UNIVERSITI PUTRA MALAYSIA

SURVIVAL TIME AND CLINICAL OUTCOME OF CATS DIAGNOSED WITH HYPERTROPHIC CARDIOMYOPATHY

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FPV 2020 96

SURVIVAL TIME AND CLINICAL OUTCOME OF CATS DIAGNOSED WITH HYPERTROPHIC CARDIOMYOPATHY

CHANG XUAN WU

A study project submitted to the
Faculty of Veterinary Medicine, Universiti Putra Malaysia
In partial fulfilment of the requirement for the
DEGREE OF DOCTOR OF VETERINARY MEDICINE
Universiti Putra Malaysia
Serdang, Selangor Darul Ehsan

2020/2021

CERTIFICATION

It is hereby that we have read this project paper entitled "**Survival Time and Clinical Outcome of Cats Diagnosed with Hypertrophic Cardiomyopathy**", by Chang Xuan Wu and in our opinion it is satisfactory in term of scope, quality, and presentation as partial fulfilment of the requirement for the course VPD 4999 – Final Year Project.

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DEDICATION

This project paper is dedicated to:

The One Almighty God who made all things possible

My beloved family for their love and care

My dearest supervisor for her great and kind help along the journey

My close friends for their continuous support

All patient involved

All educators, clinicians and UVH staff for committing themselves towards the noble cause of education

ACKNOWLEDGEMENTS

I would like to thank the Almighty God for this wonderful and fruitful experience and gave me good health and wisdom in solving problem throughout the study and those who made this project paper a reality.

I would like to express my deepest gratitude and appreciation to my caring supervisor, Dr. Khor Kuan Hua, for spending her precious time to give her endless help and helpful guidance to improve me to become better not only in this project paper but in my future life as well. Thank you for showing me how a dedicated and multi-tasking educator like you would inspire a student to become stronger and not fear of challenges.

I would also like to give my appreciation to UVH staff for helping me during these five weeks and make my project smoother and can finish on time.

Last but not least, a big thanks to my family for their encouragement and also to my best friend, Kah Yong for her continuous support and love throughout my study.

CONTENT

LIST OF ABBREVIATIONS

ACE	Angiotensin Converting Enzyme
AMVL	Anterior Mitral Valve Leaflet
Ao	Aortic
ATE	Atrial Thromboembolism
CHF	Congestive Heart Failure
CLA	Cardiac Long Axis
CSA	Cardiac Short Axis
DCM	Dilated Cardiomyopathy
DSH	Domestic Short Hair
HCM	Hypertrophic Cardiomyopathy
HOCM	Hypertrophic Obstructive Cardiomyopathy
LV	Left Ventricle
LVS	Left Ventricular Septum
LVFW	Left Ventricular Free Wall
MYBPC3	Myosin Binding Protein C-3

RAAS	Renin-Angiotensin-Aldosterone System
RCM	Restrictive Cardiomyopathy
SAM	Systolic Anterior Motion
SD	Sudden Death
UCM	Unclassified Cardiomyopathy
VHS	Vertebral Heart Score

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ABSTRAK

Abstrak daripada kertas projek yang dikemukakan kepada Fakulti Perubatan Veterinar untuk memenuhi sebahagian daripada keperluan kursus VPD 4999 - Projek

JANGKA PANJANG UMUR DAN HASIL KLINIKAL KUCING YANG DIDIAGNOSIS OLEH KARDIOMIOPATI HIPERTROFI

By

CHANG XUAN WU

2020

Penyelia: Dr. Khor Kuan Hua

Kardiomiopati hipertrofi (HCM) merupakan penyakit jantung yang paling kerap diperolehi dan daya tahan hidup kucing yang didiagnosis HCM dipengaruhi oleh beberapa faktor. Kajian retrospektif ini dijalankan di Hospital Veterinar Universiti antara tahun 2013 – 2019 bertujuan menentukan penyebab kematian yang paling kerap dan daya tahan hidup kucing yang didiagnosis HCM berdasarkan tahap penyakit, pematuhan pemilik kucing terhadap rawatan dan kewujudan penyakit serentak. Dengan merujuk pengkalan data, 184 kucing didiagnosis HCM yang mempunyai rekod perubatan pesakit yang lengkap dirujuk untuk kajian ini. Terdapat, 37 status kesihatan kucing (mati/hidup) yang

tidak dapat dikenalpasti dikecualikan daripada analisis kelangsungan hidup. Dalam kajian in, sebanyak 69% kucing telah mati (n=101/147) dan penyebab kematian yang paling biasa adalah disebabkan kardiovaskular 67 % (n=68/101), terutamanya kegagalan jantung kongestif (*CHF*) diikuti oleh tromboemboli atrium (*ATE*) dan kematian secara tiba-tiba. Median masa kelangsungan hidup kucing HCM dalam kajian ini adalah 608 hari. Terdapat perbezaan kelangsungan hidup yang ketara (p=0.001) kucing HCM diantara tahap. Median kelangsungan hidup kucing HCM (Peringkat B) adalah 1518 hari, tempoh terpanjang jika dibandingkan dengan HCM dengan *CHF* atau *ATE* (Peringkat C) dengan median kelangsungan hidup 1253 hari dan kucing HCM yang mempunyai *CHF* tidak responsif terhadap rawatan (Peringkat D) adalah 30 hari, tempoh daya tahan terpendek. Walau bagaimanapun, tidak ada perbezaan yang signifikan dalam masa kelangsungan hidup kucing HCM dengan / tanpa kepatuhan pemilik terhadap rawatan (p = 0.428) dan penyakit bersamaan (p = 0.057). Oleh itu, kucing yang didiagnosis dengan HCM kemungkinan akan meninggal dunia akibat kematian kardiovaskular dan kelangsungan hidupnya dipengaruhi oleh tahap (masa diagnosis) tetapi tidak banyak dipengaruhi oleh kepatuhan rawatan dan adanya penyakit bersamaan.

Kata kunci: felin kardiomyopati hipertrofi, jangkan panjang umur, peringkat, pematuhan terhadap rawatan, penyakit serentak

ABSTRACT

An abstract of the project presented to the Faculty of Veterinary Medicine in partial fulfilment of course VPD 4999- Project.

