at different stages of MMVD would be necessary.

Author Contributions: J.E.-M. and J.I.R.: study design, analysis, and interpretation of data; drafting of the manuscript; data analysis: J.I.R. and L.D., J.E.-M., J.I.R., J.A.M.-A., O.M.-U., Y.R.-D., J.I.M., A.C.-V. and L.G.-G.: revision of the manuscript. All authors participated in the discussion of the results, corrected, read, and approved the final manuscript. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement: Data collection and storage were performed with owner written consent, and the animal study protocol was approved by the Institutional Review Ethics and Welfare Committee of CEU Cardenal Herrera University (Spain) with registered number CEEA 22/06 for animal studies.

Informed Consent Statement: Informed consent was obtained from all subjects (owners) involved in the study.

Data Availability Statement: Data supporting the reported results can be sent to anyone interested by contacting the corresponding author.

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Conflicts of Interest: The authors declare no conflicts of interest.

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4.3.-

A New Graphical Method for Displaying Two-Dimensional Echocardiography Results in Dogs: Comprehensive Analysis of Results of Diagnostic Imaging Organized in a BOX (CARDIOBOX)

Federico J. Curra-Gagliano, Martín Ceballos, José I. Redondo and **Javier Engel-Manchado**

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A New Graphical Method for Displaying Two-Dimensional Echocardiography Results in Dogs: Comprehensive Analysis of Results of Diagnostic Imaging Organized in a BOX (CARDIOBOX)

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Simple Summary: Rapid and accurate interpretation of echocardiographic results in dogs is crucial to good clinical decision-making. In this study, we developed and evaluated a graphical method called CARDIOBOX, designed to simplify the visual representation of echocardiographic values. CARDIOBOX is a system consisting of three overlapping boxes, which house nine boxes. Each box represents a specific range of echocardiographic values. Its design is based on the results of an analysis of 2967 dogs. In this process, percentiles and cut-off points were established to delimit the boxes corresponding to normal and abnormal ranges. To evaluate the efficacy of CARDIOBOX, 55 veterinarians participated in the interpretation of echocardiographs of dogs, presented in two different formats: using CARDIOBOX and exclusively using numerical reference tables. The time taken to interpret and the accuracy of responses in each format were recorded. The results indicated that CARDIOBOX enabled veterinarians to interpret echocardiographic values more quickly without decreasing interpretation efficiency. This study shows that CARDIOBOX allows veterinarians to interpret and apply echocardiographic results more quickly and effectively, significantly facilitating clinical decision-making.

Abstract: Introduction and objective: Rapid and efficient interpretation of echocardiographic findings is critical in clinical decision-making. This study aimed to design and validate a new graphical method, called CARDIOBOX, to represent echocardiographic findings in dogs. Methods: A prospective, observational, exploratory cohort study was conducted over three years. The design of CARDIOBOX was based on baseline values obtained from 802 healthy dogs and 2165 ill dogs. Using these data, a graph consisting of nine boxes was built to show the intervals of the different echocardiographic measurements. Validation of the method was performed by a survey of 55 veterinarians, who compared the use of CARDIOBOX with the use of numerical tables. Results: CARDIOBOX demonstrated significantly faster interpretability ($p < 0.05$) without reducing its effectiveness. In addition, the staff surveyed considered it easy to use and interpret. Conclusions: The introduction of CARDIOBOX emerges as a resource that facilitates rapid and efficient interpretation of echocardiographic findings in dogs. This new graphical method is presented

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as a valuable tool for veterinary professionals in clinical decision-making in the field of veterinary cardiology.

Keywords: echocardiography; dogs; graphic method; graphic result interpretation; veterinary cardiology; clinical decision-making

1. Introduction

The exact prevalence of cardiac disease in dogs is unknown, although it may be around 10% of cases seen in daily clinical practice [1]. Echocardiography is the technique of choice in diagnosing and staging most cardiac diseases [2,3]. Echocardiographic data are usually interpreted employing tables, which use allometric formulas to predict average values based on a dog's weight [4].

Interpreting numerical values can be challenging for the human brain, designed to interpret graphs more effectively than numbers [5–7]. Human medicine has developed new strategies to present data innovatively and impactfully [8]. The efficient design of new graphical representation systems requires fast, simple, and effective implementation and interpretation, and they have been successfully employed in clinical pathology [9].

Thus, a new way of displaying these complex echocardiographic measurements could be through their graphic representation, normalising the values beforehand so that they can be easily interpreted independently of the animal's weight, as in the allometric tables used in veterinary cardiology [4]. Given the challenges faced by patients of varying sizes and weights in a clinical setting, this study sought to create, standardise, explain, and assess a visual system for interpreting echocardiographic findings, called CARDIOBOX (Comprehensive Analysis of Results of Diagnostic Imaging Organized in a BOX).

The objectives of this study were as follows: (a) to design a method for graphical representation of standardised echocardiographic results and (b) to validate the method's usefulness in a clinical setting. We hypothesise that CARDIOBOX allows the representation of echocardiographic numerical results in a simple graph that is easy and efficient to interpret and that its interpretation is faster than the traditional numerical method.

