

Doctoral Thesis No. 2024:76 Faculty of Veterinary Medicine and Animal Sciences

Echoes Across the Globe: Insights into Left Atrial Size Assessment in Dogs and Cats

Preferences, measurements, and observer variation among veterinary echocardiographers

Момо Yu-Wen Kuo



Echoes Across the Globe: Insights into Left Atrial Size Assessment in Dogs and Cats

Preferences, measurements, and observer variation among veterinary echocardiographers

Momo Yu-Wen Kuo

Faculty of Veterinary Medicine and Animal Sciences Department of Clinical Sciences Uppsala



DOCTORAL THESIS Uppsala 2024 Acta Universitatis Agriculturae Sueciae 2024:76

Cover: Illustration by Kit Kuo (kitkuo@gmail.com)

ISSN 1652-6880 ISBN (print version) 978-91-8046-367-6 ISBN (electronic version) 978-91-8046-403-1 https://doi.org/10.54612/a.1fh2v0u1j5 © 2024 Momo Yu-Wen Kuo, https://orcid.org/0000-0002-5463-2770 Swedish University of Agricultural Sciences, Department of Clinical Sciences, Uppsala, Sweden The summary chapter of this thesis is licensed under CC BY NC ND 4.0, other licences or copyright may apply to illustrations and attached articles.

Print: SLU Service/Repro, Uppsala 2024

Echoes across the globe: Insights into left atrial size assessment in dogs and cats

Abstract

Echocardiographic assessment of left atrial (LA) size is important for screening, characterizing, and monitoring heart disease in dogs and cats. Echocardiography is known to be operator-dependent, leading to potential variation in assessment of the LA size.

The thesis aimed to explore similarities and differences in LA size assessment among veterinary echocardiographers. Echocardiographers from 67 countries across six continents participated in interactive web-based studies involving image- and video-based investigations.

Most echocardiographers used linear two-dimensional (2D) echocardiography from a right parasternal short-axis view for LA size assessment, and indexed LA size to aortic (Ao) dimensions. Despite similar method of use, variations in image selection, timing, and caliper placement were observed. The echocardiographers' clinical specialist status, the number of weekly echocardiograms performed, and timing affected the mean measurement and the interobserver variation of LA and LA/Ao ratio. Furthermore, the LA size also affected the interobserver variation. Interobserver agreement of subjective assessments of LA size were comparably good, but improved after having performed linear measurements.

To conclude, the results presented in this thesis could help pave the way for more consistent and reliable echocardiographic assessment of LA size in veterinary medicine.

Keywords: 2D echocardiography, subjective assessment, quality assessment, observer variation

Author's address: Momo Yu-Wen Kuo, SLU, Department of Clinical Sciences, Box 7054, 750 07 Uppsala, Sweden. E-mail: Momo.Y-W.Kuo@slu.se

Ekon över hela världen: insikter om bedömning av vänster förmaksstorlek hos hundar och katter

Sammanfattning

Ekokardiografisk bedömning av vänster förmaks (VF) storlek är viktig för screening, karakterisering och uppföljning av hjärtsjukdom hos hundar och katter. Tekniken är operatörsberoende, vilket kan leda till variation i bedömningen av VF-storlek.

Avhandlingens syfte var att undersöka likheter och skillnader i veterinära ultraljudsundersökares (ekokardiografers) mätningar av VF-storlek. Ekokardiografer från 67 länder och sex kontinenter deltog i interaktiva bild- och videobaserade webbundersökningar.

De flesta ekokardiografer använde linjär tvådimensionell (2D) ekokardiografi från en höger parasternal kortaxelvy för VF-bedömning samt indexerade VF-storlek till aortastorlek (Ao). Trots att majoriteten hade liknande preferenser gällande metodval, observerades variationer i val av bild, timing och placering av mätpunkter. Ekokardiografernas kliniska specialiststatus, antal veckovisa utförda ekokardiogram och timing påverkade medelvärden av mätningarna samt interobservatörsvariationen rörande VF och VF/Ao kvot. Vidare påverkade storleken på VF interobservatörsvariationen. Subjektiv bedömning av VF-storlek överensstämde förhållandevis väl mellan observatörer, men förbättrades efter utförande av linjära mätningar.

Det konkluderas att resultaten i denna avhandling kan utgöra en grund för mer konsekventa och pålitliga utvärderingar av VF-storlek inom veterinärmedicinen.

Nyckelord: 2D-ekokardiografi, subjektiv bedömning, kvalitetsbedömning, observatörsvariation

Author's address: Momo Yu-Wen Kuo, SLU, Department of Clinical Sciences, P.O. Box 7054, 750 07 Uppsala, Sweden. *E-mail:* Momo.Y-W.Kuo@slu.se

Preface

I pursued a PhD for two reasons. The first was my dog, Dumbo, who was diagnosed with preclinical stage myxomatous mitral valve disease (MMVD) at the age of seven in 2013. At that time, there was no evidence to support any treatment for the preclinical stage of this disease. As a naive third-year veterinary student, it felt like my world was collapsing. I desperately wanted to save him and change the bleak outlook for such cases. Ever since then, I have explored my interest in cardiology research related to MMVD.

The second reason was the inspiration I found in Hans Rosling, a Swedish physician, academic, and public speaker. His TED talks and the book *Factfulness* resonated deeply with me. His team promoted the use of data and data visualization to explore development issues and make a better world, and I was captivated by this approach. Hans Rosling's enthusiasm was infectious, and I aspired to convey wonderful research findings through simple graphics, just as he did.

During my PhD years, I was fortunate to be guided by and collaborate with many who could be considered the Hans Rosling of the veterinary world. We all believed in the power of effectively using numbers and graphics to maximize the dissemination of knowledge. I am truly fortunate to have found someone who shares and supports my vision.

As I reach the end of my PhD journey, I reflect on my initial passion for conducting research, and my heart is still filled with enthusiasm. And Dumbo, now 18 years old, has remained clinically healthy with me! As you read this piece, I hope you enjoy this investigative journey, uncovering deeper layers and finding more intricate connections through my work in echocardiographic left atrial size assessment in dogs and cats.

Dedication

To Dumbo, my guiding star on this incredible PhD journey and my life.

To my family, who have unconditionally supported and loved me, shaping the person I am today.

"Dogs are not our whole life, but they make our lives whole."

- Roger Caras



Dumbo, Påneå, Chopi, Buzz, and Momo in Uppsala by Tsai-Hsuan Wu, 2024

Contents

List o	of publ	lication	S	13	
List	of table	es		15	
List	of figui	res		17	
Abbr	eviatio	ons		19	
1.	Back	ground	d	21	
	1.1	Heart	disease in dogs and cats	22	
		1.1.1	Common acquired and congenital heart diseases	23	
		1.1.2	Diagnosis and treatment	24	
	1.2	Left at	rium	24	
		1.2.1	Left atrial structure	25	
		1.2.2	Left atrial function and the association with the left v	entricle	
				27	
		1.2.3	Left atrial remodeling/enlargement	28	
		1.2.4	Imaging modalities for left atrial size assessment	29	
	1.3	gs and			
		cats		30	
	1.4	One- a	and two-dimensional techniques	31	
		1.4.1	Three-dimensional technique	33	
		1.4.2	Subjective impression	33	
	1.5	5 Sources of assessment variation			
	1.6 Web-based research				
2.	Aims	s		37	

3.	Mate	rials and methods	. 39			
	3.1	Experimental design	40			
		3.1.1 Global interactive web surveys (Paper I-III)	40			
		3.1.2 Video-based study (Paper IV)	44			
	3.2	Criteria for participation				
	3.3	Study distribution				
	3.4	Statistics	47			
4.	Results					
	4.1	Background information of the echocardiographers	50			
	4.2	4.2 Preferences regarding echocardiographic techniques and methods				
	for lef	t atrial size assessment in dogs and cats (Paper I & II)	51			
	4.3	Preferences regarding linear two-dimensional methods for				
	atrial	size assessment in dogs (Paper III)				
	4.4	Sources of variation in subjective assessment and linear				
	dimen	isional measurement (Paper IV)				
5.	General Discussion					
	5.1 Most common method: Indexing LA to Ao (LA/Ao) dimensions from					
	a right parasternal short-axis view					
	5.2	Sources of variation in linear two-dimensional left atrial	size			
	asses	sment	58			
		5.2.1 Sources of variation in LA size assessment: Tech	nical			
		factors	. 58			
		5.2.2 Sources of variation in LA size assessment: Oper-	ator-			
		related factors	64			
	5.3	Subjective assessment of left atrial size	65			
6.	Cond	clusions	. 67			
7.	Future perspectives					
Refe	rences	S	. 71			
Popu	ılar sc	ience summary	. 83			
•						
Popu	ılärvet	enskaplig sammanfattning	. 85			

Acknowledgements

List of publications

This thesis is based on the work contained in the following papers, referred to by Roman numerals in the text:

- Kuo MY-W, Häggström J, Gordon SG, Höglund K, Côté E, Lu T-L, Dirven M, Rishniw M, Hung Y-W, Ljungvall I. 2024. Veterinary echocardiographers' preferences for left atrial size assessment in dogs: The BENEFIT Project. *Journal of Veterinary Cardiology*. 51: 157-171.
- II. Kuo MY-W, Häggström J, Gordon SG, Höglund K, Côté E, Lu T-L, Dirven M, Rishniw M, Hung Y-W, Ljungvall I. 2024. Veterinary echocardiographers' preferences for left atrial size assessment in cats: The BENEFIT Project. *Journal of Veterinary Cardiology*. 51: 145-156.
- III. Kuo MY-W, Dirven M, Häggström J, Gordon SG, Höglund K, Côté E, Rishniw M, Lu T-L, Hung Y-W, Ljungvall I. Veterinary echocardiographers preferences for image selection, timing, and caliper placement for left atrial two-dimensional size assessment in dogs: The BENEFIT Project. (submitted)
- IV. Kuo MY-W, Häggström J, Côté E, Gordon SG, Höglund K, Rishniw M, Dirven M, Lu T-L, Hung Y-W, Ljungvall I. Sources of variation in subjective assessment and linear two-dimensional measurement of left atrial size in dogs: The BENEFIT Project. (manuscript)

Papers I-II are reproduced with the permission of the publishers.

The contribution of Momo Yu-Wen Kuo to the papers included in this thesis was as follows:

- Played a major role in the study design, data collection and analysis, and interpretation of results, and held primary responsibility for manuscript writing. Received support from supervisors and co-authors, who also contributed to the study design, data collection and analysis, and in writing and editing the manuscripts.
- II. Played a major role in the study design, data collection and analysis, and interpretation of results, and held primary responsibility for manuscript writing. Received support from supervisors and co-authors, who also contributed to the study design, data collection and analysis, and in writing and editing the manuscripts.
- III. Played a major role in the study design, data collection and analysis, and interpretation of results, and held primary responsibility for manuscript writing. Received support from supervisors and co-authors, who also contributed to the study design, data collection and analysis, and in writing and editing the manuscripts.
- IV. Played a major role in the study design, data collection and analysis, and interpretation of results, and held primary responsibility for manuscript writing. Received support from supervisors and co-authors, who also contributed to the study design, data collection and analysis, and in writing and editing the manuscripts.

List of tables

Table 1	. Summa	ry of	advantages	and	disadvantages	for	using	web-
based s	urvey							36

List of figures

Figure 1. Silicon endocast of a canine heart from a cardiac healthy Labrador Retriever. 25
Figure 2. Silicon endocasts of the canine heart from a cardiac healthy Labrador Retriever in lateral and dorsal views
Figure 3. Changes in left atrial (LA) function and size during the cardiac cycle
Figure 4. Various two-dimensional echocardiographic methods and commonly used acquisition views for measuring dimensions, circumference, area, and volume for left atrial (LA) size assessment in dogs and cats
Figure 5. Overview of study design and key findings in Paper I-IV $\dots 40$
Figure 6. Survey design process in Paper I-III
Figure 7. Question overview of echocardiographic techniques/methods for left atrial (LA) size assessment in dogs (Paper I) and cats (Paper II) 43
Figure 8. Question overview of echocardiographic linear two- dimensional methods for left atrial (LA) size assessment in dogs (Paper III)
Figure 9. The BENEFIT project website and the study platform for Paper IV

Figure 13. Analysis of data collected from 623 echocardiographers performing echocardiographic examinations in both dogs and cats. 52

Abbreviations

ACVIM	American College of Veterinary Internal Medicine
Ao	Aorta
ATE	Arterial thromboembolism
BENEFIT	gloBal caninE and feliNE leFt atrIal size assessmenT
CT	Cardiac computed tomography
CMRI	Cardiac magnetic resonance imaging
DCM	Dilated cardiomyopathy
HCM	Hypertrophic cardiomyopathy
LA	Left atrium
LA/Ao	Left atrial to aortic ratio
LAE	Left atrial enlargement
LV	Left ventricle
LVOT	Left ventricular outflow tract
MMVD	Myxomatous mitral valve disease
RCM	Restrictive cardiomyopathy
RPLAX	Right parasternal long-axis
RPSAX	Right parasternal short-axis
SD	Standard deviation
TEE	Transesophageal echocardiography

Transthoracic echocardiography
One-dimensional
Two-dimensional
Two-dimensional echocardiography
Three-dimensional
Three-dimensional echocardiography

1. Background

Cardiovascular disease is a leading cause of death in dogs and cats. Echocardiographic assessment of the left atrial (LA) size is important for effectively screening, characterizing, and monitoring progression of the majority of heart diseases affecting dogs and cats. Assessing LA size also plays a key role in predicting outcomes and determining the optimal timing of treatment in animals with left-sided heart diseases. Therefore, monitoring LA size is an important biomarker of cardiac health.

In the 1990s, the American College of Veterinary Internal Medicine (ACVIM) published guidelines recommending two-dimensional echocardiography (2DE) for assessing LA size in dogs and cats (Thomas *et al.*, 1993). This era also saw the introduction of linear methods for evaluating LA size, which remain in use today (Häggström *et al.*, 1994, Rishniw & Erb, 2000, Hansson *et al.*, 2002). Although 2DE has become widely used in clinical studies, echocardiography is highly operator-dependent, leading to potential variations in measurements. These inconsistencies may result from differences in echocardiographic techniques, training, and individual preferences among echocardiographers, which can affect the reliability of LA size assessments due to the lack of standardization and quality control.

An ideal biomarker, such as LA size assessed through echocardiography, should be safe, simple to perform, cost-effective, and highly reliable, with minimal variation (Aronson & Ferner, 2017, Bodaghi *et al.*, 2023). However, studies on the variation of echocardiographic LA size assessments in veterinary practice have mainly been limited to single-center settings, with few observers or clinically healthy animals (Dukes-McEwan *et al.*, 2002, Chetboul *et al.*, 2003, Chetboul *et al.*, 2004, van Hoek *et al.*, 2018, Fries *et al.*, 2019). This highlights the need for improved standardization to ensure consistent and accurate measurements across different practitioners.

Current ACVIM consensus guidelines concerning myxomatous mitral valve disease (MMVD) in dogs and cardiomyopathies in cats, respectively, specifically recommend the use of linear 2DE to assess LA size in dogs and cats, emphasizing the importance of consistent and reliable assessment (Keene *et al.*, 2019, Luis Fuentes *et al.*, 2020). Inconsistent LA size assessments can negatively impact evaluation of disease severity and prognosis, and also influence application of clinical study results and treatment guidelines; potentially compromising patient care.

To meet these challenges, a crucial first step is to quantitatively examine the variation in echocardiographic assessments of LA size. This thesis initiated the BENEFIT (gloBal caninE and feliNE leFt atrIal size assessmenT) project, an international research collaboration that explores veterinary echocardiographers' methods for LA size assessment in dogs and cats. The project aimed to generate insights that, in the future, could improve the reliability and standardization of echocardiographic LA size assessments in veterinary medicine.

1.1 Heart disease in dogs and cats

The heart is composed of four chambers: the right atrium receives deoxygenated blood, which is pumped by the right ventricle to the lungs. The LA receives the oxygenated blood, which is then pumped out into the body by the left ventricle (LV). The rhythmic contraction and relaxation of these chambers are controlled by electrical impulses originating from the cardiac conduction system.

Heart disease encompasses a range of abnormalities affecting the structure, function, or electrical activity of the heart. These issues may lead to irregular heartbeats and ultimately, heart failure, characterized by the heart's inability to pump sufficient blood to support vital organ function. Heart disease can be congenital (present at birth), or acquired (develop later in life). Approximately 10% of the dog population develop heart disease (Egenvall *et al.*, 2006, Fleming *et al.*, 2011). Moreover, heart diseases are one of the leading causes of death in small-bred dogs (Parker & Kilroy-Glynn, 2012, Bonnett *et al.*, 2005). Approximately 10-15% of the general cat population may be affected by feline cardiomyopathy (Côté *et al.*, 2004, Ferasin *et al.*, 2003, Paige *et al.*, 2009, Wagner *et al.*, 2010, Payne *et al.*, 2015, Follby *et al.*, 2022).

Risk factors for heart disease in dogs and cats include breed, genetics, age, medications, infections, and nutritional factors (Ford *et al.*, 2017, O'Keefe *et al.*, 1993, Walker *et al.*, 2022, Pion *et al.*, 1992). Signs of cardiovascular disease in dogs and cats involve a range of clinical signs, including respiratory distress, exercise intolerance, syncope, loss of appetite, abdominal distention (due to ascites), and unintended weight loss. In addition, some dogs with heart disease may exhibit coughing. Cats with pronounced left-sided heart disease may also experience sudden limb paresis caused by arterial thromboembolism (ATE) secondary to thrombus formation in the heart (Cheng *et al.*, 2021, Schober & Maerz, 2006).

1.1.1 Common acquired and congenital heart diseases

Myxomatous mitral valve disease is the most prevalent acquired heart disease in dogs, accounting for approximately 75-80% of all canine heart conditions (Whitney, 1974, Egenvall *et al.*, 2006, Ljungvall & Häggström, 2017). The disease commonly affects small to medium-sized breeds, such as Cavalier King Charles spaniels, Dachshunds, miniature poodles, and Yorkshire terriers (Häggström *et al.*, 1992, Beardow & Buchanan, 1993, Olsen *et al.*, 1999, Thrusfield *et al.*, 1985, Meurs *et al.*, 2019). In contrast, dilated cardiomyopathy (DCM), the most frequent form of cardiomyopathy in dogs, typically affects medium to larger breeds like Irish Wolfhounds, Doberman Pinschers, Great Danes, Boxers, and Portuguese Water Dogs (Tidholm *et al.*, 2001, Dambach *et al.*, 1999, Vollmar, 2000, Petric *et al.*, 2002).

Cardiomyopathies are the most commonly acquired heart diseases among cats, with the hypertrophic cardiomyopathic (HCM) phenotype being the most prevalent form (Follby *et al.*, 2022, Paige *et al.*, 2009), representing approximately 60% of cardiac cases (Ferasin *et al.*, 2003). Restrictive (RCM) and nonspecific cardiomyopathic phenotypes have in one study been shown to constitute 20-30% of cardiac cases in cats (Ferasin *et al.*, 2003). While most cats with HCM are non-pedigree, several pedigree breeds are recognized to be at increased risk. These breeds include the Maine Coon, Ragdoll, British Shorthair, Persian, Bengal, Sphynx, Norwegian Forest cat, and Birman (Trehiou-Sechi *et al.*, 2012, Granström *et al.*, 2011, März *et al.*, 2015, Chetboul *et al.*, 2012, Häggström *et al.*, 2016, Follby *et al.*, 2022).

The most common forms of canine congenital heart disease include pulmonic stenosis (PS), subvalvular aortic stenosis (SAS), patent ductus arteriosus (PDA), and ventricular septal defect (VSD) with various breed and sex predispositions noted (Detweiler *et al.*, 1961, Detweiler & Patterson, 1965, Tidholm, 1997, MacDonald, 2006, Brambilla *et al.*, 2020). Common congenital heart defects in cats include VSD, tricuspid/mitral valve dysplasia, and pulmonary/aortic stenosis, without consistent breed or sex predilections (MacDonald, 2006, Tidholm *et al.*, 2015).

1.1.2 Diagnosis and treatment

The diagnostic process for heart disease in dogs and cats typically begins with a review of the animal's medical history and a comprehensive physical examination. Based on the clinical signs, additional tests may include blood analysis, thoracic radiography, and an electrocardiogram (ECG) to assess heart function and detect abnormalities.

Transthoracic echocardiography (TTE) is an important diagnostic tool in veterinary cardiology, providing detailed morphological and functional insights into the heart. For more precise structural and functional information, advanced imaging techniques such as cardiac computed tomography (CCT), cardiac magnetic resonance imaging (CMRI), catheter angiography, and transesophageal echocardiography (TEE) are available, though they are rarely used in routine clinical practice.

Treatment options for heart disease in dogs and cats depend on the specific condition and disease stage. While many cardiovascular diseases are not fully curable, they can often be effectively managed with medications. Nutritional supplements and dietary changes may also help support heart function in some cases. For certain structural defects or conduction disturbances, invasive device-based interventions or surgical procedures may be necessary for effective management.

1.2 Left atrium

The term "atrium" originates from Latin, referring to a central area in a Roman household that connects multiple rooms, a concept that aligns with the function of the heart's atrial chambers (Loukas *et al.*, 2016). Figure 1 shows the anatomic relationship of the LA to other related cardiac chambers and blood vessels.

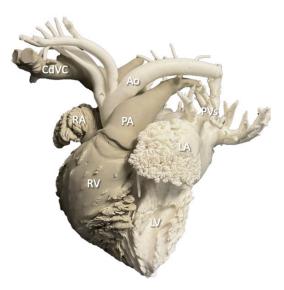


Figure 1. Silicon endocast of a canine heart from a cardiac healthy Labrador Retriever. The left atrium (LA) receives oxygen-rich blood from the lungs via the pulmonary veins (PVs), which is a part of the pulmonary circulation. The blood is then directed to the left ventricle (LV), which pumps it through the aorta (Ao) to the systemic circulation, distributing it throughout the body. Ao, aorta; CdVC, caudal vena cava; LA, left atrium; LV, left ventricle; PA, pulmonary artery; PVs, pulmonary veins; RA, right atrium; RV, right ventricle. Silicon endocast heart at the courtesy of Ranko Georgiev. Photo by the author.

Left atrial size, as determined by echocardiography, is a significant predictor of cardiovascular outcomes in both dogs and cats, as well as in humans (Borgarelli *et al.*, 2008, Payne *et al.*, 2013, Patel *et al.*, 2009, Lang *et al.*, 2015). Left atrial enlargement (LAE) is a key marker of structural remodeling in response to chronic pressure and/or volume overload in the left side of the heart, often preceding adverse clinical outcomes such as ATE in cats and cardiogenic pulmonary edema in dogs and cats.

1.2.1 Left atrial structure

The LA extends laterally and cranially, forming the left auricle (or atrial appendage) adjacent to the base of the pulmonary trunk (Figure 2, lateral view). The upper portion of the LA is situated beneath the aortic arch and the

pulmonary arteries (Figure 2, dorsal view), with the tracheal bifurcation located just behind it.

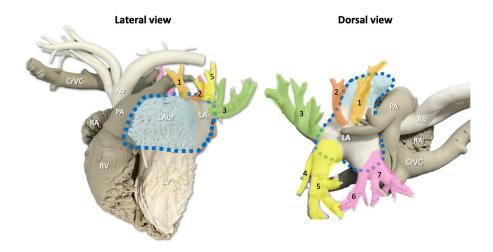


Figure 2. Silicon endocasts of the canine heart from a cardiac healthy Labrador Retriever in lateral and dorsal views. The lateral (left) and dorsal (right) views show the anatomical relationships of the left atrium (LA, blue dashed line) and left auricle (LAur, light blue) with other cardiac structures. The left cranial lobe pulmonary veins (1 and 2) merge into a single ostium. The left caudal lobe (3), accessory lobe (4), and right caudal lobe (5) pulmonary veins connect to the caudal aspect of the left atrium. The right middle lobe (6) and right cranial lobe (7) pulmonary veins join the right side of the left atrium. Different colors indicate the relative positions of the same structures in the lateral and dorsal views. Ao, aorta; CrVC, cranial vena cava; LA, left atrium; LAur, left auricle; LV, left ventricle; PA, pulmonary artery; RA, right atrium; RV, right ventricle. Silicon endocast heart at the courtesy of Ranko Georgiev. Illustration by the author.

The pulmonary trunk ends towards the posterior and lower part of the LA. The number of pulmonary veins entering the LA varies across species; for example, dogs typically have four to six pulmonary veinous ostia in the roof of the LA, whereas cats usually have three to four (Figure 1 and 2) (Panopoulos *et al.*, 2019, Kittleson & Kienle, 1998, Bezuidenhout, 2012). The interatrial septum, beginning just below the ascending aorta, separating the right and left atria (Figure 2, dorsal view).

1.2.2 Left atrial function and the association with the left ventricle

The cardiac cycle comprises two main phases: a relaxation and blood refilling phase of the ventricles known as **ventricular diastole**, which follows a contraction- and blood pumping phase of the ventricles known as **ventricular systole**. The LA contributes to cardiac performance through three components, functioning as a (booster) pump, reservoir, and conduit (Figure 3).

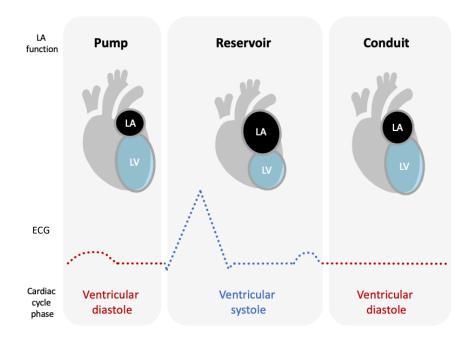


Figure 3. Changes in left atrial (LA) function and size during the cardiac cycle. The LA plays three crucial roles in the cardiac cycle: acting as a 'reservoir', collecting blood from the lungs during ventricular systole, serving as a 'conduit' for moving stored blood to the left ventricle (LV) during early ventricular diastole, and functioning as a 'pump', with atrial contraction contributing partial LV filling. This figure depicts the LA in black and the LV in blue, highlighting LA's critical role in modulating LV filling and cardiovascular function. LV, left ventricle; ECG, electrocardiography. Illustration by the author.

The functions of the atria and ventricles are closely interconnected. The LA serve as a buffer chamber to control the flow of venous blood for ventricular filling. While compliance or stiffness of the LA, along with LA contractility and relaxation, primarily influence reservoir function during ventricular systole, significant contributions also come from LV end-systolic volume and the descent of the LV base during ventricular systole. Additionally, conduit function is influenced by LA compliance and has a reciprocal association with reservoir function. However, as the mitral valve is open in ventricular diastole, conduit function is closely tied to LV compliance, with relaxation being a key determinant. The atrial contraction takes place during ventricular diastole. Atrial pump function is a reflection of the magnitude and timing of atrial contractility, which plays a significant role in determining effective ventricular stroke volume and contributes between 15 and 30% of LV stroke volume (Mitchell *et al.*, 1965, Blume *et al.*, 2011).