SURVIVAL TIME AND CLINICAL OUTCOME OF CATS DIAGNOSED WITH HYPERTROPHIC CARDIOMYOPATHY

By

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2020

Supervisor: Dr. Khor Kuan Hua

Hypertrophic cardiomyopathy (HCM) is the most common acquired heart disease and the survivability of cats diagnosed with HCM is affected by several factors. This retrospective study conducted in University Veterinary Hospital, UPM between 2013-2019 investigated the common cause of death and survival time of cats with HCM based on stage, treatment compliance and presence of concurrent disease. Using the database, 184 cats diagnosed with HCM with complete patient medical record were included in this study. However, 37 cats' health status (dead/alive) could not be determined were excluded

for the survival analysis. From this study, 69% cats did not survive (n=101/147) and the common cause of death was due to cardiovascular 67% (n=68/101), mainly congestive heart failure (CHF) followed by atrial thromboembolism (ATE) and sudden death (SD). The median survival time of HCM cats in this study was 608 days. There was significant difference (p=0.001) of survivability of HCM cats between stages. The median survival time of HCM cats (Stage B) were 1518 days, the longest compare to HCM with CHF or ATE (Stage C) with median survival time of 1253 days and HCM with refractory CHF (Stage D) with median survival time of 30 days which was the shortest. However, there were no significant different in median survival time of HCM cats with/without owner's compliance to treatment (p=0.428) and concurrent disease (p=0.057), respectively. Therefore, cats diagnosed with HCM may likely succumb to cardiovascular death and the survivability was affected by stage (time of diagnose) but did not affected much by treatment compliance and presence of concurrent disease.

Keywords: feline hypertrophic cardiomyopathy, survivability, stage, treatment compliance, concurrent disease

CHAPTER 1.0

INTRODUCTION

1.1 INTRODUCTION

Zakaria (2016) conducted a retrospective study in University Veterinary Hospital (UVH), Universiti Putra Malaysia (UPM) found that the prevalence of feline heart disease is around 1%. Cat diagnosed with cardiovascular disease can be further categorised into acquired valvular disease, cardiomyopathy, cor pulmonale and pulmonary thromboembolism, heartworm disease, pericardial disorders and cardiac tumours and lastly, congenital heart disease (Kienle, 2008). Among these diseases, HCM remains the most common acquired heart disease in cats and the occurrences remains increased (Kienle, 2008).

Cat diagnosed with HCM of either obstructive or non-obstructive may have shorter life span compared to the apparent healthy cat. Affected cats could be asymptomatic or symptomatic. According to Fox & Schober (2015), cats with asymptomatic cardiomyopathy had been reported with incidental finding of a heart murmur, gallop heart sound, or arrhythmia. As for symptomatic HCM cats, pulmonary oedema and pleural effusion were the most common radiographic findings in cats diagnosed with HCM, as a sequelae of CHF (Abbott, 2010). Besides that, some of these

cats suffered from unexpected SD. However, mortality on HCM cats not necessary cardiovascular related. Some of these cats were at risk of non-cardiovascular disease such as chronic kidney disease (CKD), cancer, chronic weight loss and diarrhoea (Fox *et. al*, 2019) and death (mortality) may not be related to heart condition.

The ultimate aim of treatment in cats diagnosed with cardiomyopathy were to delay onset of HCM clinical outcome, prolong life span, improve quality of life in diseased cats. The common cardiovascular drugs used for cat diagnosed with heart disease were vasodilator such as angiotensin-converting enzyme inhibitor (ACEi), positive inotropic drug and beta-blockers (Kienle, 2008). To date, unfortunately none of these drug therapy has shown effectiveness in prolonging life span. Schober *et al.* (2013) shown that there was no significant difference in survival time (P = 0.162) between asymptomatic HCM cat treated (mean ± SD = 1440 ± 448 days) or without treatment (mean ± SD = 1107 ± 541 days) with atenolol. The median survival time for symptomatic cats with heart disease that received benazepril was 553 days were not significantly different compared to those that did not received benazepril (median = 648 days) (King *et. al.,* 2019). But recently, Reina-Doreste *et al.* (2014) stated that pimobendan had increased the survival time of cat with heart disease (median survival time = 626 days) compared to those cats that not receiving pimobendan (median survival time = 103 days). Owner compliance was one of the considering factors toward the effectiveness of treatment and animal should be withdrawn from the study if owner failure to give full compliance (Schober *et al.*, 2013).

1.2 JUSTIFICATION

In conclusion, the survivability of cats diagnosed with cardiovascular disease may varies. None of the study looked at the survivability of cats diagnosed with HCM and compared with the stage (at the time of diagnosis), concurrent disease and treatment compliance in Malaysia. By conducting this study, information can be used by clinician in order to provide a better prognosis and suggestion to these owners with affected cats.

1.3 OBJECTIVES

The objectives of this study was to determine the common cause of death in HCM cats and their survival time based on stages, presence of concurrent disease and treatment compliance.

1.4 HYPOTHESIS

1. Null hypothesis: The common cause of death of cats diagnosed with hypertrophic cardiomyopathy is not due to cardiovascular disease.

   Alternative hypothesis: The common cause of death of cats diagnosed with hypertrophic cardiomyopathy is due to cardiovascular disease.

2. Null hypothesis: There is no different between the survival time of cats diagnosed with hypertrophic cardiomyopathy based on stages, presence of concurrent disease and with or without received cardiovascular drug.

   Alternative hypothesis: There is different between the survival time of cats diagnosed with hypertrophic cardiomyopathy based on stages, presence of concurrent disease and with or without received cardiovascular drug.

CHAPTER 2.0

LITERATURE REVIEW

2.1 TYPES OF FELINE CARDIOMYOPATHY AND ITS PREVALENCE

Feline cardiomyopathy is heart muscle disease which can be further divided into primary and secondary cardiomyopathy. Primary cardiomyopathy refers to heart muscle disease that is not affected by other factor and usually is idiopathic. Secondary cardiomyopathy occurs secondary to other factors such as nutritional (taurine deficiency), metabolic (hyperthyroidism, acromegaly), systemic disease, or other disease processes (Kienle, 2008). The primary cardiomyopathy can be classified into hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy (DCM), restrictive cardiomyopathy (RCM), arrhythmogenic right ventricular cardiomyopathy (ARVC) and unclassified cardiomyopathy (UCM) (Fuentes, 2002).

Among those primary idiopathic cardiomyopathy, HCM remained to be the most common with the prevalence of 57.5% followed by RCM, DCM and UCM with prevalence of 20.7%, 10.4% and 10.4%, respectively (Ferasin *et al.*, 2003). A CatScan program conducted by Royal Veterinary College reported the prevalence of HCM in cats was 14.7% (n=115/780) (Payne *et al.*, 2015a) and HCM remained to be the most comment disease among all cardiomyopathies.

