



**DISTRIBUTION AND RISK FACTORS OF CANINE HEART DISEASES AND
SURVEY FOR OWNERS TREATMENT INTENTION**

By

NORHIDAYAH BINTI NOORDIN

**Thesis Submitted to the School of Graduate Studies, Universiti Putra
Malaysia, in Fulfilment of the Requirements for the Degree of Master of
Veterinary Science**

February 2023

FPV 2023 1

All material contained within the thesis, including without limitation text, logos, icons, photographs and all other artwork, is copyright material of Universiti Putra Malaysia unless otherwise stated. Use may be made of any material contained within the thesis for non-commercial purposes from the copyright holder. Commercial use of material may only be made with the express, prior, written permission of Universiti Putra Malaysia.

Copyright © Universiti Putra Malaysia



Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfillment of the requirement for the degree of Master of Veterinary Science

DISTRIBUTION AND RISK FACTORS OF CANINE HEART DISEASES AND SURVEY ON OWNERS TREATMENT INTENTION

By

NORHIDAYAH BINTI NOORDIN

February 2023

Chair : Khor Kuan Hua, PhD
Faculty : Veterinary Medicine

Heart disease accounts for up to 10.0% of canine cases reported in a primary veterinary healthcare centres overseas. Risk factors may assist clinicians in establishing a differential diagnosis and planning a diagnostic approach. Early detection and treatment of heart disease had been shown to improve quality of life and prolong lifespan. This study reports the distribution and risk factors of canine heart disease and the survivability of dogs diagnosed with degenerative mitral valve disease (DMVD). The level of awareness, knowledge, and factors affecting the intention to treat canine heart disease among local dog owners were also investigated.

Records of all dogs presented to the University Veterinary Hospital (UVH) between July 2013 and July 2020 were retrospectively analysed through logistic regression. The distribution of canine heart disease patients in this population is (n=734, 7.9%). Most of these dogs had acquired valvular disease (n=528, 76.0%) and DMVD (n=291, 38.0%) was the most common valvular affliction, followed by heartworm disease (n=113, 14.8%) and dilated cardiomyopathy (DCM) (n=90, 11.6%). The risk factors identified were gender, age group and breed size. Senior (Odds ratio, OR 3.54, $p<0.001$), and small breed (OR 6.74, $p<0.001$) dogs had a higher risk for valvular disease, while the large breed (OR 7.18, $p<0.001$) dogs had a greater risk for heartworm disease. Male (OR 1.83, $p=0.02$) and large breed (OR 3.12, $p<0.001$) dogs were at risk for DCM.

A total of 261 respondents who owned or had experience caring for dogs were recruited to determine their level of awareness and knowledge of canine heart disease. The respondents' intentions to treat were investigated using the Theory of Planned Behavior (TPB) items: attitude, subjective norm, and perceived behavioural control (PBC). Empathic concern was made as a moderator through

the partial least squares method. Most of the respondents (83.5%) claimed that they were aware of the disease, however, their ability to identify clinical signs was fair. Most dog owners (92.3%) were willing to seek treatment if their pet dogs were diagnosed, but the cost (39.5%) was a primary concern for long-term treatment. Attitude, subjective norms, and PBC were significant predictors of the intention to treat. Females and owners with good knowledge of canine heart disease have a higher intention to treat it. Owners with low empathic concern can be motivated to treat affected dogs by cultivating their PBC.

The survival of dogs diagnosed with DMVD was further investigated by the Kaplan-Meier curve. Males (n= 156, 51.0%) senior-aged (n= 256, 84.7%), and small breed (n=258, 79.4%) dogs were frequently affected. Small breed dogs (OR: 3.95, p <0.001) were more likely affected by the disease compared with other breed sizes. Out of the total, 126 DMVD dogs (50.8%) had cardiac-related death. Dogs with treatment compliance had a longer median survival time (MST) (P<0.05). With compliant owners, MST of the dogs was 42.1 months (95% CI 35.7-48.5), and 25.2 months (95% CI 17.2-33.2) for stage C and stage D respectively.

In conclusion, gender, age group, and breed size were significant predictors for the likelihood of heart diseases in dogs and are best applied in the context of specific heart diseases. Compliance with long-term treatment significantly improved the lifespan of DMVD dogs. Veterinarians may play an essential role in motivating owners' intention to treat through education, support, and guidance, especially in terms of tasks perceived as challenging by the owners.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia
sebagai memenuhi keperluan untuk ijazah Master Sains Veterinar

DISTRIBUSI, FAKTOR RISIKO PENYAKIT JANTUNG ANJING DAN TINJAUAN NIAT PEMILIK UNTUK MERAWATNYA

Oleh

NORHIDAYAH BINTI NOORDIN

Februari 2023

Pengerusi : Khor Kuan Hua, PhD
Fakulti : Perubatan Veterinar

Penyakit jantung meliputi hampir 10.0% kes anjing yang dilaporkan di pusat kesihatan veterinar asas di luar negara. Faktor risiko membantu veterinawan untuk merancang diagnosis pembezaan dan pendekatan diagnostik. Pengesanan dan rawatan awal telah menunjukkan peningkatan kualiti hidup dan memanjangkan jangka hayat anjing. Kajian ini melaporkan distribusi, faktor risiko penyakit jantung anjing dan kemandirian pesakit anjing yang didiagnosis penyakit injap mitral degeneratif (DMVD). Tahap kesedaran, pengetahuan dan faktor yang mempengaruhi tujuan merawat penyakit ini dalam kalangan pemilik anjing tempatan juga diselidiki.

Rekod-rekod pesakit anjing di Hospital Veterinar Universiti (UVH) di antara Julai 2013 dan Julai 2020 dianalisis secara retrospektif menggunakan regresi logistik. Sebanyak 734 (7.9%) anjing yang didiagnosis penyakit jantung. Majoriti anjing mempunyai penyakit injap perolehan ($n=528$, 76.0%) di mana DMVD ialah penyakit injap yang paling lazim, diikuti oleh penyakit cacing jantung ($n=113$, 14.8%) dan kardiomiopati terdilat (DCM) ($n=90$, 11.6%). Faktor risiko yang dikaji adalah jantina, kumpulan umur dan saiz baka anjing. Anjing senior (Nisbah ods, (OR) 3.54, $p < 0.001$), dan baka kecil (OR 6.74, $p < 0.001$) lebih berisiko mempunyai penyakit injap, manakala baka besar (OR 7.18) berisiko tinggi mempunyai penyakit cacing jantung. Anjing jantan dan baka besar (OR 1.83, $p = 0.02$) berisiko tinggi untuk DCM.

Sebanyak 261 responden yang memiliki anjing atau mempunyai pengalaman menjaga anjing direkrut untuk menentukan tahap kesedaran dan pengetahuan tentang penyakit jantung anjing. Niat para responden untuk merawat diselidiki menggunakan metod *partial least squares structural equation modelling* melalui item-item Teori Kelakuan Terancang (TPB) iaitu sikap, norma subjektif dan

persepsi kawalan gelagat (PBC). Empati ditetapkan sebagai moderator. Majoriti responden (83.5%) menyatakan bahawa mereka sedar akan penyakit ini, walaubagaimanapun kebolehan mereka mengenalpasti tanda klinikalnya adalah di tahap sederhana. Kebanyakan responden rela mendapatkan rawatan jika anjing berpenyakit jantung, namun kos (39.5%) merupakan isu untuk rawatan jangka masa panjang. Sikap, norma subjektif, dan PBC adalah peramal niat merawat yang signifikan. Pemilik anjing wanita dan pemilik dengan pengetahuan penyakit yang tinggi lebih cenderung untuk merawat anjing mereka. Pemilik anjing yang berempati rendah boleh dimotivasikan dengan meningkatkan PBC mereka.

Kemandirian anjing yang didiagnos DMVD dikaji dengan lebih mendalam menggunakan keluk Kaplan Meier. Anjing jantan ($n=156$, 51.0%, 95% CI% 45%-56%), berusia tua (84.7%) dan baka kecil (79.4%) lazim terjejas. Anjing baka kecil (OR: 3.95, 95% CI 2.68-5.82) adalah lebih berisiko untuk menghidap DMVD berbanding saiz baka lain. Daripada jumlah keseluruhan, 126 anjing DMVD (50.8%, 95% CI 79%-90%) menghadapi kematian yang berkaitan dengan penyakit jantung. Anjing dengan pemilik yang patuh pada rawatan mempunyai masa mandiri median (MST) yang lebih panjang ($P<0.05$). Dengan pemilik yang patuh pada rawatan, MST anjing-anjing tersebut adalah selama 42.1 bulan (95% CI 35.7-48.5), dan 25.2 bulan (95% CI 17.2-33.2) di peringkat C dan D masing-masing.

Jantina, kumpulan umur dan saiz baka anjing memainkan peranan penting dalam meramal kebarangkalian penyakit jantung dalam kalangan anjing tetapi lebih sesuai diaplikasi dalam konteks penyakit jantung yang spesifik. Kepatuhan dengan rawatan jangka panjang meningkatkan jangka hayat anjing DMVD. Veterinawan memainkan peranan penting dalam menggalakkan niat merawat penyakit ini dalam kalangan pemilik anjing melalui pendidikan, sokongan dan bimbingan dalam melaksanakan tugas penjagaan yang sukar bagi pemilik.

ACKNOWLEDGEMENTS

All praises be to You Allah, Lord of the worlds, for bestowing me the chance to study Your magnificent creations and granting me the chance to complete this postgraduate study. For truly, You are the Al-Hakeem and Al-Kareem. To my family especially my beloved Mak and Ayah, for their never-ending support and faith in me.

I would like to express my gratitude to Universiti Malaysia Kelantan (UMK) and the Faculty of Veterinary Medicine, UMK for their trust and for providing me with financial support throughout the completion of my studies. To Prof Dr. Azam Khan Goriman Khan, and Prof Dr. Jasni Sabri for their assistance and faith in me. Thank you to Assoc. Prof. Dr. Ibrahim Abdul Azeez Okene and Dr. Farhan Hanif Reduan for their continuous support from the beginning.

I am forever thankful to Allah SWT for crossing my path with my supervisor Dr. Khor Kuan Hua. With grace and patience, she helped me fight my fears and was always around to guide me, especially at the toughest times. Years under her tutelage had shaped me into a better person overall. I also would like to thank her for allowing me to reproduce some of the beautiful echocardiography images from her cases in this thesis.

Thank you to my co-supervisors, Assoc. Prof. Dr. Lau Seng Fong and Dr. Siti Zubaidah Ramanoon for their patience and never-ending guidance throughout my study completion. Many thanks to Dr. Jolyne Khor Kuan Siew for her support and for being generous with her wisdom, knowledge, and opportunities for me to improve my statistical analysis skills.

I also would like to thank the University Veterinary Hospital, Universiti Putra Malaysia (UVH-UPM) staff for all the assistance given especially during the period of data collection. Special thanks to the VOs, AVOs, and VAs for their selfless assistance and for sharing their knowledge with me.

Finally, to all the four-legged buddies (of course, the three-legged ones too-Charlie the Schnauzer!) which I have met throughout completing this postgraduate study. They are the reason why I soldier on even when the going gets tough and motivate me to do better. To some of the dogs that had fallen due to these nasty diseases, they are forever free of pain and their battle stories will forever live through generations of young veterinarians to come. The experience that I gained while caring for them is my best clinical knowledge to share.

This thesis was submitted to the Senate of Universiti Putra Malaysia and has been accepted as fulfilment of the requirement for the degree of Master of Veterinary Science. The members of the Supervisory Committee were as follows:

Khor Kuan Hua, PhD

Senior Lecturer
Faculty of Veterinary Medicine
Universiti Putra Malaysia
(Chairman)

Lau Seng Fong, PhD

Associate Professor
Faculty of Veterinary Medicine
Universiti Putra Malaysia
(Member)

Siti Zubaidah Ramanoon, PhD

Senior Lecturer
Faculty of Veterinary Medicine
Universiti Putra Malaysia
(Member)

ZALILAH MOHD SHARIFF, PhD

Professor and Dean
School of Graduate Studies
Universiti Putra Malaysia

Date: 8th June 2023

Declaration by the Graduate Student

I hereby confirm that:

- this thesis is my original work;
- quotations, illustrations and citations have been duly referenced;
- this thesis has not been submitted previously or concurrently for any other degree at any institutions;
- intellectual property from the thesis and the copyright of the thesis are fully-owned by Universiti Putra Malaysia, as stipulated in the Universiti Putra Malaysia (Research) Rules 2012;
- written permission must be obtained from the supervisor and the office of the Deputy Vice-Chancellor (Research and innovation) before the thesis is published in any written, printed or electronic form (including books, journals, modules, proceedings, popular writings, seminar papers, manuscripts, posters, reports, lecture notes, learning modules or any other materials) as stated in the Universiti Putra Malaysia (Research) Rules 2012;
- there is no plagiarism or data falsification/fabrication in the thesis, and scholarly integrity is upheld in accordance with the Universiti Putra Malaysia (Graduate Studies) Rules 2003 (Revision 2015-2016) and the Universiti Putra Malaysia (Research) Rules 2012. The thesis has undergone plagiarism detection software

Signature: _____ Date: _____

Name and Matric No.: Norhidayah Binti Noordin

Declaration by Members of the Supervisory Committee

This is to confirm that:

- the research and the writing of this thesis were done under our supervision;
- supervisory responsibilities as stated in the Universiti Putra Malaysia (Graduate Studies) Rules 2003 (Revision 2015-2016) are adhered to.