1.2.3 Left atrial remodeling/enlargement

In human beings, atrial remodeling and enlargement can result from either physiological or pathological changes in the atrial myocardium (Hohendanner *et al.*, 2018, Chen *et al.*, 2021, Goette *et al.*, 2016). Documentation on physiological LAE in veterinary medicine is limited. Studies in athletic species of dogs reported only LV remodeling (Shave *et al.*, 2017, Constable *et al.*, 1994). In human athletes and normotensive pregnancies, physiological LAE is associated with increased circulation volume and improved LA function (La Gerche *et al.*, 2012, Song *et al.*, 2015). Pathological LAE is connected to adverse cardiovascular outcomes in dogs, cats, and humans (Nakamura *et al.*, 2014, Borgarelli *et al.*, 2008, Baron Toaldo *et al.*, 2018, Payne *et al.*, 2013, Häggström *et al.*, 2008, Boswood *et al.*, 2016).

In dogs and cats, pathological changes of the LA, particularly LA size, is most strongly associated with the prognosis of common heart diseases, and the chamber is, accordingly, the subject of extensive research. The LAE occurs as a compensatory response to increased pressure or volume overload within the LA chamber. This enlargement is a common feature across different common heart diseases, including MMVD and DCM in dogs, and cardiomyopathies in cats. In all cases, the LA stretches and enlarges to accommodate the increased workload, which can lead to further complications such as endocrine dysregulation, arrythmias, cardiogenic pulmonary edema, and hypercoagulability (especially in cats).

The mechanisms of LAE differ in dogs and cats depending on the underlying cardiac conditions. In dogs with MMVD, LAE primarily results from the regurgitation of blood back into the LA due to the degeneration and improper closure of the mitral valve, which, in turn, causes increased volume and pressure within the LA as it adapts to the excess blood (Parker & Kilroy-Glynn, 2012). In contrast, in dogs with DCM, LAE occurs because of weakening and dilatation of the LV, affecting its ability to pump blood efficiently into the systemic circulation, causing an accumulation of blood in the heart and backward pressure into the LA. As a result, the LA enlarges to accommodate the increased volume (O'Grady & O'Sullivan, 2004). In cats with HCM, thickening of the LV muscle makes it difficult for the ventricle to fill properly during diastole, leading to increased pressure in the LA as blood backs up, causing the atrium to stretch and enlarge over time to manage the excess blood volume (Luis Fuentes *et al.*, 2020).

1.2.4 Imaging modalities for left atrial size assessment

Echocardiography is the most commonly used quantitative noninvasive method for LA size assessment because it provides real-time images of the heart and it is widely available and portable. Left atrial size can be assessed through its dimensions, circumference, area, and volume using both one-, two-, and three-dimensional (1D, 2D, and 3D) echocardiography. However, echocardiographic assessment can be affected by various factors, such as image resolution and frame rate, geometric assumptions of LA structure, operator experience and training, and the technique/method of choice.

Thoracic radiography is a widely utilized diagnostic tool in veterinary medicine, favored for its relatively low cost, ease of use, rapid acquisition times and widespread availability in most veterinary practices. For assessing the global heart and LA size in dogs, several radiographic methods are employed, including vertebral heart size (VHS) (Lamb *et al.*, 2001), vertebral LA size (VLAS) (Malcolm *et al.*, 2018), radiographic LA dimension (RLAD) (Sánchez Salguero *et al.*, 2018), and modified-vertebral LA size (M-VLAS) (Lam *et al.*, 2021). In cats, apart from the VHS system, there is limited research data on other methods. To optimize the diagnostic quality and accuracy of thoracic radiographic interpretation, it is important to obtain radiographs that are properly positioned and captured at peak

inspiration using the correct radiographic technique. Radiographic examinations emit radiation, raising potential concerns about exposure for both animals and human operators, especially when used over long term to monitor disease progression. Similar to the challenges faced with 2D echocardiography (2DE), the interpretation of radiographic images is complicated by the superimposition of body parts, as 3D anatomical structures are projected onto 2D images. This inherent limitation requires careful analysis to ensure accurate diagnosis.

Cardiac CT (+/- gating) and CMR (+/- gating) are widely acknowledged as the gold standard methods for assessing LA volume in human medicine (Smiseth *et al.*, 2021, Rodevand *et al.*, 1999, Stojanovska *et al.*, 2011). Despite this, their everyday application is hindered by high costs, limited availability, radiation risks (CT), and the requirement for contrast agents. Additionally, general anesthesia is often necessary for dogs and cats.

1.3 Echocardiographic assessment of the left atrial size in dogs and cats

Transthoracic echocardiography (TTE) is the recommended approach for assessing LA size in dogs, cats, and humans (Lang *et al.*, 2015, Keene *et al.*, 2019, Luis Fuentes *et al.*, 2020). As a fundamental component of cardiac imaging, TTE is crucial for measuring the dimensions and performance of cardiac chambers. The TTE is the leading non-invasive modality for obtaining real-time images of the beating heart, primarily due to its practicality, safety, and availability. The prominence of TTE in clinical settings is reinforced by technological advancements that have improved the performance and reduced the cost of echocardiographic machines. Nevertheless, its widespread adoption is restricted, as it is not typically taught as an entry-level skill to veterinarians, thus limiting its use in this regard.

Transesophageal echocardiography (TEE) also offers detailed cardiac imaging and is particularly useful for guiding cardiovascular catheter and hybrid procedures. However, TEE is more invasive, requiring sedation or general anesthesia and the insertion of an esophageal probe, which carries a higher risk of complications. The TEE is not routinely used for assessing LA size in veterinary medicine. In human echocardiography, TEE does not fully capture the entire LA, and is not recommended in LA size assessment (Lang

et al., 2015). However, TEE offers effective visualization of the left auricle in dogs (Kimura *et al.*, 2014), compared to TTE.

1.4 One- and two-dimensional techniques

The Time-motion/Motion mode (M-mode) technique, also known as 1D echocardiography, was one of the first techniques developed in echocardiography. The method provides a high temporal resolution which is essential for accurately capturing rapid cardiac movements, such as valve motion. The M-mode technique for LA size assessment in dogs and cats was originally adapted from how echocardiography was used in humans and horses (Pipers & Hamlin, 1977, Long *et al.*, 1992). In veterinary cardiology, where patients often have higher heart rates than humans, the ability of M-mode to provide high frame rates and excellent temporal resolution is particularly valuable.

As echocardiographic technology advanced, 2DE began to replace Mmode in some instances. The 2DE offers real-time images of the heart's structures from multiple angles with high frame rates, allowing for more accurate assessments of cardiac anatomy and function. The advantages of 2DE, such as visualizing the heart in multiple planes and guiding interventional procedures, far exceed the limited view provided by M-mode (O'Grady *et al.*, 1986, Häggström *et al.*, 1994, Hansson *et al.*, 2002, Rishniw & Erb, 2000). Further technological advancements, such as the shift from mechanical to phased array probes and the development of systems with higher frame rates, have significantly improved the quality of 2D imaging. These innovations have enabled more detailed and precise imaging, enhancing diagnostic capabilities in the demanding cardiac environments of veterinary medicine.

Currently, 2DE is the recommended technique for assessing LA size in dogs and cats (Luis Fuentes *et al.*, 2020, Keene *et al.*, 2019). Numerous 2DE methods and common acquisition views measuring dimensions, circumference, area, and volume for LA size assessment in dogs and cats are showed in Figure 4. In human medicine, measuring LA volume by 2DE is recommended for its robust prognostic value in predicting outcomes of various heart diseases (Barnes *et al.*, 2004, Tsang *et al.*, 2001, Beinart *et al.*, 2004, Moller *et al.*, 2003, Lang *et al.*, 2015, Rossi *et al.*, 2002, Tsang *et al.*, 2006, Vyas *et al.*, 2011).

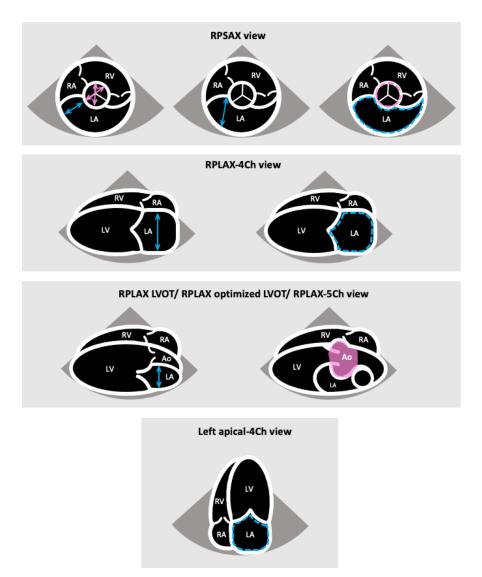


Figure 4. Various two-dimensional echocardiographic methods and commonly used acquisition views for measuring dimensions, circumference, area, and volume for left atrial (LA) size assessment in dogs and cats. Blue arrows indicate the location for LA dimension measurements, while pink arrows indicate the location for aortic (Ao) dimension measurements. The pink shaded area denotes the Ao dimension measurements, used in place of arrows due to multiple recommendations in the area. Blue dashed lines indicate LA circumference and area measurements, and pink dashed lines indicate Ao circumference and area measurements. The 2DE methods to estimate LA volume, the area length method and the Simpson's modified method of discs, are both based on volumetric assumptions based on the LA area. LV, left ventricle; RA, right

atrium; RV, right ventricle; RPSAX, right parasternal short-axis; RPLAX LVOT, right parasternal long-axis left ventricular outflow tract; RPLAX-4Ch, right parasternal long-axis four-chamber; RPLAX-4Ch, right parasternal long-axis five-chamber. Illustration by the author.

1.4.1 Three-dimensional technique

Assessing LA size with real-time three-dimensional echocardiography (RT3DE) is a feasible method in dogs (Tidholm *et al.*, 2011, Treibert *et al.*, 2024, Tidholm *et al.*, 2023). When high-resolution images are attainable, this technique is one of the most reliable for measuring cardiac chamber size, alongside cardiac computed tomography and cardiovascular magnetic resonance. Furthermore, RT3DE offers the advantage of not relying on geometric assumptions of the LA structure, thus providing more accurate measurements compared to 2D methods. However, like any other echocardiographic modality, RT3DE relies on adequate image quality, and has a comparable low temporal resolution. Even though the modality is widely available in human echocardiography laboratories, a large European survey showed that LA size was only assessed by 3DE in selected cases across European echocardiographic laboratories (Ajmone Marsan *et al.*, 2020).

1.4.2 Subjective impression

A visual assessment of LA size can be obtained from 2D images before quantitative measurements are derived from 1D, 2D, or 3D echocardiography. The acquisition views for subjective assessment have been described using right parasternal short-axis (RPSAX)- and right parasternal long-axis four-chamber (RPLAX-4Ch) views in both dogs and cats, and left parasternal apical four-chamber view in cats (Boon, 2011, Kittleson & Côté, 2021).

1.5 Sources of assessment variation

To effectively characterize and quantify the heart using echocardiography, the operator needs a comprehensive understanding of cardiovascular physiology, pathophysiology, and the factors influencing observational variation. Variation in assessing LA size can arise from several sources, including biological, technical, and operator-related factors. Biological influences include breed, age, body weight, body condition score, physique, heart rate, anesthesia, and specific heart conditions (Campbell & Kittleson, 2007, Johard *et al.*, 2018). Technical factors involve the positioning of the animal (standing or recumbent), the technique/method of use and how the echocardiography equipment (machine and probe type) is used. Operator-related variables could be related to experience and training in echocardiography.

1.6 Web-based research

With the rise of the internet and the ubiquity of computers, the World Wide Web has emerged as a crucial platform for communication, profoundly reshaping research methodologies. The World Wide Web has expanded the scope of research activities from literature reviews and collaboration with colleagues across diverse geographical locations, to recruitment of study participants who can be directed to online sites to complete web-based research - using internet as a data-collection platform.

Surveys stand as a powerful tool for research, with the internet's emergence further amplifying the efficacy of web-based surveys. A webbased survey is a common method used in web-based research. Historically, survey research was a tedious process, requiring the distribution of paper questionnaires via mail to a carefully selected group of respondents. The traditional survey was not only time-consuming but also involved a lengthy waiting period for the return of responses, followed by the labor-intensive task of manually inputting data into a database or spreadsheet for analysis. In contrast, the accessibility and efficiency of survey research have improved nowadays by automated survey software and online platforms, which have potentially simplified the process of designing, distributing, and analyzing surveys.

Before selecting and designing research tools, it is crucial to understand the advantages and drawbacks of web-based surveys (Ahern, 2005, Ball, 2019, Duffy, 2002), as outlined in Table 1. Adhering to well-established and detailed methodologies, refined over decades, is essential for both web-based and traditional survey methods. This adherence ensures the production of valid and relevant data that effectively address research questions, thereby guaranteeing the integrity and utility of research outcomes (Ball, 2019, Ponto, 2015). Researchers have employed survey methods extensively since the 1930s, establishing foundational guidelines for creating survey instruments, survey design, data collection, and analysis (Callegaro *et al.*, 2015, Rossi *et al.*, 2013, Kelley *et al.*, 2003). Additionally, the Checklist for Reporting Results of Internet E-Surveys (CHERRIES) was introduced to improve the quality of web-based survey reports submitted for publication (Eysenbach, 2004).

The American Heart Association and the European Association of Cardiovascular Imaging have chosen survey as a tool to pinpoint potential disparities between guidelines and real-world clinical application (Sahn *et al.*, 1978, Cameli *et al.*, 2019, Ajmone Marsan *et al.*, 2020, Podlesnikar *et al.*, 2022). These investigations aimed to discern variations and commonalities in the practices of echocardiographers and facilities regarding clinical imaging, with the objective of tackling complexities in these domains and enhancing future guidelines and recommendations (Sahn *et al.*, 1978, Ajmone Marsan *et al.*, 2020).

Advantages		Disadvantages	
Fo	r researchers		
•	Cost-effective alternative to paper surveys	• Limited ability to explore open- ended questions with immediate follow-ups	
•	Enhanced accessibility for sensitive topics, diverse cultural cohorts, and marginalized communities	 Sample bias in subject recruitment due to self-selection from non-random computer/internet users 	
•	Swift and extensive outreach capabilities	• Equipment and network issues may arise	
•	Reduced time consumption Versatile adaptability	• Uncertain impact on response rates	
•	Streamlined automation processes	Challenges with literacy and disabilities	
		• Constraints in internet availability	
Fo	r respondents	-	
•	Ensures anonymity	• Absence of chances to clarify ambiguous terms	
•	Allows respondents to answer at their own pace	Online privacy concerns	
•	Empowers participants with a sense of control	• Excessive web-based surveys distract respondents	
•	Sparks greater interest in participation with innovative	• Constraints in internet availability	
	and engaging approaches		

Table 1. Summary of advantages and disadvantages for using web-based survey.

2. Aims

The overall aims of this thesis were to investigate the preferences of veterinary echocardiographers for assessing LA size in dogs and cats, to identify the most commonly used methods, and to determine how different factors influence measurements performed using these methods.

The specific aims were to:

- Investigate echocardiographers' preferences concerning techniques and methods for LA size assessment in dogs and cats.
- Investigate echocardiographers' preferences for assessing LA size in subgroups based on geographic, demographic, and professional profiles.
- ♥ Investigate the linear 2D preferences of veterinary echocardiographers for acquiring and measuring LA size in dogs; specifically concerning image selection, timing method, caliper placement, and threshold for LA enlargement for different methods.
- Investigate sources of variation in subjective assessments and linear 2D measurements of LA size when using a RPSAX view.
- ♥ Investigate the additional value of linear 2D measurements of LA size in a RPSAX view to subjective assessment on interobserver variation.

3. Materials and methods

The materials and methods employed in the studies are detailed in the included papers and related supporting information. This section offers a summary of the study methods (Figure 5) and highlights comparative aspects across the various studies.

OVERVIEW OF STUDY DESIGN AND KEY FINDINGS IN PAPER

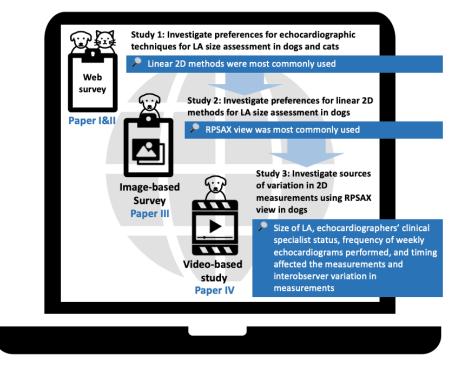


Figure 5. Overview of study design and key findings in Paper I-IV. This figure summarizes the study design, aims, methods, and main findings across Papers I-IV. All three studies conducted in the thesis were web-based studies. The initial web survey (Study 1) targeted echocardiographers examining dogs (Paper I) and cats (Paper II). Subsequent studies included an image-based survey (Study 2, Paper III) and a video-based study (Study 3, Paper IV), both focusing on echocardiographic assessment of the left atrium (LA) in dogs. RPSAX, right parasternal short-axis; 2D, two-dimensional.

3.1 Experimental design

3.1.1 Global interactive web surveys (Paper I-III)

The initial phase of this project involved the development of an interactive web survey, Study 1, structured in accordance with established guidelines (Callegaro *et al.*, 2015, Rossi *et al.*, 2013). The survey was designed to capture veterinary echocardiographers' preferences regarding different

echocardiographic techniques and methods for assessing LA size in dogs (Paper I) and cats (Paper II). The outcome of the survey highlighted a significant preference for linear 2D-technique, prompting the creation of a second, more targeted survey.

The follow-up survey, Study 2, therefore concentrated on exploring specific aspects of linear 2D methods in dogs (Paper III). Cats were deliberately excluded from this survey to avoid lengthening the questionnaire, which could negatively impact the response rate, abandonment rate, representativeness, and quality of the data (Galesic & Bosnjak, 2009).

Both surveys were designed for optimal accessibility on personal computers, tablets, and smartphones, utilizing the Netigate web platform (Netigate AB, Stockholm, Sweden). The process of survey construction and validation is summarized in Figure 6.

SURVEY DESIGN PROCESS

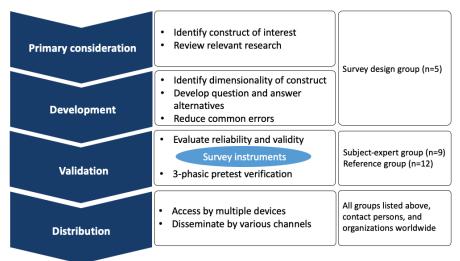


Figure 6. Survey design process in Paper I-III. The study-design group developed the questionnaire based on their expertise and by reviewing relevant literature. Questions and answer alternatives were refined to minimize errors. A three-phase pretest verified content validity by the subject-expert and reference groups. Information about the study was distributed online across various channels and countries.

In the first survey, 134 questions were created and divided into three parts to investigate echocardiographers' preferences concerning LA size assessment in dogs (Paper I) and cats (Paper II). Part 1 was designed to gather general background information on echocardiographers' geographic, demographic, and professional profiles. Part 2 concerned the techniques used for LA size assessment—including subjective assessments, M-mode, linear 2D, area, and volume (both 2D- and 3D-based methods)—and detailed information regarding animal positioning, acquisition views, indexing methods, and timing method for measurements (Figure 7). Part 3 assessed the echocardiographers' experience and training level in echocardiography.

TECHNIQUES/METHODS OF ECHOCARDIOGRAPHIC ASSESSMENT OF THE LA SIZE IN DOGS AND CATS

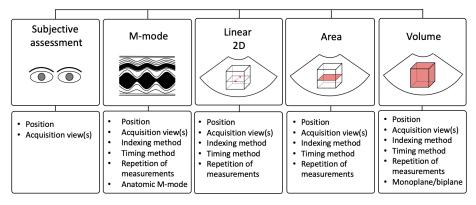


Figure 7. Question overview of echocardiographic techniques/methods for left atrial (LA) size assessment in dogs (Paper I) and cats (Paper II). This section differed between dogs and cats owing to current slightly divergent recommendations regarding assessments. Echocardiographers were instructed to answer questions specifically for the species they had practical experience examining. 2D, two-dimensional.

Building on the findings from the first survey; namely that the linear 2D technique was most commonly used, the follow-up survey was focused on this technique. The second survey required echocardiographers to evaluate a selected set of echocardiographic images and illustrations. It consisted of 98 image-based questions aimed at exploring echocardiographers' preferences for linear 2D methods when assessing LA size in dogs (Paper III). Questions related to respondents' demographic and professional profiles were identical to the first survey. Four linear 2D methods were examined, specifically concerning image selection, timing method, caliper placement, and threshold used for LA enlargement; all involving the use of right parasternal windows to obtain LA and Ao dimensions when assessing LA size in dogs. Echocardiographers who used alternative methods were requested to detail the acquisition views they used (Figure 8).

LINEAR 2D METHODS FOR ASSESSING LA AND AO DIMENSIONS IN DOGS

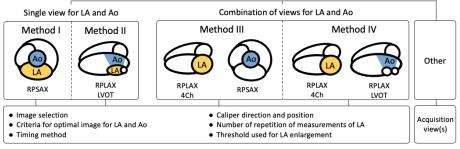


Figure 8. Question overview of echocardiographic linear two-dimensional methods for left atrial (LA) size assessment in dogs (Paper III). Ao, aorta; RPSAX, right parasternal short-axis; RPLAX-4Ch, right parasternal long-axis four chamber; RPLAX-LVOT, right-parasternal long-axis left ventricular outflow tract; 2D, two-dimensional.

3.1.2 Video-based study (Paper IV)

A study website was developed featuring echocardiographic cine-loops and multiple-choice questions (Figure 9). The platform was designed to enable echocardiographers to express their subjective impressions and perform linear 2D measurements of LA size in cine-loops, to investigate their threshold for considering LAE, and to collect their demographic and professional profiles. The platform's user interfaces were designed to replicate the ultrasound measurement process as closely as possible. Echocardiographers used this platform to measure LA and Ao dimensions; caliper placements and timing of the measurements were recorded on cineloops. Nine cine-loops, from nine different dogs, were selected to represent a range of LA sizes in RPSAX view. The selected images represented certain preferences previously described amongst veterinary echocardiographers (Paper III); with variation in angulations and image quality. Furthermore, the loops included a variation regarding visibility of pulmonary venous inlets to mimic patient-to-patient variations in the routine clinic.

THE BENEFIT PROJECT WEBSITE AND THE STUDY PLATFORM



https://benefitproject.pages.dev/

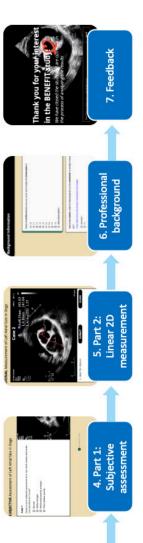


Figure 9. The BENEFIT project website and the study platform for Paper IV. The website outlined the project's aims, team, and all studies conducted in the project. To enter the study (Paper IV), echocardiographers accessed a specific study page, which introduced the video-based study's aims and displayed real-time participant data by continent and country. Initially, echocardiographers provided general background information. In Part 1, they subjectively assessed LA size in 9 randomized videos. In Part 2, they performed linear measurements on the same 9 videos, repeated three times for a total of 27 randomly videos. Finally, they provided their professional background and any feedback. The study platform featured two parts:

- 1) **Subjective assessments**: Echocardiographers assessed LA size as normal, mildly, or moderately/severely enlarged based on their visual impression of the randomly ordered cine-loops (n=9), displayed one at a time on the screen.
- 2) Linear 2D measurements: Echocardiographers measured LA and Ao dimensions on nine cine-loops repeated three times (n=9*3); displayed randomly without disclosure of the repetitions. After each measurement, the echocardiographers classified the LA size as normal, mildly, or moderately/severely enlarged based on their LA/Ao measurements. They were queried about their opinions regarding the quality of the cine-loops and their methods for timing the measurements.

3.2 Criteria for participation

Paper I and II

Veterinary echocardiographers who performed, or had previously performed echocardiography in dogs (Paper I) and/or cats (Paper II).

Paper III

Veterinary echocardiographers who performed, or had previously performed linear 2D echocardiography when assessing the LA size in dogs, and who indexed LA to Ao when assessing the chamber size.

Paper IV

Veterinary echocardiographers who performed, or had previously performed echocardiography in dogs using linear 2D assessments.

3.3 Study distribution

Veterinary echocardiographers were invited to participate in the studies through various channels: (1) National/international veterinary organizations and veterinary internal medicine/cardiology associations across 34 countries; (2) The Veterinary Information Network (VIN) - Cardiology ListServe, which includes veterinarians worldwide with a special interest in veterinary cardiology, including American and European Colleges of Veterinary Internal Medicine (ACVIM and ECVIM-CA) cardiology diplomates and candidates, as well as other interested veterinarians; (3) Presentations performed by members of the BENEFIT project at international congresses; and (4) referrals from echocardiographers who shared the study link with other veterinary echocardiographers. Two reminders were issued during the data collection phase for all studies conducted.

3.4 Statistics

Descriptive analyses of results in each paper involved performing calculations for response counts and percentages. Statistical analyses were conducted using the JMP software (JMP, v. 17.0, SAS Institute Inc, Cary, NC).

In Paper III, group median values for LA and Ao measurements were compared using the Wilcoxon test. Differences in variance between groups were assessed using a two-sided F-test.

In Paper IV, differences in LA, Ao, and LA/Ao values between groups were analyzed using one-way analysis of variance (ANOVA) and the Tukey-Kramer test for multiple comparisons. Interobserver variation and its two components, repeatability and reproducibility, were assessed using the measurement system analysis platform in the software. Differences in variation between groups were evaluated by analyses of the model residuals in each group using the Levine test for homoscedasticity and Bonferroni correction. Results are reported as standard deviation (SD) of the measurement and variance (square of SD).

4. Results

This section provides a summary of the key findings, while more comprehensive information can be accessed in Papers I-IV and the supplementary materials included in those papers.

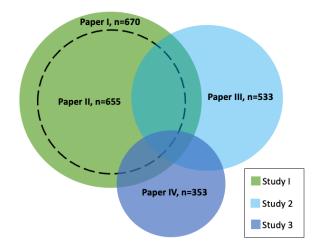
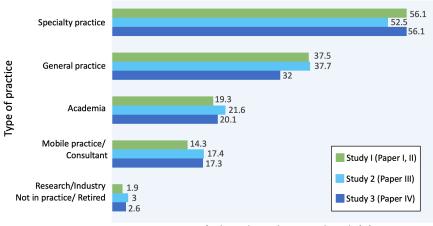


Figure 10. Distribution of echocardiographers across studies within the BENEFIT project. Study 1 corresponds to Papers I and II, Study 2 corresponds to Paper III, and Study 3 to Paper IV. The chart also shows the proportion of echocardiographers who participated in multiple studies, with approximately one-third continuing in subsequent studies. The size of the areas is approximately in proportion to the actual number of echocardiographers for each paper.