2. Material and Methods

This project received authorisation from the Institutional Committee for the Care and Use of Experimental Animals (CICUAL) at the Faculty of Veterinary Sciences, University of Buenos Aires, Argentina (Project 2019/49). All animal owners were informed about this study's objectives, methods, and purpose and gave their informed consent, which was also signed by the veterinarians involved in this clinical study. This study comprised two phases: (1) the design and standardisation of the CARDIOBOX method using echocardiographic values in dogs as a reference and (2) assessing the method's effectiveness in a clinical context.

2.1. Design and Standardisation of the CARDIOBOX Method

This descriptive, cross-sectional study was conducted to create and standardise the CARDIOBOX graphical method for assessing dog echocardiographic results. This study included 2967 dogs.

2.1.1. Patient Selection, Assessment, and Classification

All animals underwent a comprehensive evaluation, including anamnesis, detailed physical examination, and complementary diagnostic tests. These tests involved measuring systolic, diastolic, and mean arterial blood pressure with a SunTech Vet 30 oscillometric monitor (SunTech Medical Inc., Morrisville, USA), performing a six-channel electrocardiogram using a TEMIS model TM-300 digital electrocardiograph (Temis Tech., Cordoba, Argentina), right lateral and ventrodorsal radiographic views, and haematology including complete blood count (red blood cells, white blood cells, and platelets, as well as haemoglobin and haematocrit). Biochemistry, including glucose, urea, creatinine, alkaline phosphate (ALKP), cholesterol, alanine aminotransferase (ALT), total protein, globulin, albumin, and electrolytes (sodium, potassium, and chloride), was also measured.

Based on these assessments, animals were assigned to one of two groups according to health status. The HEALTHY GROUP (802 dogs) comprised dogs with no cardiac or systemic disease signs, excluding breeds with specific echocardiographic reference values (e.g., greyhounds, Labradors). Dogs diagnosed with cardiac disease formed the CARDIAC GROUP (2165 dogs). Together, the HEALTHY GROUP and the CARDIAC GROUP were called the TOTAL GROUP (2967 dogs).

2.1.2. Echocardiographic Evaluation

Echocardiography was performed following standard clinical recommendations [10] using a SonoScape A6 ultrasound machine (SonoScape Medical Corp., Guangdong, China) with 5–9 MHz microconvex probes and a Vinno 5 ultrasound machine (Vinno, Suzhou City, China) using 1–5 MHz adult phased array and 5–11 MHz microconvex probes. The left atrium and ascending aorta diameters were measured in B-mode in the right parasternal short-axis view at early diastole to calculate the left atrium/aorta (LA/Ao) index [11]. Additionally, in the right parasternal short-axis M-mode view at the level of the papillary muscles, the following parameters were measured:

- Interventricular septal thickness in diastole and systole (IVSd and IVSs)
- Left ventricular internal diameter in diastole and systole (LVIDd and LVIDs)
- Left ventricular free-wall thickness in diastole and systole (PLVWd and PLVWs)
- The principal investigator (FCG) performed all echocardiographic scans, and one additional investigator (JEM), each with over ten years of experience and specialised accreditation in veterinary cardiology, reviewed the images. Images that did not meet quality standards for accurate measurements were excluded from the analysis. Echocardiographic values for each patient were standardised to account for body weight variations using a formula derived from Cornell et al. (2004) [4]:

Standardised Value = Absolute Value (cm)/Weight (kg) ^{B}, where B is the constant *b* in the allometric equation defined by Cornell et al. (2004) [4].

2.1.3. Construction of the CARDIOBOX Graphical Method

The CARDIOBOX is a visual tool developed to evaluate graphically echocardiographic parameters in dogs. Each parameter is represented within a row of nine boxes, divided into three categories: values below the normal range (boxes 1, 2, and 3), values within the normal range (central grey boxes 4, 5, and 6), and values above the normal range (boxes 7, 8, and 9). Each box represents a specific percentile range, allowing an intuitive interpretation of a patient's data against reference values derived from a healthy population (see Figure 1).

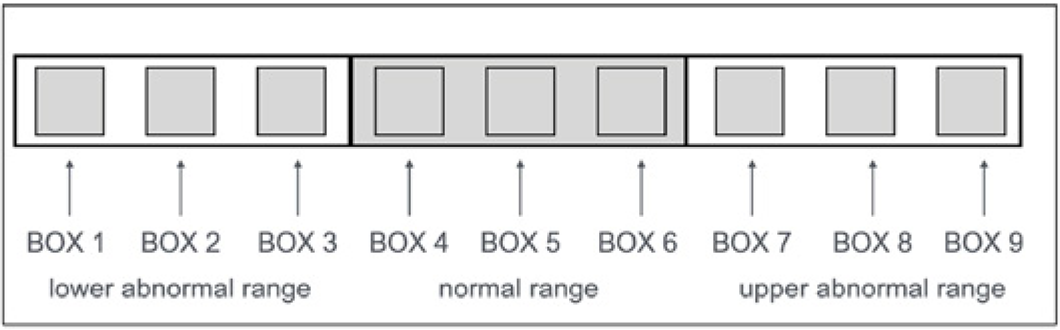

Figure 1. Basic structure of the CARDIOBOX. A marker indicates each parameter in one of the nine boxes: boxes 1, 2, and 3 for values below the normal range (white); boxes 4, 5, and 6 for values within the normal range (grey central rectangle); and boxes 7, 8, and 9 for values above the normal range (white).