2.2 HYPERTROPHIC CARDIOMYOPATHY

2.2.1 Type of hypertrophic cardiomyopathy and its prevalence

HCM is a myocardium disease where the papillary muscle and ventricular walls of the left ventricle (LV) being defined as mild to severe hypertrophy (Kienle, 2008) or as diffuse or regional increased LV wall thickness with a non-dilated LV chamber (Fuentes *et al.,* 2020). These abnormalities affect the ventricular filling due to diastolic dysfunction (ventricular stiffness and fail to relax), eventually causes increase in atrial pressure and CHF (Fuentes, 2002). The gene mutation of cardio myosin binding protein-C3 (MYBPC3) was found in Maine Coon cats (Meur *et al.*, 2005) and was then identified in Ragdoll cats (Meurs *et al*. 2007). In Maine Coon cats, HCM is an autosomal dominant inherited disease (Kittleson *et al.,* 1999) and therefore occurrence of familial HCM (Meurs *et al.,* 2007) was observed. Cat with normal interventricular septum and left ventricular free wall thickness but showed mild papillary muscle hypertrophy or there was presence of systolic anterior motion (SAM) or both, the cat was categorised as equivocal HCM cat (Granström *et al*., 2011).

Hypertrophic Obstructive Cardiomyopathy (HOCM) was describes as presence of SAM (Côté *et al.,* 2011). SAM refers to displacement of the anterior mitral valve leaflet (AMVL) into the left ventricular outflow tract (LVOT) which dynamically obstruct blood from pumping out through aorta systole. (Schober & Todd, 2010). The severity of LVOT obstruction due to AMVL can be categorised into mild (mitral valve approached interventricular septum (IVS) in systole, but without septal contact), moderate (short

mitral-septal contact), and severe (prolonged mitral-septal contact) using M-mode images (Gilbert *et al.,* 1980). SAM was very commonly seen with HCM. Around two third of HCM cats were diagnosed with SAM of the mitral valve (Fox *et al.,* 1995).

Specifically for HCM/HOCM, male cats especially the castrated male were noted to be greatly affected with high of prevalence between 71- 74 % (Fox *et al.,* 2018; Payne *et al.,* 2010). More than 50% of cats diagnosed with HCM/ HOCM were less than 7 years old and frequently diagnosed in the Domestic Shorthair, Maine Coon, Persian and Domestic Longhair (Fox *et al.,* 2018).

2.2.2 Staging of hypertrophic cardiomyopathy

Feline cardiomyopathy can be divided into 4 stages, namely stage A to D. Stage A refers to cats without myocardial disease but at high risk of cardiomyopathy. Stage B involved asymptomatic cats with cardiomyopathy which can be further categories into B1 and B2. In stage B1, cats were found to have normal or mild left atrial (LA) enlargement. However, in stage B2, cats would have moderate to severe LA enlargement, gallop sound, arrhythmia, decreased left atrial function, extreme left ventricular hypertrophy, left ventricular systolic dysfunction, spontaneous echo-contrast/thrombus and regional wall motion abnormalities. Cats with sign of CHF or ATE with or without resolving post-treatment were categories as stage C. In stage D, cats with CHF were not responded to the treatment anymore, also known as refractory CHF (Fuentes *et al.,* 2020)

2.2.3 Clinical signs and clinical outcome of hypertrophic cardiomyopathy

The most common clinical sign observed in HCM cats with CHF were dsypnoea, lethargy, anorexia, and vomiting or weight loss. With dyspnoea, affected cats with HCM will experience one or a combination of these complications of CHF; namely pulmonary oedema, pleural effusion and ascites. Other clinical signs reported were lameness, paresis, pain, syncope, collapse without loss of consciousness and ventricular premature complexes were normally associated with ATE secondary to HCM (Rush *et al.,* 2002; Trehiou-Sechi *et al*., 2012).

The three main clinic outcome of cats diagnosed with HCM were CHF, ATE and SD (Payne *et al.,* 2010,2013; Trehiou-Sechi *et al*., 2012). These outcomes may vary between cats. A large retrospective study (known as REVEAL) collected information from 21 countries, reported that HCM (24%) and HOCM (12%) cats would develop CHF and ATE, respectively. The older cats had higher chance to develop CHF but HCM cats of more than 10-year-old has lower incidence of ATE. The mean morbidity time for cats with pre-clinical HCM that developed CHF or ATE or SD was reported within 3 years, which those cats will eventually experience cardiovascular death (Fox *et al*., 2018).

2.3 IMPORTANT DIAGNOSTIC TOOLS OF HYPERTROPHIC CARDIOMYOPATHY

2.3.1 Heart auscultation

Cats with preclinical or asymptomatic HCM/HOCM will have greater chance (82%) to be auscultated with systolic heart murmurs compared to apparent healthy cat (46%). Among those apparent healthy (normal echocardiography) cats with heart murmur, 68% of cats were low grade of murmur (grades 1 to 2) while among HCM/HOCM cats with heart murmur, 71% of cats were high grade of murmur (grades 3 to 5/6) (Fox *et al*., 2018). Murmur sound had been associated with SAM due to LVOT obstruction (Rush *et al.,* 2002; Trehiou-Sechi *et al*., 2012).

Table 1: Heart murmur grading system adapted from Feline Cardiology Book (Côté *et al.*, 2011)

GRADES	DESCRIPTION
Grade I	Very soft murmur that is not immediately audible but can be heard only after careful auscultation in a quiet environment.
Grade II	Soft murmur that is audible with careful auscultation.
Grade III	Moderate murmur that is audible with auscultation.
Grade IV	Loud murmur without thrill.
Grade V	Loud murmur with a palpable thrill.
Grade VI	Audible murmur with stethoscope held slightly off chest wall

With abnormal heart sound, only 10%-13% of HCM and 18% of HOCM cats had arrhythmia and gallop heart sound, respectively (n=1008) (Fox *et al*., 2018; Payne *et al.*, 2015b). Nevertheless, premature ventricular complex arrhythmia still can be an indicator for structural heart disease and advance investigation was recommended (Côté *et al.*, 2008).