4.1 Background information of the echocardiographers

The first survey (Study 1, Papers I and II) collected responses from 670 echocardiographers in 54 countries across all six continents, and 655 of these echocardiographers performed echocardiography in both dogs and cats. The follow-up survey (Study 2, Paper III) attracted 533 echocardiographers from 48 countries, and 36% of these had also contributed to the first survey. The video-based online study (Study 3, Paper IV) was completed by 353 echocardiographers from 48 countries, and 38% of these had previously engaged in other studies within the BENEFIT Project (Figure 10).

Across all studies, the type of practice among echocardiographers remained consistent (Figure 11).



Proportion of echocardiographers in each study (%)

Figure 11. Proportion of types of practice among echocardiographers across all studies. Approximately half of the echocardiographers worked in a specialty practice and about one-third worked in general practice.

4.2 Preferences regarding echocardiographic techniques and methods for left atrial size assessment in dogs and cats (Paper I & II)

When assessing LA size in dogs and cats, 33.7% (226/670) of the echocardiographers for dogs and 34.7% (227/655) for cats combined linear 2D methods with subjective assessments. Among echocardiographers using linear 2D methods, the most commonly used view was RPSAX. Approximately 70% of the echocardiographers (436/621 for dogs and 437/612 for cats) indexed LA to Ao. Approximately 30% of the echocardiographers (191/621 for dogs and 210/612 for cats) shared identical preferences regarding positioning, acquisition views, indexing methods, and timing method for the measurements (Figure 12).

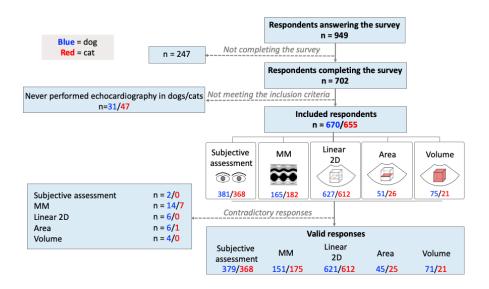


Figure 12. Distribution of responses regarding echocardiographic techniques of use for left atrial size assessment in dogs (blue) and cats (red). A total of 949 individuals participated; of which 74% completed the first survey. The analysis included responses from 670 and 655 echocardiographers who performed echocardiography on dogs (Paper I) and cats (Paper II), respectively. The chart highlights the variety of preferred techniques. MM, M-mode; 2D, two-dimensional.

When comparing echocardiographers performing echocardiography in both species (n=623), the echocardiographers favored linear 2D (96%, 600/623) and subjective assessment (55%, 345/623) for both dogs and cats. The M-mode technique was more frequently used in cats (27%, 171/623) compared with in dogs (23%, 144/623) (Figure 13).

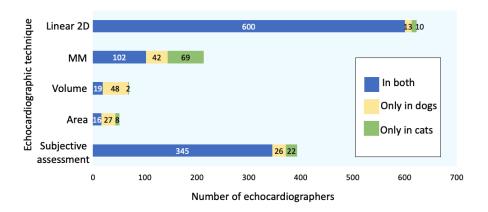


Figure 13. Analysis of data collected from 623 echocardiographers performing echocardiographic examinations in both dogs and cats. The figure shows a predominant use of linear 2D and subjective assessments for both species. The use of the M-mode technique varied; while some echocardiographers applied it to both dogs and cats, others used it exclusively for one species. MM, M-mode; 2D, two-dimensional.

4.3 Preferences regarding linear two-dimensional methods for left atrial size assessment in dogs (Paper III)

Of the 533 echocardiographers who completed the survey, 86% (459/533) used a RPSAX view for measuring LA and Ao dimensions. Within this group, 57% (261/459) preferred the same angulation of the heart and 76% (351/459) timed LA and Ao dimensions at end-systole/early-diastole. Caliper placement for LA_{SAX} dimension on the aortic side were comparatively consistent across all LA size categories, whereas caliper placement on the LA lateral wall was more variable.

Thirty-nine percent (207/533) of the echocardiographers used right parasternal long-axis (RPLAX) views - both the RPLAX four-chamber

(RPLAX-4Ch) and RPLAX optimized for left ventricular outflow (LVOT) views - for assessing LA size. Most echocardiographers (80%, 130/162) preferred the same angulation of the heart and 82% (132/162) timed the LA_{LAX} (LA dimension measured from a RPLAX-4Ch view) at end-systole/early-diastole. Caliper placement for LA_{LAX} measurements near both the septal and lateral LA walls varied substantially.

The upper limit for LAE used by the echocardiographers varied among all methods used. Training and experience did not influence interobserver variation for LA measurements in a RPSAX view, whereas these factors impacted measurements performed in a RPLAX view.

When assessing LA size subjectively, the RPSAX view and the RPLAX-4Ch view were trusted the most. About 43% (231/533) of the echocardiographers trusted the RPSAX view the most and 36% (190/533) trusted the RPLAX-4Ch view the most, respectively. The majority of echocardiographers (93.4%, 498/533) assessed LA subjectively. Seventy-seven percent (408/533) of the echocardiographers stated that they assessed the LA size identically in both dogs and cats when using linear 2D methods.

4.4 Sources of variation in subjective assessment and linear two-dimensional measurement (Paper IV)

A total of 353 echocardiographers from 49 countries across six continents completed the study. Caliper placement for LA dimension on the aortic side were comparatively consistent across all LA size categories, whereas caliper placement on the LA lateral wall was more variable.

The lowest mean values for LA measurements were recorded by echocardiographers who performed echocardiograms <6 times/week and those without specialist status. The highest mean values for LA and Ao measurements were obtained for measurements performed at ventricular end-systole/early-diastole.

Interobserver variation was higher in cine-loops that had been categorized by the majority as enlarged or borderline enlarged LA compared to normalsized LA. Lower interobserver variation occurred among board-certified specialists, echocardiographers performing echocardiograms >20 times/week, and those who timed measurements at end-systole/earlydiastole, using either aortic valve motion or a combination of timing methods. Years of experience performing echocardiography did not consistently reduce interobserver variation. Subjective LA size assessment agreement between echocardiographers improved after performing linear measurements.

5. General Discussion

This thesis highlights similarities in echocardiographers' preferences for assessing LA size in dogs and cats and identifies key technical factors that may influence these assessments, particularly during image acquisition and measurement. Additionally, we examined the effects of operator-related factors on the measurement outcomes. Sources of variation in LA size assessment, focusing on the technical and operator-related factors investigated in this thesis, are discussed below.

5.1 Most common method: Indexing LA to Ao (LA/Ao) dimensions from a right parasternal short-axis view

In both dogs and cats, over 90% of the echocardiographers prioritized the linear 2DE from a RPSAX view, indexing LA to Ao when assessing LA size (Paper I and II). Despite various techniques being reported, transthoracic 2DE is the only technique officially recommended by the ACVIM as a standard for cardiac chamber quantification (Thomas *et al.*, 1993). The popularity of the RPSAX method may stem from several factors: firstly, the method has, in multiple studies across both species, been demonstrated to have a prognostic value. Secondly, the ACVIM consensus guidelines recommend this method for staging common heart diseases in dogs and cats (Keene *et al.*, 2019, Luis Fuentes *et al.*, 2020). Lastly, the ability to capture both the LA and Ao in the same view provides operational convenience, and the LA/Ao ratio offers a BW-independent measure of LA size.

When measuring LA/Ao in dogs, the majority (86%) of echocardiographers used a RPSAX view for assessment of both LA and Ao dimensions, while 40% measured LA dimension from a RPLAX view (Paper III). Long-axis echocardiographic ratios of LA/Ao have been reported to effectively identify LAE in dogs with MMVD in one study (Strohm et al., 2018). Measuring the LA from the RPLAX-4Ch view potentially avoids incorporation of a pulmonary vein and facilitates timing of measurement precisely at end-systole (Hsue & Visser, 2020). However, very few echocardiographers prioritized the long-axis view approach (Paper I). Significant variation was observed among echocardiographers in their use of long-axis echocardiographic ratios of LA/Ao, specifically in image selection, caliper placement for LA and Ao dimensions, and the thresholds used for LAE (Paper III). The less frequent use of RPLAX views may be attributed to several factors. Obtaining LA/Ao from a RPLAX-4Ch view requires a separate view for Ao dimension, which adds complexity and consumes more time (Strohm et al., 2018, Hsue & Visser, 2020, Marchesotti et al., 2019, Visser et al., 2019, Vatne et al., 2021). Additionally, LA size assessment from a RPLAX view has not been widely used in large clinical trials, unlike the common application of LA/Ao from a single RPSAX view (Boswood et al., 2016, Häggström et al., 2008, Reynolds et al., 2012).

In cats, assessing LA size from a long-axis view, without the use of an indexing method, was used by only a few of the responding echocardiographers (Paper II), even though this approach has been suggested for use in cats in the ACVIM consensus recommendations and other

literature (Luis Fuentes *et al.*, 2020, Payne *et al.*, 2013, Schober & Maerz, 2006, Greet *et al.*, 2020). Normalizing LA size to the Ao or using allometric scaling may help to mitigate the impact of BW variations and sex on the chamber size (Häggström *et al.*, 2016, Chetboul *et al.*, 2012). Furthermore, according to the findings in the present thesis, veterinary echocardiographers prefer to use the very same methods for LA size assessment in both dogs and cats. Accordingly, the methods of recommendations for use in dogs may also have influenced the echocardiographers preferences for cats.

Few veterinary echocardiographers reported the use of volumetric methods for LA size estimation in dogs and cats (Paper I and II). This reluctance may be due to the more recent introduction of these techniques in veterinary practice and their more time-consuming and labor-intensive nature compared to linear measurements. In human medicine, LA size is typically assessed by measuring the anteroposterior dimension in a parasternal long-axis view, known in veterinary medicine as the RPLAX LVOT view, using either M-mode or linear 2D techniques (Lang *et al.*, 2015). However, relying solely on the anteroposterior dimension is discouraged as it does not accurately represent LAE (Wade *et al.*, 1987, Schabelman *et al.*, 1981, Lang *et al.*, 2015). Instead, measuring LA volumes is recommended, with extensive literature showing a strong prognostic value in humans (Tsang *et al.*, 2003, Gottdiener *et al.*, 2006, Tsang *et al.*, 2006).

5.2 Sources of variation in linear two-dimensional left atrial size assessment

Before the BENEFIT project, no large-scale veterinary study had investigated impacts of different sources of variation when assessing LA size by echocardiography. The concept and consensus of standards for operators' training, echocardiographic laboratories, and quality assurance in echocardiography have been studied and implemented in human echocardiography for more than a decade (Picard *et al.*, 2011, Masani, 2018, Popescu *et al.*, 2009, Popescu *et al.*, 2020). Similar consensus has not been established in the veterinary field. Our study found that more than half of the veterinary echocardiographers had self-learned the techniques, and that the majority of the veterinary echocardiographers were the only operator at their workplace (Paper I), limiting their opportunities for peer review and technique refinement.

5.2.1 Sources of variation in LA size assessment: Technical factors

Positioning of subject

Ninety percent of the echocardiographers assessed LA size with the dogs and cats positioned in right lateral recumbency, and approximately 10% with the animal in a standing position (Paper I-II). The popularity of lateral recumbency may be due to its ability to minimize lung interference, thereby enhancing the visualization of the heart and aiding in the collection of structural data (Thomas, 1984). One small study involving four healthy dogs, examined in standing and lateral recumbent positions by two cardiologists, revealed no significant differences between standing and recumbent positioning on LA size assessment (Chetboul *et al.*, 2005). A potential influence of the animal's position on the assessment has, however, not been investigated in the hands of many. Human studies have shown that the position of the subject influence TTE image quality and linear measurements (Felner *et al.*, 1980, Ottenhoff *et al.*, 2022).

Index normalization

Aortic indexing was the most commonly used normalization approach for LA size assessments in both species (Paper I and II). Very few echocardiographers normalized the LA size without indexing to the Ao (Paper I-III). Well-recognized normalization methods for linear LA size assessment include using an internal control, such as the Ao (Rishniw & Erb, 2000, Hansson *et al.*, 2002, Brown *et al.*, 2003, Strohm *et al.*, 2018), and normalizing chamber measurements to BW through nonlinear regression (Gonçalves *et al.*, 2002) or allometric scaling (Cornell *et al.*, 2004, Häggström *et al.*, 2016). Potential reasons for the popularity of LA/Ao indexing in dogs and cats has been discussed above.

Timing method (time-point identification)

'Valvular motion' was the most frequently used timing method when assessing LA size in Papers I-III, and 'a combination of timing methods' was most frequently used in Paper IV. The variation in findings between the papers of this thesis may be explained as follows: The first and second study (Paper I -III) were surveys that provided text, illustrations, and still images to be evaluated by the echocardiographers. The primary goal of the first and second study were to identify echocardiographers' top preferences; therefore, they were only allowed to provide a single response option per question. Study III (Paper IV), on the other hand, was conducted through a specially designed web platform that mimics the actual practice of measuring cine-loops on echocardiographic machines. Given the practical scenarios; where more than one timing method might be used for measurements, echocardiographers were allowed to select multiple response options, and accordingly more than one timing method. These findings suggest that while most echocardiographers prefer valvular motion for timing (2019, Borgarelli et al., 2012, Boswood et al., 2016, Rishniw & Erb, 2000, Häggström et al., 2008, Hansson et al., 2002, Borgarelli et al., 2008), the measurements made by identifying aortic cusps might be challenging to implement in practice. Importantly, the lowest interobserver variation in assessing LA size at endsystole/early-diastole was achievable by either relying on aortic valvular motion or using a combination of timing methods (Paper IV).

Acquisition and measurement for left atrial dimension

1. **RPSAX view** (see Figure 14, left): When acquiring images for LA dimension measurements in the RPSAX view, echocardiographers placed significant importance on the LA outline and Ao shape (Papers III and IV). Achieving an optimal image requires adjusting the imaging angulation. However, only about half of the echocardiographers favored the same angulation for the RPSAX

view, indicating differing preferences in image acquisition (Paper III).

Further variation was noted in caliper placement for measuring LA dimensions, particularly near the pulmonary venous inlets on the LA lateral wall, in both still images (Paper III) and cine-loops (Papers IV). Our findings are similar to results from one study concerning caliper placement in the LA lateral wall in dogs and cats (Rishniw, 2016). This variation is unsurprising, given the inconsistent suggestions for caliper placement in various studies (Hansson *et al.*, 2002, Rishniw & Erb, 2000) and textbooks (Boon, 2011, Penninck & d'Anjou, 2015). Reducing this variation may be achieved by unifying caliper placement near the pulmonary venous inlets, positioning it directly medial or lateral to the pulmonary venous inlets rather than relying on imaginary lines near the LA border (Hansson *et al.*, 2002).

2. **RPLAX-4Ch view** (see Figure 14, right): Over 80% of the echocardiographers preferred to use a RPLAX-4Ch view with a horizontally aligned LA and LV, when they were asked to take the orientation of the LV, LA, and mitral annulus into consideration (Paper III). Interestingly, this image angulation differs from images presented in many publications in veterinary medicine, where a tilted LV chamber or both tilted LA and LV chambers have been described (Vatne et al., 2021, Visser et al., 2019, Safian et al., 2022, Rishniw & Erb, 2000, Boon, 2011, De Madron et al., 2015). Many echocardiographers focused on the visibility of the interatrial septum and the position of the LA free and lateral walls when acquiring images, but less so for the LV wall (Paper III). However, the position of the LV wall, whether horizontal or tilted relative to the LA wall, may influence the orientation of the mitral annulus, which is an important reference for caliper placement when measuring LA dimensions in a RPLAX-4Ch view. Various caliper placements have been reported for RPLAX views in veterinary medicine (O'Grady et al., 1986, Brown et al., 2005, Strohm et al., 2018, Vatne et al., 2021, Marchesotti et al., 2019), and our findings reflect a broad range of approaches.

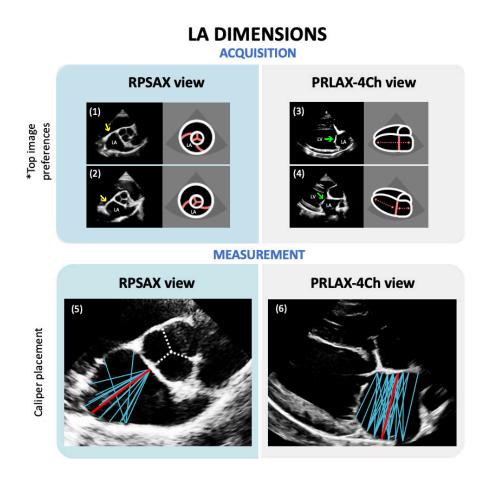


Figure 14. Echocardiographers' acquisition and measurement preferences for left atrial (LA) dimension assessment using right parasternal short-axis (RPSAX)- and right parasternal long-axis four-chamber (RPLAX-4Ch) views. Images (1) and (2) show variations in the orientation of the aortic commissures and interatrial septum (yellow arrows) in the RPSAX view, while images (3) and (4) demonstrate different orientations of the left ventricle (LV) and mitral annulus (green arrows). Caliper placement and directions in images (5) and (6) are indicated by blue lines. The red lines indicate the most used placements in the RPSAX and RPLAX-4Ch views, respectively.

*Echocardiographers were asked to take the orientation of specific anatomical structures into consideration when selecting their options. According to instructions given: attention should be focused on the aortic cusps, interatrial septum, and left auricle for the RPSAX view; and on the LA, LV, and mitral annulus for the RPLAX-4Ch view.

Acquisition and measurement for aortic dimension

- RPSAX view (see Figure 15, lower left): The direction of measuring Ao in a RPSAX view exhibited little variation among echocardiographers (Paper III and IV). This stands in contrast to the measurement of Ao from a RPLAX LVOT view, which varied substantially (Paper III). Different landmarks were proposed in two publications that focused on measuring the LA/Ao from a RPSAX view offering guidance for the Ao measurement (Rishniw & Erb, 2000, Hansson *et al.*, 2002), and these two approaches are proved as interchangeable (Georgiev *et al.*, 2013). The most commonly used method found in this thesis; measuring the Ao dimension at the junction of the noncoronary and left coronary aortic cusps (Hansson *et al.*, 2002), has been widely applied in large clinical trials for managing MMVD (Häggström *et al.*, 2008, Boswood *et al.*, 2016, Wess *et al.*, 2020) and is recommended by the ACVIM consensus guidelines (Keene *et al.*, 2019).
- 2. RPLAX LVOT views (see Figure 15, upper and lower right): When measuring the Ao dimension from a long-axis LVOT view, substantial variations were seen in echocardiographers' responses regarding angulation of the selected view, appearance of specific anatomical structures in the acquisition view, and valvular position; the latter reflecting timing in the cardiac cycle (Paper III). As illustrations/images published across different literature sources vary regarding these above-mentioned parameters, a variety in application of the method for measuring Ao dimension may easily be explained (De Madron *et al.*, 2015, Boon, 2011, Luis Fuentes V., 2010, Strohm *et al.*, 2018).

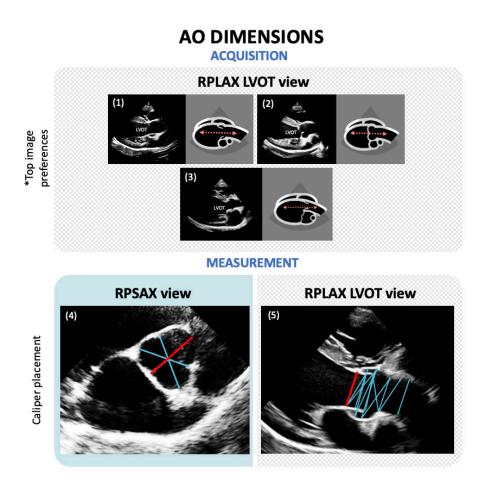


Figure 15. Echocardiographers' acquisition and measurement preferences for aortic (Ao) dimensional assessment using right parasternal short-axis (RPSAX)and right parasternal long-axis left ventricular outflow (RPLAX LVOT) views. Images (1) and (2) show variations in aortic valvular position at different time-points in the cardiac cycle within a RPLAX LVOT view. Images (1) and (3) show the same aortic valvular position, but with different angulations of the RPLAX LVOT view. Caliper placement and directions in (4) and (5) are indicated by blue lines. The red lines indicate the most the most used placements in the RPSAX and RPLAX LVOT views, respectively.

* Echocardiographers were asked to take the orientation and size of specific anatomical structures into consideration when selecting their option. According to instructions given: attention should be focused on the LVOT/ascending aorta, and timing in the cardiac cycle.

Timing of measurements in a RPSAX view

In Paper III, 77% of echocardiographers stated that they performed measurements during end-systole or early-diastole. An analysis of the cineloops in Paper IV, which examined the echocardiographers' actual application of their preferred measurement techniques rather than just their stated preferences, did however show a discrepancy from the results in Paper III. Only around half of the echocardiographers adhered to the end-systole/early-diastole timing when making their measurements. Left atrial size varies during the cardiac cycle (Braunwald *et al.*, 1961, Järvinen *et al.*, 1994, Spencer *et al.*, 2001, Posina *et al.*, 2013) and differences in time-point selection may accordingly have an important effect on the LA size assessment and the application of published reference values.

5.2.2 Sources of variation in LA size assessment: Operator-related factors

Echocardiographers' professional profiles

In Paper IV, we found that specialty training, number of performing examinations, and specific timing conditions improved LA measurement consistency, which aligned with results from other studies (Dukes-McEwan *et al.*, 2002, Chetboul *et al.*, 2004, Safian *et al.*, 2022). The number of years performing echocardiography was not consistently linked to lower variation in 2D measurements, indicating that specialized training and regular practice are more crucial for consistent measurements than experience duration.

Precise timing for measurements is of great importance for achieving a lower interobserver variation in LA measurements (Paper IV). Board-certified specialists and/or those performing echocardiography >20 times/week were more consistent in timing their measurements during the same cardiac cycle phases (end-systole/early-diastole) compared to others. The findings in Paper III, which showed no significant differences in LA measurements from a RPSAX view among echocardiographers with varied professional profiles, may primarily result from the inability to evaluate actual timing of measurements in an image-based survey.

5.3 Subjective assessment of left atrial size

Most echocardiographers combined their objective assessment with a subjective estimate of LA size (Paper I and II). The top two commonly used acquisition views for subjectively assessing LA size in dogs and cats were RPSAX and RPLAX-4Ch views (Paper I and II). When subjectively assessing LA size in dogs, echocardiographers trusted a RPSAX view the most (43%) (Paper III). Estimating the LA size from a short-axis view offers the advantage of visualizing a reference structure, the Ao, simultaneously, which is intuitive and time-saving. In paper IV, we found interobserver agreement of subjective assessments of LA size were comparably good, and improved after having performed linear measurements.

6. Conclusions

This thesis has investigated veterinary echocardiographers' preferences for LA size assessment in dogs and cats; to identify common methods of use, and to determine how different factors influence measurements performed using these methods. The following specific conclusions can be drawn:

- Veterinary echocardiographers most commonly used linear 2D methods in combination with subjective assessment to assess LA size in dogs and cats.
- The echocardiographers' preferences for techniques and methods for LA size assessment in dogs and cats were similar across geographic, demographic, and professional profiles.
- For linear 2D methods, a single RPSAX view was most favored for LA size assessment in dogs, but variations existed in image selection, timing, caliper placement, and threshold used for LAE.
- ♥ The size of the LA, the clinical specialist status of the echocardiographers, the number of weekly performed echocardiograms, and timing affected the measurements and interobserver variation in measurements of LA and LA/Ao, but not of Ao measurements.
- Interobserver agreement of subjective assessments of LA size were comparably good but improved after having performed linear measurements.

7. Future perspectives

The findings in this thesis reveal both similarities and differences in LA size assessments in dogs and cats among veterinary echocardiographers. Furthermore, factors contributing to the variation in assessment have been identified. These insights suggest several areas for further research to be conducted to harmonize echocardiographic LA size assessment among veterinary echocardiographers. These studies are important to serve as background information for establishing guidelines that could be generally accepted and implemented in the veterinary cardiology community. Future studies could focus on the following areas:

- Investigate if factors identified contributing to variation in LA assessment in cats and dogs, respectively, can be implemented in future assessment instructions; thereby reducing interobserver variation.
- Investigate the agreement between linear 2D LA assessment protocols, constructed based upon results from the above-mentioned studies, and volumetric assessments of the chamber using different diagnostic modalities, such as 3DE and CMRI.
- Test future protocols for LA size assessment, constructed upon results from the above-mentioned studies, in the hands of many; including a group of veterinary echocardiographers with different levels of experience/specialist status.
- Establish guidelines for LA size assessment in clinical practice, and furthermore, and thereafter, establish reference values for normalityincluding a large population of dogs and cats- investigated in the hands of many.

References

Ahern, N. R. (2005). Using the Internet to conduct research. Nurse Res 13, 55-70.

- Ajmone Marsan, N., Michalski, B., Cameli, M., Podlesnikar, T., Manka, R., Sitges, M., Dweck, M. R. & Haugaa, K. H. (2020). EACVI survey on standardization of cardiac chambers quantification by transthoracic echocardiography. *Eur Heart J Cardiovasc Imaging* 21, 119-123.
- Aronson, J. K. & Ferner, R. E. (2017). Biomarkers-A General Review. Curr Protoc Pharmacol 76, 9.23.21-29.23.17.
- Ball, H. L. (2019). Conducting Online Surveys. J Hum Lact 35, 413-417.
- Barnes, M. E., Miyasaka, Y., Seward, J. B., Gersh, B. J., Rosales, A. G., Bailey, K. R., Petty, G. W., Wiebers, D. O. & Tsang, T. S. M. (2004). Left Atrial Volume in the Prediction of First Ischemic Stroke in an Elderly Cohort Without Atrial Fibrillation. *Mayo Clinic Proceedings* 79, 1008-1014.
- Baron Toaldo, M., Romito, G., Guglielmini, C., Diana, A., Pelle, N. G., Contiero, B.
 & Cipone, M. (2018). Prognostic value of echocardiographic indices of left atrial morphology and function in dogs with myxomatous mitral valve disease. *Journal of veterinary internal medicine* 32, 914-921.
- Beardow, A. W. & Buchanan, J. W. (1993). Chronic mitral valve disease in cavalier King Charles spaniels: 95 cases (1987-1991). J Am Vet Med Assoc 203, 1023-1029.
- Beinart, R., Boyko, V., Schwammenthal, E., Kuperstein, R., Sagie, A., Hod, H., Matetzky, S., Behar, S., Eldar, M. & Feinberg, M. S. (2004). Long-term prognostic significance of left atrial volume in acute myocardial infarction. *Journal of the American College of Cardiology* 44, 327-334.
- Bezuidenhout, A. (2012). The Heart and Arteries. *Miller's Anatomy of the Dog-E-Book*. Elsevier health sciences.
- Blume, G. G., McLeod, C. J., Barnes, M. E., Seward, J. B., Pellikka, P. A., Bastiansen, P. M. & Tsang, T. S. M. (2011). Left atrial function: physiology, assessment, and clinical implications. *European Journal of Echocardiography* 12, 421-430.
- Bodaghi, A., Fattahi, N. & Ramazani, A. (2023). Biomarkers: Promising and valuable tools towards diagnosis, prognosis and treatment of Covid-19 and other diseases. *Heliyon* **9**, e13323.
- Bonnett, B. N., Egenvall, A., Hedhammar, A. & Olson, P. (2005). Mortality in over 350,000 insured Swedish dogs from 1995-2000: I. Breed-, gender-, ageand cause-specific rates. *Acta Vet Scand* 46, 105-120.
- Boon, J. A. (2011). Evaluation of size, function, and hemodynamics. Veterinary echocardiography-2nd ed. John Wiley & Sons.153-247.