Signature: _____
Name of
Chairman of
Supervisory
Committee: Khor Kuan Hua, PhD

Signature: _____
Name of
Member of
Supervisory
Committee: Lau Seng Fong, PhD

Signature: _____
Name of
Member of
Supervisory
Committee: Siti Zubaidah Ramanoon, PhD

TABLE OF CONTENTS

	Page
ABSTRACT	i
ACKNOWLEDGEMENTS	v
APPROVAL	vi
DECLARATION	viii
LIST OF TABLES	xiii
LIST OF FIGURES	xv
LIST OF ABBREVIATIONS	xvii
1 INTRODUCTION	1
1.1 Background of Study	1
1.2 Problem Statement	2
1.3 Objectives	3
1.4 Hypotheses	3
1.5 Justification of Study	4
1.6 Relationship Between the Objectives	4
2 LITERATURE REVIEW	6
2.1 Canine Heart Diseases	6
2.1.1 Types of Canine Heart Disease	6
2.1.2 Acquired canine heart diseases	6
2.1.3 Congestive heart failure (CHF)	12
2.1.4 Canine Heart Disease Reports in Malaysia	15
2.1.5 Diagnosis of canine heart disease	15
2.2 Risk Factors of The Canine Heart Diseases	19
2.2.1 Gender	19
2.2.2 Age Group	20
2.2.3 Breed size	20
2.2.4 Risk Factors of Heartworm Disease	21
2.3 Treatment and Management of Canine Heart Diseases	21
2.4 Compliance with Treatment	23
2.5 Awareness, Knowledge, And Intention to Treat Canine Heart Disease	24
2.5.1 Role of owners' awareness and knowledge	24
2.5.2 Theory of Planned Behaviour (TPB)	24
2.6 Role Of Empathic Concern	25
2.7 Statistical Analysis	26
2.7.1 Logistic regression	26
2.7.2 Partial Least Squares Method of Structural Equation Modelling	26
2.7.3 Kaplan-Meier Curve Estimator	27

3	DISTRIBUTION, RISK FACTORS FOR HEART DISEASE IN PET DOGS ATTENDED AT A VETERINARY TEACHING HOSPITAL IN MALAYSIA	28
3.1	Introduction	29
3.2	Methods	30
3.2.1	Study design	30
3.2.2	Definition of diseases	30
3.2.3	Data collection, inclusion, and exclusion criteria	30
3.2.4	Definition of risk factors	31
3.2.5	Statistical analysis	31
3.3	Results	31
3.4	Discussion	42
3.5	Conclusion	45
	References	46
	Proof of Publication	52
4	DOG OWNERS' AWARENESS, KNOWLEDGE, AND INTENTION TO TREAT CANINE HEART DISEASE IN KLANG VALLEY, MALAYSIA	53
4.1	Introduction	54
4.2	Materials and Methods	56
4.2.1	Respondents	56
4.2.2	Questionnaire	56
4.2.3	Statistical Analysis	58
4.3	Results	59
4.3.1	Descriptive Analysis	59
4.3.2	Common Method Variable (CMV)	64
4.3.3	Measurement Model Assessment	65
4.3.4	Structural Model Assessment	68
4.4	Discussion	71
4.5	Conclusions	74
	References	75
	Proof of Publication	79
5	THE ASSOCIATED RISK FACTORS, STAGING, AND MEDIAN SURVIVAL TIME OF DOG PATIENTS DIAGNOSED WITH DEGENERATIVE MITRAL VALVE DISEASE (DMVD)	80
5.1	Introduction	81
5.2	Methods	82
5.2.1	Study population	82
5.2.2	Data collection and categorization	82
5.2.3	Survival data analysis	82
5.2.4	Treatment Compliance	83
5.2.5	Statistical analysis	83
5.3	Results	83
5.3.1	Risk Factor Analysis	85
5.3.2	Survival Analysis	86
5.4	Discussion	93

5.5	Conclusion	96
	References	97
	Proof of Publication	100
6	SUMMARY, CONCLUSION, AND RECOMMENDATIONS FOR FUTURE RESEARCH	101
	REFERENCES	106
	APPENDICES	129
	BIODATA OF STUDENT	135
	LIST OF PUBLICATIONS	136



LIST OF TABLES

Table		Page
2.1	ACVIM Staging of DMVD Patients	7
2.2	Canine heartworm disease classification	10
3.1	Frequency (n), percentage (%), and 95% CI of distribution of heart and non-heart disease dogs presented to the UVH	33
3.2	Distribution of heart disease diagnosed among the heart disease cases (n=765) presented to the UVH	36
3.3	Frequency (n), percentage (%), and 95% CI of distribution of clinical signs related to heart disease (n=532)	37
3.4	Univariable and multivariable logistic regression analyses between risk factors (gender, age group, and breed size) and heart disease in 9255 dogs	39
3.5	Univariable and multivariable logistic regression analyses between risk factors (gender, age group, and breed size) and valvular disease, heartworm disease, and dilated cardiomyopathy in 9255 dogs	39
4.1	Demographic profiles of the participating dog owners (n = 261) and the association with ability to identify clinical signs with the intention to treat canine heart disease	60
4.2	Purpose of having pet dogs among dog owners (n = 261)	61
4.3	Source of information used by the dog owners (n = 261) in acquiring information on canine heart disease	61
4.4	Willingness to seek treatment, barriers to seeking treatment, and perception towards lifelong treatment among the dog owners (n = 261)	62
4.5	Awareness, understanding of dog owners (n = 261), and their ability to identify clinical signs of canine heart disease	62
4.6	Full collinearity testing output	64
4.7	Convergent validity of the measurement items	66
4.8	Discriminant validity of the measurement model	68

4.9	Path coefficients of the structural model and results of hypothesis testing (H): The moderating influence of empathic concern (EC) on the relationship between attitude (ATT), subjective norm (SN), perceived behavioral control (PBC), and intention to treat (INT) dogs with heart disease	70
5.1	Descriptive analysis of DMVD dogs (n=306)	84
5.2	Descriptive analysis of DMVD dogs based on compliance (n=242) with the long-term treatment	86
5.3	Univariable and multivariable logistic regression analyses between DMVD cases presented to the UVH-UPM between July 2013 and July 2020 (n=306) with risk factors (gender, age group, and breed size)	87
5.4	Descriptive analysis of DMVD cases based on mortality status and cause of death (n=248) based on owner's observation	88
5.5	Median Survival Time (MST) of dogs diagnosed with DMVD (n=248) based on gender, age group, breed size, and stages of the disease	89
5.6	Median Survival Time of dogs diagnosed with DMVD at different stages and the effect of survival based on treatment compliance (n=242)	91

LIST OF FIGURES

Figure		Page
2.1	Echocardiographic findings of a Stage C DMVD in a Shih Tzu dog	8
2.2	Echocardiographic (Duplex view of B-mode and M-mode) of DCM in a Miniature Poodle	11
2.3	Simplified pathophysiology of congestive heart failure (CHF)	14
2.4	Right lateral view of the thorax in an 11-year-old Shih-Tzu showing a VHS measurement	16
2.5	Right lateral view of a 12-years old Shih Tzu showing a VLAS measurement	17
2.6	M-mode echocardiography (lower) in a dog through the 2-Dimensional right parasternal short axis at the level of the papillary muscle	18
2.7	Theory of Perceived Behaviour (TPB)	25
4.1	The research framework of the study exhibits an extended theory of planned behaviour with empathic concern as the moderating variable	59
4.2	The relationship between the ability to identify clinical signs and the level of awareness of canine heart disease among dog owners (n = 261) in the study	63
4.3	The relationship between the ability to identify clinical signs and the level of understanding of canine heart disease among dog owners (n = 261) in the study	64
4.4	The output of structural model analysis shows the relationship between attitude, subjective norm, perceived behavioral control, empathic concern, and the interaction terms with the intention to treat. Solid lines denote significant relationship ($p < 0.05$), whereas dotted line denotes insignificant relationship. *Denotes the interaction	69
5.1	Outline of recruited DMVD dogs included for analysis	84
5.2	Kaplan-Meier curve estimator of DMVD dogs with known survival status (n=242) in UVH from July 2013-July 2020. Solid line: Stage B2, dashed line: Stage C, and dash-dotted line: Stage D	90

- 5.3 Kaplan-Meier curve estimator of Stage B2 DMVD (n=65) dogs with owner compliance to treatment versus non-compliance. Solid line: compliant cases, dashed lines: non-compliant cases, dotted line: median 92
- 5.4 Kaplan-Meier curve estimator of Stage C DMVD (n=141) dogs with owner compliance to treatment versus non-compliance. Solid line: compliant cases, dashed lines: non-compliant cases, dotted line: median 92
- 5.5 Kaplan-Meier curve estimator of Stage D DMVD (n=36) dogs with owner compliance to treatment versus non-compliance. Solid line: compliant cases, dashed lines: non-compliant cases, dotted line: median 93



COPYRIGHT



LIST OF ABBREVIATIONS

5-HT	5-hydroxytryptamine, 5-HT
ACEI	angiotensin-converting enzyme inhibitor
AngII	angiotensin II
AT1-R	angiotensin type 1- receptor
ATP	adenosine triphosphate
AUC	area under curve
CHF	congestive heart failure
CMV	common method variable
DCM	dilated cardiomyopathy
DMVD	degenerative mitral valve disease
HDL	high-density lipoprotein
L-carnitine	levocarnitine
LVIDDn	left ventricle internal diameter at diastole normalized to body weight
MST	median survival time
NTproBNP	N-terminal-pro B- type natriuretic peptide
PDK4	pyruvate dehydrogenase kinase 4
PLS-SEM	partial least squares structural equation modelling
SNP	single nucleotide polymorphism
STRTN	Straitin gene
TGF β	transforming growth factor-beta
TPB	Theory of Perceived Behaviour
UPM	Universiti Putra Malaysia

UVH	University Veterinary Hospital
VHS	vertebral heart score
VIF	variation inflation factor
VLAS	vertebral left atrium score
vLDL	very low-density lipoprotein



© COPYRIGHT UPM

CHAPTER 1

INTRODUCTION

1.1 Background of Study

Heart disease is commonly reported among dogs; approximately 10.0% of dog cases were presented to primary veterinary healthcare practices (Keene et al., 2019). For acquired heart diseases, 75.0 % of the cases consist of valvular disease. The mitral valve was the most affected (Mattin et al, 2015). Local data on canine heart disease is still lacking. However, a retrospective study in a veterinary centre in Kuala Lumpur revealed a similar finding, where degenerative mitral valve disease (DMVD), followed by dilated cardiomyopathy (DCM), was the most diagnosed heart disease among dogs (Yap et al., 2021).

Early detection and treatment of heart disease allow the chance to prolong the preclinical period and lifespan (Boswood et al., 2016; Summerfield et al., 2012). Therefore, as a provider and caretakers, dog owners' awareness and knowledge play an important role in early screening and pursuance of diagnosis and treatment. Combinations of patient history, physical examination findings, and diagnostic imaging assist the clinician in establishing the heart disease diagnosis and planning the necessary prescription. In facilities where diagnostic modalities may be limited or when faced with owners with cost constraints, risk factors helped clinicians in establishing a more accurate differential diagnosis. Heart disease requires long-term treatment to prolong the preclinical period, relieving clinical signs and reducing the heart workload. Successful management of chronic diseases relies on compliance with long-term prescriptions and commitment to nursing tasks. Proper commitment allows the disease to be managed appropriately, and check-ups and monitoring allow surfacing complications or worsening of the disease to be picked up quickly, hence allowing change or improvement in the prescription.