The boundaries for each box in a specific parameter were determined as follows:

1. Define overall bounds (minimum and maximum): The minimum and maximum values were established using data from the TOTAL POPULATION, including HEALTHY and CARDIAC groups (n = 2967). The minimum value defines the lower bound of box 1, while the maximum value defines the upper bound of box 9.
2. Calculate boxes 4, 5, and 6 (normal range): The central normal range was established using data from the HEALTHY GROUP (n = 802). This standard range spans from the 1st to the 99th percentiles and consists of three central boxes. The intervals between boxes 4, 5, and 6 are equal, with box five centred precisely at the median:
   - Box 5 is centred on the median (50th percentile), representing the midpoint of the normal distribution.
   - Box 4 begins at the 1st percentile of the data of the HEALTHY GROUP and extends to a central boundary between the 1st percentile and the median, defining the transition from box 4 to box 5.
   - Box 6 begins at this equidistant boundary on the other side of the median and extends to the 99th percentile of the data of the HEALTHY GROUP.
3. Calculate boxes 1, 2, 3 and 7, 8, 9 (values outside the normal range): To represent values below and above the normal range, the following steps were applied:
   - Boxes 1, 2, and 3 capture values below the 1st percentile of the normal range (the lower bound of box 4). These boxes are set with equidistant boundaries that span the range from the minimum value (the lower bound of box 1) to the start of the normal range.
   - Boxes 7, 8, and 9 capture values above the 99th percentile of the normal range (the upper bound of box 6). These boxes are also set with equidistant boundaries, covering the range from the end of the normal range to the maximum value (the upper bound of box 9).

2.2. Validation of the CARDIOBOX

A survey was designed to assess the clinical utility of the CARDIOBOX graphical tool. This survey was created following the CHERRIES checklist [12]. The survey was developed and hosted on the JOTFORM platform (https://form.jotform.com/223278319852059, last accessed on 19 August 2023, also accessible on Supplementary Materials Figure S1), automatically recording each question's response time. The survey was active from 25 November to 6 December 2022. It was distributed in specialised veterinary groups, including cardiology, anaesthesiology, and general clinical practice. Participation was anonymous and voluntary.

The survey included four prominent clinical cases with echocardiographic findings: two patients without pathology and two with myxomatous mitral valve disease (MMVD) at different stages. Each case was presented using two formats: (a) a panel of numerical echocardiographic values accompanied by a reference table and (b) a CARDIOBOX chart displaying the values graphically.

The four cases were presented randomly, two using the CARDIOBOX method (one healthy and one pathological case) and two using the traditional numerical method with reference values (one healthy and one pathological case).

Key variables studied included response time (automatically measured by JOTFORM) and the percentage of correct answers for the seven variables under analysis. Additionally, participants were asked to rate the effectiveness and ease of use of the CARDIOBOX method compared to the traditional numerical format using a 5-point Likert scale. A final question gauged their willingness to adopt CARDIOBOX in clinical practice.

Statistical Analysis

The statistical analysis was done using the R language program (4.4.2). The first step is calculating the percentiles for the studied standardised echocardiographic variables to build the CARDIOBOX graph.

In the second step, a detailed statistical analysis was conducted to assess the effect of the presentation method (CARDIOBOX vs. numerical) and the presence of pathology on response time and accuracy. It was also used to analyse participants' perceptions using Likert-type questions.

The parameters analysed in the survey were response time (TIME) and percentage of correct answers (CORRECT), which were compared in two cases: CARDIOBOX and cases with numerical results and reference tables. Using the Shapiro–Wilk test, the null hypothesis of normality could be rejected. As the response data (time and correct answers) did not have a normal distribution, to validate the results of the form and detect statistical differences, the Wilcoxon test was used to compare the variables' percentage of correct answers and response time between groups. The significance level was set at 5% ($p < 0.05$).

Descriptive statistics, such as means and standard deviations, were calculated for response time and percentage of correct responses, grouped by method of presentation and presence of pathology. Shapiro–Wilk normality tests indicated that the data did not follow a normal distribution, justifying non-parametric tests in subsequent analyses.

The non-parametric Friedman test for repeated-measures data was applied to compare the median response time and percentage of correct responses among the different cases. After finding significant differences, post hoc comparisons were performed using the Wilcoxon paired signed-rank test with Bonferroni correction to adjust the significance level due to multiple comparisons. A linear mixed model was also used to analyse the effect of the method of presentation, presence of pathology, and order of presentation on response time and percentage of correct responses. These models allow for repeated measures of data and intra- and inter-subject variability. The lmer function of the lme4 R package was used, incorporating fixed effects for the method of assessment, the presence or absence of pathology, and the order in which cases were presented, as well as their interactions, in addition to a random effect for the participant's identifier (identifier variable). A similar model was fitted for the percentage of correct answers.

Cronbach's alpha coefficient was calculated to measure the reliability of the scales used in the questionnaire and assess the internal consistency of the Likert-type questions related to the perceived ease of use and effectiveness of CARDIOBOX.

3. Results

A total of 2967 dogs participated in this study. Of these, 802 were classified as healthy, forming the HEALTHY GROUP, while 2165 were diagnosed with cardiac diseases and were included in the CARDIAC GROUP. Table 1 shows the calculated percentiles for data parameters for the HEALTHY GROUP and TOTAL GROUP. The CARDIOBOX boxes' limits were determined and shown in Table 2 using this data.

Table 1. Calculated percentiles using the normalised data from 802 healthy dogs and the total population (n = 2967).