2.3.2 Thoracic radiography

Thoracic radiography helps to diagnose cardiac enlargement, pulmonary oedema, enlarged great veins and pleural effusion secondary to HCM (Kienle, 2008). 'Valentine' heart shape (left atrial enlargement or biatrial enlargement) could be seen from the dorsal-ventral (DV) or ventral-dorsal (VD) of thoracic radiography but it did not different the different type of cardiomyopathy (Côté *et al.*, 2011).

Cats with left-sided cardiac disorder or moderate to severe LA enlargement will have Vertebral Heart Score (VHS) more than 7.9 shown in lateral thoracic radiography (Guglielmini *et al.*, 2014). For further investigation, echocardiography was recommended in these cats.

2.3.3 Echocardiography

Cardiomyopathies in cats can be diagnosed via echocardiography in clinical setting as it provides a real time assessment of both the heart function and structures. Two-dimension (2D) guided M-mode echocardiographic on short-axis view were used for measurements of LV wall thickness, LA and aortic (Ao) diameter. Leading edge-to-leading edge technique was recommended on the M-mode image to obtain an accurate reading of the LV wall measured (Fuentes *et al*, 2020).

From echocardiography, normal cat will have end-diastolic LV wall thickness less than or equal to 5 mm while LV hypertrophy will have reading more than or equal to 6mm (Fox *et al*., 2020). However, if left ventricular free wall (LVFW) was between 5.5-5.9mm, the cats were described as equivocal HCM (Côté *et al.*, 2011). By measuring LA/Ao ratio, left atrium enlargement can be suspected if the reading more than 1.5 (Granström *et al*., 2011). If the ratio of end-diastole IVS/LVFW at end-diastole was 0.7-1.3, then the hypertrophy was symmetric, but if the ratio was less than 0.7 or more than 1.3, then the hypertrophic is consider asymmetric (Chetboul *et al.*, 2003).

Cat with HOCM or SAM will have mitral regurgitation which can be diagnosed via colour flow imaging, concave and asymmetrical shaped waveform due to abnormal contact of distal tip of AMVL with ventricular septum causing abnormal outflow velocities during systole. Cats with SAM will have subaortic pressure gradient more than 25 mmHg together with peak outflow velocity of more than 2.5 m/s during continuous-wave Doppler assessment (Fox *et al*., 1995).

2.4 TREATMENT FOR HYPERTROPHIC CARDIOMYOPATHY

The options of drugs currently used to treat cats with mild to severe HCM without CHF were diltiazem, atenolol, benazepril, and enalapril (Kienle, 2008). However, treatment of cats diagnosed with HCM may varies depending on the disease staged (Fuentes *et al.*, 2020). Studies had described that cats with subclinical HCM may not clinically benefits from treatment such as atenolol, angiotensin converting enzyme (ACE) inhibitor (ramipril, benazapril) nor spironolactone (MacDonald *et al.,* 2006, 2008; King *et al.,* 2019; Schober *et al.,* 2013). Cats with HCM treatment with ramipril or spironolactone did not change neither the LV mass nor diastolic function as expected (MacDonald *et al.,* 2006, 2008). However, these studies had its own limitation and findings might affect the real benefit of the treatment (King *et al.,* 2019; Schober *et al.,* 2013).

When a cat diagnosed with HCM had developed CHF, diuretic drug such as furosemide and torsemide will be given to resolve pulmonary oedema and pleural effusion (Fox *et al.,* 2020). Besides that, once the risk of ATE due to HCM had been determined, clopidogrel can be used as prophylatic drug (Fox *et al.,* 2020) and to prevent the detrimental effect post-ATE.

ACE inhibitor such as enalapril were used when there was LA enlargement as it inhibits Renin-Angiotensin-Aldosterone System (RAAS) to reduce neuroendocrine activation in order to protect myocardial (Taillefer, 2006) as angiotensin II cause increase in left ventricular mass and affect the diastole function (Di Zhang *et al.,* 2008). Atenolol

was indicated to reduce the severity of LVOTO due to SAM by increasing diastolic filling time in HOCM cats (Gordon *et al.,* 2015). Diltiazem had been reported beneficial toward treatment in cats with HCM by reducing the pulmonary congestion and improve ventricular filling (Bright *et al.,* 1991).

A recent report by Reina-Doreste (2014) shown that pimobendan has beneficial effects toward cats with CHF due to HCM. However, Gordon (2015) suggested that pimobendan was not encouraged in cats with LVOT obstruction as worsening of LVOT obstruction had been seen after pimobendan administration and if used, the cat must be closely monitored (Gordon *et al.,* 2015). To-date, recommendation on the use of pimobendan in HCM is still an off-label advised usage.

In human study, patients' knowledge and understanding plays an important role to increase the compliance in long term treatment. Patients were considered compliance to treatment regime when they always or most of the time would follow the treatment protocol while if patients seldom or never or some of the time follow the treatment protocol will be considered as non-compliance (van der Wal *et al.,* 2006). It has been shown that elderly patients with CHF had higher chance to become worsen due to non-compliance to salt-restricted diet (52%) and medication (30%) (Diaz *et al.,* 2011).

2.5 SURVIVABILITY OF HYPERTROPHIC CARDIOMYOPATHY

HCM cats with CHF was reported with a median survival time of 194 days and cats with SAM had a longer life span than those without SAM (Payne *et al.,* 2010). Cats

diagnosed with SAM that has murmur auscultated were associated with heart disease at earlier stage (Payne *et al.,* 2015b). However, both murmur and SAM cannot be associated with survivability in cats with CHF, as CHF did not always occur concurrently with murmur (Payne *et al.,* 2010). Gallop sound and arrhythmia were considered as poor prognostic indicator as both had been associated with increased risk of cardiovascular death (Payne *et al.,* 2013, 2015b). LA enlargement had been associated with increased risk of death in cats with CHF (Payne *et al.*, 2010). The first clinical presentation of cats either with CHF or ATE were reported as an important prognosis factor because the first presentation may influence the mortality within 2 years of diagnosis (Payne *et al.*, 2015b).

Fox *et al.* (2018) stated that once cats developed CHF or ATE, the mean survival years reported was 1.3 ± 1.7 years. The survival time was not influenced by age after development of CHF or ATE. Approximately, 28% cats with HCM/HOCM experienced cardiovascular death. In the same group of population, 30% of cats with HCM/HOCM had non-cardiovascular death such as death related to anaesthesia, respiratory diseases, central nervous system diseases, hepatobiliary diseases, toxicosis, endocrine diseases, and trauma. Among those non-cardiovascular death, cancer is the most common cause followed by CKD (Fox *et al.,* 2019). Cardiovascular disease was commonly reported as the cause of death in cats with CKD. The incidence of cardiovascular disease was becoming more frequent in CKD patient due to the same risk factor such as aging, hypertension, diabetes and others. (Subbiah *et al.,* 2016) In a human study, it showed that people was in higher risk of cardiovascular death with lower glomerular filtration rate (Manjunath *et al.,* 2003).