Barriers to long-term treatment among dog owners may include exhaustible or bounded factors such as cost and time. Other than that, owners' internal limitations and motivations may also play an important role in their decision to pursue treatment. According to Ajzen (1991) in the Theory of Planned Behaviour (TPB), a behaviour can be predicted by the intention to engage in the behaviour. The intention can be influenced by attitude, subjective norms, and perceived behavioural control. Empathy, which is the ability to perceive, identify, and share in another being's emotional state (Eisenberg, 2000), may also play a role in strengthening their owners' intention to pursue treatment, especially upon witnessing their pets battling the clinical signs.

This study documented the distribution and risk factors of developing heart disease among dogs presented in UVH-UPM from July 2013 to July 2020. Gender, age group, and breed size were selected as the risk factors and tested using two different logistic regression models. The models were: i) involving overall heart disease dogs, and ii) a model where the dogs were separated based on the three common heart diseases, which were valvular disease, heartworm disease, and dilated cardiomyopathy. As DMVD was commonly diagnosed in the population, a specific survival analysis was carried out where the relationship between median survival time (MST) with the aforementioned risk factors and owners' compliance was investigated. Finally, a two-part questionnaire study was carried out to a) investigate the awareness and knowledge of canine heart disease, barriers to long-term treatment, and willingness to treat canine heart disease in their dogs, and b) investigate the role of TPB items which were attitude, subjective norm, and perceived behavioural control in intention to treat canine heart disease with empathic concern as its moderator. The results of this study would improve the knowledge of clinicians on canine heart disease in dogs within the local population and assist clinicians in the diagnosis and outline of a suitable treatment and management plan for heart disease and other chronic diseases.

1.2 Problem Statement

It was observed that heart disease was among the common chronic illnesses diagnosed in senior-aged dogs. Prevalence and survival of canine DMVD have been documented on specific predisposed breeds worldwide (Borgarelli et al., 2008; Mattin et al., 2015; Yap et al., 2021), but information may not be applied readily due to the differences in the presentation of the dog population locally. Hence, preliminary data from this study will allow comparison with previous studies. The relevancy of previous studies for local use can be considered. Despite the abundance of survival analyses that reported the positive roles of treatment and management of valvular diseases, the role of compliance to treatment on the lifespan of the patients remained under-studied. By understanding the owners' level of awareness and knowledge of canine heart disease, reasonable efforts can be taken by the clinicians to educate the owners. This may in return help owners in their decision-making, and increase the quality of care received by the pets at home. Unfortunately, this information is not widely studied locally. Similarly, factors affecting the intention to treat the disease among dog owners locally are also unknown. Both aspects are important for successful canine heart disease management as early intervention can help prolong lifespan and provide good quality of life for affected dogs. However, long-term treatment requires commitment and compliance from their owner(s).

1.3 Objectives

The objectives of this study were as follows:

1. To determine common heart diseases among canine patients in UVH-UPM and respective prevalence and risk factors.
2. To evaluate awareness and knowledge on canine heart disease among canine owners and barriers to long-term heart disease treatment
3. To evaluate the role of attitude, subjective norm, perceived behavioural control, and empathic concern in affecting the intention to treat canine heart disease among local dog owners
4. To determine the survival probability and factors affecting it in canine valvular disease patients in UVH-UPM

1.4 Hypotheses

The hypotheses for this study were:

1. Valvular disease is the most common type of heart disease among canine patients in UVH-UPM.
2. There is a relationship between gender, breed size, age group, and risk of having heart disease, valvular disease, heartworm disease and DCM.
3. There is a relationship between gender, breed size, age group, and treatment compliance in MST of DMVD patients.
4. Awareness and knowledge of canine heart diseases are still low among local dog owners
5. Attitude, subjective norm, perceived behavioural control, and empathic concern positively affect the intention to treat canine heart disease among dog owners
6. Empathic concern positively moderates attitude, subjective norm, and perceived behavioural control in leading to the intention to treat heart disease by dog owners

1.5 Justification of Study

To date, there is a lack of information regarding the distribution and risk factors of dogs being diagnosed with heart disease locally (Yap et al., 2021). Information from worldwide may vary geographically, for example, with the different breeds (Swift et al., 2017) and genetic predisposition (Lewis et al., 2010). Other than that, knowledge of risk factors and characteristics of common heart disease will assist clinicians in making a differential diagnosis. Data from survival analysis of dogs with valvular heart disease can help manage the owner's expectations and assist in clinical therapeutic decision-making (Borgarelli et al., 2008). There is a need to understand the level of knowledge and awareness among dog owners locally. Besides that, it is essential to understand factors affecting the owner's intention to treat canine heart disease, as clinicians can strategise and plan to assist client needs, manage their expectations, and eventually motivate owners to provide their dog(s) to improve quality of life despite being diagnosed with heart disease.

In general, this study was conducted to answer the following research questions:

1. What is the common heart disease diagnosed among dog patients in UVH-UPM?
2. How do gender, age group, and breed size affect the risk of heart disease among dog patients in UVH-UPM?
3. What is the MST of canine DMVD patients in UVH-UPM?
4. How do treatment compliance, gender, age group, and breed size affect MST of canine DMVD patients?
5. What is the level of awareness and knowledge on canine heart disease among local dog owners?
6. How does attitude, subjective norm, perceived behavioural control, and empathic concern affect intention to treat heart disease among local dog owners?

1.6 Relationship Between the Objectives

Successful management of canine heart disease requires a diagnosis, suitable treatment, and dog owners' pursuance and compliance with the treatment. Investigation of risk factors for canine heart disease among the local population of dogs may assist clinicians in deriving diagnoses and promoting early screening. Previous studies have documented that DMVD as the most common acquired heart disease. However, local data with regards to incidents of DMVD

remain lacking, despite that the disease has been noted as very common among dogs with a long preclinical period. After receiving the diagnosis, understanding the survival rate and effect of compliance on prolonging the lifespan of DMVD dogs may motivate owners to pursue treatment. Being a progressive chronic disease that often requires lifelong medication and management, it is of utmost importance to identify and acknowledge the challenges and barriers among local dog owners in treating heart disease beyond materialistic aspects. Following the prospect of adjustments to their daily activities, and having the emotional burden of witnessing the suffering of their dogs, decisions on becoming a caregiver for a chronically ill dog may require psychosocial consideration. Therefore, by predicting their intention to treat and understanding factors influencing it, efforts can be made by clinicians to assure the need of both dog owners and their pet dogs fairly.



© COPYRIGHT

References

- American Kennel Club* (2020). Retrieved July 1, 2020, from <https://www.akc.org/>
- 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. *Journal of Veterinary Internal Medicine*, 22(1): 120–128.
- Borgarelli, M., Zini, E., D'Agnolo, G., Tarducci, A., Santilli, R. A., Chiavegato, D., Tursi, M., Prunotto, M., & Häggström, J. (2004). Comparison of primary mitral valve disease in German Shepherd dogs and in small breeds. *Journal of Veterinary Cardiology*, 6(2): 27–34.
- Borgarelli, M., & Buchanan, J. W. (2012). Historical review, epidemiology and natural history of degenerative mitral valve disease. *Journal of Veterinary Cardiology*, 14(1):93–101.
- Boswood, A., Häggström, J., Gordon, S. G., Wess, G., Stepien, R. L., et al. (2016). Effect of Pimobendan in Dogs with Preclinical Myxomatous Mitral Valve Disease and Cardiomegaly: The EPIC Study—A Randomized Clinical Trial. *Journal of Veterinary Internal Medicine*, 30(6): 1765–1779.
- Buchanan, J. W., Sci, M., Bucheler, J., & Ver, M. (1995). Vertebral scale system to measure canine heartsize in radiographs. In *Journal of The American Veterinary Medical Association*, 206(2): 194–199.
- Chetboul, V., & Tissier, R. (2012). Echocardiographic assessment of canine degenerative mitral valve disease. In *Journal of Veterinary Cardiology*, 14(1):127-148.
- De Madron, E., King, J. N., Strehlau, G., & Valle White, R. (2011). Survival and echocardiographic data in dogs with congestive heart failure caused by mitral valve disease and treated by multiple drugs: A retrospective study of 21 cases. *Canadian Veterinary Journal*, 52(11): 1219–1225.
- Fox, P. R. (2012). Pathology of myxomatous mitral valve disease in the dog. In *Journal of Veterinary Cardiology*, 14(1):103-126.
- Grave, K. & Tanem, H. (1999), Compliance with short-term oral antibacterial drug treatment in dogs. *Journal of Small Animal Practice*, 40(4): 158-162.
- Häggström, J., Hansson, K., Kvart, C., & Swenson, L. (1992). Chronic valvular disease in the cavalier King Charles spaniel in Sweden. *The Veterinary Record*, 131(24): 549–553.

- Häggström, J., Kwart, C., & Hansson, K. (1995). Heart Sounds and Murmurs: Changes Related to Severity of Chronic Valvular Disease in the Cavalier King Charles Spaniel. *Journal of Veterinary Internal Medicine*, 9(2): 75–85.
- Jones, P., Chase, K., Martin, A., Davern, P., Ostrander, E. A., & Lark, K. G. (2008). Single-nucleotide-polymorphism-based association mapping of dog stereotypes. *Genetics*, 179(2):1033–1044.
- Keene B.W., Atkins CE, Bonagura JD, Fox PR, Häggström J, Fuentes VL, et al. (2019). ACVIM consensus guidelines for the diagnosis and treatment of myxomatous mitral valve disease in dogs. *Journal of Veterinary Internal Medicine*;33(3):1127–40.
- Kim, H. T., Han, S. M., Song, W. J., Kim, B., Choi, M., Yoon, J., & Youn, H. Y. (2017). Retrospective study of degenerative mitral valve disease in small-breed dogs: survival and prognostic variables. *Journal of Veterinary Science*, 18(3): 369–376.
- Madsen, M.B., Olsen, L.H., Häggström, J., Höglund, K., Ljungvall, I., et al., (2011). Identification of 2 loci associated with development of myxomatous mitral valve disease in Cavalier King Charles Spaniels. *The Journal of Heredity*. 102(Suppl-1).
- Martin, M. W. S., Stafford Johnson, M. J., & Celona, B. (2009). Canine dilated cardiomyopathy: a retrospective study of signalment, presentation and clinical findings in 369 cases. *Journal of Small Animal Practice*, 50(1): 23–29.
- Noordin N, Khor K.H., Ee K.L., Lau S.F., & Ramanoon S.Z.(2022). Risk factors for heart disease in pet dogs attended at a veterinary teaching hospital in Malaysia. *International Journal of Veterinary Science* 11(4): 504-513.
- Noordin, N., Khor, K. H., Khor, K. S., Lim, Y. J., & Lee, Y. C. (2022). Dog Owners' Perspectives on Canine Heart Disease in Klang Valley, Malaysia. *Animals*, 12(8), 985.
- Olsen, L. H., Fredholm, M., & Pedersen, H. D. (1999). Epidemiology and inheritance of mitral valve prolapse in Dachshunds. *Journal of Veterinary Internal Medicine*, 13(5): 448–456.
- Oyama M.A., Rush J.E., O'Sullivan M.L., Williams R.M., Rozanski E.A., Petrie J.P., et al. (2008). Perceptions and priorities of owners of dogs with heart disease regarding quality versus quantity of life for their pets. *233(1)*, 104–108
- Pelio, D. C., Russell, N. J., Passley, B. S., Rosson, C. D., Weller, J. B., et al. (2021). Evaluation of owner medication adherence for canine

cardiovascular disease in the referral setting. *Journal of Veterinary Cardiology*, 37: 42–51.