- Borgarelli, M., Crosara, S., Lamb, K., Savarino, P., La Rosa, G., Tarducci, A. & Haggstrom, J. (2012). Survival characteristics and prognostic variables of dogs with preclinical chronic degenerative mitral valve disease attributable to myxomatous degeneration. J Vet Intern Med 26, 69-75.
- Borgarelli, M., Savarino, P., Crosara, S., Santilli, R. A., Chiavegato, D., Poggi, M., Bellino, C., La Rosa, G., Zanatta, R., Haggstrom, J. & Tarducci, A. (2008). Survival characteristics and prognostic variables of dogs with mitral regurgitation attributable to myxomatous valve disease. *J Vet Intern Med* 22, 120-128.
- Boswood, A., Häggström, J., Gordon, S. G., Wess, G., Stepien, R., Oyama, M. A., Keene, B. W., Bonagura, J., MacDonald, K. A. & Patteson, M. (2016). Effect of pimobendan in dogs with preclinical myxomatous mitral valve disease and cardiomegaly: the EPIC study—a randomized clinical trial. J Vet Intern Med. 30, 1765-1779.
- Brambilla, P. G., Polli, M., Pradelli, D., Papa, M., Rizzi, R., Bagardi, M. & Bussadori, C. (2020). Epidemiological study of congenital heart diseases in dogs: Prevalence, popularity, and volatility throughout twenty years of clinical practice. *PLoS One* 15, e0230160.
- Braunwald, E., Frahm, C. J. & Ross, J., Jr. (1961). Studies on Starling's law of the heart. V. Left ventricular function in man. J Clin Invest 40, 1882-1890.
- Brown, D. J., Rush, J. E., MacGregor, J., Ross, J. N., Jr., Brewer, B. & Rand, W. M. (2003). M-mode echocardiographic ratio indices in normal dogs, cats, and horses: a novel quantitative method. *J Vet Intern Med* 17, 653-662.
- Brown, D. J., Rush, J. E., MacGregor, J., Ross, J. N., Jr., Brewer, B. & Rand, W. M. (2005). Quantitative echocardiographic [corrected] evaluation of mitral endocardiosis in dogs using ratio indices. *J Vet Intern Med* 19, 542-552.
- Callegaro, M., Manfreda, K. L. & Vehovar, V. (2015). Web survey methodology. Sage.
- Cameli, M., Marsan, N. A., D'Andrea, A., Dweck, M. R., Fontes-Carvalho, R., Manka, R., Michalski, B., Podlesnikar, T., Sitges, M., Popescu, B. A., Edvardsen, T., Fox, K. F. & Haugaa, K. H. (2019). EACVI survey on multimodality training in ESC countries. *Eur Heart J Cardiovasc Imaging* 20, 1332-1336.
- Campbell, F. E. & Kittleson, M. D. (2007). The effect of hydration status on the echocardiographic measurements of normal cats. *J Vet Intern Med* **21**, 1008-1015.
- Chen, Y. C., Voskoboinik, A., Gerche, A., Marwick, T. H. & McMullen, J. R. (2021). Prevention of Pathological Atrial Remodeling and Atrial Fibrillation: JACC State-of-the-Art Review. J Am Coll Cardiol 77, 2846-2864.
- Cheng, W. C., Wilkie, L., Kurosawa, T. A., Dobromylskyj, M., Priestnall, S. L., Luis Fuentes, V. & Connolly, D. J. (2021). Immunohistological Evaluation of Von Willebrand Factor in the Left Atrial Endocardium and Atrial Thrombi from Cats with Cardiomyopathy. *Animals (Basel)* 11, 1240.

- Chetboul, V., Athanassiadis, N., Concordet, D., Nicolle, A., Tessier, D., Castagnet, M., Pouchelon, J. L. & Lefebvre, H. P. (2004). Observer-dependent variability of quantitative clinical endpoints: the example of canine echocardiography. *J Vet Pharmacol Ther* 27, 49-56.
- Chetboul, V., Concordet, D., Pouchelon, J. L., Athanassiadis, N., Muller, C., Benigni, L., Munari, A. C. & Lefebvre, H. P. (2003). Effects of inter- and intra-observer variability on echocardiographic measurements in awake cats. J Vet Med A Physiol Pathol Clin Med 50, 326-331.
- Chetboul, V., Petit, A., Gouni, V., Trehiou-Sechi, E., Misbach, C., Balouka, D., Carlos Sampedrano, C., Pouchelon, J. L., Tissier, R. & Abitbol, M. (2012).
 Prospective echocardiographic and tissue Doppler screening of a large Sphynx cat population: reference ranges, heart disease prevalence and genetic aspects. *J Vet Cardiol* 14, 497-509.
- Chetboul, V., Tidholm, A., Nicolle, A., Sampedrano, C. C., Gouni, V., Pouchelon, J. L., Lefebvre, H. P. & Concordet, D. (2005). Effects of animal position and number of repeated measurements on selected two-dimensional and Mmode echocardiographic variables in healthy dogs. J Am Vet Med Assoc 227, 743-747.
- Constable, P. D., Hinchcliff, K. W., Olson, J. & Hamlin, R. L. (1994). Athletic heart syndrome in dogs competing in a long-distance sled race. *J Appl Physiol* (1985) **76**, 433-438.
- Cornell, C. C., Kittleson, M. D., Della Torre, P., Häggström, J., Lombard, C. W., Pedersen, H. D., Vollmar, A. & Wey, A. (2004). Allometric scaling of Mmode cardiac measurements in normal adult dogs. *J Vet Intern Med* 18, 311-321.
- Côté, E., Manning, A. M., Emerson, D., Laste, N. J., Malakoff, R. L. & Harpster, N. K. (2004). Assessment of the prevalence of heart murmurs in overtly healthy cats. *J Am Vet Med Assoc* 225, 384-388.
- Dambach, D. M., Lannon, A., Sleeper, M. M. & Buchanan, J. (1999). Familial dilated cardiomyopathy of young Portuguese water dogs. *J Vet Intern Med* 13, 65-71.
- De Madron, E. (2016). Normal echocardiographic values: TM, 2D, and Doppler spectral modes. *Clinical echocardiography of the dog and cat*. Elsevier Health Sciences. 21-37.
- Detweiler, D. K. & Patterson, D. F. (1965). The prevalence and types of cardiovascular disease in dogs. Annals of the New York Academy of Sciences 127, 481-516.
- Detweiler, D. K., Patterson, D. F., Hubben, K. & Botts, R. P. (1961). The prevalence of spontaneously occurring cardiovascular disease in dogs. *Am J Public Health Nations Health* **51**, 228-241.
- Duffy, M. E. (2002). Methodological issues in Web-based research. J Nurs Scholarsh 34, 83-88.

- Dukes-McEwan, J., French, A. T. & Corcoran, B. M. (2002). Doppler echocardiography in the dog: measurement variability and reproducibility. *Vet Radiol Ultrasound* 43, 144-152.
- Egenvall, A., Bonnett, B. N. & Häggström, J. (2006). Heart disease as a cause of death in insured Swedish dogs younger than 10 years of age. *J Vet Intern Med* **20**, 894-903.
- Eysenbach, G. (2004). Improving the quality of Web surveys: the Checklist for Reporting Results of Internet E-Surveys (CHERRIES). *J Med Internet Res* **6**, e34.
- Felner, J. M., Blumenstein, B. A., Schlant, R. C., Carter, A. D., Alimurung, B. N., Johnson, M. J., Sherman, S. W., Klicpera, M. W., Kutner, M. H. & Drucker, L. W. (1980). Sources of variability in echocardiographic measurements. *The American Journal of Cardiology* 45, 995-1004.
- Ferasin, L., Sturgess, C. P., Cannon, M. J., Caney, S. M., Gruffydd-Jones, T. J. & Wotton, P. R. (2003). Feline idiopathic cardiomyopathy: a retrospective study of 106 cats (1994-2001). *J Feline Med Surg* 5, 151-159.
- Fleming, J. M., Creevy, K. E. & Promislow, D. E. (2011). Mortality in north american dogs from 1984 to 2004: an investigation into age-, size-, and breed-related causes of death. *J Vet Intern Med* 25, 187-198.
- Follby, A., Pettersson, A., Ljungvall, I., Ohlsson, Å. & Häggström, J. (2022). A Questionnaire Survey on Long-Term Outcomes in Cats Breed-Screened for Feline Cardiomyopathy. *Animals (Basel)* 12, 2782.
- Ford, J., McEndaffer, L., Renshaw, R., Molesan, A. & Kelly, K. (2017). Parvovirus Infection Is Associated With Myocarditis and Myocardial Fibrosis in Young Dogs. *Vet Pathol* 54, 964-971.
- Fries, R. C., Gordon, S. G., Saunders, A. B., Miller, M. W., Hariu, C. D. & Schaeffer, D. J. (2019). Quantitative assessment of two- and three-dimensional transthoracic and two-dimensional transesophageal echocardiography, computed tomography, and magnetic resonance imaging in normal canine hearts. *J Vet Cardiol* 21, 79-92.
- Galesic, M. & Bosnjak, M. (2009). Effects of Questionnaire Length on Participation and Indicators of Response Quality in a Web Survey. *The Public Opinion Quarterly* 73, 349-360.
- Georgiev, R., Rishniw, M., Ljungvall, I. & Summerfield, N. (2013). Common twodimensional echocardiographic estimates of aortic linear dimensions are interchangeable. *J Vet Cardiol* 15, 131-138.
- Goette, A., Kalman, J. M., Aguinaga, L., Akar, J., Cabrera, J. A., Chen, S. A., Chugh,
 S. S., Corradi, D., D'Avila, A., Dobrev, D., Fenelon, G., Gonzalez, M.,
 Hatem, S. N., Helm, R., Hindricks, G., Ho, S. Y., Hoit, B., Jalife, J., Kim,
 Y. H., Lip, G. Y., Ma, C. S., Marcus, G. M., Murray, K., Nogami, A.,
 Sanders, P., Uribe, W., Van Wagoner, D. R. & Nattel, S. (2016).
 EHRA/HRS/APHRS/SOLAECE expert consensus on atrial
 cardiomyopathies: definition, characterization, and clinical implication.
 Europace 18, 1455-1490.

- Gonçalves, A. C., Orton, E. C., Boon, J. A. & Salman, M. D. (2002). Linear, logarithmic, and polynomial models of M-mode echocardiographic measurements in dogs. *Am J Vet Res* 63, 994-999.
- Gottdiener, J. S., Kitzman, D. W., Aurigemma, G. P., Arnold, A. M. & Manolio, T. A. (2006). Left Atrial Volume, Geometry, and Function in Systolic and Diastolic Heart Failure of Persons ≥65 Years of Age (The Cardiovascular Health Study). *The American Journal of Cardiology* **97**, 83-89.
- Granström, S., Godiksen, M. T., Christiansen, M., Pipper, C. B., Willesen, J. L. & Koch, J. (2011). Prevalence of hypertrophic cardiomyopathy in a cohort of British Shorthair cats in Denmark. *J Vet Intern Med* 25, 866-871.
- Greet, V., Sargent, J., Brannick, M. & Fuentes, V. L. (2020). Supraventricular tachycardia in 23 cats; comparison with 21 cats with atrial fibrillation (2004–2014). *Journal of Veterinary Cardiology* 30, 7-16.
- Häggström, J., Andersson Å, O., Falk, T., Nilsfors, L., U, O. I., Kresken, J. G., Höglund, K., Rishniw, M., Tidholm, A. & Ljungvall, I. (2016). Effect of Body Weight on Echocardiographic Measurements in 19,866 Pure-Bred Cats with or without Heart Disease. J Vet Intern Med 30, 1601-1611.
- Häggström, J., Boswood, A., O'Grady, M., Jöns, O., Smith, S., Swift, S., Borgarelli, M., Gavaghan, B., Kresken, J. G., Patteson, M., Ablad, B., Bussadori, C. M., Glaus, T., Kovacević, A., Rapp, M., Santilli, R. A., Tidholm, A., Eriksson, A., Belanger, M. C., Deinert, M., Little, C. J., Kvart, C., French, A., Rønn-Landbo, M., Wess, G., Eggertsdottir, A. V., O'Sullivan, M. L., Schneider, M., Lombard, C. W., Dukes-McEwan, J., Willis, R., Louvet, A. & DiFruscia, R. (2008). Effect of pimobendan or benazepril hydrochloride on survival times in dogs with congestive heart failure caused by naturally occurring myxomatous mitral valve disease: the QUEST study. *J Vet Intern Med* 22, 1124-1135.
- Häggström, J., Hansson, K., Karlberg, B. E., Kvart, C. & Olsson, K. (1994). Plasma concentration of atrial natriuretic peptide in relation to severity of mitral regurgitation in Cavalier King Charles Spaniels. *Am J Vet Res* 55, 698-703.
- Häggström, J., Hansson, K., Kvart, C. & Swenson, L. (1992). Chronic valvular disease in the cavalier King Charles spaniel in Sweden. *Vet Rec* 131, 549-553.
- Hansson, K., Häggström, J., Kvart, C. & Lord, P. (2002). Left atrial to aortic root indices using two-dimensional and M-mode echocardiography in cavalier King Charles spaniels with and without left atrial enlargement. *Vet Radiol Ultrasound* 43, 568-575.
- Hohendanner, F., Messroghli, D., Bode, D., Blaschke, F., Parwani, A., Boldt, L. H. & Heinzel, F. R. (2018). Atrial remodelling in heart failure: recent developments and relevance for heart failure with preserved ejection fraction. *ESC Heart Fail* 5, 211-221.
- Hsue, W. & Visser, L. C. (2020). Reproducibility of echocardiographic indices of left atrial size in dogs with subclinical myxomatous mitral valve disease. J Vet Intern Med 34, 1779-1786.

- Järvinen, V., Kupari, M., Hekali, P. & Poutanen, V. P. (1994). Assessment of left atrial volumes and phasic function using cine magnetic resonance imaging in normal subjects. *Am J Cardiol* 73, 1135-1138.
- Johard, E., Tidholm, A., Ljungvall, I., Häggström, J. & Höglund, K. (2018). Effects of sedation with dexmedetomidine and buprenorphine on echocardiographic variables, blood pressure and heart rate in healthy cats. *J Feline Med Surg* **20**, 554-562.
- Keene, B. W., Atkins, C. E., Bonagura, J. D., Fox, P. R., Häggström, J., Fuentes, V. L., Oyama, M. A., Rush, J. E., Stepien, R. & Uechi, M. (2019). ACVIM consensus guidelines for the diagnosis and treatment of myxomatous mitral valve disease in dogs. *J Vet Intern Med.* 33, 1127-1140.
- Kelley, K., Clark, B., Brown, V. & Sitzia, J. (2003). Good practice in the conduct and reporting of survey research. *International Journal for Quality in Health Care* 15, 261-266.
- Kimura, T., Takatsuki, S., Miyoshi, S., Katsumata, Y., Nishiyama, T., Nishiyama, N., Tanimoto, Y., Aizawa, Y., Jinzaki, M. & Fukuda, K. (2014). Pericardial Endoscopy–Guided Left Atrial Appendage Ligation. *Circulation: Cardiovascular Interventions* 7, 844-850.
- Kittleson, M. D. & Côté, E. (2021). The Feline Cardiomyopathies: 2. Hypertrophic cardiomyopathy. J Feline Med Surg 23, 1028-1051.
- Kittleson, M. D. & Kienle, R. D. (1998). Small animal cardiovascular medicine.
- La Gerche, A., Burns, A. T., Taylor, A. J., Macisaac, A. I., Heidbüchel, H. & Prior, D. L. (2012). Maximal oxygen consumption is best predicted by measures of cardiac size rather than function in healthy adults. *Eur J Appl Physiol* 112, 2139-2147.
- Lam, C., Gavaghan, B. J. & Meyers, F. E. (2021). Radiographic quantification of left atrial size in dogs with myxomatous mitral valve disease. *J Vet Intern Med* 35, 747-754.
- Lamb, C. R., Wikeley, H., Boswood, A. & Pfeiffer, D. U. (2001). Use of breedspecific ranges for the vertebral heart scale as an aid to the radiographic diagnosis of cardiac disease in dogs. *Vet Rec* 148, 707-711.
- Lang, R. M., Badano, L. P., Mor-Avi, V., Afilalo, J., Armstrong, A., Ernande, L., Flachskampf, F. A., Foster, E., Goldstein, S. A., Kuznetsova, T., Lancellotti, P., Muraru, D., Picard, M. H., Rietzschel, E. R., Rudski, L., Spencer, K. T., Tsang, W. & Voigt, J. U. (2015). Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr 28, 1-39.e14.
- Ljungvall, I. & Häggström, J. (2017). Adult-onset valvular heart disease. *Textbook* of Veterinary Internal Medicine. Diseases of the Dog and the Cat. Elsevier Saunders, 3033-3057.

- Long, K. J., Bonagura, J. D. & Darke, P. G. (1992). Standardised imaging technique for guided M-mode and Doppler echocardiography in the horse. *Equine Vet* J 24, 226-235.
- Loukas, M., Youssef, P., Gielecki, J., Walocha, J., Natsis, K. & Tubbs, R. S. (2016). History of cardiac anatomy: a comprehensive review from the Egyptians to today. *Clin Anat* 29, 270-284.
- Luis Fuentes, V., Abbott, J., Chetboul, V., Côté, E., Fox, P. R., Häggström, J., Kittleson, M. D., Schober, K. & Stern, J. A. (2020). ACVIM consensus statement guidelines for the classification, diagnosis, and management of cardiomyopathies in cats. J Vet Intern Med 34, 1062-1077.
- Luis Fuentes V., J. L., Dennis S. (2010). *BSAVA Manual of Canine and Feline Cardiorespiratory Medicine*. BSAVA British Small Animal Veterinary Association.
- MacDonald, K. A. (2006). Congenital Heart Diseases of Puppies and Kittens. Veterinary Clinics of North America: Small Animal Practice 36, 503-531.
- Malcolm, E. L., Visser, L. C., Phillips, K. L. & Johnson, L. R. (2018). Diagnostic value of vertebral left atrial size as determined from thoracic radiographs for assessment of left atrial size in dogs with myxomatous mitral valve disease. J Am Vet Med Assoc 253, 1038-1045.
- Marchesotti, F., Vezzosi, T., Tognetti, R., Marchetti, F., Patata, V., Contiero, B., Zini, E. & Domenech, O. (2019). Left atrial anteroposterior diameter in dogs: reference interval, allometric scaling, and agreement with the left atrial-to-aortic root ratio. *J Vet Med Sci* 81, 1655-1662.
- März, I., Wilkie, L. J., Harrington, N., Payne, J. R., Muzzi, R. A., Häggström, J., Smith, K. & Luis Fuentes, V. (2015). Familial cardiomyopathy in Norwegian Forest cats. *J Feline Med Surg* 17, 681-691.
- Masani, N. (2018). The Echocardiography Quality Framework: a comprehensive, patient-centered approach to quality assurance and continuous service improvement. *Echo Res Pract* **5**, G35-41.
- Meurs, K. M., Adin, D., O'Donnell, K., Keene, B. W., Atkins, C. E., DeFrancesco, T. & Tou, S. (2019). Myxomatous mitral valve disease in the miniature poodle: A retrospective study. *Vet J* 244, 94-97.
- Mitchell, J. H., Gupta, D. N. & Payne, R. M. (1965). Influence of Atrial Systole on Effective Ventricular Stroke Volume. *Circulation Research* 17, 11-18.
- Moller, J. E., Hillis, G. S., Oh, J. K., Seward, J. B., Reeder, G. S., Wright, R. S., Park, S. W., Bailey, K. R. & Pellikka, P. A. (2003). Left atrial volume: a powerful predictor of survival after acute myocardial infarction. *Circulation* 107, 2207-2212.
- Nakamura, K., Osuga, T., Morishita, K., Suzuki, S., Morita, T., Yokoyama, N., Ohta, H., Yamasaki, M. & Takiguchi, M. (2014). Prognostic value of left atrial function in dogs with chronic mitral valvular heart disease. *J Vet Intern Med* 28, 1746-1752.

- O'Grady, M. R., Bonagura, J. D., Powers, J. D. & Herring, D. S. (1986). Quantitative cross-sectional echocardiography in the normal dog. *Veterinary Radiology* 27, 34-49.
- O'Grady, M. R. & O'Sullivan, M. L. (2004). Dilated cardiomyopathy: an update. *Veterinary Clinics: Small Animal Practice* **34**, 1187-1207.
- O'Keefe, D. A., Sisson, D. D., Gelberg, H. B., Schaeffer, D. J. & Krawiec, D. R. (1993). Systemic toxicity associated with doxorubicin administration in cats. J Vet Intern Med 7, 309-317.
- Olsen, L. H., Fredholm, M. & Pedersen, H. D. (1999). Epidemiology and inheritance of mitral valve prolapse in Dachshunds. *J Vet Intern Med* **13**, 448-456.
- Ottenhoff, J., Hewitt, M., Makonnen, N., Kongkatong, M. & Thom, C. D. (2022). Comparison of the Quality of Echocardiography Imaging Between the Left Lateral Decubitus and Supine Positions. *Cureus* 14, e31835.
- Paige, C. F., Abbott, J. A., Elvinger, F. & Pyle, R. L. (2009). Prevalence of cardiomyopathy in apparently healthy cats. *J Am Vet Med Assoc* 234, 1398-1403.
- Panopoulos, I., Auriemma, E., Specchi, S., Diana, A., Pietra, M., Papastefanou, A., Zini, E. & Cipone, M. (2019). 64-multidetector CT anatomical assessment of the feline bronchial and pulmonary vascular structures. *J Feline Med Surg* 21, 893-901.
- Parker, H. G. & Kilroy-Glynn, P. (2012). Myxomatous mitral valve disease in dogs: does size matter? J Vet Cardiol 14, 19-29.
- Patel, D. A., Lavie, C. J., Milani, R. V., Shah, S. & Gilliland, Y. (2009). Clinical implications of left atrial enlargement: a review. *Ochsner J* 9, 191-196.
- Payne, J. R., Borgeat, K., Connolly, D. J., Boswood, A., Dennis, S., Wagner, T., Menaut, P., Maerz, I., Evans, D., Simons, V. E., Brodbelt, D. C. & Luis Fuentes, V. (2013). Prognostic indicators in cats with hypertrophic cardiomyopathy. *J Vet Intern Med* 27, 1427-1436.
- Payne, J. R., Brodbelt, D. C. & Luis Fuentes, V. (2015). Cardiomyopathy prevalence in 780 apparently healthy cats in rehoming centres (the CatScan study). J Vet Cardiol 17 Suppl 1, S244-257.
- Penninck, D. & d'Anjou, M.-A. (2015). Atlas of small animal ultrasonography, Second Edition. John Wiley & Sons.
- Petric, A. D., Stabej, P. & Zemva, A. (2002). Dilated cardiomyopathy in Doberman Pinschers: Survival, Causes of Death and a Pedigree Review in a Related Line. *J Vet Cardiol* **4**, 17-24.
- Picard, M. H., Adams, D., Bierig, S. M., Dent, J. M., Douglas, P. S., Gillam, L. D., Keller, A. M., Malenka, D. J., Masoudi, F. A., McCulloch, M., Pellikka, P. A., Peters, P. J., Stainback, R. F., Strachan, G. M. & Zoghbi, W. A. (2011). American Society of Echocardiography recommendations for quality echocardiography laboratory operations. J Am Soc Echocardiogr 24, 1-10.
- Pion, P. D., Kittleson, M. D., Thomas, W. P., Skiles, M. L. & Rogers, Q. R. (1992). Clinical findings in cats with dilated cardiomyopathy and relationship of findings to taurine deficiency. *J Am Vet Med Assoc* 201, 267-274.

- Pipers, F. S. & Hamlin, R. L. (1977). Echocardiography in the horse. J Am Vet Med Assoc 170, 815-819.
- Podlesnikar, T., Cardim, N., Ajmone Marsan, N., D'Andrea, A., Cameli, M., Popescu, B. A., Schulz-Menger, J., Stankovic, I., Toplisek, J., Maurer, G., Haugaa, K. H. & Dweck, M. R. (2022). EACVI survey on hypertrophic cardiomyopathy. *Eur Heart J Cardiovasc Imaging* 23, 590-597.
- Ponto, J. (2015). Understanding and Evaluating Survey Research. J Adv Pract Oncol 6, 168-171.
- Popescu, B. A., Andrade, M. J., Badano, L. P., Fox, K. F., Flachskampf, F. A., Lancellotti, P., Varga, A., Sicari, R., Evangelista, A., Nihoyannopoulos, P., Zamorano, J. L., Derumeaux, G., Kasprzak, J. D., Roelandt, J. R. T. C. & on behalf of the European Association of Echocardiography, D. R. (2009). European Association of Echocardiography recommendations for training, competence, and quality improvement in echocardiography. *European Journal of Echocardiography* 10, 893-905.
- Popescu, B. A., Stefanidis, A., Fox, K. F., Cosyns, B., Delgado, V., Di Salvo, G. D., Donal, E., Flachskampf, F. A., Galderisi, M., Lancellotti, P., Muraru, D., Sade, L. E. & Edvardsen, T. (2020). Training, competence, and quality improvement in echocardiography: the European Association of Cardiovascular Imaging Recommendations: update 2020. *Eur Heart J Cardiovasc Imaging* 21, 1305-1319.
- Posina, K., McLaughlin, J., Rhee, P., Li, L., Cheng, J., Schapiro, W., Gulotta, R. J., Berke, A. D., Petrossian, G. A., Reichek, N. & Cao, J. J. (2013). Relationship of phasic left atrial volume and emptying function to left ventricular filling pressure: a cardiovascular magnetic resonance study. J Cardiovasc Magn Reson 15, 99.
- Reynolds, C. A., Brown, D. C., Rush, J. E., Fox, P. R., Nguyenba, T. P., Lehmkuhl, L. B., Gordon, S. G., Kellihan, H. B., Stepien, R. L., Lefbom, B. K., Meier, C. K. & Oyama, M. A. (2012). Prediction of first onset of congestive heart failure in dogs with degenerative mitral valve disease: the PREDICT cohort study. J Vet Cardiol 14, 193-202.
- Rishniw, M. (2016). ESVC-O-14 Interobserver variability in two-dimensional echocardiographic left atrial measurements is complex. *Research Communication, 25th ECVIM-CA Congress, Lisbon, Portugal.*
- Rishniw, M. & Erb, H. N. (2000). Evaluation of four 2-dimensional echocardiographic methods of assessing left atrial size in dogs. J Vet Intern Med 14, 429-435.
- Rodevand, O., Bjornerheim, R., Ljosland, M., Maehle, J., Smith, H. J. & Ihlen, H. (1999). Left atrial volumes assessed by three- and two-dimensional echocardiography compared to MRI estimates. *The International Journal* of Cardiac Imaging 15, 397-410.
- Rossi, A., Cicoira, M., Zanolla, L., Sandrini, R., Golia, G., Zardini, P. & Enriquez-Sarano, M. (2002). Determinants and prognostic value of left atrial volume

in patients with dilated cardiomyopathy. *Journal of the American College of Cardiology* **40**, 1425-1430.