	Percentile										
HEALTHY GROUP	**Min**	**1**	**2.5**	**5**	**25**	**50**	**75**	**95**	**97.5**	**99**	**Max**
AIDn	0.49	0.56	0.59	0.62	0.70	0.75	0.82	0.92	0.96	1.00	1.23
IVSSDn	0.25	0.29	0.31	0.32	0.38	0.42	0.46	0.54	0.56	0.58	0.69
LVIDDn	0.84	1.12	1.19	1.22	1.38	1.47	1.55	1.66	1.68	1.69	1.74
PLVWDn	0.23	0.26	0.29	0.30	0.37	0.42	0.47	0.56	0.58	0.62	0.69
IVSSn	0.33	0.43	0.43	0.46	0.54	0.59	0.64	0.74	0.77	0.82	0.92
LVIDSn	0.28	0.47	0.54	0.58	0.73	0.82	0.90	1.01	1.04	1.06	1.09
PLVWSn	0.37	0.41	0.44	0.47	0.54	0.61	0.68	0.77	0.80	0.83	0.95
TOTAL POPULATION											
AIDn	0.35	0.58	0.61	0.64	0.73	0.80	0.91	1.20	1.37	1.52	2.22
IVSSDn	0.22	0.28	0.30	0.32	0.38	0.43	0.48	0.56	0.60	0.65	0.84
LVIDDn	0.68	1.07	1.16	1.22	1.41	1.54	1.69	2.12	2.29	2.46	3.04
PLVWDn	0.19	0.27	0.29	0.31	0.38	0.43	0.49	0.57	0.61	0.65	0.86
IVSSn	0.11	0.40	0.44	0.47	0.55	0.62	0.68	0.81	0.85	0.90	1.22
LVIDSn	0.24	0.45	0.52	0.59	0.75	0.86	0.97	1.18	1.34	1.58	2.55
PLVWSn	0.32	0.41	0.44	0.47	0.56	0.63	0.70	0.81	0.85	0.89	1.12

AIDn: normalised left atrial internal diameter in diastole. IVSSDn: normalised interventricular septal thickness in diastole. LVIDDn: normalised left ventricular internal diameter at diastole. PLVWDn: normalised left ventricular free-wall thickness in diastole. IVSSn: normalised interventricular septal thickness in systole. LVIDSn: normalised left ventricular internal diameter at systole. PLVWSn: normalised left ventricular free-wall thickness in systole.

Table 2. Limits for each box for constructing the CARDIOBOX for the studied echocardiographic variables.

	BOX 1		BOX 2		BOX 3		BOX 4		BOX 5		BOX 6		BOX 7		BOX 8		BOX 9	
AIDn	0.35	0.41	0.42	0.48	0.49	0.55	0.56	0.70	0.71	0.85	0.86	1.00	1.01	1.26	1.27	1.52	1.53	2.22
IVSSDn	0.22	0.24	0.25	0.26	0.27	0.28	0.29	0.39	0.40	0.48	0.49	0.58	0.59	0.61	0.62	0.65	0.66	0.84
LVIDDn	0.68	0.82	0.83	0.96	0.97	1.11	1.12	1.31	1.32	1.50	1.51	1.69	1.70	2.07	2.08	2.46	2.47	3.04
PLVWDn	0.19	0.21	0.22	0.23	0.24	0.25	0.26	0.38	0.39	0.50	0.51	0.62	0.63	0.63	0.64	0.65	0.66	0.86
IVSSn	0.11	0.21	0.22	0.32	0.33	0.42	0.43	0.56	0.57	0.69	0.70	0.82	0.83	0.85	0.86	0.90	0.91	1.22
LVIDSn	0.24	0.31	0.32	0.39	0.40	0.46	0.47	0.67	0.68	0.86	0.87	1.06	1.07	1.32	1.33	1.58	1.59	2.55
PLVWSn	0.32	0.35	0.36	0.38	0.39	0.40	0.41	0.55	0.56	0.69	0.70	0.83	0.84	0.86	0.87	0.89	0.90	1.12

AIDn: normalised left atrial internal diameter in diastole. IVSSDn: normalised interventricular septal thickness in diastole. LVIDDn: normalised left ventricular internal diameter at diastole. PLVWDn: normalised left ventricular free-wall thickness in diastole. IVSSn: normalised interventricular septal thickness in systole. LVIDSn: normalised left ventricular internal diameter at systole. PLVWSn: normalised left ventricular free-wall thickness in systole.

Validation of the CARDIOBOX

A total of 55 surveys were collected. Results indicated that evaluation times were significantly shorter with CARDIOBOX than with the traditional numerical method ($p < 0.0001$), with no significant time difference between cases with or without pathology (CARDIOBOX: $p = 0.28$; Numeric: $p = 0.80$). CARDIOBOX also yielded a higher percentage of correct answers compared to the numerical method ($p = 0.02793$), and there was no significant difference in accuracy between cases with and without pathology as shown in Table 3 (CARDIOBOX: $p = 1$; Numeric: $p = 0.224$).

Table 3. Mean time and standard deviation employed in the evaluation of echocardiographic data from the cases using the traditional numerical method and the proposed graphical method (CARDIOBOX) and percentage of correct answers in evaluating echocardiographic data of the cases using the conventional numeric method and the proposed graphical method (CARDIOBOX).