- Pouchelon, J. L., Atkins, C. E., Bussadori, C., Oyama, M. A., Vaden, S. L., et al. (2015). Cardiovascular-renal axis disorders in the domestic dog and cat: A veterinary consensus statement. *Journal of Small Animal Practice*, 56(9): 537–552.
- Raggi, P., Callister, T. Q., Lippolis, N. J., & Russo, D. J. (2000). Is mitral valve prolapse due to cardiac entrapment in the chest cavity? A CT view. *Chest*, 117(3): 636–642.
- Serfass, P., Chetboul, V., Sampedrano, C. C., Nicolle, A., Benalloul, T., Laforge, H., Gau, C., Hébert, C., Pouchelon, J. L., & Tissier, R. (2006). Retrospective study of 942 small-sized dogs: Prevalence of left apical systolic heart murmur and left-sided heart failure, critical effects of breed and sex. *Journal of Veterinary Cardiology*, 8(1): 11–18.
- Stepien, R. L., Rak, M. B., & Blume, L. M. (2020). Use of radiographic measurements to diagnose stage B2 preclinical myxomatous mitral valve disease in dogs. *Journal of the American Veterinary Medical Association*, 256(10), 1129–1136. <https://doi.org/10.2460/JAVMA.256.10.1129>
- Swenson, L., Häggström, J., Kvarn, C., & Juneja, R. K. (1996). Relationship between parental cardiac status in Cavalier King Charles spaniels and prevalence and severity of chronic valvular disease in offspring. *Journal of the American Veterinary Medical Association*, 208(12): 2009–2012.
- Urfer, S. R., Kaeberlein, M., Promislow, D. E. L., & Creevy, K. E. (2020). Lifespan of companion dogs seen in three independent primary care veterinary clinics in the United States. *Canine Medicine and Genetics*, 7(1): 7.
- Whitney, J. G. (1974). Observations on the effect of age on the severity of heart valve lesions in the dog. *Journal of Small Animal Practice*, 15(8): 511–522.
- Yap, K. S., Ghanabadi, S., Ibrahim Abdul-Azeez Okene, A. S., & Ayahsamy, S. (2021). Retrospective Echocardiographic Survey of Canine Cardiac Conditions in Kuala Lumpur, Malaysia. *Journal of Animal Health and Production Retrospective*, 9(2): 198–204.
- Wang, J., Zhou, J., Powell-Braxton, L., & Bondy, C. (1999). Effects of Igf1 gene deletion on postnatal growth patterns. *Endocrinology*, 140(7): 3391–3394.

REFERENCES

- Abbott, J.A. (2010) The effect of pregnancy on echocardiographic variables in healthy bitches. *Journal of Veterinary Cardiology*, 12(2): 123–128.
- Abi-Gerges, N., Small, B. G., Lawrence, C. L., Hammond, T. G., Valentin, J. P., & Pollard, C. E. (2004). Evidence for gender differences in electrophysiological properties of canine Purkinje fibres. *British Journal of Pharmacology*, 142(8): 1255–1264.
- Adin, D., Kurtz, K., Atkins, C., Papich, M.G., & Vaden, S. (2020) Role of electrolyte concentrations and renin-angiotensin-aldosterone activation in the staging of canine heart disease. *Journal of Veterinary Internal Medicine*. 34(1): 53–64.
- Adin, D., DeFrancesco, T. C., Keene, B., Tou, S., Meurs, K., Atkins, C., Aona, B., Kurtz, K., Barron, L., & Saker, K. (2019). Echocardiographic phenotype of canine dilated cardiomyopathy differs based on diet type. *Journal of Veterinary Cardiology*, 21: 1–9.
- Ajzen, I. (1991). The theory of planned behavior. *Organizational Behavior and Human Decision Processes*, 50(2): 179–211.
- Ajzen, I. (2020). The theory of planned behavior: Frequently asked questions. *Human Behavior and Emerging Technologies*, 2(4): 314–324.
- Alho, A. M., Fiarresga, A., Landum, M., Lima, C., Gamboa, Ó., Meireles, J., Sales Luís, J., & Madeira De Carvalho, L. (2016). A Homemade Snare: An Alternative Method for Mechanical Removal of *Dirofilaria immitis* in Dogs. *Veterinary Medicine International*, 5780408
- American Heartworm Society. (2020). Current Canine Guidelines for the Prevention, Diagnosis, and Management of Heartworm (*Dirofilaria immitis*) Infection in Dogs. Retrieved from <https://www.heartwormsociety.org/veterinary-resources/american-heartworm-society-guidelines>
- American Kennel Club (2020). Retrieved July 1, 2020, from <https://www.akc.org/>
- Amin, A., & Maleki, M. (2012). Positive inotropes in heart failure: A review article. *Heart Asia*, 4(1):16-22.
- Andrei, B., & Vulpe, V. (2021) Prevalence of cardiac diseases in small animals: A five-year single-center retrospective study. *Revista Romana de Medicina Veterinara*, 31(1): 35-40
- Aonuma, H., Yoshimura, A., Perera, N., Shinzawa, N., Bando, H., Oshiro, S., Nelson, B., Fukumoto, S., & Kanuka, H. (2009). Loop-mediated isothermal amplification applied to filarial parasites detection in the

- mosquito vectors: *Dirofilaria immitis* as a study model. *Parasites and Vectors*, 2(1): 1–7.
- Arrigo, M., Huber, L. C., Winnik, S., Mikulicic, F., Guidetti, F., Frank, M., Flammer, A. J., & Ruschitzka, F. (2019). Right Ventricular Failure: Pathophysiology, Diagnosis and Treatment. *Cardiac Failure Review*, 5(3): 140.
- Aupperle, H., & Disatian, S. (2012). Pathology, protein expression and signaling in myxomatous mitral valve degeneration: Comparison of dogs and humans. *Journal of Veterinary Cardiology*. 14(1):59-71.
- Aupperle, H., März, I., Thielebein, J., & Schoon, H. A. (2008). Expression of transforming growth factor-beta1, -beta2 and -beta3 in normal and diseased canine mitral valves. *Journal of Comparative Pathology*, 139(2–3): 97–107.
- Avierinos, J.F., Gersh, B.J., Melton, L.J., Bailey, K.R., Shub, C., et al. (2002). Natural history of asymptomatic mitral valve prolapse in the community. *Circulation* 106:1355–1361.
- Azhar, M., Brown, K., Gard, C., Chen, H., Rajan, S., Elliott, D. A., Stevens, M. V., Camenisch, T. D., Conway, S. J., & Doetschman, T. (2011). Transforming growth factor Beta2 is required for valve remodeling during heart development. *Developmental Dynamics : An Official Publication of the American Association of Anatomists*, 240(9): 2127–2141.
- Ballantyne K.C, & Buller K. (2015). Experiences of veterinarians in clinical behavior practice: A mixed-methods study. *Journal of Veterinary Behaviour*. 10(5):376–83.
- Baron, R. M., & Kenny, D. A. (1986). The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. *Journal of Personality and Social Psychology*, 51(6): 1173–1182.
- Batson C.D., Duncan, B. D., Ackerman, P., Buckley, T., & Birch, K. (1981). Is empathic emotion a source of altruistic motivation? *Journal of Personality and Social Psychology*. 40(2):290–302.
- Beardow, A. W., & Buchanan, J. W. (1993). Chronic mitral valve disease in cavalier King Charles spaniels: 95 cases (1987-1991). *Journal of the American Veterinary Medical Association*, 203(7): 1023–1029.
- Beaumier, A., Rush, J. E., Yang, V. K., Freeman, L. M., & John Rush, C. E. (2018). Clinical findings and survival time in dogs with advanced heart failure. *Journal of Veterinary Internal Medicine*, 32(3):944–950.
- BENCH (BENazepril in Canine Heart disease) Study Group. (1999). The effect of benazepril on survival times and clinical signs of dogs with congestive

- heart failure: Results of a multicenter, prospective, randomized, double-blinded, placebo-controlled, long-term clinical trial. *Journal of Veterinary Cardiology: The Official Journal of the European Society of Veterinary Cardiology*, 1(1): 7–18.
- Bernay, F., Bland, J. M., Häggström, J., Baduel, L., Combes, B., Lopez, A., & Kaltsatos, V. (2010). Efficacy of Spironolactone on Survival in Dogs with Naturally Occurring Mitral Regurgitation Caused by Myxomatous Mitral Valve Disease. *Journal of Veterinary Internal Medicine*, 24(2): 331–341.
- Birkegård, A. C., Reimann, M. J., Martinussen, T., Häggström, J., Pedersen, H. D., & Olsen, L. H. (2016). Breeding Restrictions Decrease the Prevalence of Myxomatous Mitral Valve Disease in Cavalier King Charles Spaniels over an 8- to 10-Year Period. *Journal of Veterinary Internal Medicine*, 30(1): 63–68.
- Blanco, P.G., Tórtora, M., Rodriguez, R., Arias, D.O., & Gobello, C. (2011). Ultrasonographic assessment of maternal cardiac function and peripheral circulation during normal gestation in dogs. *The Veterinary Journal*.190(1): 154–159.
- Bogucki, S., & Noszczyk-Nowak, A. (2015). Short-term heart rate variability (HRV) in healthy dogs. *Polish Journal of Veterinary Sciences*, 18(2): 307–312.
- Boon, J. A. (2011). Chapter 4- Evaluation of Size, Functions and Hemodynamics. pp.225-387. In *Veterinary Echocardiography*. (2nd ed.). Iowa: Wiley-Blackwell.
- Boonyapakorn, C., Punyapornwithaya, V., Sawatphakdee, G., Poolsawat, N., & Pongkan, W. (2020) Estrogen deprivation induces lipid profile impairment but not cardiac dysfunction in ovariohysterectomized dogs. *Polish Journal of Veterinary Sciences*, 23(4): 521–528.
- Bopassa, J. C., Eghbali, M., Toro, L., & Stefani, E. (2010). A novel estrogen receptor GPER inhibits mitochondria permeability transition pore opening and protects the heart against ischemia-reperfusion injury. *American Journal of Physiology. Heart and Circulatory Physiology*, 298(1): H16–H23.
- Borgarelli M., & Haggstrom, J. (2010). Canine degenerative myxomatous mitral valve disease: Natural history, clinical presentation and therapy. In *Veterinary Clinics of North America - Small Animal Practice* 40(4): 651-663.
- Borgarelli, M., & Buchanan, J. W. (2012). Historical review, epidemiology and natural history of degenerative mitral valve disease. *Journal of Veterinary Cardiology*, 14(1):93–101.

- 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. *Journal of Veterinary Internal Medicine*, 22(1): 120–128.
- Borgarelli, M., Zini, E., D'Agnolo, G., Tarducci, A., Santilli, R. A., Chiavegato, D., Tursi, M., Prunotto, M., & Häggström, J. (2004). Comparison of primary mitral valve disease in German Shepherd dogs and in small breeds. *Journal of Veterinary Cardiology*, 6(2): 27–34.
- Boswood, A., Häggström, J., Gordon, S. G., Wess, G., Stepien, R. L., et al. (2016). Effect of Pimobendan in Dogs with Preclinical Myxomatous Mitral Valve Disease and Cardiomegaly: The EPIC Study—A Randomized Clinical Trial. *Journal of Veterinary Internal Medicine*, 30(6): 1765–1779.
- Boyko, A.R., Quignon, P., Li, L., Schoenebeck, J.J., & Degenhardt, J.D. (2010) A Simple Genetic Architecture Underlies Morphological Variation in Dogs. *PLoS Biol.* 8, 1000451.
- Boyle, K. L., & Leech, E. (2012). A review of the pharmacology and clinical uses of pimobendan. *Journal of Veterinary Emergency and Critical Care*, 22(4): 398–408.
- 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(7): e0230160.
- Brooks, V.L., & Keil, L.C. (1994). Changes in the baroreflex during pregnancy in conscious dogs: heart rate and hormonal responses. *Endocrinology*. 135(5): 1894–1901.
- Brown B. R. (2018). The Dimensions of Pet-Owner Loyalty and the Relationship with Communication, Trust, Commitment and Perceived Value. *Veterinary Sciences*. 5(4):95.
- Buchanan, J. W., Sci, M., Bucheler, J., & Ver, M. (1995). Vertebral scale system to measure canine heartsize in radiographs. In *Journal of The American Veterinary Medical Association*, 206(2): 194–199.
- Buchanan, J.W. (1977) Chronic valvular disease (endocardiosis) in dogs. *Advances in Veterinary Science and Comparative Medicine*. 21: 75–106.
- Byrne BM. *Structural Equation Modelling with AMOS: Basic Concepts, Applications, and Programming*. 2nd ed. New York: Routledge; 2001.