- Rossi, P. H., Wright, J. D. & Anderson, A. B. (2013). *Handbook of survey research*. Academic press.
- Safian, A. M., Menciotti, G., Lahmers, S. M., Jeong, H., Franchini, A. & Borgarelli, M. (2022). Performance of Different Echocardiographic Measurements of Left Atrial Size in Dogs by Observers with Different Levels of Experience. *Animals (Basel)* 12.
- Sahn, D. J., DeMaria, A., Kisslo, J. & Weyman, A. (1978). Recommendations regarding quantitation in M-mode echocardiography: results of a survey of echocardiographic measurements. *Circulation* 58, 1072-1083.
- Sánchez Salguero, X., Prandi, D., Llabrés-Díaz, F., Manzanilla, E. G. & Bussadori, C. (2018). A radiographic measurement of left atrial size in dogs. *Ir Vet J* 71, 25.
- Schabelman, S., Schiller, N. B., Silverman, N. H. & Ports, T. A. (1981). Left atrial volume estimation by two-dimensional echocardiography. *Cathet Cardiovasc Diagn* 7, 165-178.
- Schober, K. E. & Maerz, I. (2006). Assessment of left atrial appendage flow velocity and its relation to spontaneous echocardiographic contrast in 89 cats with myocardial disease. *J Vet Intern Med* 20, 120-130.
- Shave, R., Howatson, G., Dickson, D. & Young, L. (2017). Exercise-Induced Cardiac Remodeling: Lessons from Humans, Horses, and Dogs. *Vet Sci* **4**.
- Smiseth, O. A., Baron, T., Marino, P. N., Marwick, T. H. & Flachskampf, F. A. (2021). Imaging of the left atrium: pathophysiology insights and clinical utility. *Eur Heart J Cardiovasc Imaging* 23, 2-13.
- Song, G., Liu, J., Ren, W., Qiao, W., Zhang, J., Zhan, Y. & Bi, W. (2015). Reversible Changes of Left Atrial Function during Pregnancy Assessed by Two-Dimensional Speckle Tracking Echocardiography. *PLoS One* 10, e0125347.
- Spencer, K. T., Mor-Avi, V., Gorcsan, J., 3rd, DeMaria, A. N., Kimball, T. R., Monaghan, M. J., Perez, J. E., Weinert, L., Bednarz, J., Edelman, K., Kwan, O. L., Glascock, B., Hancock, J., Baumann, C. & Lang, R. M. (2001). Effects of aging on left atrial reservoir, conduit, and booster pump function: a multi-institution acoustic quantification study. *Heart* 85, 272-277.
- Stojanovska, J., Cronin, P., Patel, S., Gross, B. H., Oral, H., Chughtai, K. & Kazerooni, E. A. (2011). Reference Normal Absolute and Indexed Values From ECG-Gated MDCT: Left Atrial Volume, Function, and Diameter. *American Journal of Roentgenology* **197**, 631-637.
- Strohm, L. E., Visser, L. C., Chapel, E. H., Drost, W. T. & Bonagura, J. D. (2018). Two-dimensional, long-axis echocardiographic ratios for assessment of left atrial and ventricular size in dogs. *J Vet Cardiol* 20, 330-342.
- Takemoto, Y., Barnes, M. E., Seward, J. B., Lester, S. J., Appleton, C. A., Gersh, B. J., Bailey, K. R. & Tsang, T. S. M. (2005). Usefulness of Left Atrial Volume in Predicting First Congestive Heart Failure in Patients ≥65 Years

of Age With Well-Preserved Left Ventricular Systolic Function. *The American Journal of Cardiology* **96**, 832-836.

- Thomas, W. P. (1984). Two-dimensional, real-time echocardiography in the dog technique and anatomic validation. *Veterinary Radiology* **25**, 50-64.
- Thomas, W. P., Gaber, C. E., Jacobs, G. J., Kaplan, P. M., Lombard, C. W., Moise, N. S. & Moses, B. L. (1993). Recommendations for standards in transthoracic two-dimensional echocardiography in the dog and cat. Echocardiography Committee of the Specialty of Cardiology, American College of Veterinary Internal Medicine. J Vet Intern Med 7, 247-252.
- Thrusfield, M. V., Aitken, C. G. G. & Darker, P. G. G. (1985). Observations on breed and sex in relation to canine heart valve incompetence. *Journal of Small Animal Practice* 26, 709-717.
- Tidholm, A. (1997). Retrospective study of congenital heart defects in 151 dogs. *Journal of Small Animal Practice* **38**, 94-98.
- Tidholm, A., Bodegård-Westling, A., Höglund, K., Ljungvall, I. & Häggström, J. (2011). Comparisons of 2- and 3-dimensional echocardiographic methods for estimation of left atrial size in dogs with and without myxomatous mitral valve disease. J Vet Intern Med 25, 1320-1327.
- Tidholm, A., Häggström, J., Borgarelli, M. & Tarducci, A. (2001). Canine idiopathic dilated cardiomyopathy. Part I: Aetiology, clinical characteristics, epidemiology and pathology. *Vet J* 162, 92-107.
- Tidholm, A., Ljungvall, I., Michal, J., Häggström, J. & Höglund, K. (2015). Congenital heart defects in cats: a retrospective study of 162 cats (1996– 2013). *Journal of Veterinary Cardiology* 17, S215-S219.
- Tidholm, A., Menciotti, G. & Borgarelli, M. (2023). Current use of real-time threedimensional transthoracic echocardiography in animals. J Vet Cardiol 51, 97-104.
- Trehiou-Sechi, E., Tissier, R., Gouni, V., Misbach, C., Petit, A. M., Balouka, D., Sampedrano, C. C., Castaignet, M., Pouchelon, J. L. & Chetboul, V. (2012). Comparative echocardiographic and clinical features of hypertrophic cardiomyopathy in 5 breeds of cats: a retrospective analysis of 344 cases (2001-2011). J Vet Intern Med 26, 532-541.
- Treibert, J., Friederich, J., Fischer, S., Küchenhoff, H. & Wess, G. (2024). Reference intervals for various measurements of canine left atrial size and function obtained using two-dimensional and three-dimensional echocardiography. *J Vet Cardiol* 52, 43-60.
- Tsang, T. S. M., Abhayaratna, W. P., Barnes, M. E., Miyasaka, Y., Gersh, B. J., Bailey, K. R., Cha, S. S. & Seward, J. B. (2006). Prediction of Cardiovascular Outcomes With Left Atrial Size: Is Volume Superior to Area or Diameter? *Journal of the American College of Cardiology* 47, 1018-1023.
- Tsang, T. S. M., Barnes, M. E., Bailey, K. R., Leibson, C. L., Montgomery, S. C., Takemoto, Y., Diamond, P. M., Marra, M. A., Gersh, B. J., Wiebers, D. O., Petty, G. W. & Seward, J. B. (2001). Left atrial volume: important risk

marker of incident atrial fibrillation in 1655 older men and women. *Mayo Clinic Proceedings* **76**, 467-475.

- Tsang, T. S. M., Barnes, M. E., Gersh, B. J., Takemoto, Y., Rosales, A. G., Bailey, K. R. & Seward, J. B. (2003). Prediction of risk for first age-related cardiovascular events in an elderly population: the incremental value of echocardiography. *Journal of the American College of Cardiology* 42, 1199-1205.
- van Hoek, I., Payne, J. R., Feugier, A. & Connolly, D. J. (2018). Inter-observer variability for cardiac ultrasound measurements in cats repeated at different time points in early adult life. *Vet Anim Sci* 5, 44-46.
- Vatne, L., Dickson, D., Tidholm, A., Caivano, D. & Rishniw, M. (2021). The effects of activity, body weight, sex and age on echocardiographic values in English setter dogs. *J Vet Cardiol* 37, 26-41.
- Visser, L. C., Ciccozzi, M. M., Sintov, D. J. & Sharpe, A. N. (2019). Echocardiographic quantitation of left heart size and function in 122 healthy dogs: A prospective study proposing reference intervals and assessing repeatability. J Vet Intern Med 33, 1909-1920.
- Vollmar, A. C. (2000). The prevalence of cardiomyopathy in the Irish wolfhound: a clinical study of 500 dogs. *J Am Anim Hosp Assoc* **36**, 125-132.
- Vyas, H., Jackson, K. & Chenzbraun, A. (2011). Switching to volumetric left atrial measurements: impact on routine echocardiographic practice. *European Journal of Echocardiography* 12, 107-111.
- Wade, M. R., Chandraratna, P. A. N., Reid, C. L., Lin, S.-L. & Rahimtoola, S. H. (1987). Accuracy of nondirected and directed M-mode echocardiography as an estimate of left atrial size. *The American Journal of Cardiology* 60, 1208-1211.
- Wagner, T., Fuentes, V. L., Payne, J. R., McDermott, N. & Brodbelt, D. (2010). Comparison of auscultatory and echocardiographic findings in healthy adult cats. *J Vet Cardiol* 12, 171-182.
- Walker, A. L., DeFrancesco, T. C., Bonagura, J. D., Keene, B. W., Meurs, K. M., Tou, S. P., Kurtz, K., Aona, B., Barron, L., McManamey, A., Robertson, J. & Adin, D. B. (2022). Association of diet with clinical outcomes in dogs with dilated cardiomyopathy and congestive heart failure. *J Vet Cardiol* 40, 99-109.
- Wess, G., Kresken, J. G., Wendt, R., Gaugele, J., Killich, M., Keller, L., Simak, J., Holler, P., Bauer, A., Küchenhof, H. & Glaus, T. (2020). Efficacy of adding ramipril (VAsotop) to the combination of furosemide (Lasix) and pimobendan (VEtmedin) in dogs with mitral valve degeneration: The VALVE trial. J Vet Intern Med 34, 2232-2241.
- Whitney, J. C. (1974). Observations on the effect of age on the severity of heart valve lesions in the dog. *J Small Anim Pract* **15**, 511-522.

Popular science summary

Cardiovascular disease is one of the leading causes of death in both dogs and cats. These types of diseases affect the heart's structure, function, or electrical signals, which can lead to heart failure, a state which is characterized by a heart that no longer can pump enough blood to meet the body's needs. Heart disease can either be congenital (present at birth) or acquired later in life. Approximately 10% of the dog population and 10-15% of the cat population are diagnosed with heart disease.

Echocardiography, which is an ultrasound examination of the heart, is a key imaging modality used in both veterinary and human medicine to assess the anatomy, size and function of the heart chambers and valves. It provides real-time dynamic images, is non-invasive, and is widely accessible. However, the quality and accuracy of echocardiographic results can vary depending on how the operators perform the examination.

Echocardiographic assessment of the left atrial (LA) size is a fundamental part of the examination because it is important for screening, characterizing, and monitoring progression of heart disease in dogs and cats. Over the years, several different echocardiographic techniques and methods for LA size assessment in dogs and cats have been presented and published, often differing in acquisition view, instructions for caliper placement (measurement points), and/or reference values for normality. Currently in veterinary medicine, there is a lack of widely accepted guidelines for echocardiographic LA size assessment. This could contribute to interobserver variability, potentially resulting in differences in how dogs/cats are managed in clinical and research practice.

To address these challenges, this thesis initiated the BENEFIT project (gloBal caninE and feliNE leFt atrIal size assessmenT), an international study investigating how veterinary echocardiographers assess LA size in dogs and cats. The thesis aimed to explore similarities and differences in LA size assessment among veterinary echocardiographers. Veterinary echocardiographers from 67 countries across six continents participated in image and video web-based studies to assess how LA size is assessed.

We found that most echocardiographers used two-dimensional (2D) echocardiography from a right parasternal short-axis view (with the dog lying on its right side) and indexed LA size to the aorta (using the LA/Ao ratio). While most echocardiographers had similar preferences regarding method of choice for assessing the LA size, a large variation existed in image selection, timing, and caliper placement when measuring the dimensions of the LA and aorta. Factors like the echocardiographer's formal training, the number of echocardiograms performed per week, and timing in the cardiac cycle used for measurements affected the assessment and contributed to variation between observers. Although interobserver agreement in subjective assessments was comparably good, but improved after having performed linear measurements.

The thesis presents results that could help pave the way for more consistent and reliable echocardiographic assessment of LA size in veterinary medicine.

Populärvetenskaplig sammanfattning

Hjärt-kärlsjukdom är en av de främsta dödsorsakerna hos både hundar och katter. Dessa sjukdomar påverkar hjärtats struktur, funktion eller elektriska signaler, vilket kan leda till utveckling av hjärtsvikt, vilket karakteriseras av att hjärtat inte längre kan pumpa tillräckligt med blod för att tillgodose kroppens behov. Hjärtsjukdom kan vara antingen medfödd (finns vid födseln) eller förvärvas senare i livet. Cirka 10 % av hundpopulationen och 10-15 % av kattpopulationen diagnostiseras med hjärtsjukdom.

Ekokardiografi är en ultraljudsbaserad undersökningsmetod som används både inom veterinär- och humanmedicinen för att utvärdera hjärtats anatomi och storlek samt funktionen av hjärtats kamrar och klaffar. Tekniken möjliggör dynamiska bilder i realtid, är icke-invasiv och är vida tillgänglig. Undersökningens kvalitet och de ekokardiografiska mätningarnas precision kan emellertid variera beroende på hur operatörerna utför undersökningen.

Bedömning av vänster förmak (VF) är en fundamental del av en ekokardiografisk undersökning eftersom information om dets storlek är viktig vid screening-, karakterisering- och övervakning av hjärtsjukdom hos hundar och katter. Genom åren har flera olika ekokardiografiska tekniker och metoder presenterats och publicerats för bedömning av VF-storlek hos hundar och katter. Ofta skiljer sig olika presenterade metoder sig åt rörande val av bildplan, instruktioner för placering av mätpunkter och/eller normala referensvärden. För närvarande föreligger det inom veterinärmedicinen en brist på allmänt accepterade riktlinjer rörande ekokardiografisk bedömning av VF-storlek, vilket potentiellt kan bidra till interobservatörsvariabilitet och därmed resultera i skillnader i hur hundar/katter hanteras i klinisk och forskningsrelaterad praxis. För att adressera dessa utmaningar utgör denna avhandling början av det så kallade BENEFIT (gloBal caninE and feliNE leFt atrIal size assessmenT) projektet, vilket är ett internationellt projekt som undersöker hur veterinära ekokardiografer bedömer VF-storlek hos hundar och katter. Avhandlingen syftade till att utforska likheter och skillnader i bedömningen av VF-storlek bland veterinära ekokardiografer. Deltagare från 67 länder och sex kontinenter deltog i olika webbaserade studier innehållande både bild- och videomaterial för bedömning av VF-storlek.

Vi fann att de flesta ekokardiografer använde tvådimensionell (2D) ekokardiografi från en höger parasternal kortaxelvy och indexerade VFstorleken till aortan (stora kroppspulsådern). De flesta ekokardiografer hade liknande metodpreferenser för utvärdering av VF-storlek, men det förelåg stora variationer i bildval, timing och placering av mätpunkter vid mätning VF:s dimensioner. Faktorer av och aortas som operatörens specialiseringsnivå, hur ofta utförde operatören ekokardiografiundersökningar per vecka, och när i hjärtcykeln mätningarna utfördes, påverkade och bidrog till variation mellan observatörer. Subjektiv bedömning av VF-storlek överensstämde förhållandevis väl mellan observatörer, men förbättrades efter utförande av linjära mätningar.

Avhandlingen presenterar resultat som kan bidra till att bana väg för en mer konsekvent och tillförlitlig ekokardiografisk bedömning av VF-storlek inom veterinärmedicinen.

Acknowledgements

The present thesis was carried out at the Department of Clinical Sciences, at the Swedish University of Agricultural Sciences (SLU), Uppsala. The work in this thesis was supported by Scholarships for Taiwanese Studying in the Focused Fields, Ministry of Education, Taiwan.

This thesis would not have been possible without help and support from friends, colleagues, and my family.

I would also like to express my sincere thanks to *all the participating veterinary echocardiographers and veterinary associations around the globe* who helped us validate the study content, distributed the studies, participated in studies, and shared profoundly touching feedback with us. Thanks to your enthusiastic participation, I've been able to uncover these findings and persevere through this long journey.

I am deeply grateful for the opportunities I had to present our research findings at conferences during my PhD. These events were organized by ACVIM, ECVIM, Boehringer Ingelheim, and the British Cardiovascular Society, which made the journey even more meaningful and unforgettable.

I would especially like to express my genuine gratitude to:

Associate Professor **Ingrid Ljungvall**, my main supervisor and a truly wonderful woman, embodies generosity, humor, and wisdom. She is deeply committed to excellence, passionate about research, and has profound love and compassion for all living creatures. You are not only my mentor and an outstanding work partner but also a cherished friend in life. Thank you for exemplifying the rigor a researcher must bring to scientific inquiry while also nurturing my creative pursuits. Meeting you has been one of the most beautiful and transformative experiences of my life!

Professor **Jens Häggström**, my co-supervisor, is filled with wit and humor, easygoing and patient. He always provides timely encouragement, courage, and is generous with praise. Thank you for your unwavering support and affirmation in every moment of our research collaboration. Your positive attitude, along with your experience and intuition in research, have swiftly lifted me through challenges, ready to face them anew. Thank you for believing in and trusting me; I am honored to have been supervised by you.

Associate Professor **Katja Höglund**, my co-supervisor, shows profound care and support for her students and approaches science with meticulous rigor. Each of your greetings has dispelled the loneliness and hardship of this journey, making the path of scientific research feel secure with your presence. You care not only for my doctoral research but also teach me how to balance my physical, mental health, and work. I am deeply appreciative of your holistic approach to guidance.

Professor **Sonya G. Gordon**, my co-supervisor, is incredibly wise, confident, energetic, and charismatic. Your insightful ideas, creativity, networking have greatly contributed to our BENEFIT project. Thank you for all your valuable input, even from across the globe—I especially cherish our memorable meetings with you on the treadmill. I look forward to continuing to learn from you in my future!

Professor Etienne Côté and Adjunct Professor Mark Rishniw, collaborators on the BENEFIT project, thank you for the time you've dedicated to each of our study designs and manuscripts. Your valuable perspectives, experiences, and suggestions have greatly refined our work! I truly appreciate having you on our team. Your involvement inspires me even more to improve the development of veterinary echocardiography.

Mark Dirven, a collaborator on the BENEFIT project and a friend who supports and cares for both Hung-Ting and me in our life in Sweden, has shared his wide-ranging experiences and insights on different culture, life, and clinical practice. I am deeply grateful for your mentorship and friendship! Working with you has been a joy, and I know we will continue collaborating in the future.

Ta-Li Lu and **Yong-Wei Hung**, collaborators on the BENEFIT project and pivotal figures in introducing me to the field of small animal cardiology, have been essential to my achievements and the researcher I am today. Without

meeting you, none of this would have been possible. You have been role models in my growth, showing me that curiosity about knowledge and the world knows no bounds. Here's to creating a better future together for veterinarians, researchers, pet owners, and animals. Cheers!

Liv and Todd, without you both by my side during those final thesis writing sessions, sharing our stresses and supporting each other, I might not have been able to remain optimistic. I am truly thrilled and moved that we all made it through! Thank you for always being so reliable, for sharing so much, and for helping me extensively. Cheers to my wonderful partners!

Johanna and **Karin**, colleagues who always assist me with issues big and small, are empathetic, generously giving, and humorously spirited. You both have made my work in Sweden and my trips abroad for conferences filled with laughter and comfort, even providing chocolate during those tough office hours. You also embody a serious and courageous approach to life and work that is truly inspirational. I am so fortunate to know two brilliant women from whom I have so much to learn.

Aleks, Net, and Pack, thank you for your companionship during this journey. Whether discussing life in Sweden, our PhD experiences, or observations from our varied cultural backgrounds, you have enriched my life beyond our work. Together, we even navigated the challenges of COVID. I am grateful for each of you! Here's to us all taking big strides toward our dream futures.

Malin, Ninni, Pia, Jeanette, Åsa, Ylva and Susanne, thank you for the fikas and corridor chats that have shaped the beautiful memories of my PhD life in Sweden and deepened my understanding of Swedish culture. Your kindness and warmth have made the Swedish cold and darkness much more bearable! Thank you all.

Hao-Han, **Wen-Yen**, **Tung-Ju**, and **Chia-Hsin**, my former colleagues and good friends from the veterinary cardiology hospital in Taiwan, it feels like just yesterday that we shared those challenging and rewarding times together. Thank you for your support and encouragement these years. Five years have passed, and I believe we've all moved closer to our ideal selves. Let's continue to live earnestly for cardiology, for the animals, and for ourselves in the future.

Ι

Journal of Veterinary Cardiology (2024) 51, 157-171





www.elsevier.com/locate/jvc

Veterinary echocardiographers' preferences for left atrial size assessment in dogs: the BENEFIT project^{*}



M.Y.-W. Kuo^{a,*}, J. Häggström^a, S.G. Gordon^b, K. Höglund^c, E. Côté^d, T.-L. Lu^e, M. Dirven^f, M. Rishniw^g, Y.-W. Hung^h, I. Ljungvall^a

^a Department of Clinical Sciences, Faculty of Veterinary Medicine and Animal Science, Swedish University of Agricultural Sciences, Uppsala, Sweden

^b Department of Small Animal Clinical Science, Texas A&M University, College Station, TX, USA

^c Department of Anatomy, Physiology and Biochemistry, Faculty of Veterinary Medicine and Animal Science, Swedish University of Agricultural Sciences, Uppsala, Sweden ^d Department of Companion Animals, Atlantic Veterinary College, University of Prince Edward Island, Prince Edward Island, Canada

^e Chuan Animal Hospital, Taipei, Taiwan

^f Evidensia Södra Animal Hospital, Kungens Kurva, Sweden

^g Veterinary Information Network, Davis, CA, USA

^h Cardiospecial Veterinary Hospital, Taipei, Taiwan

Received 16 September 2022; received in revised form 13 October 2023; accepted 5 November 2023

KEYWORDS Cardiology; Echocardiography;

Abstract Introduction/objectives: Veterinary echocardiographers' preferences for left atrial (LA) size assessment in dogs have never been systematically investigated. The primary aim of this international survey study was to investigate

The preliminary data of the study were presented in abstract form at the 31st European College of Veterinary Internal Medicine-Companion Animals Online Congress on September 3, 2021.

* Corresponding author.

https://doi.org/10.1016/j.jvc.2023.11.002

1760-2734/© 2023 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

^{*} A unique aspect of the Journal of Veterinary Cardiology is the emphasis of additional web-based materials permitting the detailing of procedures and diagnostics. These materials can be viewed (by those readers with subscription access) by going to http://www.sciencedirect.com/science/journal/17602734. The issue to be viewed is clicked and the available PDF and image downloading is available via the Summary Plus link. The supplementary material for a given article appears at the end of the page. To view the material is to go to http://www.doi.org and enter the doi number unique to this paper which is indicated at the end of the manuscript.

E-mail address: Momo.Y-W.Kuo@slu.se (M.Y.-W. Kuo).

Heart failure; Valvular disease; Cardiomyopathy	 echocardiographers' preferences for LA size assessment in dogs. The secondary aim was to investigate echocardiographers' preferences for assessing LA size in subgroups based on geographic, demographic, and professional profiles. <i>Animals, materials, and methods</i>: An online survey instrument was designed, verified, and distributed globally to the veterinary echocardiographers. <i>Results</i>: A total of 670 echocardiographers from 54 countries on six continents completed the survey. Most echocardiographers (n = 621) used linear two-dimensional (2D)-based methods to assess LA size, 379 used subjective assessment, and 151 used M-mode-based methods. Most commonly, echocardiographers (n = 436) using linear 2D-based methods alone. Most echocardiographers (n = 436) using linear 2D-based methods alone. Most echocardiographers (n = 436) using linear 2D-based methods alone. Most echocardiographers shared the same preferences regarding dog position, acquisition view, indexing method, and identification of the time-point used for the measurement. The responses were comparably homogeneous across geographic location, training level, years of performing echocardiography, and type of practice. <i>Discussion/conclusion:</i> Most veterinary echocardiographers assessed LA size in dogs using linear 2D echocardiography from a right parasternal short-axis view, and by indexing the LA to the aorta. The respondents' preferences were similar across geographic, demography, and professional backgrounds. © 2023 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

Abbre	Abbreviations	
2D	2-dimensional	
Ao	aorta	
LA	left atrium, left atrial	
мм	M-mode	

Introduction/objectives

Assessment of left atrial (LA) size plays an important role in establishing diagnosis and prognosis, grading disease severity, and timing of treatment in dogs with cardiac disease [1-5]. Echocardiographers can evaluate LA size qualitatively (subjectively) and quantitatively (objectively) using one-dimensional (M-mode, MM), two-dimensional (2D), and three-dimensional echocardiographic techniques, and various methods have been suggested for this purpose [6-9]. Multiple factors may influence how veterinary echocardiographers assess LA size, including the modalities available in the ultrasonographic system, the level of experience and training features, and personal preference for using specific methods [10,11].

Expert groups have created and disseminated recommendations for standardizing the methodology used to quantify cardiac chambers in humans [12,13], but no similar recommendations currently exist in veterinary medicine. Investigators have proposed reference intervals for specific echocardiographic methods assessing LA size in dogs [8,9,14–19], which might, in part, reflect the variation in assessment between echocardiographers rather than between methods. A lack of consistency in assessments could negatively impact the assessment of disease severity and prognosis, as well as how published clinical study results and expert treatment guidelines are interpreted and implemented.

Prior to proposing actions to address these concerns, an essential first step is to quantitatively investigate the variability of echocardiographic assessment of LA size in dogs. The gloBal caninE and feliNE leFt atrial size assessmenT (BENEFIT) project is an international research collaboration aimed at exploring how veterinary echocardiographers assess LA size in dogs and cats, which may provide useful information for future work to improve echocardiographic LA size assessment in dogs and cats. The American Society of Echocardiography and the European Association of Cardiovascular Imaging have surveyed echocardiographers to examine potential sources of inter-observer variability in echocardiographic assessments and to identify potential discrepancies between recommendations and everyday clinical practice [20-24]. These studies aimed to identify differences and similarities in how echocardiographers and centers perform clinical imaging, in order to address challenges in complex areas and further improve guidelines and recommendations in the future [21,25,26]. Although it is widely acknowledged that veterinary echocardiographers use a variety of methods and have different preferences for assessing LA size in dogs, the extent of this variation has, to our knowledge, never been investigated systematically.

The primary aim of this prospective study was to investigate echocardiographers' preferences concerning LA size assessment in dogs, including echocardiographic techniques (MM, linear 2D, area-based, volume-based, and subjective assessment) and methods (positioning of the dog, acquisition views, indexing methods, and identification of the time-point used for the measurement). The secondary aim was to investigate echocardiographers' preferences for assessing LA size in subgroups based on geographic, demographic, and professional profiles.