Method	Pathology	Mean Time	SD Time	Correct
CARDIOBOX	NO	65	35	97.7%
CARDIOBOX	YES	72	32	94.6%
Numeric	NO	109	52	92.7%
Numeric	YES	128	61	93.5%

Participants' perceptions of the CARDIOBOX graphical tool were also assessed using Likert-type questions, and the effect of the presentation method (traditional vs. CARDIOBOX) was analysed.

Mean scores and standard deviations were obtained for two critical aspects of the tool. Ease of use received a mean score of 4.49 (out of 5) with a standard deviation of 0.98, indicating that participants perceived the tool as easy to use. The tool's effectiveness received a mean score of 4.18 (out of 5) with a standard deviation of 1.19, suggesting that users consider CARDIOBOX effective for interpreting echocardiographic results.

The frequency analysis showed that most participants gave high scores in terms of ease of use: 40 people rated it a five, 7 a four, and only 8 gave scores of three or lower. For the tool's effectiveness, 32 participants rated it a five and 10 a four, while 13 scored three or less. Results are shown in Figure 2.

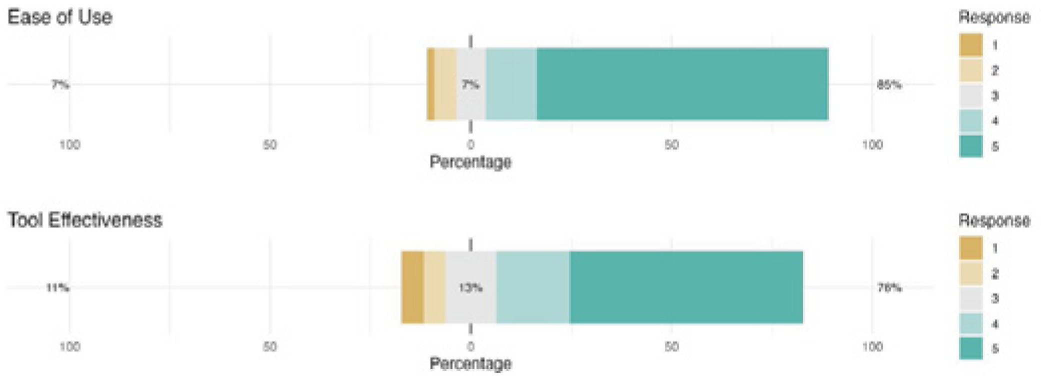

Figure 2. Likert graphs for perceived ease of use and tool effectiveness.

Interest in the future implementation of CARDIOBOX was high, with 44 respondents (80%) considering it beneficial for patient information. A smaller group of 10 respondents (18.18%) expressed uncertainty about its usefulness, while only 1 (1.82%) deemed it irrelevant.

Cronbach's alpha was calculated for the first two Likert-type questions (ease of use and effectiveness of the tool), obtaining a value of 0.76. This result indicates good internal consistency between items, supporting the measures' reliability.

For the analysis of turnaround time and accuracy, a linear mixed model was fitted to assess the effect of presentation method, presence of pathology, and order of presentation on turnaround time. The results showed that the traditional method was associated with a significant increase in turnaround time compared to CARDIOBOX. Specifically, using the conventional method increased response time by 49.49 s (standard error = 4.65, t-value = 10.64). Pathology had no significant effect on response time (t-value = −0.18), nor did pathology significantly affect the order of presentation (t-value = 1.21).

A linear mixed model was used to calculate the percentage of correct answers. The results indicated that the traditional method tended to slightly decrease the rate of correct answers compared to CARDIOBOX, with a reduction of 0.0299 (standard error = 0.0154, t-value = −1.94). However, this effect did not reach statistical significance. The presence of pathology showed no significant impact on the accuracy of responses (t-value = 1.47), and the order of presentation had no considerable effect either (t-value = 1.27). Analysis of the impact of the order of presentation revealed that this factor had no significant influence on either response time or the percentage of correct answers. This indicates that no learning or fatigue effects were observed that could bias this study's results.

The Likert-type questions indicated a positive trend in participants' perceptions of CARDIOBOX. Most participants gave high ratings for ease of use and effectiveness, and many showed interest in its future implementation.

4. Discussion

The CARDIOBOX graphical method was developed to provide a standardised, efficient, and intuitive means for interpreting dog echocardiographic parameters. Our findings support our hypothesis that CARDIOBOX could facilitate rapid and reliable clinical assessments. Clinicians found the tool user-friendly and effective in distinguishing between healthy and pathological cases, with significantly faster assessment times than traditional numerical methods, such as the Cornell allometric scaling charts [4].

Defining the range limits within the nine CARDIOBOX boxes was critical for clinical accuracy and utility. The method was constructed using a percentile-based approach, where the outer bounds (minimum and maximum) were defined from the TOTAL POPULATION, which included both healthy and cardiac groups. At the same time, the central boxes (4, 5, and 6) were determined exclusively from the HEALTHY GROUP. This combined approach aims to balance sensitivity for pathological cases with specificity for healthy cases, providing a reliable diagnostic aid for veterinarians.