- Calvert, C. A., Hall, G., Jacobs, G., & Pickus, C. (1997). Clinical and pathologic findings in Doberman pinschers with occult cardiomyopathy that died suddenly or developed congestive heart failure: 54 cases (1984-1991). *Journal of the American Veterinary Medical Association*, 210(4): 505–511.
- Campbell, D. J. (2013). Do intravenous and subcutaneous angiotensin II increase blood pressure by different mechanisms? *Clinical and Experimental Pharmacology and Physiology*, 40(8): 560–570.
- Casey, R. A., & Bradshaw, J. W. S. (2008). Owner compliance and clinical outcome measures for domestic cats undergoing clinical behavior therapy. *Journal of Veterinary Behavior: Clinical Applications and Research*, 3(3), 114–124.
- Chelliah, M., & Šlapeta, J. (2019). The prevalence and trends of canine heartworm (*Dirofilaria immitis*) in Kuala Lumpur, Malaysia (1970-2018). *Veterinary Parasitology, Regional Studies and Reports*, 16, 100272.
- Chen, C. H., Budas, G. R., Churchill, E. N., Disatnik, M. H., Hurley, T. D., & Mochly-Rosen, D. (2008). Activation of aldehyde dehydrogenase-2 reduces ischemic damage to the heart. *Science*, 321(5895): 1493–1495.
- Chetboul, V., & Tissier, R. (2012). Echocardiographic assessment of canine degenerative mitral valve disease. In *Journal of Veterinary Cardiology*, 14(1):127-148.
- Chetboul, V., Pouchelon, J.L., Menard, J., Blanc, J., Desquilbet, L., et al. (2017) Short-Term Efficacy and Safety of Torasemide and Furosemide in 366 Dogs with Degenerative Mitral Valve Disease: The TEST Study. *Journal of Veterinary Internal Medicine*. 31(6): 1629–1642.
- Chetboul, V., Tissier, R., Villaret, F., Nicolle, A., Déan, E., et al. (2004). Epidemiological, clinical, echo-doppler characteristics of mitral valve endocardiosis in Cavalier King Charles in France: a retrospective study of 451 cases (1995 to 2003). *Canadian Veterinary Journal*. 45(12):1012-5.
- Chin W.W. (2010). How to write up and report PLS analyses. In: Handbook of partial least squares. pp. 655–90. Berlin: Springer.
- Christiansen S.B., Kristensen AT, Sandøe P, Lassen J. Looking After Chronically Ill Dogs: Impacts on the Caregiver's Life.; *Anthrozoös*, 26(4):519–33.
- Coffman, M., Guillot, E., Blondel, T., Garelli-Paar, C., Feng, S., Heartsill, S., & Atkins, C. E. (2021). Clinical efficacy of a benazepril and spironolactone combination in dogs with congestive heart failure due to myxomatous

mitral valve disease: The BENazepril Spironolactone Study (BESST). *Journal of Veterinary Internal Medicine*, 35(4): 1673–1687.

- Cohen S. P. (2002). Can pets function as family members?. *Western Journal of Nursing Research*, 24(6): 621–638.
- Cohn, J. N., Ferrari, R., & Sharpe, N. (2000). Cardiac remodeling--concepts and clinical implications: a consensus paper from an international forum on cardiac remodeling. Behalf of an International Forum on Cardiac Remodeling. *Journal of the American College of Cardiology*, 35(3): 569–582.
- Côté, E., Edwards, N. J., Ettinger, S. J., Fuentes, V. L., MacDonald, K. A., Scansen, B. A., David Sisson, D., & Abbott, J. A. (2015). Management of incidentally detected heart murmurs in dogs and cats. *Journal of the American Veterinary Medical Association*, 246(10): 1076–1088.
- Davis, M.H. (1980) A Multidimensional Approach to Individual Differences in Empathy. *JSAS Catalog of Selected Documents in Psychology*, 10:85
- De Madron, E., King, J. N., Strehlau, G., & Valle White, R. (2011). Survival and echocardiographic data in dogs with congestive heart failure caused by mitral valve disease and treated by multiple drugs: A retrospective study of 21 cases. *Canadian Veterinary Journal*, 52(11): 1219–1225.
- De Madron, E., King, J. N., Strehlau, G., & Valle White, R. (2011). Survival and echocardiographic data in dogs with congestive heart failure caused by mitral valve disease and treated by multiple drugs: A retrospective study of 21 cases. *Canadian Veterinary Journal*, 52(11): 1219–1225
- Decety J., Bartal I.B.A., Uzefovsky F., Knafo-Noam A. (2016). Empathy as a driver of prosocial behaviour: highly conserved neurobehavioural mechanisms across species. *Philosophical Transactions of Royal Society B*.371201500772015007771:1686)
- Del Buono, M. G., Arena, R., Borlaug, B. A., Carbone, S., Canada, J. M., Kirkman, D. L., Garten, R., Rodriguez-Miguel, P., Guazzi, M., Lavie, C. J., & Abbate, A. (2019). Exercise Intolerance in Patients With Heart Failure: JACC State-of-the-Art Review. *Journal of the American College of Cardiology*, 73(17): 2209–2225.
- Department of Statistics Malaysia Official Portal [Internet]. Retrieved 10th November 2021. <https://www.dosm.gov.my/v1>.
- 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(1): 481–516.
- Dillon, A. R., Dell'Italia, L. J., Tillson, M., Killingsworth, C., Denney, T., Hathcock, J., & Botzman, L. (2012). Left ventricular remodeling in preclinical

- experimental mitral regurgitation of dogs. *Journal of Veterinary Cardiology*, 14(1):73–92.
- Disatian, S., Ehrhart, E. J., Zimmerman, S., & Orton, E. C. (2008). Interstitial cells from dogs with naturally occurring myxomatous mitral valve disease undergo phenotype transformation. *Journal of Heart Valve Disease*, 17(4): 402–412.
- Donath, M.Y., Zapf, J., Eppenberger-Eberhardt, M., Froesch, E.R., & Eppenberger, H.M. (1994) Insulin-like growth factor I stimulates myofibril development and decreases smooth muscle α -actin of adult cardiomyocytes. *Medical Sciences*, 91: 1686–1690.
- Drake, J., & Wiseman, S. (2018). Increasing incidence of *Dirofilaria immitis* in dogs in USA with focus on the southeast region 2013–2016. *Parasites & Vectors*, 11(1):39.
- Dutton, E., & López-Alvarez, J. (2018). An update on canine cardiomyopathies – is it all in the genes? *Journal of Small Animal Practice*, 59(8): 455–464.
- Edvinsson, M. L., Uddman, E., Edvinsson, L., & Andersson, S. E. (2014). Brain natriuretic peptide is a potent vasodilator in aged human microcirculation and shows a blunted response in heart failure patients. *Journal of Geriatric Cardiology*, 11(1): 50.
- Egenvall, A., Bonnett, B. N., Hedhammar, Å., & Olson, P. (2005). Mortality in over 350,000 insured Swedish dogs from 1995-2000: II. Breed-specific age and survival patterns and relative risk for causes of death. *Acta Veterinaria Scandinavica*, 46(3): 121–136.
- Ellingsen K, Zanella AJ, Bjerkås E, Indrebø A. (2010). The relationship between empathy, perception of pain and attitudes toward pets among Norwegian dog owners. *Anthrozoos*, 23(3):231–43.
- Erling, P., Mazzafero, E. M. (2008). Left-sided congestive heart failure in dogs: Pathophysiology and diagnosis. *Compendium (Yardley, PA)*, 30(2): 79–91.
- Everett, R. M., McGann, J., Wimberly, H. C., & Althoff, J. (1999). Dilated cardiomyopathy of Doberman pinschers: retrospective histomorphologic evaluation of heart from 32 cases. *Veterinary Pathology*, 36(3): 221–227.
- Falk, T., Ljungvall, I., Zois, N. E., Höglund, K., Olsen, L. H., Pedersen, H. D., & Häggström, J. (2013). Cardiac Troponin-I Concentration, Myocardial Arteriosclerosis, and Fibrosis in Dogs with Congestive Heart Failure because of Myxomatous Mitral Valve Disease. *Journal of Veterinary Internal Medicine*, 27(3): 500–506.

- Fascetti, A. J., Reed, J. R., Rogers, Q. R., & Backus, R. C. (2003). Taurine deficiency in dogs with dilated cardiomyopathy: 12 cases (1997-2001). *Journal of the American Veterinary Medical Association*, 223(8): 1137–1141.
- FDA-NIH Biomarker Working Group. BEST (Biomarkers, EndpointS, and other Tools) Resource [Internet]. Silver Spring (MD): Food and Drug Administration (US); 2016-. Retrieved from: <https://www.ncbi.nlm.nih.gov/books/NBK326791/>. Accessed on 12th February 2021
- Ferasin, L., & Linney, C. (2019) Coughing in dogs: what is the evidence for and against a cardiac cough? *Journal of Small Animal Practice*. 60(3):139–145.
- Ferasin, L., Crews, L., Biller, D. S., Lamb, K. E., & Borgarelli, M. (2013). Risk factors for coughing in dogs with naturally acquired myxomatous mitral valve disease. *Journal of Veterinary Internal Medicine*, 27(2), 286–292
- Fine, D. M., DeClue, A. E., & Reiner, C. R. (2008). Evaluation of circulating amino terminal-pro-B-type natriuretic peptide concentration in dogs with respiratory distress attributable to congestive heart failure or primary pulmonary disease. *Journal of the American Veterinary Medical Association*, 232(11), 1674–1679.
- Fioretti, M., & Delli, C. (1988) Epidemiological survey of dilatative cardiomyopathy in dogs. *Veterinaria*, 2(8):1.
- Ford, J., McEndaffer, L., Renshaw, R., Molesan, A., & Kelly, K. (2017). Parvovirus Infection Is Associated With Myocarditis and Myocardial Fibrosis in Young Dogs. *Veterinary Pathology*, 54(6): 964–971.
- Fornell C, Larcker DF. Evaluating Structural Equation Models with Unobservable Variables and Measurement Error. *J Mark Res*. 1981;18(1):39.
- Fox, P. R. (2012). Pathology of myxomatous mitral valve disease in the dog. In *Journal of Veterinary Cardiology*, 14(1):103-126.
- Frank, K., & Heald, R. D. (2010). The emerging role of Wolbachia species in heartworm disease. *Compendium (Yardley, PA)*, 32(4):E4.
- Frazier P.A., Tix A.P., Barron K.E. (2004). Testing moderator and mediator effects in counseling psychology research. *Journal of Counselling and Psychology* ;51(1):115–34.
- Freeman, L. M., Stern, J. A., Fries, R., Adin, D. B., & Rush, J. E. (2018). Diet-associated dilated cardiomyopathy in dogs: what do we know? *Journal of the American Veterinary Medical Association*, 253(11), 1390–1394.

- Freid, K. J., Freeman, L. M., Rush, J. E., Cunningham, S. M., Davis, M. S., Karlin, E. T., & Yang, V. K. (2021). Retrospective study of dilated cardiomyopathy in dogs. *Journal of Veterinary Internal Medicine*, 35(1): 58–67.
- Fülöp, L., Bányász, T., Szabó, G., Tóth, I. B., Bíró, T., Lôrincz, I., Balogh, Á., Petô, K., Mikó, I., & Nánási, P. P. (2006). Effects of sex hormones on ECG parameters and expression of cardiac ion channels in dogs. *Acta Physiologica*, 188(3–4): 163–171.
- Funder, J. W. (2017). Chapter 21 - Aldosterone and Mineralocorticoid Receptors. In G. Fink (Ed.), *Stress: Neuroendocrinology and Neurobiology* (1st ed.), pp. 221–225. Academic Press. London.
- Gouni, V., Serres, F. J., Pouchelon, J. L., Tissier, R., Lefebvre, H. P., Nicolle, A. P., Sampedrano, C. C., & Chetboul, V. (2007). Quantification of mitral valve regurgitation in dogs with degenerative mitral valve disease by use of the proximal isovelocity surface area method. *Journal of the American Veterinary Medical Association*, 231(3): 399–406.
- Graham, W., Rubin, S.B., President, P., Boeckh, A., President, V., et al. (2012). *Current Canine Guidelines for the Diagnosis, Prevention, and Management of Heartworm (Dirofilaria immitis) Infection in Dogs*. American Heartworm Association.
- Grave, K. & Tanem, H. (1999), Compliance with short-term oral antibacterial drug treatment in dogs. *Journal of Small Animal Practice*, 40(4): 158-162.
- Greco, A., Meomartino, L., Raiano, V., Fatone, G., & Brunetti, A. (2008). Effect of left vs. right recumbency on the vertebral heart score in normal dogs. *Veterinary Radiology & Ultrasound*, 49(5): 454–455.
- Guglielmini, C. (2003). Cardiovascular Diseases in the Ageing Dog: Diagnostic and Therapeutic Problems. *Veterinary Research Communications*, 27(1): 555–560.
- Gulanber, E., & Gulanber. (2005). Vertebral Scale System to Measure Heart Size in Thoracic Radiographs of Turkish Shepherd (Kangal) Dogs. *Turkish Journal of Veterinary and Animal Sciences*, 29, 723–726.
- Haritha, G (2020) Pericardial Effusion in Dogs. *Veterinary Medicine and Pharmaceutical*,. 89051
- Haenlein, M., & Kaplan, A. M. (2004). A Beginner's Guide to Partial Least Squares Analysis. *Understanding Statistics*, 3(4): 283–297.
- Hagemeyer, F. (1993). Calcium sensitization with pimobendan: pharmacology, haemodynamic improvement, and sudden death in patients with chronic congestive heart failure. *European Heart Journal*, 14(4): 551–566.