Animals, materials and methods

An English-language survey instrument was constructed and validated using recognized principles [27-31], and it was deployed using an online platform¹. The survey design process is depicted in Supplemental Table A. Respondents were instructed to participate only once, and the survey could only be accessed once, using the same device. All respondents participated anonymously. There was no incentive provided to respondents other than contributing to the development of knowledge. The period of collection of responses was September 18th to November 1st, 2020. Respondents were asked to answer questions based on their situation prior to the COVID-19 restrictions. Respondents who were no longer in clinical practice were asked to answer questions based on their past practice.

Study enrollment

Inclusion criteria

Individuals who performed, or had previously performed, echocardiogram in dogs.

Exclusion criteria

Individuals who did not meet the inclusion criteria and those who provided contradictory responses (e.g. respondents who stated, in an initial question, that they performed echocardiogram in dogs, or that they used a specific echocardiographic technique, but then stated the opposite in a subsequent question).

Survey instrument

The 134 survey questions were divided into three parts (Fig. 1). Respondents were directed to relevant subsequent questions according to their answers to the preceding questions; thus, they were not required to respond to all the questions. Most questions (129/134) were mandatory and were primarily formatted as multiple-choice questions comprising both single- and multipleanswer possibilities. Respondents could provide free-text answers if their option was missing from the listed response options. Five optional questions were open-ended. The guestions in Parts 1 (12 questions) and 3 (16 questions) were for all respondents. Respondents who performed echocardiogram in both dogs and cats were directed to all questions in Part 2 (106 questions); respondents who only performed echocardiogram in dogs or cats were directed to the relevant questions in Part 2 (53 questions). The filter questions and illustrations were designed to reduce misconceptions regarding animal species and technique of use for each question. The survey question stems, associated answer alternatives, and illustrations are reported in Supplemental Document I.

PART 1: general background of respondents

Questions related to respondents' geographic, demographic, and professional profiles in echocardiography.

PART 2: techniques/methods of echocardiographic assessment of left atrial size in dogs

Questions included in part 2.1 were related to the following echocardiographic techniques: (1) subjective assessment, (2) MM, (3) linear 2D, (4) area, and (5) volume. Respondents were asked to specify their most commonly used technique(s) for assessing LA size (multiple answers were possible) and were then directed to relevant questions regarding their technique(s) of choice to share details. Questions in part 2.2 were related to respondents' opinions of their technique(s)/method(s) of choice.

PART 3: self-assessment regarding echocardiographic preferences and training

Questions were related to the respondents' preferences regarding echocardiography, echocardiographic experiences, and their level of training.

ⁱ Netigate AB, Stockholm, Sweden.

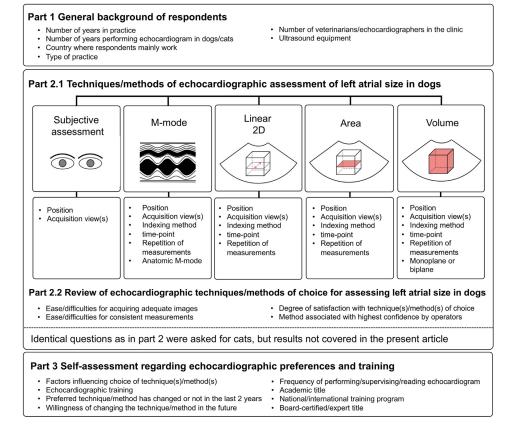


Figure 1 Survey construction and overview of questions. Illustrations correspond to the five different echocardiographic techniques evaluated in the survey. See Supplemental Document I for further details about the survey questions and answer alternatives. 2D: two-dimensional.

Pretest verification

A three-phase pretest was performed in the survey design process (Supplemental Table A) using the modified Delphi method [32]:

Phase 1

A group of subject-matter experts (n = 9), consisting of board-certified cardiologists and researchers working in academia or private clinical practice, from Canada, Sweden, Taiwan, the Netherlands, and the United States, reviewed the survey instrument with the goal of identifying perceived flaws and limitations, and stating recommended changes. Revisions were made according to the comments received.

Phase 2

A reference group (n = 12), consisting of echocardiographers who regularly performed

echocardiography in dogs and cats, but who were not working in academia and were not boardcertified cardiologists, and who worked in various fields of veterinary medicine (cardiology, diagnostic imaging, emergency and critical care, and internal medicine) in different countries and territories (Australia, China, Hong Kong, Japan, Singapore, Sweden, the Netherlands, the United States, and Zambia), tested the survey. Most echocardiographers (9/12) in the reference group were non-native English speakers. Revisions were made according to the comments received. The subject-matter experts involved in Phase 1 were not eligible to participate in Phase 2.

Phase 3

The survey was tested and amended again by nine subject-matter experts prior to the survey distribution.

Data collection

Veterinary echocardiographers were invited to participate in the study, which was distributed through the following channels: (1) Chairpersons of national veterinary organizations and key-opinion leaders of veterinary internal medicine/cardiology associations in 34 countries; (2) American and European Colleges of Veterinary Internal Medicine, Cardiology ListServe, hosted by the Veterinary Information Network. The subscribers of ListServe include veterinarians globally who had voluntarily registered to receive ListServe emails because of their interest in veterinary cardiology and include all American and European College of Veterinary Internal Medicine cardiology diplomates and candidates, as well as other interested veterinarians; and (3) international cardiology virtual congresses. Reminders were sent out after 14 and 30 days in groups (1) and (2).

Statistical analysis

Descriptive analyses of the survey results were performed. The response counts and percentages were calculated.

Results

A total of 949 individuals provided responses, of which 702 (74.0%) completed the survey. Entries from 32 respondents were considered invalid and were excluded (Fig. 2). The results described below are from responses provided by the 670 respondents. Respondents (n = 3) from one country reported that

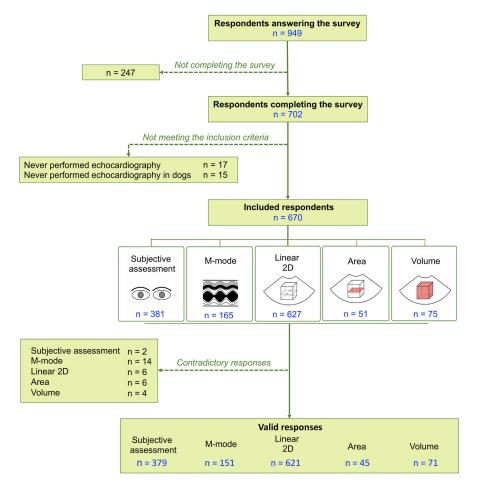


Figure 2 Flow chart demonstrating the process of extracting valid survey responses. Contradictory responses for an echocardiographic technique led to exclusion of survey responses for that particular technique, whereas the remaining responses from these respondents were retained. 2D: two-dimensional.

the survey link could not be opened without access to VPN in their country.

Geographic, demographic, and professional profile

Echocardiographers providing responses worked in 54 countries on six continents (Fig. 3 and Supplemental Table B). The demographic and professional profiles of the respondents are presented in Supplemental Figure I. Most echocardiographers (n = 644/670, 96.1%) reported that they performed echocardiograms regularly in the 12 months preceding the survey (or portion of 12 months excluding COVID-19 restrictions, as relevant). In general, respondents with longer experience in echocardiography performed and supervised/taught more echocardiographic examinations and read more echocardiograms per week compared to respondents with fewer years of experience (Supplemental Figure IB). Twenty-four % (n = 164/ 670) had been trained in an international specialty training program (e.g. ACVIM/ECVIM/Asian College of Veterinary Internal Medicine, AiCVIM), 22.5% (n = 151/670) in a national specialty training program, and 2.7% (n = 18/670) in both a national and international specialty training program. Respondents had mostly learned to perform echocardiograms from echocardiography courses (n = 428/670, 63.9%) and/or were self-taught (n = 302/670, 45.1%). Approximately half of the respondents (n = 317/670,

47.3%) were the only echocardiographers who regularly practiced echocardiography at their workplace.

Preferences for echocardiographic approach for LA size assessment in dogs

The respondents most commonly used the linear 2D technique (n = 621/670, 92.7%) when assessing LA size, followed by the subjective assessment (n = 379/670, 56.6%), and the MM technique (n = 151/670, 22.5%) (Fig. 4A). Most commonly, respondents combined the linear 2D technique with subjective assessment (n = 222/670, 33.1%), followed by the linear 2D technique alone (n = 191/670, 28.5%), or by combining the MM technique, linear 2D, and subjective assessment (n = 68/670, 10.1%) (Fig. 4B). Most respondents (n = 512/670, 76.4%) trusted the linear 2D technique the most when assessing LA size.

Quantitative assessment

Linear two-dimensional

Most of the 621 respondents (n = 470/621, 75.7%) who assessed LA size using a linear 2D technique preferred to acquire images with dogs positioned in right lateral recumbency and using the right parasternal short-axis view (Fig. 5). Similarly, most respondents preferred indexing the LA dimension to the aortic (Ao) dimension, using 2D echocardiographic guidance for timing the

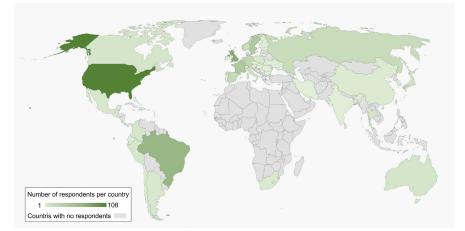


Figure 3 Geographic distribution of 670 veterinary echocardiographers spanning 54 countries. Detailed information of geographic location of the respondents are reported in Supplemental Table B.

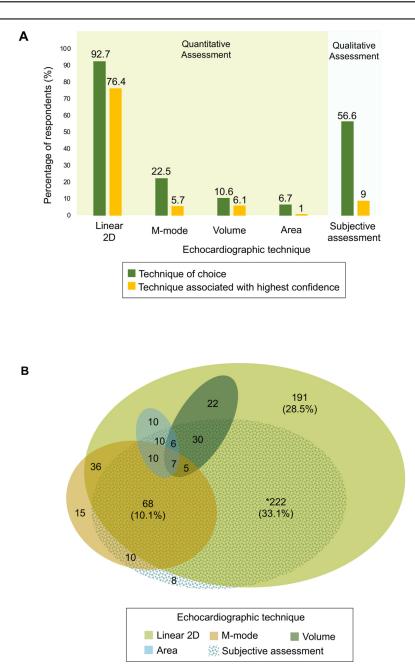


Figure 4 An overview of the veterinary echocardiographers' preferences for left atrial size assessment in dogs (n = 670), showing (A) the most commonly used (multiple-choice) and trusted (single-choice) echocardiographic technique for the purpose, and (B) the different approaches for assessing the left atrial size. Respondents that used other echocardiographic techniques (n = 17) and other combinations (n = 3) were not included in (B). The size of the areas in (B) are approximately in proportion to the actual number of the responses for each technique, and the numbers represent the number of the responses for each method and the combination of techniques. *222 echo-cardiographers combined linear technique and subjective assessment when assessing LA size in dogs.

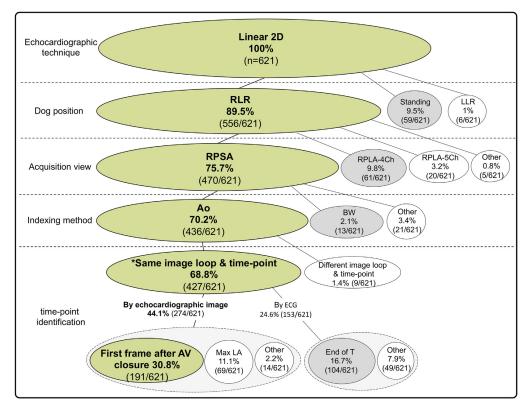


Figure 5 Linear 2D preferences for assessment of the left atrial size in dogs based on responses from 621 veterinary echocardiographers. Questions regarding dog position, acquisition view, indexing method and time-point identification for measurements had single discrete options for responding. The answers with the most (green) and second most (gray) responses in each layer are marked. The branch was only extended from the answers with most responses in the previous question. Answer alternatives receiving less than 2% of the responses for the linear 2D method were grouped as 'other'. 2D: two-dimensional; Ao: aorta; AV: aortic valve; BW: body weight; LLR: left lateral recumbency; RLR: right lateral recumbency; RPSA: right parasternal short-axis view; RPLA-4Ch: right parasternal long-axis four chamber view; assessment.

measurement by identifying the first frame after aortic valve closure. Of the respondents using the linear 2D technique, 30.8% (n = 191/621) had identical preferences regarding the position of the dog during the examination, acquisition view, indexing method, and identification of the timepoint used for the measurements. Approximately two-thirds of these respondents (n = 422/621, 68.0%) acquired replicate measurements over several cardiac cycles and averaged these.

M-mode

Most of the 151 respondents (n = 69/151, 45.7%) who assessed LA size using a MM technique preferred acquiring images with dogs positioned in right lateral recumbency, using the right parasternal short-axis view (Supplemental Figure II). Half of these respondents (n = 76/151, 50.3%) used anatomic MM. Most respondents preferred indexing the LA dimension to the Ao dimension, using echocardiographic guidance for timing the measurement of these two structures. To measure the Ao dimension, most respondents identified the time-point on the MM showing two Ao cusps. To measure the LA dimension, most respondents identified the time-point on the MM showing the maximal LA size. Few respondents using MM (n = 8/151, 5.3%) had identical preferences regarding positioning of the dog, acquisition view, indexing method, and identification of timepoint used for the measurements. Approximately two-thirds of these respondents (n = 100/151,

66.2%) acquired replicate measurements over several cardiac cycles and averaged these.

Volume

Most of the 71 respondents (n = 26/71, 36.6%) who measured LA size using the biplane Simpson's modified method of discs preferred to acquire images with dogs positioned in left lateral recumbency and using the left apical four-chamber and two-chamber views (Supplemental Figure III). Similarly, most respondents preferred indexing LA volume to body weight, using 2D echocardiographic guidance for timing the measurement by identifying the last frame before mitral valve opening. Of these respondents, 43.7% (n = 31/71) acquired replicate measurements over several cardiac cycles and averaged these.

Area

Most of the 45 respondents (n = 16/45, 35.6%) who assessed LA areas preferred to acquire images with dogs positioned in right lateral recumbency and using the right parasternal short-axis view (Supplemental Figure IV). Similarly, most respondents preferred indexing the LA area to the Ao area, using 2D echocardiographic guidance for timing the measurement by identifying the image showing the maximal LA area. Forty-nine percent (n = 22/45) of these respondents acquired replicate measurements over several cardiac cycles and averaged these.

Qualitative assessment

Subjective assessment

Most of the 379 respondents (n = 358/379, 94.5%) who assessed LA size subjectively also assessed it quantitatively (Fig. 4B). Most examined images with dogs were positioned in right lateral recumbency and imaged the LA from both right parasternal short-axis views (n = 277/379, 73.1%) and right parasternal long-axis four-chamber views (n = 265/379, 69.9%) (Supplemental Figure V).

Factors influencing choice of echocardiographic technique/method and respondents' willingness to change methods

Respondents reported being substantially influenced by clinical studies/guidelines/textbooks, echocardiography courses, and supervisors in their preferences for LA size assessment (Fig. 6).

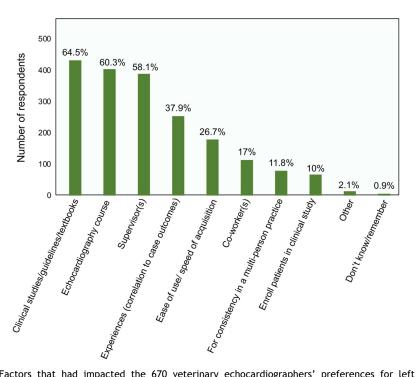


Figure 6 Factors that had impacted the 670 veterinary echocardiographers' preferences for left atrial size assessment in dogs.

Echocardiographers' preferences were comparably similar across the groups based on geographic location, level of training, years performing echocardiography and type of practice, as shown in Supplemental Figures VI, VII, Table C, and D. Most respondents stated that they were willing to change the method of assessing LA size in the future (Supplemental Table C).

Discussion

To our knowledge, this study represents the first, and currently the only, large-scale investigation examining how veterinary echocardiographers with a variety of training backgrounds evaluate LA size. The present survey instrument, constructed using scientifically tested methods with rigorous validation, sampling from academia and practice, and from 54 countries, generated a large volume of data that showed veterinary echocardiographers' preferences concerning LA size assessment in dogs. Most veterinary echocardiographers assessed LA size in dogs using linear 2D echocardiography from a right parasternal short-axis view and indexing the LA to the Ao. However, despite the apparent agreement for this imaging plane, only approximately one-third of those who used a linear 2D technique shared the same preferences regarding dog position, acquisition view, indexing method, and identification of the time-point used for measurement. Additionally, most echocardiographers combined their objective assessment with a subjective estimate of LA size. We found that the respondents' preferences were similar across geographic, demographic, and professional backgrounds.

More than 90% of echocardiographers assessed LA size in dogs using a linear 2D technique with or without another technique. Most echocardiographers who used a linear 2D technique assessed LA size from a right parasternal short-axis view and indexed the LA dimension to the Ao. Only 13% of the respondents used a right parasternal long-axis view, regardless of dog positioning. This view was more frequently used by echocardiographers working in North America and/or academia and by respondents with more than 20 years of echocardiographic experience and/or being international specialists. The overwhelming preference for estimating the LA:Ao ratio from a right parasternal short-axis view may be related to a wealth of published studies in which this method has been used [2-5,33,34], along with the ease of acquiring an image that includes both the Ao and the LA in the same view. The Ao short-axis dimension has been widely used for normalizing LA size,

presumably because few diseases in dogs change the Ao size, and because it is not influenced by body condition score [14]. The American College of Veterinary Internal Medicine consensus guidelines for staging and treating myxomatous mitral valve disease, which is the most prevalent heart disease in dogs, recommend using the right parasternal short-axis method [35,36]. Such recommendations likely influenced the preference of echocardiographers. The method has, furthermore, been reported to be more sensitive at detecting LA enlargement than MM-based estimates [15], and it has, in several studies, been demonstrated to be one of only a few variables that consistently shows a high prognostic value in dogs with heart diseases [1-4]. Even though the lateral LA wall may, in some cases, be more readily identified in the right parasternal long-axis view, comparably few respondents used this method.

Approximately one-third of the respondents using a linear 2D technique reported relying solely on this technique when assessing LA size in dogs, again presumably reflecting a high confidence in linear 2D-based methods, whereas the other twothirds preferred to combine various techniques, most commonly with subjective assessment. Respondents identified subjective assessment as the second most trusted technique according to the results in the self-assessment part of the study. However, most respondents trusted quantitative measurements more. More than half of the respondents assessed the LA subjectively, but almost none reported using this technique alone. Even though subjective assessment appeared to be a popular approach for evaluating LA size, its utility and performance in the hands of veterinary echocardiographers is currently unknown. Respondents trained in international specialty programs subjectively assessed LA size more frequently than respondents with other backgrounds. A possible explanation for this finding might be that the echocardiographers who have undergone international specialty training in cardiology have received extensive practical supervised training, and, thus, have gained more experience leading to greater confidence in their subjective assessment. In addition, 55% (n = 72/132) of the respondents working in North America were international specialists, which might explain why respondents working in this location favored subjective assessment more than those working in other continents.

Approximately 30% (n = 191/621) of the echocardiographers who used a linear 2D technique shared the same preferences regarding dog position, acquisition view, indexing method and identification of time-point used for the measurement.

Although echocardiographers mostly preferred linear 2D-based methods for assessing LA size in dogs, the specific preferences varied: those who preferred calculating the LA:Ao ratio from a right parasternal short-axis view (n = 436/621, 70.2%) had comparably homogeneous preferences for dog positioning (right lateral). Imaging the dogs in a standing position was more frequently performed by echocardiographers working in Europe and South America compared to those working in other continents. Approximately 80% (n = 364/436) of the respondents who calculated LA:Ao from a short-axis view measured the LA dimension in a similar time phase (ventricular end-systole/early diastole and end of T wave, namely at the maximal LA size), but their preferences for identification of time-point varied substantially. Approximately 45% (n = 191/436) performed the measurement at the first frame after Ao valve closure, which is in agreement with initial studies describing the method [15,16]. One potential explanation for why the rest identified the timepoint for measuring the LA dimension differently might be that the active ventricular myocardial motion in systole and early-diastole can sometimes blur the outline of the cardiac structures, including the aortic cusps [19,37]. Another possibility of the observed variation in time-point identification for LA size assessment may be due to non-uniform descriptions and variable recommendations for echocardiographic methods in textbooks [6–9], published literature, and echocardiography courses. Comparably, few respondents prioritized the right parasternal long-axis view for assessing LA size, making it difficult to draw any conclusions about their preference for this technique.

approximately one-quarter of Although respondents used a MM technique for assessing LA size in dogs, few trusted the technique the most. Similarly, few respondents stated that they assessed LA size solely with this technique. No clear pattern was identified when characterizing the respondents who used MM, except that the technique was more frequently used by echocardiographers working in North America, compared to those in other continents, and by echocardiographers not working in academia. The use of MM-based methods for assessing LA size is rarely described in recent literature, which contrasts with the number of echocardiographers who still commonly use this technique. Despite several inherent limitations of this technique [14,15,38,39], possible explanations for its popularity could be high temporal and image resolutions, which are of value for border detection and timing, thereby facilitating appropriate cursor

placement when measuring the chamber [40,41], training, and personal habits.

Few respondents reported using volume- or areabased methods to quantitatively assess LA size in dogs. The low numbers made it difficult to draw strong conclusions about these respondents. A comparably high proportion of echocardiographers had confidence in volume-based methods, but a small proportion expressed confidence in areabased methods. Those who used volumetric methods most commonly used Simpson's modified method of discs applied to 2D biplane images for assessing LA size, similar to findings from an echocardiographic survey on cardiac chamber quantification in people [21]. Based on the results of the present study, the three-dimensional technique is not currently widely used for LA volume assessment in dogs. The finding that comparably few echocardiographers assessed LA size using volume- or area-based methods may be explained by the later introduction of these methods in veterinary medicine, the need for specialized equipment with the required software, and that they are more timeconsuming and laborious compared to the MM and linear 2D methods. Furthermore, the use of volumetric assessment is presumably also limited by a shortage of reliable reference intervals, and currently, it is unknown which method most accurately estimates the true LA size. Furthermore, the published large clinical trials [3,33,42,43] have hitherto not included volumetric assessment as a major inclusion criterion or primary outcome variable. The absence of methods for estimating LA volume in these trials may have influenced the results of the current study. Finally, no clinical study has shown that more complex 2D and three-dimensional methods are better prognosticators of clinical outcomes than simple linear estimates of LA enlargement [44].

Respondents reported being substantially influenced by clinical studies/guidelines/textbooks, echocardiography courses and supervisors in their preferences for assessing LA size, and most respondents had learned to perform echocardiograms at echocardiography courses and/or were self-taught. This is not surprising, as most respondents were not cardiologists or radiologists who would have had formal extended training. Only approximately one guarter of the respondents stated that ease of use or speed of acquisition influenced their preferences for certain methods. Nearly half of the respondents reported that they were the only person practicing echocardiography regularly at their workplace. These findings highlight the importance of training, continuing education, and guidelines/recommendations for veterinary echocardiographers and people aspiring to start performing echocardiograms.

Well-designed survey instruments provide a rigorous approach to research with scientifically tested methods to ensure a high-quality process and outcome [31,45,46]. Appropriately designed survey studies in echocardiography can, accordingly, have the potential to identify differences and similarities in veterinary clinical imaging and serve as a valuable base for future work in the area. The method of this study mirrors the approach recently chosen by the European Association of Cardiovascular Imaging for a similar purpose [25].

A limitation of this study was that the results are based on self-reported responses that could not be verified independently. The subjectivity of the respondents' interpretations of certain terms, such as 'regularly performed echocardiograms,' could have introduced inter-respondent variability. The data analyzed and reported were based on all valid responses, and no lower limit of participants for each category of geographic, demographic, or professional profile was set. Another limitation was that, similar to many other published survey studies, no inferential statistics were included because these types of studies are inherently associated with several steps of selection bias and other limitations, making statistical analysis less appropriate [21,47]. The online survey was structured in English, which might have impacted the interpretation and understanding of some of the questions and answer alternatives for non-native English respondents. However, to ensure as little language confusion as possible, we invited 12 echocardiographers (three native and nine non-native English speakers) working in different countries/fields to validate the survey content prior to broad distribution during the study design. We performed several rounds of pretest by echocardiographers of various backgrounds in the 3-phase verification to ensure the quality and validity of the survey data. Only respondents who had access to the internet could participate in the survey, and some respondents reported that access to the survey link was denied in their countries. As the number of respondents in each country could also be affected by how the local chairpersons or key-opinion leaders promoted the survey, the respondents from each country might not have been in proportion to the real number of echocardiographers in a specific country. A further limitation with this study is that the definition of international and national specialist might vary between different countries. In the survey, the specialty-relevant questions

and alternatives were phrased attentively, with annotations if possible, and free-text answers were allowed to overcome this issue.

The present study aimed to identify the veterinary echocardiographers' most prioritized echocardiographic method in daily practice for assessing LA size in dogs, and many questions had single, discrete options for responding. Thus, the study could not capture every possible choice if respondents preferred more than one option for response alternatives, or had a nuanced response. Adding more questions could have addressed this limitation, but at the expense of greater length and thus, respondent fatigue [48]. Therefore, the investigators acknowledged this limitation with the understanding that alternatives were not necessarily superior.

Conclusions

Veterinary echocardiographers most commonly used and trusted linear 2D-based methods to assess LA size in dogs. Most preferred to use the right parasternal short-axis view indexed to the Ao in combination with subjective assessment for the purpose. Although these broad preferences were comparably homogeneous across echocardiographers, fewer than one third shared the exact same combination of preferences regarding position of the dog during the examination, acquisition view, indexing method, and identification of time-point used for the measurements. Echocardiographers reported that clinical studies/guidelines/textbooks, echocardiography courses and supervisors exerted the most influence on their preferences for assessing LA size. The respondents' preferences were similar across geographic, demographic, and professional backgrounds. Findings of the present study could have important implications for future work aimed at optimizing and uniforming the assessment of LA size among veterinary echocardiographers.

Funding

Scholarships for Taiwanese Studying in the Focused Fields, Ministry of Education, Taiwan.

Conflict of Interest Statement

The authors do not have any conflicts of interest to disclose.

Acknowledgments

The authors would like to thank Myriam Baranger-Ete, Marlies Böhm, Thomas J. Boumans, Ayaka Chen, Anna Djupsjöbacka, Johanna Frank, Weibin Guo, Adam Honeckman, Hanneke van Meeuwen, Sharon Troiano Shull, and Shih-Ping Yeh for helping in the pretest verification and disseminating the survey; the chairpersons/key-opinion leaders who disseminated and promoted the survey; and all the respondents globally who participated in the survey.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.jvc.2023.11.002.