CHAPTER 3.0

MATERIAL AND METHODS

3.1 SOURCE OF DATA

This retrospective study was conducted in UVH, UPM. The feline case log book (CLB) from 2013-2019 was retrieved. Case file number of each cats diagnosed or suspected with HCM were recorded. Patient's medical record files were retrieved and data inclusive of patient signalmant, clinical signs, physical examination, radiography and echocardiography findings, date of diagnosed, type of treatment given, concurrent disease, date and cause of death were recorded.

3.2 INCLUSION CRITERIA

The inclusion criteria of cats diagnosed with HCM recruited in this study were based on, (i) retrievable patient file medical record, (ii) available information on clinical signs and physical examination findings at presentation, (iii) retrievable archived radiography and echocardiography images. Cats diagnosed with HCM with no complete information will be excluded out. Cats with unknown survival status due to uncontactable owner or missing cats will be excluded from our survivability analysis.

3.3 DATA COLLECTION

3.3.1 Patient Signalment

The age, breed, sex (male or female and the neutering status) and body weight of each feline patient were recorded. Based on age categories established by American Association of Feline Practitioners (AAFP) and American Animal Hospital Association (AAHA), feline age can be classified as (i) Kitten (birth to 6 months old), (ii) Junior (7 months to 2 years old), (iii) Prime (3 to 6 years old), (iv) Mature (7 to 11 years old), (v) Senior (12 to 14 years old) and (vi) Geriatric (more than 15 years old).

3.3.2 Clinical Signs

Clinical signs related to heart disease such as tachypnoea (more than 40 breaths per minute), dyspnoea, open mouth breathing, open mouth breathing, exercise intolerance, coughing, weight lost, hind limb paralysis, seizure and syncope that had been observed by owner or veterinarian during first presentation were recorded.

3.3.3 Physical Examination

Heart auscultation findings done by veterinarian to determine presence of arrhythmia, gallop sound, tachycardia which is more than 180 beat per minutes, murmur, muffled sound and thumping sound were recorded. Abnormal lung sound findings that was described as harsh, dull, wheezing or crackles sound were noted.

3.3.4 Thoracic radiography

Thoracic radiography of each feline patient identified were retrieved, the findings were reconfirmed and recorded. Thoracic radiography in lateral and DV view were evaluated. On the lateral thoracic radiograph, the VHS was determined. The cardiac long axis (CLA) and the cardiac short axis (CSA) was measured and compared with the length of thoracic vertebrae starting from the cranial edge of 4^{th} thoracic vertebrae. CLA was measured from the ventral border of main stem bronchi to the heart apex. CSA was measured perpendicularly to the measurement of CLA at the point of maximum heart width (Guglielmini *et al.,* 2015). Any presence of pulmonary oedema or pleural effusion or pericardia effusion from the radiograph were recorded.

3.3.5 Echocardiography

Echocardiography findings were retrieved and measurement of the interventricular septum at end-diastole (IVSd) and left ventricular free wall at end-diastole (LVFWd) thickness, fractional shortening, left atrium (LA) diameter and LA to aorta (Ao) ratio were recorded. Cats are diagnosed as HCM when either IVSd or LVFWd thickness were more than 6 mm. Cats were diagnosed as equivocal HCM when IVSd or LVFWd thickness was showed mild hypertrophy (5.5-5.9 mm) or there was presence of LVOT obstruction when IVSd or LVFWd thickness were normal. If HOCM was diagnosed, the LVOT obstruction due to SAM of mitral valve and mitral regurgitation observed from

two-dimension (2D) echocardiography and colour flowing imaging would be reviewed, respectively.

3.3.6 Staging of Hypertrophic Cardiomyopathy

According to Fox (2020), feline cardiomyopathy can be categorised into A, B1, B2, C and D. All the information obtained from the clinical signs, physical examination, radiological finding and treatment were used to further staged the cats diagnosed with HCM. Cats are classified as B when cat initial presentation were normal (asymptomatic). Cats were classified as C when cat showed clinical sign of CHF or ATE at the first presentation. Cats were classified as stage D when cats were at chronic stage and not responding to treatment regime hence required hospitalisation and/or constant revisit as outpatient (refer Table 2).

Table 2: Staging of feline cardiomyopathy (Fuentes *et al.,* 2020)

Stage	Description
A	Predisposed breeds
B1	Subclinical (Normal/mild atrial enlargement)
B2*	Subclinical (Moderate/severe atrial enlargement)
C	Current or previous CHF/ATE
D	Refractory CHF

*Additional risk factors in B2 include a gallop sound, arrhythmia, decreased left atrial function, extreme left ventricular hypertrophy, left ventricular systolic dysfunction, spontaneous echo-contrast/thrombus, regional wall motion abnormalities

3.3.7 Treatment Compliance

From the patient medical record file, drugs related to heart which had been prescribed such as diuretic (furosemide and spironolactone), ACE inhibitor (benazapril and imidapri), beta-blocker (atenolol), positive inotropic drug (pimobendan), calcium channel blocker (diltiazem and amlodipine) and antiplatelet drug (clopidogrel) were recorded. Owner compliance was determined from the patient medical record file or by contacting these owners via the telephone. These cats will be recorded as compliance if the cat owner continued the long term treatment as prescribed while the cat is still alive or dead (did not survive despite treatment). Owner will be recorded as non-compliance when owner had stop the heart medication by themselves or did not start the treatment while the cat patient is still alive or dead.

3.3.8 Concurrent disease

From the patient medical record, any concurrent disease of each cats diagnosed with HCM such as kidney disease, respiratory disease, cancer, mycoplasmosis, oral disease or liver disease and cause of death were recorded. When the cause of death cannot be determined from patient medical record file, description of cats' death was obtained from their owner. Any description related to clinical signs such as dyspnoea, suddenly collapse or death was categorised as cardiovascular death.