- Häggström, J., Hansson, K., Kvarn, C., & Swenson, L. (1992). Chronic valvular disease in the cavalier King Charles spaniel in Sweden. *The Veterinary Record*, 131(24): 549–553.
- Häggström, J., Kvarn, C., & Hansson, K. (1995). Heart Sounds and Murmurs: Changes Related to Severity of Chronic Valvular Disease in the Cavalier King Charles Spaniel. *Journal of Veterinary Internal Medicine*, 9(2): 75–85.
- Hair J.F., Fisher J.J., Sarstedt M, Ringle CM.,(2019). When to use and how to report the results of PLS-SEM. *European Business Review*, 31(1):2-24.
- Hair Jr, J., Sarstedt, M., Hopkins, L. & G. Kuppelwieser, V. (2014), "Partial least squares structural equation modeling (PLS-SEM): An emerging tool in business research", *European Business Review*, 26(2), 106-121.
- Hair, J.F., Black, W.C., Babin, B.J., Anderson RE. Multivariate Data Analysis. 7th ed. Upper Saddle River, New Jersey: Prentice Hall.
- Hair, J.F., Hult, G.T.M., Ringle, C.M. & Sarstedt, M. (2017) A Primer on Partial Least Squares Structural Equation Modeling (PLS-SEM). 2nd Edition, Thousand Oaks, CA.:Sage Publications.
- Hallman, B. E., Hauck, M. L., Williams, L. E., Hess, P. R., & Suter, S. E. (2019). Incidence and risk factors associated with development of clinical cardiotoxicity in dogs receiving doxorubicin. *Journal of Veterinary Internal Medicine*, 33(2), 783.
- Harpster, N. (1983). Boxer cardiomyopathy. In *Current veterinary therapy VIII*. (pp. 329–337). Philadelphia: W.B. Saunders.
- Hayward, C. S., Kelly, R. P., & Collins, P. (2000). The roles of gender, the menopause and hormone replacement on cardiovascular function. *Cardiovascular Research*, 46(1): 28–49.
- Herzog HA. Gender differences in human-animal interactions: A review. *Anthrozoos*. 2007;20(1):7–21.
- Hezzell, M. J., Boswood, A., Chang, Y. M., Moonarmart, W., Souttar, K., & Elliott, J. (2012). The Combined Prognostic Potential of Serum High-Sensitivity Cardiac Troponin I and N-Terminal pro-B-Type Natriuretic Peptide Concentrations in Dogs with Degenerative Mitral Valve Disease. *Journal of Veterinary Internal Medicine*, 26(2): 302–311.
- Hezzell, M.J., Foster, J.D., Oyama, M.A., Buch, J., Farace, G., Quinn, J.J., & Yerramilli, M. (2020). Measurements of echocardiographic indices and biomarkers of kidney injury in dogs with chronic kidney disease. *Veterinary Journal*, 255:105420.

- Holliday, R. (1997). Understanding Ageing. *Philosophical Transactions: Biological Sciences*, 352(1363): 1793–1797.
- Hori, Y., Takusagawa, F., Ikadai, H., Uechi, M., Hoshi, F., & Higuchi, S. I. (2007). Effects of oral administration of furosemide and torsemide in healthy dogs. *American Journal of Veterinary Research*, 68(10):1058–1063.
- Hwang, H., Malhotra, N. K., Kim, Y., Tomiuk, M. A., & Hong, S. (2010). A comparative study on parameter recovery of three approaches to structural equation modeling. *Journal of Marketing Research*, 47:699–712.
- Inoue, M., Hasegawa, A., Hosoi, Y., & Sugiura, K. (2016). Association between breed, gender and age in relation to cardiovascular disorders in insured dogs in Japan. *Journal of Veterinary Medical Science*, 78(2): 347–350.
- Janke N., Coe J.B., Bernardo T.M., Dewey C.E., Stone E.A. (2021). Pet owners' and veterinarians' perceptions of information exchange and clinical decision-making in companion animal practice. *PLoS One*, 16(2).
- Janus, I., Noszczyk-Nowak, A., Nowak, M., Cepiel, A., Ciaputa, R., Paśławska, U., Dzięgiel, P., & Jabłońska, K. (2014). Myocarditis in dogs: Etiology, clinical and histopathological features (11 cases: 2007-2013). *Irish Veterinary Journal*, 67(1): 1–8.
- Jones, P., Chase, K., Martin, A., Davern, P., Ostrander, E. A., & Lark, K. G. (2008). Single-nucleotide-polymorphism-based association mapping of dog stereotypes. *Genetics*, 179(2):1033–1044.
- Kai Lee E. (2019) Retrospective study on canine heart disease in University Veterinary Hospital, Universiti Putra Malaysia (UVH-UPM) from 2014-2018. Final Year Project Thesis. Universiti Putra Malaysia.
- Kaplan J.L., Stern J.A., Fascetti A.J., Larsen J.A., Skolnik H., et al. (2018) Taurine deficiency and dilated cardiomyopathy in golden retrievers fed commercial diets. *PLOS ONE*, 13(12): e0210233.
- Kealy, J. K. (1987). *Diagnostic radiology of the dog and cat*. (2nd ed.). pp.220. St Louis: Saunders WB.
- Keene BW, Atkins CE, Bonagura JD, Fox PR, Häggström J, Fuentes VL, et al. (2019). ACVIM consensus guidelines for the diagnosis and treatment of myxomatous mitral valve disease in dogs. *Journal of Veterinary Internal Medicine*;33(3):1127–40.
- 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. *Journal of Veterinary Internal Medicine*, 33(3):1127–1140.

Khor, K. H., Campbell, F., Rathbone, M. J., Greer, R. M., Mills, P. C. (2012). Acceptability and compliance of atenolol tablet, compounded paste and compounded suspension prescribed to healthy cats. *Journal of Feline Medicine and Surgery*, 14(2): 99–106.

Khor, K. H., Khor, K. S., Lee, Y. C., & Lim, J. Y. (2020). Would Cat Owners Intend to Treat their Cats If Diagnosed with Heart Disease? *Journal of Veterinary Behavior*, 41:39–46.

Kim, H. T., Han, S. M., Song, W. J., Kim, B., Choi, M., Yoon, J., & Youn, H. Y. (2017). Retrospective study of degenerative mitral valve disease in small-breed dogs: survival and prognostic variables. *Journal of Veterinary Science*, 18(3): 369–376.

Klabunde, E. R. (2012). Cardiovascular Physiology Concepts 2nd Edition. *Cardiovascular Physiology Concepts 2nd Edition*. pp.243. Baltimore: Lippincott Williams & Wilkins.

Klinge, C. M. (2017). Estrogens regulate life and death in mitochondria. *Journal of Bioenergetics and Biomembranes*, 49(4): 307–324.

Klüser, L., Maier, E. T., & Wess, G. (2019). Evaluation of a high-sensitivity cardiac troponin I assay compared to a first-generation cardiac troponin I assay in Doberman Pinschers with and without dilated cardiomyopathy. *Journal of Veterinary Internal Medicine*, 33(1), 54–63.

Kock N., Lynn G.S. (2012). Lateral collinearity and misleading results in variance-based SEM: An illustration and recommendations. *Journal of the Association for Information System*, 13(7):546–580.

Kogan, L. R., Schoenfeld-Tacher, R., & Viera, A. R. (2012). The internet and health information: Differences in pet owners based on age, gender, and education. *Journal of the Medical Library Association*, 100(3): 197–204.

Kolimenakis, A., Heinz, S., Wilson, M. L., Winkler, V., Jakob, L., Michaelakis, A., Papachristos, D., Richardson, C., & Horstick, O. (2021). The role of urbanisation in the spread of Aedes mosquitoes and the diseases they transmit—A systematic review. *PLOS Neglected Tropical Diseases*, 15(9): e0009631.

Kruger, K, Mccune, S, & Merrill, R (2017). *WALTHAM® Pocket Book of Human-Animal Interactions*. USA: Mars Petcare

LaCaille L. (2013). Theory of Reasoned Action. In: Gellman M.D., Turner J.R., (Eds.). *Encyclopedia of Behavioral Medicine*. New York: Springer;

- Lau, S. F. (2017). Canine vector borne diseases of zoonotic concern in three dog shelters in Peninsular Malaysia: The importance of preventive measures. *Tropical Biomedicine*, 34(1): 72–79.
- Leon AC. Descriptive and Inferential Statistics. *Comparative Clinical Psychology*. 1998;243–85.
- Levine, R., Hagège, A., Judge, D. et al., (2015). Mitral valve disease—morphology and mechanisms. *Nature Review Cardiology*, 12(12): 689–710
- Li, D., Lu, C.-J., Hao, G., Wright, H., Woodward, L., Liu, K., Vergari, E., Surdo, N. C., Herring, N., Zaccolo, M., & Paterson, D. J. (2015). Efficacy of B-Type Natriuretic Peptide Is Coupled to Phosphodiesterase 2A in Cardiac Sympathetic Neurons. *Hypertension*, 66(1),:190–198.
- Linklater, A. K. J., Lichtenberger, M. K., Thamm, D. H., Tilley, L., & Kirby, R. (2007). Serum concentrations of cardiac troponin I and cardiac troponin T in dogs with class IV congestive heart failure due to mitral valve disease. *Journal of Veterinary Emergency and Critical Care*, 17(3): 243–249.
- Lira, R. P. C., Antunes-Foschini, R., & Rocha, E. M. (2020). Survival analysis (Kaplan-Meier curves): a method to predict the future. *Arquivos Brasileiros de Oftalmologia*, 83(2): v–vii.
- Ljungvall, I., Höglund, K., Tidholm, A., Olsen, L. H., Borgarelli, M., Venge, P., & Häggström, J. (2010). Cardiac troponin I is associated with severity of myxomatous mitral valve disease, age, and C-reactive protein in dogs. *Journal of Veterinary Internal Medicine*, 24(1): 153–159.
- Lu, T. L., Wong, J. Y., Tan, T. L., & Hung, Y. W. (2017). Prevalence and epidemiology of canine and feline heartworm infection in Taiwan. *Parasites & Vectors*, 10(Suppl 2): 484.
- Lue, T. W., Pantenburg, D. P., & Crawford, P. M. (2008). Impact of the owner-pet and client-veterinarian bond on the care that pets receive. *Journal of the American Veterinary Medical Association*, 232(4): 531–540.
- Madsen, M.B., Olsen, L.H., Häggström, J., Höglund, K., Ljungvall, I., et al., (2011). Identification of 2 loci associated with development of myxomatous mitral valve disease in Cavalier King Charles Spaniels. *The Journal of Heredity*. 102(Suppl-1).
- Markby, G., Summers, K. M., MacRae, V. E., Del-Pozo, J., & Corcoran, B. M. (2017). Myxomatous Degeneration of the Canine Mitral Valve: From Gross Changes to Molecular Events. *Journal of Comparative Pathology*, 156(4): 371–383.