References

- [1] Borgarelli M, Crosara S, Lamb K, Savarino P, La Rosa G, Tarducci A, Häggström J. Survival characteristics and prognostic variables of dogs with preclinical chronic degenerative mitral valve disease attributable to myxomatous degeneration. J Vet Intern Med 2012;26:69–75.
- [2] Borgarelli M, Savarino P, Crosara S, Santilli R, Chiavegato D, Poggi M, Bellino C, La Rosa G, Zanatta R, Häggström J, Tarducci A. Survival characteristics and prognostic variables of dogs with mitral regurgitation attributable to myxomatous valve disease. J Vet Intern Med 2008;22:120-8.
- [3] Boswood A, Häggström J, Gordon SG, Wess G, Stepien R, Oyama MA, Keene BW, Bonagura J, MacDonald KA, Patteson M, Smith M, Fox PR, Sanderson K, Woolley R, Szatmári V, Menaut P, Church WM, O'Sullivan ML, Jaudon J-P, Kresken J-G, Rush J, Barrett KA, Rosenthal SL, Saunders AB, Ljungvall I, Deinert M, Bomassi E, Estrada AH, Fernandez Del Palacio MJ, Moise NS, Abbott JA, Fujii Y, Spier A, Luethy MW, Santilli RA, Uechi M, Tidholm A, Watson P. Effect of pimobendan in dogs with preclinical myxomatous mitral valve disease and cardiomegaly: the EPIC study—a randomized clinical trial. J Vet Intern Med 2016;30:1765—79.
- [4] Dukes-McEwan J, Borgarelli M, Tidholm A, Vollmar AC, Häggström J, ESVC Taskforce for Canine Dilated Cardiomyopathy. Proposed guidelines for the diagnosis of canine idiopathic dilated cardiomyopathy. J Vet Cardiol 2003;5:7–19.
- [5] Saunders AB, Gordon SG, Boggess MM, Miller MW. Longterm outcome in dogs with patent ductus arteriosus: 520 cases (1994–2009). J Vet Intern Med 2014;28:401–10.
- [6] Boon J. Evaluation of size, function, and hemodynamics. Veterinary echocardiography. Hoboken: Wiley-Blackwell; 2011. p. 153–247.

- [7] Fuentes L. Echocardiography and Doppler ultrasound. In: Smith F, Tilley L, Oyama M, Sleeper M, editors. Manual of canine and feline cardiology. Philadelphia: Saunder; 2015. p. 77–92.
- [8] Fuentes L. Echocardiography. In: Fuentes L, Johnson LR, Dennis S, editors. BSAVA manual of canine and feline cardiorespiratory medicine. Castle Donington: British Small Animal Veterinary Association; 2010. p. 79–97.
- [9] de Madron E. Normal echocardiographic values: TM, 2D, and Doppler spectral modes. In: de Madron E, Chetboul V, Bussadori C, editors. Clinical Echocardiography of the dog and cat. St. Louis: Elsevier; 2016. p. 21–37.
- [10] Chetboul V, Athanassiadis N, Concordet D, Nicolle A, Tessier D, Castagnet M, Pouchelon J, Lefebvre H. Observer-dependent variability of quantitative clinical endpoints: the example of canine echocardiography. J Vet Pharmacol Ther 2004;27:49–56.
- [11] Chetboul V. Intra-and interoperator variability. In: de Madron E, Chetboul V, Bussadori C, editors. Clinical echocardiography of the dog and cat. St. Louis: Elsevier; 2016. p. 39–43.
- [12] Delgado V, Cardim N, Cosyns B, Donal E, Flachskampf F, Galderisi M, Gerber B, Gimelli A, Haugaa KH, Kaufmann PA, Lancellotti P, Magne J, Masci PG, Muraru D, Habib G, Edvardsen T, Popescu B. Criteria for recommendation, expert consensus, and appropriateness criteria papers: update from the European Association of Cardiovascular Imaging Scientific Documents Committee. Eur Heart J Cardiovasc Imaging 2018;19:835–7.
- [13] Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, Flachskampf FA, Foster E, Goldstein SA, Kuznetsova T, Lancellotti P, Muraru D, Picard MH, Rietzschel ER, Rudski L, Spencer KT, Tsang W, Voigt J-U. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging 2015;16:233–70.
- [14] Rishniw M, Erb HN. Evaluation of four 2-dimensional echocardiographic methods of assessing left atrial size in dogs. J Vet Intern Med 2000;14:429–35.
- [15] Hansson K, Häggström J, Kvart C, Lord P. Left atrial to aortic root indices using two-dimensional and M-mode echocardiography in cavalier King Charles spaniels with and without left atrial enlargement. Vet Radiol Ultrasound 2002;43:568–75.
- [16] Rishniw M, Caivano D, Dickson D, Vatne L, Harris J, Matos J. Two-dimensional echocardiographic left-atrial-toaortic ratio in healthy adult dogs: a reexamination of reference intervals. J Vet Cardiol 2019;26:29–38.
- [17] Visser LC, Ciccozzi MM, Sintov DJ, Sharpe AN. Echocardiographic quantitation of left heart size and function in 122 healthy dogs: a prospective study proposing reference intervals and assessing repeatability. J Vet Intern Med 2019;33:1909–20.
- [18] Strohm L, Visser LC, Chapel E, Drost W, Bonagura J. Twodimensional, long-axis echocardiographic ratios for assessment of left atrial and ventricular size in dogs. J Vet Cardiol 2018;20:330–42.
- [19] Chetboul V, Sampedrano CC, Concordet D, Tissier R, Lamour T, Ginesta J, Gouni V, Nicolle AP, Pouchelon J-L, Lefebvre HP. Use of quantitative two-dimensional color

tissue Doppler imaging for assessment of left ventricular radial and longitudinal myocardial velocities in dogs. Am J Vet Res 2005;66:953-61.

- [20] Sahn DJ, DeMaria A, Kisslo J, Weyman A. Recommendations regarding quantitation in M-mode echocardiography: results of a survey of echocardiographic measurements. Circulation 1978;58:1072–83.
- [21] Marsan NA, Michalski B, Cameli M, Podlesnikar T, Manka R, Sitges M, Dweck MR, Haugaa KH. EACVI survey on standardization of cardiac chambers quantification by transthoracic echocardiography. Eur Heart J Cardiovasc Imaging 2020;21:119–23.
- [22] Podlesnikar T, Cardim N, Marsan NA, D'Andrea A, Cameli M, Popescu BA, Schulz-Menger J, Stankovic I, Toplisek J, Maurer G, Haugaa KH, Dweck MR. EACVI survey on hypertrophic cardiomyopathy. Eur Heart J Cardiovasc Imaging 2022;23:590-7.
- [23] Sitges M, Marsan NA, Cameli M, D'Andrea A, Carvalho RF, Holte F, Michalski B, Podlesnikar T, Popescu BA, Schulz-Menger J, Stankovic I, Haugaa KH, Dweck MR. EACVI survey on the evaluation of left ventricular diastolic function. Eur Heart J Cardiovasc Imaging 2021;22:1098–105.
- [24] Michalski B, Dweck MR, Marsan NA, Cameli M, D'Andrea A, Carvalho RF, Holte E, Podlesnikar T, Manka R, Haugaa KH. The evaluation of aortic stenosis, how the new guidelines are implemented across Europe: a survey by EACVI. Eur Heart J Cardiovasc Imaging 2020;21:357–62.
- [25] Haugaa KH, Marsan NA, Cameli M, D'Andrea A, Dweck MR, Carvalho RF, Holte E, Manka R, Michalski B, Podlesnikar T, Popescu BA, Schulz-Menger J, Sitges M, Stankovic I, Maurer G, Edvardsen T. Criteria for surveys: from the European Association of Cardiovascular Imaging Scientific Initiatives Committee. Eur Heart J Cardiovasc Imaging 2019;20:963-6.
- [26] Cameli M, Marsan NA, D'Andrea A, Dweck MR, Fontes-Carvalho R, Manka R, Michalski B, Podlesnikar T, Sitges M, Popescu BA, Edvardsen T, Fox KF, Haugaa KH. EACVI survey on multimodality training in ESC countries. Eur Heart J Cardiovasc Imaging 2019;20:1332–6.
- [27] Marsden PV, Wright JD. Handbook of survey research. Bingley: Group Publishing Limited; 2010.
- [28] Hinkin TR. A brief tutorial on the development of measures for use in survey questionnaires. Organ Res Methods 1998; 1:104–21.
- [29] Dillman DA, Smyth JD, Christian LM. Web questionnaires and implementation. In: Dillman DA, Smyth JD, Christian LM, editors. Web questionnaires and implementation. Internet, phone, mail and mixed-mode surveys: the tailored design method. Hoboken: John Wiley & Sons; 2014. p. 301–50.
- [30] Tsang S, Royse CF, Terkawi AS. Guidelines for developing, translating, and validating a questionnaire in perioperative and pain medicine. Saudi J Anaesth 2017;11:80–9.
- [31] Couper MP, Traugott MW, Lamias MJ. Web survey design and administration. Publ Opin Q 2001;65:230–53.
- [32] Dalkey N, Helmer O. An experimental application of the Delphi method to the use of experts. Manag Sci 1963;9: 458–67.
- [33] Häggström J, Boswood A, O'Grady M, Jöns O, Smith S, Swift S, Borgarelli M, Gavaghan B, Kresken JG, Patteson M, Åblad B, Bussadori CM, Glaus T, Kovačević A, Rapp M, Santilli RA, Tidholm A, Eriksson A, Bélanger MC, Deinert M, Little CJL, Kvart C, French A, Rønn-Landbo M, Wess G, Eggertsdottir A, O'Sullivan ML, Schneider M, Lombard CW, Dukes-McEwan J, Willis R, Louvet A, DiFruscia R.

Longitudinal analysis of quality of life, clinical, radiographic, echocardiographic, and laboratory variables in dogs with myxomatous mitral valve disease receiving pimobendan or benazepril: the QUEST study. J Vet Intern Med 2013;27:1441–51.

- [34] Summerfield NJ, Boswood A, O'Grady MR, Gordon SG, Dukes-McEwan J, Oyama MA, Smith S, Patteson M, French AT, Culshaw GJ, Braz-Ruivo L, Estrada A, O'Sullivan ML, Loureiro J, Willis R, Watson P. Efficacy of pimobendan in the prevention of congestive heart failure or sudden death in Doberman Pinschers with preclinical dilated cardiomyopathy (the PROTECT Study). J Vet Intern Med 2012;26:1337–49.
- [35] Atkins C, Bonagura J, Ettinger S, Fox P, Gordon SG, Häggström J, Hamlin R, Keene B, Luis-Fuentes V, Stepien R. Guidelines for the diagnosis and treatment of canine chronic valvular heart disease. J Vet Intern Med 2009;23:1142–50.
- [36] Keene BW, Atkins CE, Bonagura JD, Fox PR, Häggström J, Fuentes VL, Oyama MA, Rush JE, Stepien R, Uechi M. ACVIM consensus guidelines for the diagnosis and treatment of myxomatous mitral valve disease in dogs. J Vet Intern Med 2019;33:1127–40.
- [37] Dickson D, Caivano D, Patteson M, Rishniw M. The times they are a-changin': two-dimensional aortic valve measurements differ throughout diastole. J Vet Cardiol 2016; 18:15–25.
- [38] Lombard C. Normal values of the canine M-mode echocardiogram. Am J Vet Res 1984;45:2015-8.
- [39] Tidholm A, Westling A, Höglund K, Ljungvall I, Häggström J. Comparisons of 3-, 2-dimensional, and Mmode echocardiographical methods for estimation of left chamber volumes in dogs with and without acquired heart disease. J Vet Intern Med 2010;24:1414–20.
- [40] Brown DJ, Rush JE, MacGregor J, Ross Jr JN, Brewer B, Rand WM. M-mode echocardiographic ratio indices in normal dogs, cats, and horses: a novel quantitative method. J Vet Intern Med 2003;17:653–62.
- [41] Oyama MA, Sisson DD. Assessment of cardiac chamber size using anatomic M-mode. Vet Radiol Ultrasound 2005;46: 331–6.
- [42] Borgarelli M, Ferasin L, Lamb K, Bussadori C, Chiavegato D, D'Agnolo G, Migliorini F, Poggi M, Santilli RA, Guillot E, Garelli-Paar C, Toschi Corneliani R, Farina F, Zani A, Dirven M, Smets P, Guglielmini C, Oliveira P, Di Marcello M, Porciello F, Crosara S, Ciaramella P, Piantedosi D, Smith S, Vannini S, Dall'Aglio E, Savarino P, Quintavalla C, Patteson M, Silva J, Locatelli C, Baron Toaldo M. Delay of appearance of symptoms of canine degenerative mitral valve disease treated with spironolactone and benazepril: the DELAY Study. J Vet Cardiol 2020;27:34–53.
- [43] Wess G, Kresken JG, Wendt R, Gaugele J, Killich M, Keller L, Simak J, Holler P, Bauer A, Küchenhof H, Glaus T. Efficacy of adding ramipril (VAsotop) to the combination of furosemide (Lasix) and pimobendan (VEtmedin) in dogs with mitral valve degeneration: the VALVE trial. J Vet Intern Med 2020;34:2232–41.
- [44] Tidholm A, Häggström J. Prognostic value of selected one-, two- and three-dimensional and Doppler echocardiographic methods to assess severity in dogs with myxomatous mitral valve disease. J Vet Cardiol 2021;39: 89–101.
- [45] Bennett C, Khangura S, Brehaut JC, Graham ID, Moher D, Potter BK, Grimshaw JM. Reporting guidelines for survey

research: an analysis of published guidance and reporting practices. PLoS Med 2011;8:e1001069.

- [46] Ponto J. Understanding and evaluating survey research. J Adv Pract Oncol 2015;6:168-71.
- [47] Morello SL, Colopy SA, Chun R, Buhr KA. Work, life, and the gender effect: perspectives of ACVIM Diplomates in

2017. Part 1—specialty demographics and measures of professional achievement. J Vet Intern Med 2020;34: 1825–36.

[48] Porter SR, Whitcomb ME, Weitzer WH. Multiple surveys of students and survey fatigue. New Dir Inst Res 2004;2004: 63-73.

Available online at www.sciencedirect.com



Π

Journal of Veterinary Cardiology (2024) 51, 145-156





www.elsevier.com/locate/jvc

Veterinary echocardiographers' preferences for left atrial size assessment in cats: the BENEFIT project $\stackrel{\star}{\sim}$



M.Y.-W. Kuo^{a,*}, J. Häggström^a, S.G. Gordon^b, K. Höglund^c, E. Côté^d, T.-L. Lu^e, M. Dirven^f, M. Rishniw^g, Y.-W. Hung^h, I. Ljungvall^a

^a Department of Clinical Sciences, Faculty of Veterinary Medicine and Animal Science, Swedish University of Agricultural Sciences, Uppsala, Sweden

^b Department of Small Animal Clinical Science, Texas A&M University, College Station, TX, USA

^c Department of Anatomy, Physiology and Biochemistry, Faculty of Veterinary Medicine and Animal Science, Swedish University of Agricultural Sciences, Uppsala, Sweden ^d Department of Companion Animals, Atlantic Veterinary College, University of Prince Edward Island, Prince Edward Island, Canada

^e Chuan Animal Hospital, Taipei, Taiwan

^f Evidensia Södra Animal Hospital, Kungens Kurva, Sweden

^g Veterinary Information Network, Davis, CA, USA

^h Cardiospecial Veterinary Hospital, Taipei, Taiwan

Received 1 February 2023; received in revised form 13 October 2023; accepted 5 November 2023

KEYWORDS Cardiology; Echocardiography; Abstract Introduction/objectives: Veterinary echocardiographers' preferences for left atrial (LA) size assessment in cats have not been systematically investigated. The primary aim of this prospective exploratory study was to investigate

Preliminary data of the study were presented in abstract form at the 39th ACVIM Forum, June 24th 2022.

- * Corresponding author.
 - E-mail address: Momo.Y-W.Kuo@slu.se (M.Y.-W. Kuo).

https://doi.org/10.1016/j.jvc.2023.11.001

1760-2734/© 2023 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

^{*} A unique aspect of the Journal of Veterinary Cardiology is the emphasis of additional web-based materials permitting the detailing of procedures and diagnostics. These materials can be viewed (by those readers with subscription access) by going to http://www.sciencedirect.com/science/journal/17602734. The issue to be viewed is clicked and the available PDF and image downloading is available via the Summary Plus link. The supplementary material for a given article appears at the end of the page. To view the material is to go to http://www.doi.org and enter the doi number unique to this paper which is indicated at the end of the manuscript.

Heart failure; Cardiomyopathy; Feline	ary aim was to investigate echocardiographers' preferences for assessing LA size in subgroups based on geographic, demographic, and professional profiles. <i>Animals, materials, and methods</i> : An online survey instrument was designed, verified, and distributed globally to veterinary echocardiographers. <i>Results</i> : A total of 655 veterinary echocardiographers from six continents and 54 countries, working in specialty practice (56%) and in general practice (38%), provided data. Linear two-dimensional (2D) technique was favored by most echocardiographers (n = 612) for LA size assessment. Most commonly, respondents combined linear 2D with subjective assessment (n = 227), while 209 used linear 2D-based methods alone. Most echocardiographers using linear 2D-based methods preferred the right parasternal short-axis view and to index the LA to the aorta (Ao). Approximately 10% of the respondents obtained LA dimensions from a right parasternal long-axis four-chamber view. Approximately one-third of echocardiographers that made linear measurements from 2D echocardiograpms shared the same preferences regarding cat position, acquisition view, indexing method and time point identification for the LA measurement. The responses were comparably homogeneous across geographic location, level of training, years performing echocardiography, and type of practice. <i>Discussion/conclusion:</i> Most veterinary echocardiographers assessed LA size in cats using linear 2D echocardiography from a right parasternal short-axis view, and indexed LA to Ao. Respondents' preferences were similar over geographic, demographer, and professional backgrounds.
---	--

Abbreviations

2D	2-dimensional
Ao	aorta
LA	left atrium, left atrial
LAE	left atrial enlargement
MM	M-mode
RLR	right lateral recumbency

Introduction/objectives

Quantification of LA size is regarded as one of the most clinically important measurements in feline echocardiography. Identification of substantial LA enlargement (LAE) on an echocardiogram suggests underlying cardiac disease in cats presenting with signs of respiratory distress [1,2]. Decisions about treatment strategies and establishment of prognoses for cats affected by cardiomyopathies are, furthermore, also partly based on the degree of LAE demonstrated on an echocardiogram [3–9].

The current state of knowledge regarding LA size assessment in cats is characterized by a lack of updated and universally acknowledged guidelines. This can potentially be attributed to the absence of consensus on the optimal approach for conducting such assessments. Various echocardiographic techniques and methods, as well as various specific recommendations for each of these, have been suggested for LA size assessment in cats. The absence of uniformity in LA size assessments may have negative effects on the accurate evaluation of disease severity and prognosis. Furthermore, this can impede the proper interpretation and implementation of published clinical study findings and expert treatment guidelines. In human medicine, large scale surveys have identified similarities and differences between echocardiog raphic methods used in everyday clinical practice and methods recommended in guidelines [10-12] to comprehend challenges in complex areas like current LA size assessment in cats [11,13–15]. The gloBal caninE and feliNE leFt atrial size assessmenT (BENEFIT) project is an international research collaboration aiming to explore veterinary echocardiographers' methods regarding LA size assessment in dogs and cats, aimed at harmonizing or standardizing LA size assessment in veterinary medicine. We recently submitted the results of the canine portion of this research collaboration for publication¹.

ⁱ Dog manuscript: Veterinary echocardiographers' preferences for left atrial size assessment in dogs: The BENEFIT Project (which is Conditional Accept in JVC).

Echocardiographers' preferences of the techniques and methods for assessing LA size in cats has, to our knowledge, not been systematically investigated previously in a large-scale study. Accordingly, the primary aim of this study was to investigate echocardiographers' preferences concerning LA size assessment in cats, including echocardiographic techniques (M-mode (MM), linear 2D, area-based, volume-based, and subjective assessment) and methods (positioning of the cat, acquisition views, indexing methods, and identification of the time point used for the measurement). A secondary aim was to investigate echocardiographers' preferences for assessing LA size in subgroups based on geographic, demographic, and professional profiles.

Animals, materials and methods

An English-language survey instrument was constructed and validated using recognized principles [16-20], and it was deployed using an online platform¹. Respondents' echocardiographic preferences for dogs and cats were investigated in the same survey¹, and this manuscript includes the part concerning cats. Respondents were instructed to only participate once, and the survey could only be accessed once using the same device. The respondents participated anonymously. Respondents received no incentives to participate. The period of collection of responses was September 18th to November 1st, 2020. Respondents were asked to answer the questions based on their situations prior to COVID-19 restrictions. Respondents who were no longer in clinical practice were asked to answer the questions according to their practice in the past.

Study enrollment

Inclusion criteria

Individuals who performed, or had previously performed, echocardiograms in cats.

Exclusion criteria

Individuals who did not meet the inclusion criteria, and those who provided contradictory responses (e.g. respondents who stated, in an initial question, that they performed echocardiograms in cats, or that they used a specific echocardiographic technique, but then stated the opposite in a subsequent question).

^j Netigate AB, Stockholm, Sweden.

Survey instrument

A total of 134 questions were created and divided into three parts (Fig. 1). Respondents were directed to relevant subsequent questions according to their answers to preceding questions; thus, they were not required to respond to all questions. Most questions (129/134) were mandatory and primarily formatted as multiple-choice questions comprising both single- and multiple-answer possibilities; free-text answers were made possible if the respondent's choice was missing from the alternatives listed. Five optional questions were openended. Questions in parts 1 (12 questions) and 3 (16 questions) were for all respondents. Respondents performing echocardiograms in both dogs and cats were directed to all questions in part 2 (106 questions); respondents only performing echocardiograms in dogs or cats were directed to the relevant questions in part 2 (53 questions). The filter questions and illustrations were designed to reduce the misconceptions regarding animal species for each question. Survey question stems, associated answer alternatives, and illustrations are reported in the Supplemental Document I.

PART 1: general background of respondents

Questions related to the respondents' geographic, demographic, and professional roles related to echocardiography.

PART 2: techniques/methods of echocardiographic assessment of left atrial size in cats

Questions included in part 2.1 were related to the following echocardiographic techniques: (1) subjective assessment, (2) MM (3) linear 2D, (4) area, and (5) volume. Respondents were asked to specify their most commonly used technique(s) for assessing LA size (multiple answers were possible), and respondents were then directed to relevant questions related to their selected technique(s) of choice to provide details. Questions in part 2.2 were related to respondents' opinion of their technique(s)/method(s) of choice.

PART 3: self-assessment regarding echocardiographic preferences and training

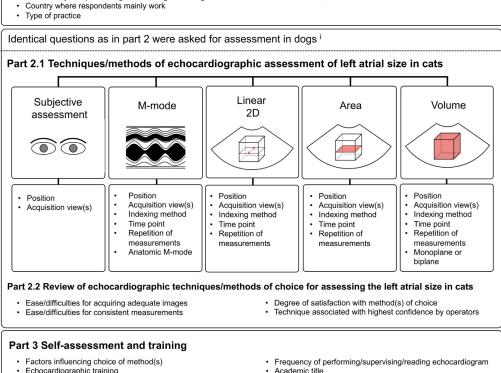
Questions related to the respondents' preferences regarding echocardiography, echocardiographic experience, and their level of training.

Pretest verification

A three-phase pretest was performed using the modified Delphi method [21]:

· Number of veterinarians/echocardiographers in the clinic

· Ultrasound equipment



- Echocardiographic training
- Preferred method has changed or not in the last 2 years
- Willingness of changing the method in the future
- National/international training program
- · Board-certified/expert title

Survey construction and overview of questions. Illustrations correspond to the five different echo-Figure 1 cardiographic methods evaluated in the survey. See Supplemental Document | for further details about the survey questions and answer alternatives. 2D: two-dimensional.

Phase 1

A group of subject-matter experts (n = 9), consisting of board-certified cardiologists and researchers working in academia or private clinical practice, from Canada, Sweden, Taiwan, the Netherlands, and the United States, reviewed the survey instrument with the goal of identifying perceived flaws and limitations, and stating recommended changes. Revisions were made according to the comments received.

Phase 2

A reference group (n = 12), consisting of echocardiographers who regularly performed echocardiograms in dogs and cats, but who were not working in academia and were not board-certified cardiologists, and who worked in various fields of veterinary medicine (cardiology, diagnostic imaging, emergency and critical care, and internal medicine) in different countries and territories (Australia, China, Hong-Kong, Japan, Singapore, Sweden, the Netherlands, the United States, and Zambia), tested the survey. Most echocardiographers (9/12) in the reference group were non-native English speakers. Revisions were made according to the comments received. Subject matter experts involved in phase 1 were not eligible to take part in phase 2.

Phase 3

The survey was tested and amended again by the nine subject-matter experts prior to distribution to potential respondents.

Part 1 General background of respondents

- · Number of years in practice
- Number of years performing echocardiogram in dogs/cats

Data collection

echocardiographers Veterinary received an invitation to participate in the study, which was distributed through the following channels: (1) Chairpersons of national veterinary organizations and key opinion leaders of veterinary internal medicine/cardiology associations in 34 countries; (2) American and European Colleges of Veterinary Internal Medicine - Cardiology ListServe, hosted by the Veterinary Information Network. The subscribers of the Listserve included veterinarians globally who had voluntarily registered to receive Listserve emails because of their interest in veterinary cardiology and included all American and European College of Veterinary Internal Medicine cardiology diplomates and candidates, as well as other interested veterinarians; (3) international cardiology virtual congresses. Reminders were sent out after 14 and 30 days to both groups (1) and (2).

Statistical analysis

Descriptive analyses of the survey results were performed. Response counts and percentages were calculated.

Results

A total of 949 individuals provided data, and of these, 702 (74%) completed the entire survey. The mean response time for the participants was 21 min and 18 s. Entries from 47 respondents were considered invalid and were excluded (Fig. 2), and results described below were accordingly based on analyses of responses from 655 respondents. Respondents (n = 3) from one country reported that they could not participate as the survey link could not be opened in their country (without access to a VPN).

Geographic, demographic, and professional information

Echocardiographers providing responses worked on six continents and in 54 countries (Supplemental Table A). Most echocardiographers (n = 633/655, 96.6%) self-reported that they performed echocardiograms regularly in the preceding 12 months (or portion of 12 months excluding COVID-19 restrictions, as relevant). Respondents' demographic and professional information is shown in Supplemental Figure I and Supplemental Table A. Respondents predominantly learned to perform echocardiograms from echocardiography courses (n = 419/655, 64.0%) and/or were self-taught (n = 293/655, 44.7%). Approximately half of respondents (n = 310/655, 47.3%) were the only echocardiographers regularly practicing echocardiography at their workplace.