Using the TOTAL POPULATION to define the minimum and maximum values (boxes 1 and 9) ensures that CARDIOBOX captures the full range of values encountered in practice, enhancing sensitivity by encompassing the entire data spectrum. This is essential, as a narrow outer range might exclude clinically relevant values. Including data from both healthy and cardiac groups at the extremes allows CARDIOBOX to reflect the broad echocardiographic variation seen in practice, making it suitable for diverse cases [4,13]. However, defining the central boxes (4, 5, and 6) from the HEALTHY GROUP ensures that standard range cutoffs remain strictly derived from non-pathological values, preserving high specificity. Previous research suggests that using only healthy populations for reference intervals is crucial for avoiding skewed ranges, which could misrepresent the normal distribution [3].

Another potential approach to constructing the CARDIOBOX would be to define the central and extreme boxes exclusively from the HEALTHY GROUP data. While this might yield a tighter distribution, such a configuration would likely result in pathological values clustering at the outermost edges (boxes 1 and 9). This clustering could reduce diagnostic efficacy, as it may limit the method's ability to differentiate degrees of abnormality, making distinguishing between mild and severe pathology harder. Practical diagnostic tools benefit from capturing a spectrum of abnormal values, enabling clinicians to detect deviations at varying stages [8]. By using healthy-only data to set the normal range while relying on the broader total population for the extremes, CARDIOBOX enhances both specificity and sensitivity across clinical cases.

CARDIOBOX was validated by 55 veterinarians, who responded positively to its ease of use and effectiveness. While the feedback suggests high user satisfaction, expanding this study to include veterinarians with varying experience in cardiology would provide more comprehensive validation. Additional insights from general practitioners and specialists would help confirm that CARDIOBOX is universally accessible. Given that veterinary technology can sometimes face resistance due to learning curves, the ease-of-use scores indicate that this tool could integrate smoothly into clinical practice, regardless of users' prior experience [13].

A further consideration is this study's focus on dogs under 20 kg, which restricts generalisability to larger breeds with differing cardiac morphologies. The variability in cardiac parameters across breeds underscores the importance of expanding CARDIOBOX to include larger dogs and diverse morphologies and validating its applicability for other canine populations. Further research in this direction would strengthen CARDIOBOX as a versatile tool and extend its clinical relevance.

Standardised echocardiographic values adjusted for weight through allometric scaling ensure consistency in measurement across dogs of different body sizes (see Supplementary Materials Tables S1 and S2). However, a more detailed explanation of how allometric scaling integrates with the graphical method could provide a more robust theoretical basis. This explanation would enhance readers' understanding of the method's applicability across different body sizes, further supporting CARDIOBOX's validity as a tool for diverse veterinary populations.

Although this study provides valuable cross-sectional data, longitudinal studies could offer additional insights into how well CARDIOBOX performs over time, especially in monitoring disease progression or assessing treatment efficacy. Applying CARDIOBOX in a longitudinal context could reveal its potential for tracking individual changes in echocardiographic parameters, broadening its utility in veterinary practice.

In human medicine, graphical data representation is widely recognised as beneficial for diagnostic accuracy, interpretive speed, and error reduction, mainly when it balances central tendencies with extremes [14]. CARDIOBOX follows these principles by adopting percentile-based limits, enhancing sensitivity and specificity for a reliable, clinically useful tool. By employing a clear, percentile-based visual differentiation, CARDIOBOX supports prompt and accurate decision-making in clinical settings [15]. Additionally, user feedback in this study highlights the positive reception of CARDIOBOX's layout, suggesting that graphical tools of this type could be beneficial across veterinary and human medicine for complex data interpretation [13].

The unique advantages of this new graphical method are summarized as follows: (A) It solves a critical problem. Traditional numerical representation of echocardiographic data often leads to delays and errors in interpretation, particularly in scenarios requiring quick decisions or for practitioners without immediate access to reference materials (see Supplementary Materials Figure S2). By providing a straightforward graphical representation, the method significantly reduces interpretation time while maintaining diagnostic accuracy. Furthermore, (B) it fills an existing gap. While echocardiography and its result-representation methods are well-established, no simple and easily adaptable method exists for future integration into ultrasound software. This approach bridges the gap by enabling automated, reliable, and simplified interpretations directly within ultrasound devices, empowering clinicians to make immediate decisions without external resources. Lastly, (C) it simplifies and modernizes an existing solution. Beyond its graphical design, it is built to seamlessly integrate with emerging technologies such as Deep Learning and Artificial Intelligence (AI). These advancements promise faster and more accurate interpretations, while the system's scalability allows practitioners to build personalized reference tables tailored to their patients and clinical approaches, making it a dynamic and evolving tool for modern veterinary practice. It has the potential to be integrated into ultrasound software, facilitating real-time graphical representation and automatic interpretation of echocardiographic data, which further enhances its utility in clinical settings. CARDIOBOX could integrate AI and machine learning to enhance diagnostic capabilities. Developing automated algorithms for segmentation and measurement could provide clinicians with immediate, standardized echocardiographic assessments. Tests in simulated environments show that using computer vision in ultrasound devices can streamline data acquisition and offer real-time feedback in CARDIOBOX outputs. These improvements would aid in monitoring disease progression and treatment efficacy, expanding CARDIOBOX's impact in veterinary cardiology.