3.3.9 Survivability

The survivability of the patient was determined by calculating the number of days these HCM cats survive or dead as the squealae of the disease. If alive, the calculated numbers of survival days begun from the first date of diagnosis till August 2012. If dead, the calculated numbers of survival days begun from the first date of diagnosis till the date of euthanasia or found dead. If there was no information on the survival status that can be obtained from the patient medical record, the cat owner will be contacted via the telephone for information and updates.

3.4 CLINICAL OUTCOME

The clinical outcome was determined based one the information obtained from the file of the patient medical record and radiography. CHF was defined as the presence of pulmonary oedema or pericardial effusion from radiography findings with clinical signs such as dyspnoea, abdominal breathing, open mouth breathing, crackles lung sound or gallop sound (Fox *et al.,* 2020). ATE was described as the presence of paralysis, cyanotic at the extremities or tachypnea due to pain (Cote *et al.,* 2011). SD was described as cat was found death unexpected when cat condition was stable (Payne *et al.,* 2015).

3.5 DATA ANALYSIS

All the data were obtained were recorded in Microsoft Office Excel for descriptive analysis. Kalpan-Meier survival analysis in IBM SPSS version 23 was used to analyse survivability at 95 % Cl ($p<0.05$) of HCM based on stage, treatment compliance and presence of concurrent disease.

CHAPTER 4.0

RESULTS

In this study, 188 feline patients diagnosed with HCM were identified from 2013-2019 in UVH. However, 4 cats were excluded due to non-retrievable patient medical file. As for the survivability study, 37 cats from 184 cats were excluded due to unclear status of survival, such as cat went missing (n=4), or cat owners were uncontactable (n=33).

4.1 PATIENT SIGNALMENT FINDINGS OF FELINE HYPERTROPHIC CARDIOMYOPATHY

4.1.1 Age

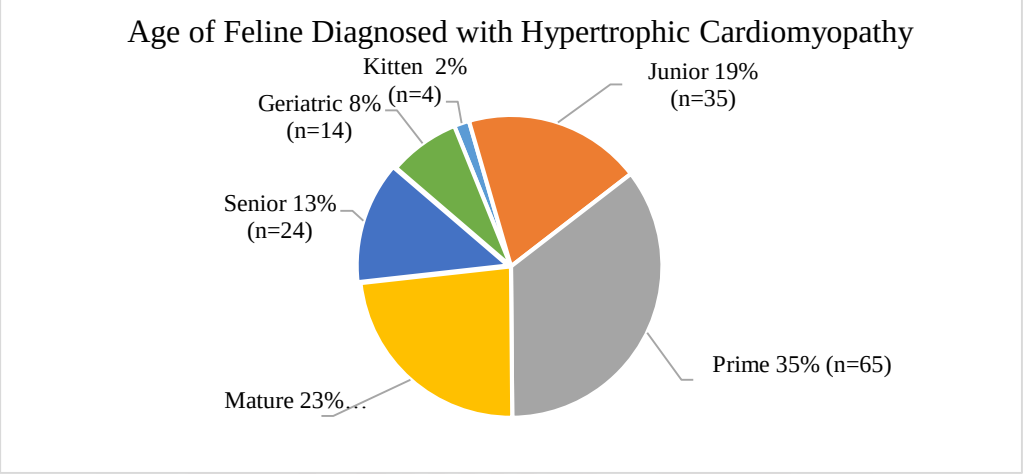
The mean age of cats with diagnosed with HCM were 6.7 years old (age range 4-month to 20-year-old). Majority of the cats were in prime age group (35%; *n*=65), followed by mature (23%, *n*=42), junior (19%, *n*=35), senior (13%, *n*=24), geriatric (8%, *n*=14) and lastly, the kitten (2%, *n*= 4) (refer Figure 1).

4.1.2 Breed

The most common cat breed diagnosed with HCM were Domestic Short Hair (DSH) (57%, n=103), followed by Persian (22%, n=41), others (10%, n=18), Siamese

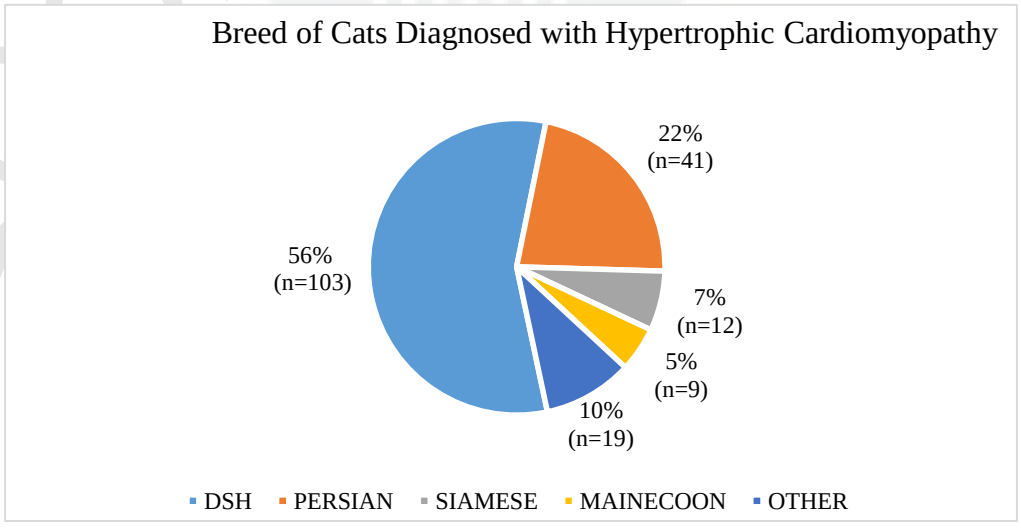
(7%, n=12), and lastly was Maine Coon (5%, n=9). The others breed consists of 4 Bengal, 3 Domestic long hair, 3 Scottish Fold, 2 Exotic short hair, and one each for the following breeds; Sphynx, Medium Long Hair, Siberian, Himalayan, British Short Hair, European short hair and American Short Hair (refer Figure 2).