Echocardiographic approaches for LA size assessment in cats

Respondents most commonly used linear 2D-based methods when assessing LA size, followed by subjective assessment, and MM-based methods (Fig. 3A). Most commonly, respondents combined linear 2D-based methods with subjective assessment, followed by using linear 2D-based methods alone, and, finally, by combining MM-based methods, linear 2D, and subjective assessment (Fig. 3B). Most respondents (n = 499/655, 76.2%) trusted linear 2D-based methods the most when assessing LA size. Virtually all respondents imaged cats in right lateral recumbency when obtaining either shortaxis or long-axis views of the LA.

Quantitative assessment

Linear two-dimensional

Most of the 612 respondents who assessed LA size using linear 2D-based methods preferred the right parasternal short-axis view (Fig. 4). Similarly, most respondents preferred indexing the LA dimension to the aortic dimension, and most preferred timing the measurement at approximately ventricular end-systole/early-diastole by identifying the first frame after aortic valve closure. Of respondents using linear 2D, 34.3% had identical preferences regarding positioning of the cat during the examination, acquisition view, indexing method and identification of time point used for the measurements. Approximately 61% of respondents acquired repeat measurements over more than one cardiac cycle and subsequently averaged them.

M-mode

Most of the 175 respondents who assessed LA size using MM-based methods preferred the right parasternal short-axis view (Supplemental Figure II). Fifty percent of these respondents used anatomic MM. Most respondents preferred indexing the LA dimension to the aortic dimension, using echocardiographic guidance for timing the measurement of these two structures. For measuring the aortic dimension, most respondents identified the time point on the MM immediately before aortic valve opening. For measuring the LA dimension, most respondents identified the time point on the MM showing the maximal LA size. For respondents using MM, 11.4% had identical preferences regar ding positioning of the cat, acquisition view,

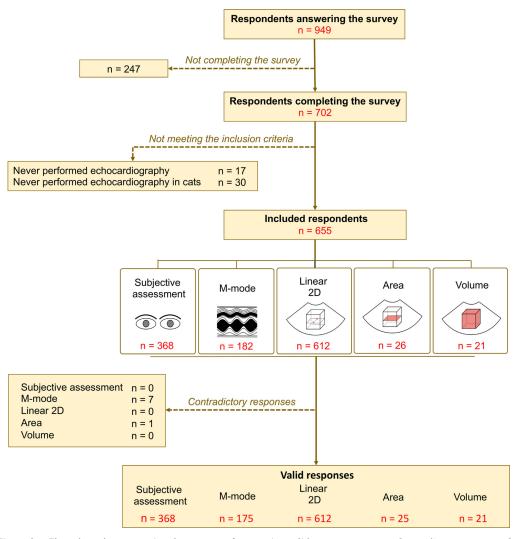


Figure 2 Flow chart demonstrating the process of extracting valid survey responses. Contradictory responses for an echocardiographic method led to exclusion of survey responses for that particular technique, whereas the remaining responses from these respondents were retained. 2D: two-dimensional.

indexing method, and identification of time point used for the measurements. Approximately two thirds of these respondents (66%) acquired repeat measurements over more than one cardiac cycle and subsequently averaged them.

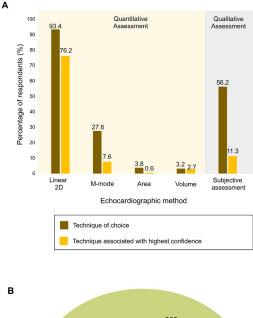
Area

Most of the 25 respondents who assessed LA areas preferred the right parasternal short-axis view (Supplemental Figure III). Most respondents did not use any indexing method for LA area

assessment and used 2D guidance for timing the measurement by identifying the image showing the maximal LA area. Forty percent of these respo ndents acquired repeat measurements over more than one cardiac cycle and subsequently averaged them.

Volume

Most of the 21 respondents who assessed LA volumes preferred the right parasternal long-axis fourchamber view, to which they applied a monoplane



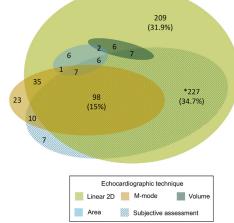


Figure 3 An overview of veterinary echocardiographers' preferences for left atrial size assessment in cats (n = 655), showing (A) the most commonly used (multiple-choice) and trusted (single-choice) echocardiographic technique for the purpose, and (B) demonstrates how echocardiographers combined different techniques for left atrial size assessment in cats and highlights the popularity of each combination. Respondents that used other echocardiographic technigues (n = 17) and other combinations (n = 5) were not included in (B). The size of the areas in (B) are approximately in proportion to the actual number of the responses for each technique, and the numbers represent the number of responses for each technique and the combination of techniques. *227 echocardiographers combined linear 2D-based methods and subjective assessment when assessing left atrial size in cats.

or biplane (modified) Simpson's method of discs (Supplemental Figure IV). Similarly, most respond ents preferred indexing LA volume to body surface area or body weight, using 2D echocardiographic guidance for timing the measurement by visualizing maximal LA size or identifying the last frame before mitral valve opening. Thirty five percent of these respondents acquired repeat measurements over more than one cardiac cycle, and subsequently averaged them.

Qualitative assessment

Subjective assessment

Most of the 368 respondents who subjectively assessed LA size also used a quantitative assess ment (Fig. 3B) and examined both right parasternal short-axis and long-axis four-chamber views (Supplemental Figure V).

Factors influencing choice of echocardiographic technique/method and respondents' willingness to change methods

Approximately two-thirds of the respondents stated that clinical studies and expert opinion had influenced their preferences for assessing LA size the most (Fig. 5). The echocardiographers' preferences were comparably similar across the groups based on geographic location, level of training, years performing echocardiography and type of practice, as shown in Supplemental Figures VI, VII and Supplemental Tables B and C. Most respon dents were willing to change the method of use for assessing LA size in the future (Supplemental Table B).

Discussion

Our large survey-based study provides information about the methods cardiologists and other echocardiographers used to assess LA size in cats. Out of all respondents, 93% performed linear 2D echocardiographic measurements for LA size assessment in cats. This technique was the most trusted by 76% of all respondents. Common approaches were to acquire images from a right parasternal short-axis view with the cat positioned in right lateral recumbency, measuring the LA dimensions at approximately ventricular end-systole/early diastole, and indexing the LA size to the aortic dimension on the same image. However, considerable variability exists between respondents among these approaches, only 34% of those using 2D imaging shared identical preferences. This suggests

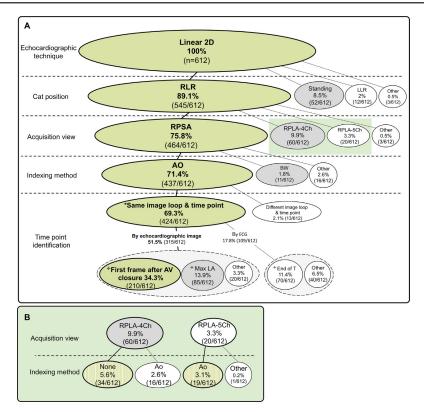


Figure 4 Linear two-dimensional preferences for assessment of left atrial size in cats based on responses from 612 veterinary echocardiographers preferences for assessment of left atrial size in cats based on responses from 612 veterinary echocardiographers. Questions regarding cat position, acquisition view, indexing method and time point identification for measurements had single discrete options for responding. The answers with the most (green) and the second most (gray) responses in each layer are marked. In (A), the branch was only extended from the answers with most responses in the previous question; therefore, totals at some individual levels can be less than the total on the previous level. (B) shows information regarding what indexing method were chosen by the respondents (the green square in A). Answer alternatives receiving less than 1.5% of the responses for the linear 2D method were grouped as 'other'. 2D: two-dimensional; Ao: aorta; AV: aortic valve; BW: body weight; LLR: left lateral recumbency; RLR: right lateral recumbency; RPSA: right parasternal short-axis view; RPLA-4Ch: right parasternal long-axis four-chamber view, *The respondents used the same image loop (acquisition view) and time point for both aortic and LA dimension for LA size assessment. *These time points were categorized as at the period approximately end-systole/early-diastole in the present study.

that considerable inconsistencies exist between respondents, underscoring the need for a more standardized approach (or approaches). For the assessment, linear 2D was often combined with subjective assessment.

For linear 2D methods, respondents acquired images from a right parasternal short-axis view (76%) much more commonly than from a right parasternal long-axis four-chamber view (10%). In the American College of Veterinary Internal Medicine consensus statement [6] and in other literature [22–24] concerning feline cardiology, it has been suggested that the LA dimension should be measured from a right parasternal short-axis view and be indexed to the Ao using the same frame; another common suggestion is to measure the LA dimension from a right parasternal longaxis four-chamber view, without indexing [25]. The LA and aortic dimensions have been reported to vary with body weight and sex in cats [26,27]. Accordingly, normalization of the LA size to either the Ao or by allometric scaling has been shown to

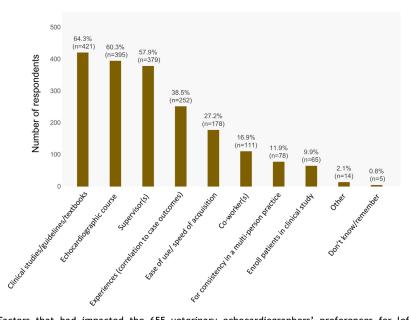


Figure 5 Factors that had impacted the 655 veterinary echocardiographers' preferences for left atrial size assessment in cats.

limit the impact of body weight [26,28]. Assessing LA size without indexing might be misleading with regards to the extent of LAE [26,28]. This might explain why the right parasternal long-axis fourchamber view was unfavored in the present study.

Of the respondents who shared comparably similar preferences regarding cat positioning, view of choice and indexing method in linear 2D, only one-third shared identical preferences in time point identification. More respondents timed their measurement at approximately ventricular endsystole/early-diastole, though they identified this period in the cardiac cycle using variable methods. For identifying ventricular end-systole/earlydiastole, most respondents visualized aortic valve motion, but many also used either the size of LA or ECG gating. This suggests that some respondents experience difficulty in clearly visualizing the aortic commissures at ventricular early-diastole in some cats. Furthermore, different approaches (i.e. visualizing aortic valve motion, size of LA or ECG gating) [5,22,29] and different timings in the cardiac cycle have been reported in publications for LA measurement in cats, providing respondents with a range of options from which to choose their timing [29,30]. However, whether this has any clinical impact remains undetermined.

The most used approach for assessing LA size in cats was to combine subjective (gualitative) and linear 2D-based (quantitative) assessments rather than using linear 2D alone. A single linear measurement would not fully capture three-dimens ional asymmetric LA dilation. As the left auricle in cats may sometimes be more prominently enlarged compared to the LA body [5], measuring LA size by this approach only might lead to underestimation of left auricular dilation, and could, accordingly, lead to underestimation of LAE. Combining the subjective assessment with linear 2D, to allow full inspection of the LA border. has been recommended for LA size assessment in cats [5]. In the present survey, assessing LA size subjectively was found to be the second most used method and was presented as the second most trusted when examining the LA in cats. One explanation might be that subjective assessment is intuitive and time-saving. Another explanation might be that enlargement of the LA in each feline cardiomyopathy stage was only described qualitatively [6], without quantification. These form the possible challenges of subjective assessment:

the consistency between different operators and accuracy in diagnosis and prognosis has never been systematically investigated in veterinary medi cine.

Respondents reported using MM less commonly than 2D methods. The prognostic value of LA size in feline cardiomyopathies was initially identified by using MM-based measurements [23]. The high temporal resolution of MM overcame some of the difficulties for visualizing rapid heart rate and small hearts in cats. However, with advances in imaging technology, frame rates and temporal resolution became less limiting in identifying appropriate measurement time-points. M-modebased methods were more commonly performed for LA size assessment in one study concerning measurements in cats compared to dogs'. In cats, more than 1/4 of the respondents used MM-based methods, but only less than 1/10 of the total respondents trusted it the most. The MM technique was more frequently used by echocardiographers working in North and South America compared to the other continents, and by echocardiographers who had performed echocardiograms for <5 years or >20 years. A potential explanation for this finding is that respondents presumably had their habitual preferences, and beginners were willing to perform all the techniques taught by supervisors or outlined in textbooks.

Very few respondents used area- or volumebased methods for LA size assessment in cats. Using area- and volume-based methods for LA size assessment in cats has been reported to be timeconsuming, and to have high sampling variation, low intra-operator repeatability, and low sensitivity for detecting LAE [27–31]. Moreover, the reference interval for normal LA volume reported in one study was established mainly based on measurements in cats of a single breed [32]. In the context of human medicine, evaluation of LA size and remodeling typically involves measurement of LA volume [33]. Unlike LA diameter, LA volume exhibits a more robust association with stronger prediction of outcomes in human [34]. Volumetric assessment in cats is likely constrained by the scarcity of dependable normal values of LA volume. Additionally, there is a lack of clinical studies demonstrating that intricate area- or volume-based methods offer superior prognostic value compared to simple linear estimates of LAE.

Survey research has developed into a rigorous branch of science that includes objectively tested strategies for obtaining representative samples [17,20,35,36]. In this study, we implemented an

approach that has recently been utilized in human medicine to explore the divergences and commonalities in clinical imaging. By adopting similar methodology, we aimed to comprehensively address the obstacles encountered in a particularly contentious and intricate domain, namely the assessment of LA size in cats [11-13,37]. In addition to studying the preferred methods of examining LA size, the study also investigated the positioning of the cat, acquisition views, indexing methods, and identification of the time point used for the measurement for each method. We already know that the LA chamber assessed by echocardiography is a powerful clinical variable for disease assessment and prognostication [3-8,30]. We designed a survey instrument and used it to gather information from a wide range of veterinary echocardiographers worldwide. Accordingly, we find it of interest to evaluate current preferences amongst veterinary echocardiographers. This does not, however, indicate that methods assessed as being more accurate should be abandoned from future use systematically in favor of more efficient ones, but rather that the methods should be better described and optimized, to be practical in the hands of many. Obtaining information from this prospective exploratory study regarding 1) which and how specific techniques and methods are employed, 2) similarities and differences in LA size assessment in cats amongst veterinary echocardiographers, as well as 3) the underlying rationales for choosing the specific method for LA size assessment, can inform future developments in harmonization of LA size assessment in veterinary medicine.

Our study has some limitations. The responses could not be verified independently because the results were based on self-reported responses, a situation shared with many other survey studies [10–13,15]. No specific minimum number of participants was established for each category of geographic, demographic, or professional profiles, and the data that were analyzed and reported encompassed all valid responses. As in many other published survey studies, no inferential statistics were applied; only descriptive statistics were used, as inherent selection bias and other limitations could lead to inappropriate statistical conclusions. The survey was formulated in English, which might lead to misunderstanding or misinterpretation of the questions and answer alternatives to non-native English respondents. To overcome the language barrier and the respondents' potential differences in familiarity with

various echocardiographic terminologies, we invited 12 veterinarians (nine non-native English speakers) working in various fields and countries to validate the survey content. Only the respondents who had access to the internet and the survey link could participate in the study. The number of respondents in each country could have been affected by how the local contact person promoted the survey, and therefore might not be in proportion to the exact number of echocardiographers in any specific country. Respondents' preferences for echocardiographic LA size assessment in dogs and cats were investigated in the same surveyⁱ; thus, the respondents' answers for cats might be affected by their answers for dogs.

Conclusions

Most veterinary echocardiographers assessed LA size in cats using linear 2D-based methods. The majority of respondents employed the right parasternal short-axis view, indexed the LA to the aorta, and timed the measurement during endsystole/early-diastole. This approach was often combined with subjective assessment. Although the responses for linear 2D preferences appeared comparably homogeneous across respondents, less than one-third shared the exact same combination of preferences regarding position of the cat during the examination, acquisition view, indexing method, and identification of time point used for the measurements. The MM technique was used by one-third of echocardiographers and area- or volume-based method was infrequently used for assessment LA size in cats. Respondents' preferences were similar over geographic, demographic, and professional backgrounds.

Funding

Scholarships for Taiwanese Studying in the Focused Fields, Ministry of Education, Taiwan.

Conflict of Interest Statement

The authors do not have any conflicts of interest to disclose.

Acknowledgments

The authors would like to thank Myriam Baranger-Ete, Marlies Böhm, Thomas J. Boumans, Ayaka Chen, Anna Djupsjöbacka, Johanna Frank, Weibin Guo, Adam Honeckman, Hanneke van Meeuwen, Sharon Troiano Shull, and Shih-Ping Yeh for helping in the pretest verification and disseminating the survey; the chairpersons/key-opinion leaders who disseminated and promoted the survey; and all the respondents globally who participated in the survey.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.jvc.2023.11.001.

References

- [1] Ward JL, Lisciandro GR, Ware WA, Viall AK, Aona BD, Kurtz KA, Reina-Doreste Y, DeFrancesco TC. Evaluation of point-of-care thoracic ultrasound and NT-proBNP for the diagnosis of congestive heart failure in cats with respiratory distress. J Vet Intern Med 2018;32:1530–40.
- [2] Janson CO, Hezzell MJ, Oyama MA, Harries B, Drobatz KJ, Reineke EL. Focused cardiac ultrasound and point-of-care NT-proBNP assay in the emergency room for differentiation of cardiac and noncardiac causes of respiratory distress in cats. J Vet Emerg Crit Care 2020;30:376–83.
- [3] Fox PR, Liu S-K, Maron BJ. Echocardiographic assessment of spontaneously occurring feline hypertrophic cardiomyopathy: an animal model of human disease. Circulation 1995;92:2645–51.9.
- [4] Rush JE, Freeman LM, Fenollosa NK, Brown DJ. Population and survival characteristics of cats with hypertrophic cardiomyopathy: 260 cases (1990–1999). J Am Vet Med Assoc 2002;220:202–7.
- [5] Payne J, Borgeat K, Brodbelt D, Connolly D, Fuentes VL. Risk factors associated with sudden death vs. congestive heart failure or arterial thromboembolism in cats with hypertrophic cardiomyopathy. J Vet Cardiol 2015;17:S318–28.
- [6] Luis Fuentes V, Abbott J, Chetboul V, Côté E, Fox PR, Häggström J, Kittleson MD, Schober K, Stern JA. ACVIM consensus statement guidelines for the classification, diagnosis, and management of cardiomyopathies in cats. J Vet Intern Med 2020;34:1062–77.
- [7] Kittleson MD, Côté E. The feline cardiomyopathies: 2. Hypertrophic cardiomyopathy. J Feline Med Surg 2021;23: 1028–51.
- [8] Hogan DF, Fox PR, Jacob K, Keene B, Laste NJ, Rosenthal S, Sederquist K, Weng H-Y. Secondary prevention of cardiogenic arterial thromboembolism in the cat: the doubleblind, randomized, positive-controlled feline arterial thromboembolism; clopidogrel vs. aspirin trial (FAT CAT). J Vet Cardiol 2015;17:S306–17.
- [9] Linney CJ, Dukes-McEwan J, Stephenson H, López-Alvarez J, Fonfara S. Left atrial size, atrial function and left ventricular diastolic function in cats with hypertrophic cardiomyopathy. J Small Anim Prac 2014;55:198–206.
- [10] Sahn DJ, DeMaria A, Kisslo J, Weyman A. Recommendations regarding quantitation in M-mode

echocardiography: results of a survey of echocardiographic measurements. Circulation 1978;58:1072-83.

- [11] Marsan NA, Michalski B, Cameli M, Podlesnikar T, Manka R, Sitges M, Dweck MR, Haugaa KH. EACVI survey on standardization of cardiac chambers quantification by transthoracic echocardiography. Eur Heart J Cardiovasc Imaging 2020;21:119–23.
- [12] Podlesnikar T, Cardim N, Marsan NA, D'Andrea A, Cameli M, Popescu BA, Schulz-Menger J, Stankovic I, Toplisek J, Maurer G, Haugaa KH, Dweck MR. EACVI survey on hypertrophic cardiomyopathy. Eur Heart J Cardiovasc Imaging 2022;23:590-7.
- [13] Sitges M, Marsan NA, Cameli M, D'Andrea A, Carvalho RF, Holte F, Michalski B, Podlesnikar T, Popescu BA, Schulz-Menger J, Stankovic I, Haugaa KH, Dweck MR. EACVI survey on the evaluation of left ventricular diastolic function. Eur Heart J Cardiovasc Imaging 2021;22:1098–105.
- [14] Haugaa KH, Marsan NA, Cameli M, D'Andrea A, Dweck MR, Carvalho RF, Holte E, Manka R, Michalski B, Podlesnikar T, Popescu BA, Schulz-Menger J, Sitges M, Stankovic I, Maurer G, Edvardsen T. Criteria for surveys: from the European Association of Cardiovascular Imaging Scientific Initiatives Committee. Eur Heart J Cardiovasc Imaging 2019;20:963–6.
- [15] Cameli M, Marsan NA, D'Andrea A, Dweck MR, Fontes-Carvalho R, Manka R, Michalski B, Podlesnikar T, Sitges M, Popescu BA, Edvardsen T, Fox KF, Haugaa KH. EACVI survey on multimodality training in ESC countries. Eur Heart J Cardiovasc Imaging 2019;20:1332–6.
- [16] Marsden PV, Wright JD. Handbook of survey research. Bingley: Group Publishing Limited; 2010.
- [17] Hinkin TR. A brief tutorial on the development of measures for use in survey questionnaires. Organ Res Methods 1998;1: 104–21.
- [18] Dillman DA, Smyth JD, Christian LM. Web questionnaires and implementation. In: Dillman DA, Smyth JD, Christian LM, editors. Web questionnaires and implementation. Internet, phone, mail and mixed-mode surveys: the tailored design method. Hoboken: John Wiley & Sons; 2014. p. 301–50.
- [19] Tsang S, Royse CF, Terkawi AS. Guidelines for developing, translating, and validating a questionnaire in perioperative and pain medicine. Saudi J Anaesth 2017;11:80–9.
- [20] Couper MP, Traugott MW, Lamias MJ. Web survey design and administration. Public Opin Q 2001;65:230–53.
- [21] Dalkey N, Helmer O. An experimental application of the Delphi method to the use of experts. Manag Sci 1963;9: 458–67.
- [22] de Madron E. Normal echocardiographic values: TM, 2D, and Doppler spectral modes. In: de Madron E, Chetboul V, Bussadori C, editors. Clinical echocardiography of the dog and cat. St. Louis: Elsevier; 2016. p. 21–37.
- [23] Payne J, Borgeat K, Connolly D, Boswood A, Dennis S, Wagner T, Menaut P, Maerz I, Evans D, Simons V, Brodbelt DC, Fuentes VL. Prognostic indicators in cats with hypertrophic cardiomyopathy. J Vet Intern Med 2013;27:1427–36.
- [24] Maerz I, Schober K, Oechtering GU. Echocardiographic measurement of left atrial dimension in healthy cats and cats with left ventricular hypertrophy. Tierarztl Prax Ausg Kleintiere Heimtiere 2006;34:331.

- [25] Greet V, Sargent J, Brannick M, Fuentes VL. Supraventricular tachycardia in 23 cats; comparison with 21 cats with atrial fibrillation (2004–2014). J Vet Cardiol 2020;30: 7–16.
- [26] Häggström J, Andersson ÅO, Falk T, Nilsfors L, Olsson U, Kresken J, Höglund K, Rishniw M, Tidholm A, Ljungvall I. Effect of body weight on echocardiographic measurements in 19,866 pure-bred cats with or without heart disease. J Vet Intern Med 2016;30:1601–11.
- [27] Mottet E, Amberger C, Doherr M, Lombard C. Echocardiographic parameters in healthy young adult Sphynx cats. Schweiz Arch Tierheilkd 2012;154:75.
- [28] Chetboul V, Petit A, Gouni V, Trehiou-Sechi E, Misbach C, Balouka D, Sampedrano CC, Pouchelon J-L, Tissier R, Abitbol M. Prospective echocardiographic and tissue Doppler screening of a large Sphynx cat population: reference ranges, heart disease prevalence and genetic aspects. J Vet Cardiol 2012;14:497–509.
- [29] Abbott JA, Maclean HN. Two-dimensional echocardiographic assessment of the feline left atrium. J Vet Intern Med 2006;20:111-9.
- [30] Chetboul V, Passavin P, Trehiou-Sechi E, Gouni V, Poissonnier C, Pouchelon J, Desquilbet. Clinical, epidemiological and echocardiographic features and prognostic factors in cats with restrictive cardiomyopathy: a retrospective study of 92 cases (2001-2015). J Vet Intern Med 2019;33:1222–31.
- [31] Duler L, Scollan KF, LeBlanc NL. Left atrial size and volume in cats with primary cardiomyopathy with and without congestive heart failure. J Vet Cardiol 2019;24: 36–47.
- [32] Rauch J, Fehr M, Beyerbach M, Hungerbuehler SO. Comparative assessment of left atrial volume in healthy cats by two-dimensional and three-dimensional echocardiography. BMC Vet Res 2020;16:1–14.
- [33] Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, Flachskampf FA, Foster E, Goldstein SA, Kuznetsova T, Lancellotti P, Muraru D, Picard MH, Rietzschel ER, Rudski L, Spencer KT, Tsang W, Voigt J-U. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging 2015;16:233–70.
- [34] Pritchett AM, Jacobsen SJ, Mahoney DW, Rodeheffer RJ, Bailey KR, Redfield MM. Left atrial volume as an index of left atrial size: a population-based study. J Am Coll Cardiol 2003; 41:1036–43.
- [35] Bennett C, Khangura S, Brehaut JC, Graham ID, Moher D, Potter BK, Grimshaw JM. Reporting guidelines for survey research: an analysis of published guidance and reporting practices. PLoS Med 2011;8:e1001069.
- [36] Ponto J. Understanding and evaluating survey research. J Adv Pract Oncol 2015;6:168.
- [37] Michalski B, Dweck MR, Marsan NA, Cameli M, D'Andrea A, Carvalho RF, Holte E, Podlesnikar T, Manka R, Haugaa KH. The evaluation of aortic stenosis, how the new guidelines are implemented across Europe: a survey by EACVI. Eur Heart J Cardiovasc Imaging 2020;21:357–62.

Available online at www.sciencedirect.com

ScienceDirect

Acta Universitatis Agriculturae Sueciae

DOCTORAL THESIS NO. 2024:76

Assessing left atrial (LA) size by echocardiography is important for managing heart disease in dogs and cats. Various factors can affect how echocardiographers assess LA size. Veterinary echocardiographers from 67 countries across six continents participated in interactive web-based studies involving image- and video-based investigations. Despite similar linear two-dimensional method of use, variations in image selection, timing, and caliper placement were observed. The thesis presents results that may pave the way for more consistent and reliable echocardiographic assessment of LA size in pets.

Momo Yu-Wen Kuo received her postgraduate education at the Department of Clinical Sciences, Swedish University of Agricultural Sciences, Uppsala. She obtained her degree of Doctor of Veterinary Medicine and master's degree at the Faculty of Veterinary Medicine, National Taiwan University, Taipei.

Acta Universitatis Agriculturae Sueciae presents doctoral theses from the Swedish University of Agricultural Sciences (SLU).

SLU generates knowledge for the sustainable use of biological natural resources. Research, education, extension, as well as environmental monitoring and assessment are used to achieve this goal.

ISSN 1652-6880 ISBN (print version) 978-91-8046-367-6 ISBN (electronic version) 978-91-8046-403-1