- Martin, M. W. S., Stafford Johnson, M. J., & Celona, B. (2009). Canine dilated cardiomyopathy: a retrospective study of signalment, presentation and clinical findings in 369 cases. *Journal of Small Animal Practice*, 50(1): 23–29.
- Mattin, M. J., Boswood, A., Church, D. B., Lopez-Alvarez, J., McGreevy, P. D., et al., (2015). Prevalence of and risk factors for degenerative mitral valve disease in dogs attending primary-care veterinary practices in England. *Journal Of Veterinary Internal Medicine*, 29(3): 847–854
- McCauley, S. R., Clark, S. D., Quest, B. W., Streeter, R. M., & Oxford, E. M. (2020). Review of canine dilated cardiomyopathy in the wake of diet-associated concerns. *Journal of Animal Science*, 98(6): 1–10.
- Medlock, J., Barrass, I., Bennett, E., Taylor, M., & Leach, S. (2007). Analysis of Climatic Predictions for Extrinsic Incubation of *Dirofilaria* in The United Kingdom. *Vector Borne and Zoonotic Diseases*, 7(1): 4–14.
- Menciotti, G., Borgarelli, M., Aherne, M., Wesselowski, S., Häggström, J., Ljungvall, I., Lahmers, S. M., & Abbott, J. A. (2017). Mitral valve morphology assessed by three-dimensional transthoracic echocardiography in healthy dogs and dogs with myxomatous mitral valve disease. *Journal of Veterinary Cardiology*, 19(2): 113–123.
- Mercier, E., Mathieu, M., Sandersen, C.F., Delvaux, F.H., Clercx, C.M., et al. (2010). Evaluation of the influence of age on pulmonary arterial pressure by use of right ventricular catheterization, pulsed-wave Doppler echocardiography, and pulsed-wave tissue Doppler imaging in healthy Beagles. *American Journal of Veterinary Research*. 71(8): 891–897.
- Meurs, K. M., Stern, J. A., Sisson, D. D., Kittleson, M. D., Cunningham, S. M., et al. (2013). Association of dilated cardiomyopathy with the striatin mutation genotype in boxer dogs. *Journal of Veterinary Internal Medicine*, 27(6): 1437–1440.
- Meurs, K.M., Friedenber, S. G., Kolb, J., Saripalli, C., Tonino, P., Woodruff, K., Olby, N. J., Keene, B. W., Adin, D. B., Yost, O. L., DeFrancesco, T. C., Lahmers, S., Tou, S., Shelton, G. D., & Granzier, H. (2019). A missense variant in the titin gene in Doberman pinscher dogs with familial dilated cardiomyopathy and sudden cardiac death. *Human Genetics*, 138(5): 515–524.
- Meurs, K.M., Lahmers, S., Keene, B. W., White, S. N., Oyama, M. A., Mauceli, E., & Lindblad-Toh, K. (2012). A splice site mutation in a gene encoding for PDK4, a mitochondrial protein, is associated with the development of dilated cardiomyopathy in the Doberman pinscher. *Human Genetics*, 131(8): 1319–1325.
- Meurs, K.M., Miller, M.W., & Wright, N.A. (2001). Clinical features of dilated cardiomyopathy in Great Danes and results of a pedigree analysis: 17

- cases (1990-2000). *Journal of the American Veterinary Medical Association*. 218(5): 729–732.
- Mohd-Zaki, A. H., Brett, J., Ismail, E., & L'Azou, M. (2014). Epidemiology of Dengue Disease in Malaysia (2000–2012): A Systematic Literature Review. *PLoS Neglected Tropical Diseases*, 8(11), e0003156.
- Montoya-Alonso, J. A., Mellado, I., Carretón, E., Cabrera-Pedrero, E. D., Morchón, R., & Simón, F. (2010). Canine dirofilariosis caused by *Dirofilaria immitis* is a risk factor for the human population on the island of Gran Canaria, Canary Islands, Spain. *Parasitology Research*, 107(5): 1265–1269.
- Mukherjee, J., Das, P. K., Ghosh, P. R., Banerjee, D., Sharma, T., Basak, D., & Sanyal, S. (2015). Electrocardiogram pattern of some exotic breeds of trained dogs: A variation study. *Veterinary World*, 8(11): 1317–1320.
- Mukherjee, J., Mohapatra, S. S., Jana, S., Das, P. K., Ghosh, P. R., Das, K., & Banerjee, D. (2020). A study on the electrocardiography in dogs: Reference values and their comparison among breeds, sex, and age groups. *Veterinary World*, 13(10): 2216.
- Muñoz-Durango, N., Fuentes, C. A., Castillo, A. E., González-Gómez, L. M., Vecchiola, A., Fardella, C. E., & Kalergis, A. M. (2016). Role of the Renin-Angiotensin-Aldosterone System beyond Blood Pressure Regulation: Molecular and Cellular Mechanisms Involved in End-Organ Damage during Arterial Hypertension. *International Journal of Molecular Sciences*, 17(7): 797
- Murphy M.D., Larson J, Tyler A, Kvam V, Frank K, Eia C, Bickett-Weddle D., Flaming K., Baldwin C.J., Petersen C.A. (2013). Assessment of owner willingness to treat or manage diseases of dogs and cats as a guide to shelter animal adoptability. *Journal of the American Veterinary Medical Association*. 242(1): 46–53
- Muzzi, R. AL, de Araújo, R. B., Muzzi, L. AL, Pena, J. L., & Silva, E. F. (2003). Regurgitant jet area by Doppler color flow mapping: quantitative assessment of mitral regurgitation severity in dogs. *Journal of Veterinary Cardiology*, 5(2): 33–38.
- Nelson, R. W., & Couto, G. C. (2014). Chapter 3- Management of Heart Failure (pp. 54-71) In: *Small Animal Internal Medicine* (Fifth Ed). St. Louis: Elsevier.
- Nickels, B. M., & Feeley, T. H. (2018). Breaking Bad News in Veterinary Medicine. *Health communication*, 33(9): 1105–1113.
- Noack, S., Harrington, J., Carithers, D. S., Kaminsky, R., & Selzer, P. M. (2021). Heartworm disease - Overview, intervention, and industry perspective.

- Noordin N, Khor K.H., Ee K.L., Lau S.F., & Ramanoon S.Z.(2022). Risk factors for heart disease in pet dogs attended at a veterinary teaching hospital in Malaysia. *International Journal of Veterinary Science* 11(4): 504-513.
- Noordin, N., Khor, K. H., Khor, K. S., Lim, Y. J., & Lee, Y. C. (2022). Dog Owners' Perspectives on Canine Heart Disease in Klang Valley, Malaysia. *Animals*, 12(8), 985.
- Noszczyk-Nowak, A. (2011). NT-pro-BNP . troponin I as predictors of mortality in dogs with heart failure. *Polish Journal of Veterinary Sciences*, 14(4): 551–556.
- Noszczyk-Nowak, Agnieszka, Michałek, M., Kałuża, E., Cepiel, A., & Paślawska, U. (2017). Prevalence of Arrhythmias in Dogs Examined between 2008 and 2014. *Journal of Veterinary Research*, 61(1): 103.
- O'Brien, M. J., Beijerink, N. J., & Wade, C. M. (2021). *Genetics of canine myxomatous mitral valve disease*. *Animal Genetics*, 52(4): 409–421.
- O'Neill, D.G., Church, D.B., McGreevy, P.D., Thomson, P.C., & Brodbelt, D.C., (2013) Longevity and mortality of owned dogs in England. *Veterinary Journal*. 198(3): 638–643.
- Offord, D. R., & Kraemer, H. C. (2000). Risk factors and prevention. *Evidence-Based Mental Health*, 3(3): 70–71.
- Oliveira, P., Domenech, O., Silva, J., Vannini, S., Bussadori, R., & Bussadori, C. (2011). Retrospective review of congenital heart disease in 976 dogs. *Journal of Veterinary Internal Medicine*, 25(3): 477–483.
- Olsen, L. H., Fredholm, M., & Pedersen, H. D. (1999). Epidemiology and inheritance of mitral valve prolapse in Dachshunds. *Journal of Veterinary Internal Medicine*, 13(5): 448–456.
- Olsson, K., Lagerstedt, A.S., Bergström, A., & Häggström, J. (2003) Change of Diurnal Heart Rate Patterns During Pregnancy and Lactation in Dogs (Canis familiaris). *Acta Veterinaria Scandinavica*, 44:105.
- Ontiveros, E.S., Whelchel, B.D., Yu, J., Kaplan, J.L., Sharpe., A.N., Fousse, S.L., Crofton, A.E., Fascetti, A.J., & Stern, J.A. (2020) Development of plasma and whole blood taurine reference ranges and identification of dietary features associated with taurine deficiency and dilated cardiomyopathy in golden retrievers: A prospective, observational study. *PLoS One*, 15: e0233026
- Oyama M.A., Rush J.E., O'Sullivan M.L., Williams R.M., Rozanski E.A., Petrie J.P., et al. (2008). Perceptions and priorities of owners of dogs with heart

- disease regarding quality versus quantity of life for their pets.233(1), 104–108
- Oyama, M. A., & Singletary, G. E. (2010). The use of NT-proBNP assay in the management of canine patients with heart disease. *The Veterinary Clinics of North America. Small Animal Practice*, 40(4): 545–558.
- Oyama, M. A., & Solter, P. F. (2004). Validation of an immunoassay for measurement of canine cardiac troponin-I. *Journal of Veterinary Cardiology*, 6(2): 17–24.
- Oyama, M. A., Rush, J. E., O'Sullivan, M. L., Williams, R. M., Rozanski, E. A., et al. (2008). *Perceptions and priorities of owners of dogs with heart disease regarding quality versus quantity of life for their pets*, 233(1): 104–108
- Oyama, MA, Kraus, MS, and Gelzer, AR (2020) *Rapid review of ECG interpretation in small animal practice* (2nd ed.) Taylor & Francis.
- Pallant, J. (2010). *SPSS survival manual : a step by step guide to data analysis using SPSS*. Maidenhead: Open University Press/McGraw-Hill.
- Park, R. M., Gruen, M. E., & Royal, K. (2021). Association between Dog Owner Demographics and Decision to Seek Veterinary Care. *Veterinary Sciences*, 8(1), 7.
- Park, H. A. (2013). An introduction to logistic regression: from basic concepts to interpretation with particular attention to nursing domain. *Journal of Korean Academy of Nursing*, 43(2): 154–164.
- Park, K., Gaze, D., Collinson, P., & Marber, M. (2017). Cardiac troponins: From myocardial infarction to chronic disease. *Cardiovascular Research*, 113(14):1708–1718.
- Parker, H. G., & Kilroy-Glynn, P. (2012). Myxomatous mitral valve disease in dogs: Does size matter? *Journal of Veterinary Cardiology*, 14(1): 19–29.
- Peek C.W., Dunham C.C., Dietz B.E.(1997). Gender, relational role orientation, and affinity for animal rights. *Sex Roles*. 37(11):905–20.
- Pelio, D. C., Russell, N. J., Passley, B. S., Rosson, C. D., Weller, J. B., et al. (2021). Evaluation of owner medication adherence for canine cardiovascular disease in the referral setting. *Journal of Veterinary Cardiology*, 37: 42–51.
- Philipp, U, Vollmar, A, Häggström, J, Thomas, A, & Distl, O (2012) Multiple Loci Are Associated with Dilated Cardiomyopathy in Irish Wolfhounds. *PLOS ONE*, 7: e36691.

- Pouchelon, J. L., Atkins, C. E., Bussadori, C., Oyama, M. A., Vaden, S. L., et al. (2015). Cardiovascular-renal axis disorders in the domestic dog and cat: A veterinary consensus statement. *Journal of Small Animal Practice*, 56(9): 537–552.
- Prošek, R., Sisson, D. D., Oyama, M. A., & Solter, P. F. (2007). Distinguishing Cardiac and Noncardiac Dyspnea in 48 Dogs Using Plasma Atrial Natriuretic Factor, B-Type Natriuretic Factor, Endothelin, and Cardiac Troponin-I. *Journal of Veterinary Internal Medicine*, 21(2): 238–242.
- Quest, B. W., Leach, S. B., Garimella, S., Konie, A., & Clark, S. D. (2022). Incidence of Canine Dilated Cardiomyopathy Diagnosed at Referral Institutes and Grain-Free Pet Food Store Sales: A Retrospective Survey. *Frontiers in Animal Science*, 3:846227.
- Raggi, P., Callister, T. Q., Lippolis, N. J., & Russo, D. J. (2000). Is mitral valve prolapse due to cardiac entrapment in the chest cavity? A CT view. *Chest*, 117(3): 636–642.
- Rai, S., Mishra, P., & Ghoshal, U. C. (2021). Survival analysis: A primer for the clinician scientists. *Indian Journal of Gastroenterology*, 40(5): 541–549.
- Reboldi, G., Angeli, F., & Verdecchia, P. (2013). Multivariable Analysis in Cerebrovascular Research: Practical Notes for the Clinician. *Cerebrovascular Diseases*, 35(2), 187–193.
- Reust, C. E., & Mattingly, S. (1996). Family involvement in medical decision making. *Family Medicine*, 28(1): 39–45.
- Romero-Rodríguez, P., García-y-González, E., Santos-Sotomaior, C., Pineda-Burgos, B., Olivar-Valladolid, G., et al. (2019). Prevalence of *Dirofilaria immitis* in domestic canines from two municipalities in the tropic of Guerrero, Mexico. *Abanico Veterinario*, 9(1):1-11.
- Saleeza, S. N., Norma-Rashid, Y., & Azirun, M. S. (2013). Mosquito species and outdoor breeding places in residential areas in Malaysia. *The Southeast Asian Journal Of Tropical Medicine And Public Health*, 44(6), 963–969.
- Sanderson, S. L., Gross, K. L., Ogburn, P. N., Calvert, C., Jacobs, G., et al. (2001). Effects of dietary fat and L-carnitine on plasma and whole blood taurine concentrations and cardiac function in healthy dogs fed protein-restricted diets. *American Journal of Veterinary Research*, 62(10):1616–1623.
- Santilli, R. A., Battaia, S., Perego, M., Tursi, M., Grego, E., et al., (2017). Bartonella-associated inflammatory cardiomyopathy in a dog. *Journal of Veterinary Cardiology*, 19(1):74–81.