Figure 1: Age of Feline Diagnosed with Hypertrophic Cardiomyopathy (*n*=184)



Age category adapted from American Association of Feline Practitioners (AAFP) and American Animal Hospital Association (AAHA)

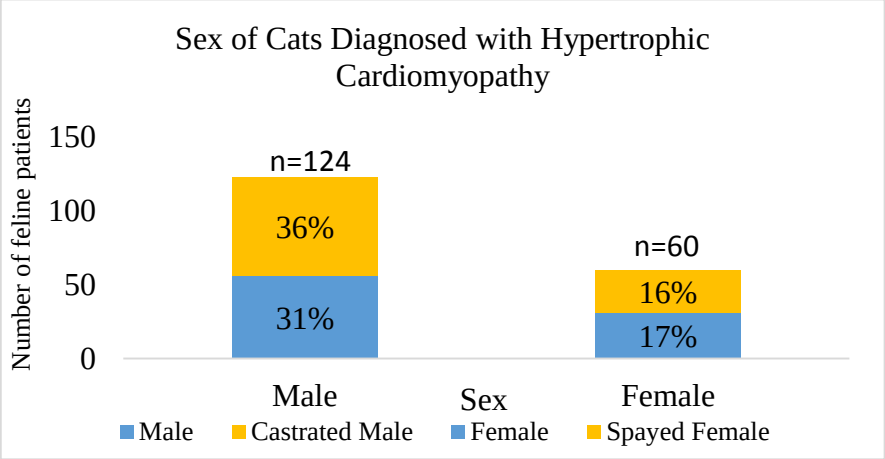
Figure 2: Breed of Cats Diagnosed with Hypertrophic Cardiomyopathy (*n*=184)



4.1.3 Sex

In this study, the castrated male cats were more frequently diagnosed with HCM. Among the 184 HCM cats, 67 cats were castrated male (36%), 57 cats were male (31%), 31 cats were female (17%) and 29 cats were spayed female (16%) (refer Figure 3).

Figure 3: Sex of Cats Diagnosed with Hypertrophic Cardiomyopathy (*n*=184)

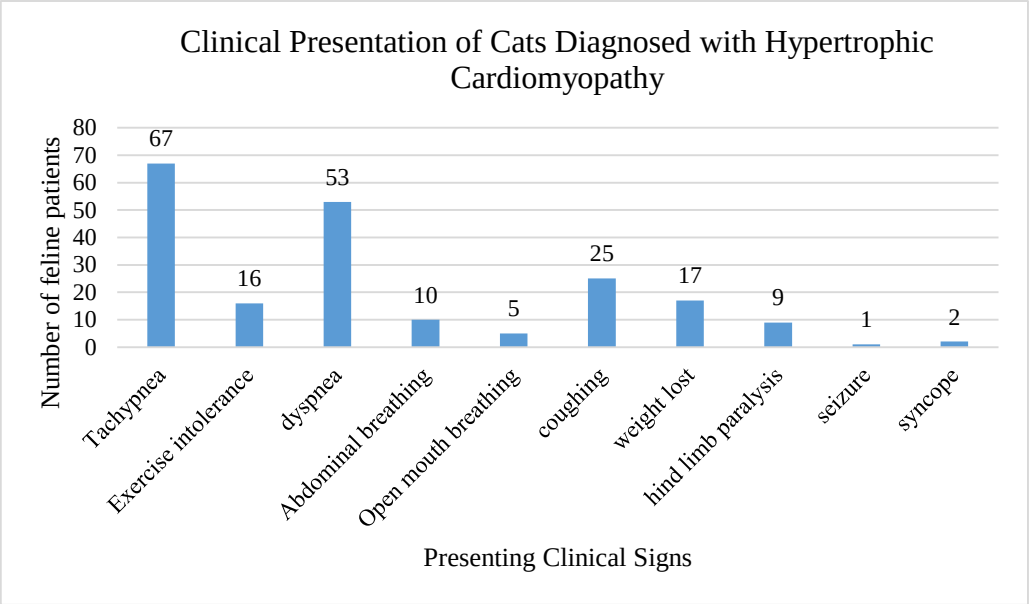


4.2 COMMON PHYSICAL EXAMINATION FINDINGS OF FELINE HYPERTROPHIC CARDIOMYOPATHY

4.2.1 Clinical Presentation

Based on Figure 4, tachypnoea (*n*=67) was the most common presented clinical signs followed by dsypnoea (*n*=53). Other clinical presentation seen in this study were coughing (*n*=25), weight lost (*n*=17), exercise intolerance (*n*=16) and abdominal breathing (*n*=10). The less common clinical signs seen were hind limb paralysis (*n*=9), open mouth breathing (*n*=5), syncope (*n*=2) and seizure (*n*=1).

Figure 4: Clinical Presentation of Cats Diagnosed with Hypertrophic Cardiomyopathy (*n*=184)



4.2.2 Heart Auscultation

Tachycardia (69%, *n*=127) was often auscultated followed by 37% of cats that had murmur (*n*=68), gallop heart sound (n=14; 8%), muffled heart sound (n=7; 4%) and arrhythmia (n=1; 1%).

4.2.3 Lung Auscultation

There was equal opportunity for cats diagnosed with HCM to have normal respiratory sound (n=92/184) and abnormal lung sound (*n*=92/184). Harsh lung sound

was the most commonly reported (87%, *n*=80/92) followed by wheezing and crackles sound (17%, *n*=16/92) and dull lung sound (9%, *n*=8/92).

4.3 THORACIC RADIOGRAPHIC FINDINGS

Based on the thoracic radiography, among 160 cats with abnormal findings, 124 cats had radiographic findings of pulmonary oedema, 35 cats with pleural effusion and 3 cats with pericardial effusion. Using the VHS measurement of the heart, majority of the cats had cardiomegaly with VHS of more than or equal 8 (n= 143; 78%) and 41 (22%) cats were less than 8.

4.4 ECHOCARDIOGRAPHIC FINDINGS

In this group of cats (*n*=184) (refer Figure 5), 147 cats were diagnosed with HCM (80%), 34 cats were categorised as equivocal HCM (18%) and 3 cats with focal HCM (2%). Symmetric hypertrophy affecting the entire LV was the most common finding, presenting at 76% of 147 HCM cats (n=112). Asymmetric which refers to hypertrophy affecting either the LVS or LVFW was noted in 24% of the cats diagnosed with HCM. Seventeen (9%) cats diagnosed with HOCM due to presence of LVOT obstruction (n=13) and SAM (n=4) (refer Figure 6).