This study has certain limitations. At present, this first study does not consider all the echocardiographic parameters. In this publication, we have focused on introducing the CARDIOBOX system using the main absolute parameters that vary with body weight. In addition, the CARDIOBOX system is validated on breeds with standard weight-adjusted reference tables, excluding Greyhounds, Labradors, and other giant breeds that are not represented in the demographic studied, as well as specific brachycephalic breeds that require customised reference tables. Future research should investigate the applicability of this system to these excluded breeds, also exploring variations between breed types (brachycephalic, mesocephalic, and dolichocephalic) and size (small vs. giant). In addition, extending the research to other species, such as cats and even humans, is essential to realise the full potential of this system. In conclusion, CARDIOBOX represents an effective tool for interpreting echocardiographic results in dogs, significantly improving interpretation speed without compromising diagnostic accuracy. The balance between sensitivity and specificity through the combined use of healthy and total population data enhances its applicability across clinical scenarios, from general practice to specialised cardiology. However, expanding the tool's validation to larger breeds, and conducting longitudinal studies would further strengthen CARDIOBOX's potential. These findings suggest that CARDIOBOX could become a widely applicable alternative to traditional methods, advancing clinical data interpretation and optimising patient care in veterinary medicine.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/vetsci12010034/s1; Figure S1: Form template used to validate the Cardiobox (jotform English.docx). Table S1: Table showing reference values of echocardiographic parameters using the CARDIOBOX system for dogs weighing up to 17 kg; Table S2: Table showing reference values of echocardiographic parameters using the CARDIOBOX system for dogs weighing 20 to 50 kg. Figure S2: (CARDIOBOX REPORT.doc) ecochardiographic report including the template of Cardiobox.

Author Contributions: F.J.C.-G. and J.E.-M. study design, interpretation of data and drafting of manuscript; F.J.C.-G. and J.I.R. data analysis; F.J.C.-G., J.E.-M., J.I.R. and M.C. revision of manuscript. All authors have read and agreed to the published version of the manuscript.

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Informed Consent Statement: Informed consent was obtained from all subjects involved in this study.

Data Availability Statement: Data supporting the reported results can be sent to anyone interested by contacting the corresponding author.

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Conflicts of Interest: The authors declare no conflicts of interest.

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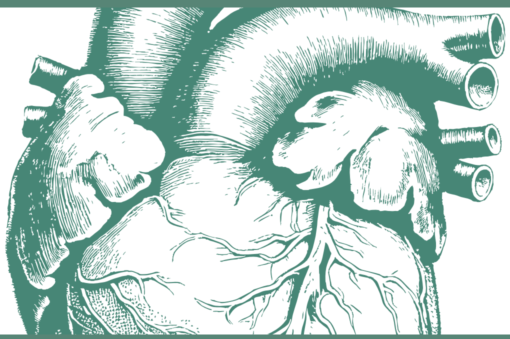


5.-
Conclusiones/Conclusions

5.1.- Los resultados de nuestro trabajo apoyan la validez de la versión española del cuestionario **FETCH-Q™** para evaluar la evolución de la calidad de vida de los pacientes caninos con MMVD, a medida que evoluciona la enfermedad en los distintos estadios ACVIM.

5.2.- Las técnicas de aprendizaje automático, basadas en una encuesta de calidad de vida, el historial clínico y la exploración física, pueden ser herramientas adicionales útiles a la hora de abordar perros con MMVD en las clínicas generalistas. En la mayoría de los casos, el modelo propuesto pudo clasificar perros sanos y pacientes en estadios ACVIM B y C.

5.3.- El sistema **CARDIOBOX** representa una herramienta eficaz para interpretar los resultados ecocardiográficos en perros, mejorando significativamente la velocidad de interpretación sin comprometer la precisión diagnóstica. Estos resultados sugieren que **CARDIOBOX** podría convertirse en una alternativa ampliamente aplicable a los métodos tradicionales de datos clínicos y optimizar la atención al paciente en medicina veterinaria.

5.1.- The results of our work support the validity of the Spanish version of the **FETCH-Q™** questionnaire in evaluating the evolution of quality of life for canine patients with MMVD as the disease progresses through the various ACVIM stages.

5.2.- Based on a quality-of-life survey, clinical history, and physical examination, machine learning techniques may serve as helpful additional tools for treating dogs with MMVD in generalist clinics. In most cases, the proposed model could classify healthy dogs as well as ACVIM stage B and C patients.

5.3.- The **CARDIOBOX** system is an effective tool for interpreting echocardiographic findings in dogs. It significantly enhances the speed of interpretation without compromising diagnostic accuracy. These results indicate that **CARDIOBOX** could serve as a widely applicable alternative to traditional clinical data methods and optimise patient care in veterinary medicine.

6.-

Resumen/Sumary

En el primer trabajo se evaluó la utilidad de la encuesta de calidad de vida **FETCH-Q™** en pacientes caninos con MMVD con tutores de habla hispana. El objetivo fue evaluar si los datos de la encuesta se correlacionaban con el empeoramiento de los signos clínicos a medida que avanzaba el estadio ACVIM de la enfermedad mixomatosa de la válvula mitral. Se estudiaron 228 perros de 51 tutores, de 7 clínicas privadas y 2 hospitales universitarios, y se hizo un seguimiento a dos semanas para repetir la prueba. Nuestro trabajo confirma que el cuestionario **FETCH-Q™** puede ser utilizado para evaluar la evolución clínica de la MMVD.