- Saunders, AB (2012) The diagnosis and management of age-related veterinary cardiovascular disease. *The Veterinary Clinics of North America. Small Animal Practice*, 42(4), 655–668.
- Schaffer, S., & Kim, H. W. (2018). Effects and Mechanisms of Taurine as a Therapeutic Agent. *Biomolecules & Therapeutics*, 26(3):225–241.
- Schrope, D. P. (2015). Prevalence of congenital heart disease in 76,301 mixed-breed dogs and 57,025 mixed-breed cats. *Journal of Veterinary Cardiology*, 17(3): 192–202.
- Schulz R., Tompkins C.A., Rau M.T. (1988). A longitudinal study of the psychosocial impact of stroke on primary support persons. *Psychology and Aging*, 3(2): 131–141.
- Scott-Moncrieff, J. C. (2012). Thyroid Disorders in the Geriatric Veterinary Patient. *Veterinary Clinics of North America: Small Animal Practice*, 42(4): 707–725.
- Sedgwick, P. (2010). The log rank test. *BMJ*, 341(7765): 207.
- Self, S. W., Pulaski, C. N., McMahan, C. S., Brown, D. A., Yabsley, M. J., et al. (2019). Regional and local temporal trends in the prevalence of canine heartworm infection in the contiguous United States: 2012–2018. *Parasites & Vectors*, 12(1): 380.
- Serfass, P., Chetboul, V., Sampedrano, C. C., Nicolle, A., Benalloul, T., Laforge, H., Gau, C., Hébert, C., Pouchelon, J. L., & Tissier, R. (2006). Retrospective study of 942 small-sized dogs: Prevalence of left apical systolic heart murmur and left-sided heart failure, critical effects of breed and sex. *Journal of Veterinary Cardiology*, 8(1): 11–18.
- Simón, F, Siles-Lucas, M, Morchón, R, González-Miguel, J, Mellado, I, Carretón, E, & Montoya-Alonso, JA (2012) Human and Animal Dirofilariasis: the Emergence of a Zoonotic Mosaic. *Clinical Microbiology Reviews*, 25(3): 507–544.
- Sleeper, M. M., Clifford, C. A., & Laster, L. L. (2001). Cardiac troponin I in the normal dog and cat. *Journal of Veterinary Internal Medicine*, 15(5): 501–503.
- Smolkovic I, Fajfar M, & Mlinaric V., (2012). Attachment to pets and interpersonal relationships: Can a four-legged friend replace a two-legged one? *Journal of European Psychology Students*, 3(1): 15–23
- Speranza, R., Giada, B., Anna, E., Chiara, L., Rosita, S., et al., (2006). Association of Atrial Natriuretic Peptide and Type A Natriuretic Peptide Receptor Gene Polymorphisms With Left Ventricular Mass in Human

Essential Hypertension. *Journal of the American College of Cardiology*, 48(3): 499–505.

Swift, S., Baldin, A. and Cripps, P. (2017), Degenerative Valvular Disease in the Cavalier King Charles Spaniel: Results of the UK Breed Scheme 1991–2010. *Journal of Veterinary Internal Medicine*, 31: 9-14.

Stel, V. S., Dekker, F. W., Tripepi, G., Zoccali, C., & Jager, K. J. (2011). Survival Analysis I: The Kaplan-Meier Method. *Nephron Clinical Practice*, 119(1): c83–c88.

Stephenson, H.M., Fonfara, S., López-Alvarez, J., Cripps, P., & Dukes-McEwan, J. (2012). Screening for Dilated Cardiomyopathy in Great Danes in the United Kingdom. *Journal of Veterinary Internal Medicine*, 26(5): 1140–1147.

Stepien, R. L., Rak, M. B., & Blume, L. M. (2020). Use of radiographic measurements to diagnose stage B2 preclinical myxomatous mitral valve disease in dogs. *Journal of the American Veterinary Medical Association*, 256(10): 1129–1136.

Strasser, A., Simunek, M., Seiser, M., and Hofecker, G. (1997) Age-dependent changes in cardiovascular and metabolic responses to exercise in beagle dogs. *Zentralblatt Fur Veterinarmedizin*, 44:449–460.

Strickland, K. N. (1998). Canine and feline caval syndrome. *Clinical Techniques in Small Animal Practice*, 13(2): 88–95.

Summerfield N.J., Boswood A, O'Grady M.R., Gordon S.G., Dukes-McEwan J., Oyama M.A., Smith S., Patteson M., French A.T., Culshaw G.J., Braz-Ruivo L., Estrada A., O'Sullivan M.L., Loureiro J., Willis R., Watson P.(2012). Efficacy of Pimobendan in the Prevention of Congestive Heart Failure or Sudden Death in Doberman Pinschers with Preclinical Dilated Cardiomyopathy (The PROTECT Study). *Journal of Veterinary Internal Medicine*, 26(6): 1337–1349.

Surachetpong S. (2010). Myxomatous Degenerative Mitral Valve Disease: An Update. *Thai Journal of Veterinary Medicine*, 40:151–7.

Sutter, N.B., Bustamante, C.D., Chase, K., Gray, M.M., Zhao, K., et al., (2007).A Single IGF1 Allele Is a Major Determinant of Small Size in Dogs. *Science*, 316: 112.

Svensson C, Emanuelson U, Bard AM, Forsberg L, Wickström H, Reyher KK. Communication styles of Swedish veterinarians involved in dairy herd health management: A motivational interviewing perspective. *Journal of Dairy Science*,102(11): 10173–10185.

Swenson, L., Häggström, J., Kvarn, C., & Juneja, R. K. (1996). Relationship between parental cardiac status in Cavalier King Charles spaniels and

- prevalence and severity of chronic valvular disease in offspring. *Journal of the American Veterinary Medical Association*, 208(12): 2009–2012.
- Sykes, JE, Kittleson, MD, Chomel, BB, MacDonald, KA, & Pesavento, PA (2006) Clinicopathologic findings and outcome in dogs with infective endocarditis: 71 cases (1992-2005). *Journal of the American Veterinary Medical Association*, 228(11): 1735–1747
- Szumilas, M. (2010). Explaining Odds Ratios. *Journal of the Canadian Academy of Child and Adolescent Psychiatry*, 19(3): 227.
- Taguchi, D., Kanemoto, I., Yokoyama, S., Mizuno, M., & Washizu, M. (2014). Mitral valve replacement with a mechanical valve for severe mitral regurgitation in a small dog. *Case Reports in Veterinary Medicine*, 892625.
- Talamonti, Z., Cassis, C., Brambilla, P. G., Scarpa, P., Stefanello, D., et.al., (2015). Preliminary Study of Pet Owner Adherence in Behaviour, Cardiology, Urology, and Oncology Fields. *Veterinary Medicine International*, 618216.
- Taylor N. & Signal T.D., (2005) Empathy and attitudes to animals. *Anthrozoos*. 18(1):18–27.
- Thirunavukkarasu, P. (2019). Prevalence of Canine Acquired Heart Diseases in Chennai, India. *International Journal of Livestock Research*, 9(3), 331-339.
- Thrusfield, M V., Aitken, CGG, & Darker, PGG (1985) Observations on breed and sex in relation to canine heart valve incompetence. *Journal of Small Animal Practice* 26(12): 709–717.
- Tidholm, A, & Jönsson, L (1997) A retrospective study of canine dilated cardiomyopathy (189 cases). *Journal of the American Animal Hospital Association*, 33(6): 544–550.
- Tilley, L., Smith, F., Oyama, M., & Sleeper, M. (2008). *Manual of Canine and Feline Cardiology*. St. Louis: Blackwell
- Tremont, G., Davis, J.D., & Spitznagel, M.B. (2005). *Understanding and Managing Caregiver Burden in Cerebrovascular Disease*. pp.305. In: Paul, R.H., Cohen, R., Ott, B.R., Salloway, S. (eds) *Vascular Dementia. Current Clinical Neurology*. New Jersey: Humana Press.
- Uechi, M. (2012). Mitral valve repair in dogs. *Journal of Veterinary Cardiology*, 14(1): 185–192.

- Urfer, S. R., Kaeberlein, M., Promislow, D. E. L., & Creevy, K. E. (2020). Lifespan of companion dogs seen in three independent primary care veterinary clinics in the United States. *Canine Medicine and Genetics*, 7(1): 7.
- Urfer, S.R., Kaeberlein, T.L., Mailheau, S., Bergman, P.J., Creevy, K.E., et al., (2017) Asymptomatic heart valve dysfunction in healthy middle-aged companion dogs and its implications for cardiac aging. *GeroScience* 39: 43–50.
- Vinnie-Siow, Low, V. L., Tan, T. K., Teoh, Y. B., Prakash, B. K., & Lim, Y. A. L. (2021). Serological survey of canine vector-borne diseases in two animal shelters in central Peninsular Malaysia. *Tropical Biomedicine*, 38(1): 145–149.
- Vitulli W. F. (2006). Attitudes toward empathy in domestic dogs and cats. *Psychological reports*, 99(3): 981–991.
- Volpe, M., Carnovali, M., & Mastromarino, V. (2016). The natriuretic peptides system in the pathophysiology of heart failure: from molecular basis to treatment. *Clinical Science*, 130(2): 57–77.
- Wang, J., Zhou, J., Powell-Braxton, L., & Bondy, C. (1999). Effects of Igf1 gene deletion on postnatal growth patterns. *Endocrinology*, 140(7): 3391–3394.
- Ward, J, Mochel, JP, Seo, YJ, & Sathe, S (2020) Effects of the estrous cycle and pregnancy status on cardiovascular variables in healthy bitches. *Journal of Veterinary Cardiology*, 30: 57–68.
- Ware, W. A. (2007). *Cardiovascular disease in small animal medicine*. pp. 396. London: Manson
- Ware, WA, & Hopper, DL (1999) Cardiac Tumors in Dogs: 1982–1995. *Journal of Veterinary Internal Medicine*, 13(2): 95–103.
- Waxman, A. S., Kornreich, B. G., Gould, R. A., Sydney, N., Moise, M., et al. (2012). Interactions between TGFb1 and cyclic strain in modulation of myofibroblastic differentiation of canine mitral valve interstitial cells in 3D culture. *Journal of Veterinary Cardiology*, 14(1): 211–221.
- Wess G. (2022). Screening for dilated cardiomyopathy in dogs. *Journal Of Veterinary Cardiology*, 40, 51–68
- Whitney, J. G. (1974). Observations on the effect of age on the severity of heart valve lesions in the dog. *Journal of Small Animal Practice*, 15(8): 511–522.
- Wrobel, J. P., Thompson, B. R., & Williams, T. J. (2012). Mechanisms of pulmonary hypertension in chronic obstructive pulmonary disease: a

pathophysiologic review. *The Journal of Heart and Lung Transplantation*, 31(6): 557–564.

Yap, K. S., Ghanabadi, S., , Ibrahim Abdul-Azeez Okene, A. S., & Ayahsamy, S. (2021). Retrospective Echocardiographic Survey of Canine Cardiac Conditions in Kuala Lumpur, Malaysia. *Journal of Animal Health and Production Retrospective*, 9(2): 198–204.

Yin, F. C., Spurgeon, H. A., Greene, H.L., Lakatta, E. G., & Weisfeldt, M. L. (1979). Age-associated decrease in heart rate response to isoproterenol in dogs. *Mechanisms of Ageing and Development*, 10(1-2): 17–25.

Youssef, G (2021) Valvular heart diseases in women. *Egyptian Heart Journal*, 73: 1–6.

Zhu, X., Tang, Z., Cong, B., Du, J., Wang, C., Wang, L., Ni, X., & Lu, J. (2013). Estrogens increase cystathionine- γ -lyase expression and decrease inflammation and oxidative stress in the myocardium of ovariectomized rats. *Menopause*, 20(10): 1084–1091.