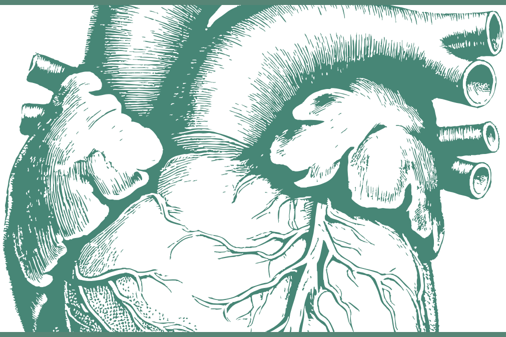
La enfermedad mixomatosa de la válvula mitral es la cardiopatía adquirida más frecuente en los perros. La prueba estándar para su diagnóstico definitivo es la ecocardiografía. El objetivo del segundo trabajo fue desarrollar una herramienta que utilice una encuesta de calidad de vida, una anamnesis estructurada y una exploración física para predecir los estadios de la clasificación del Colegio Americano de Medicina Interna Veterinaria. Identificar con precisión el estadio de un paciente es crucial para evaluar cuándo debe iniciarse el tratamiento y adaptarlo a su estadio ACVIM. El estudio analizó 1011 perros de 23 hospitales, y los resultados mostraron que la mayoría de los pacientes se clasificaron con éxito en el grupo de control (perros sanos), estadio B (perros con soplo cardíaco pero asintomáticos) y estadio C (perros con insuficiencia cardíaca). Sin embargo, no se obtuvieron resultados eficientes para diferenciar entre el estadio B1 (perros con soplo cardíaco y sin agrandamiento del corazón) y el estadio B2 (perros con soplo cardíaco y agrandamiento del corazón).

En este trabajo, desarrollamos y evaluamos el método **CARDIOBOX**, diseñado para simplificar la representación visual de los valores ecocardiográficos. Para evaluar la eficacia de **CARDIOBOX**, 55 veterinarios participaron en la interpretación de ecocardiografías de perros, presentadas en dos formatos diferentes: utilizando **CARDIOBOX** y utilizando exclusivamente tablas numéricas de referencia. Se registraron el tiempo empleado en la interpretación y la precisión de las respuestas en cada formato. Los resultados indicaron que **CARDIOBOX** permitía a los veterinarios interpretar más rápidamente los valores ecocardiográficos sin disminuir la eficacia de la interpretación. Este estudio demuestra que **CARDIOBOX** permite a los veterinarios interpretar y aplicar los resultados ecocardiográficos con mayor rapidez y eficacia, facilitando significativamente la toma de decisiones clínicas.

In this paper was evaluated the utility of the **FETCH-Q™** quality of life survey in canine MMVD patients with Spanish-speaking owners. The aim is to determine whether the survey data correlates with worsening clinical signs as the ACVIM stage of myxomatous mitral valve disease progresses. Two hundred twenty-eight dogs from 51 owners, seven private clinics, and two university veterinary hospitals were studied and followed up for repeat testing for up to 2 weeks. Our work confirms that the **FETCH-Q™** questionnaire effectively assesses the clinical course of MMVD.

Myxomatous mitral valve disease is the most common acquired heart disease in dogs. The gold standard for definitive diagnosis is echocardiography. The aim of this second study was to develop a tool that utilises a quality-of-life survey, structured anamnesis, and physical examination to predict the classification stages of the American College of Veterinary Internal Medicine (ACVIM). Accurately identifying a patient's stage is crucial for determining when treatment should be initiated and for tailoring it to their ACVIM stage. The study analyzed 1,011 dogs from 23 hospitals, and the results indicated that most patients were successfully classified into the control group (healthy dogs), stage B (dogs with a heart murmur but are asymptomatic), and stage C (dogs with heart failure). However, efficient results were not achieved in differentiating between stage B1 (dogs with a heart murmur and without heart enlargement) and stage B2 (dogs with a heart murmur and heart enlargement).

In this study, we developed and evaluated a graphical method called **CARDIOBOX**, which aims to simplify the visual representation of echocardiographic values. To assess the efficacy of **CARDIOBOX**, 55 veterinarians participated in interpreting echocardiographs of dogs presented in two formats: using **CARDIOBOX** and solely utilising numerical reference tables. We recorded the time taken for interpretation and the accuracy of responses in each format. The results indicated that **CARDIOBOX** enabled veterinarians to interpret echocardiographic values more quickly without compromising the efficiency of interpretation. This study demonstrates that **CARDIOBOX** allows veterinarians to interpret and apply echocardiographic results swiftly and effectively, significantly aiding clinical decision-making.



7.-

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Will Rogers, comediante y actor estadounidense nacido en 1879 dijo:
"El mejor médico del mundo es el veterinario: él no puede preguntarles a sus pacientes qué les pasa. Simplemente, lo tiene que saber".

La enfermedad mixomatosa de la válvula mitral representa la cardiopatía adquirida más común en la práctica veterinaria, afectando a una proporción significativa de pacientes caninos. El presente trabajo surge como resultado de una investigación orientada a optimizar el abordaje diagnóstico de esta patología. Se propone brindar a los clínicos veterinarios herramientas diagnósticas actualizadas y basadas en la evidencia, con el objetivo de facilitar una detección precoz y una gestión clínica más eficaz. Asimismo, se espera que esta contribución constituya un punto de partida para futuras investigaciones que permitan profundizar en el entendimiento de la enfermedad y, en consecuencia, mejorar la calidad de vida de los pacientes afectados.

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