In this study, the mean LA:Ao and LA size of cats diagnosed with HCM were 1.73 and 14.2 mm respectively. 70% of cats with LA:Ao ratio more than 1.5 (n=117/167) while

Figure 5: Type of Hypertrophy in Cats Diagnosed with Hypertrophic Cardiomyopathy (*n*=184)

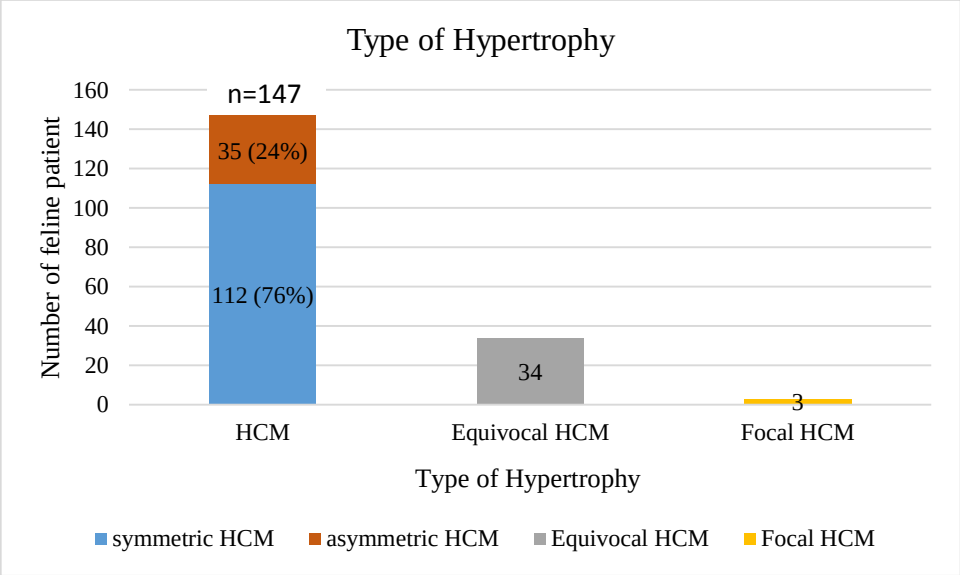
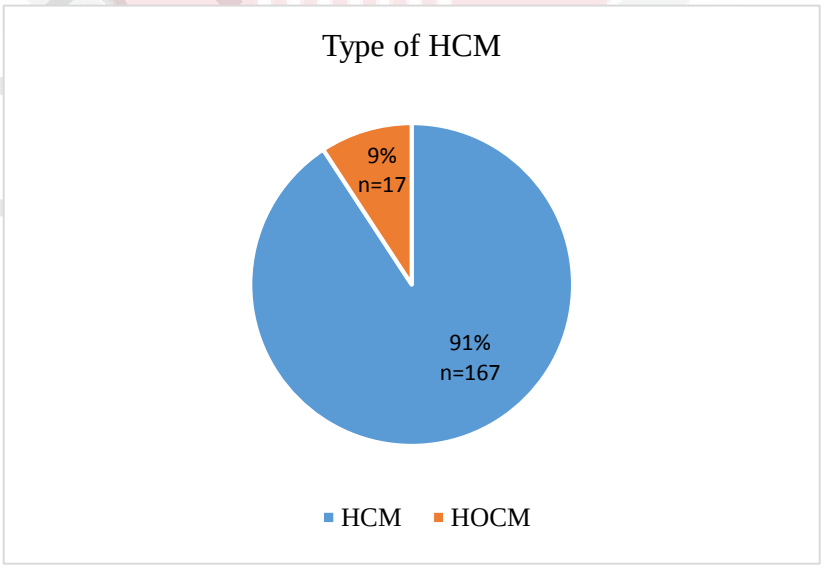


Figure 6: Type of Hypertrophic Cardiomyopathy in Cats Diagnosed with Hypertrophy Cardiomyopathy (*n*=184)

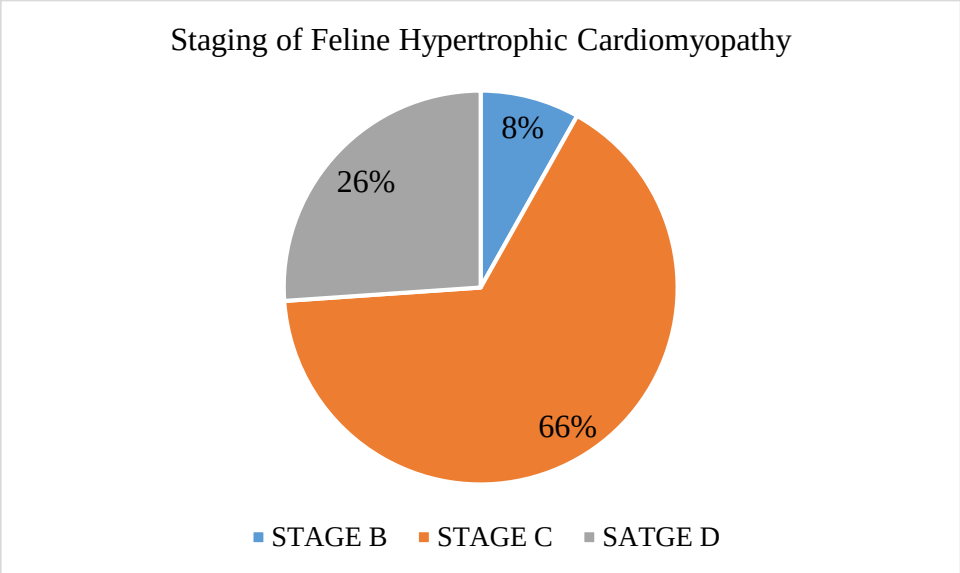


30% of cats were having LA:Ao ratio less than 1.5 (n=50/167) and 17 cats excluded due to unretrievable data. 26% of cats were having LA enlargement with size more than or equal to 16mm (*n*=43/166) while 74% of cats were having LA size less than 16mm (*n*=123/166) and 18 cat were excluded due to unretrievable data.

4.5 STAGING OF FELINE HYPERTROPHIC CARDIOMYOPATHY

Based on the staging of feline cardiomyopathy described by Fuentes *et al.* (2020), 15 cats were categorised as Stage B (8%) which was asymptomatic. Majority of the cats (n=121) cats were classified as Stage C (66%) as the initial presentation of cat shown one of the clinical sign of CHF or ATE. 48 cats were in Stage D (26%) as the cats had refractory CHF and did not well response to treatment (refer Figure 7).

Figure 7: Staging of Feline Hypertrophic Cardiomyopathy (*n*=184)



The staging was adapted from Fuentes *et al.* (2020).

4.6 COMMON CAUSE OF DEATH

Among 147 cats with known status of survival, 101 cats were deceased (69%) and 46 cats were still alive. Within those 101 deceased cats, 68 cats were died due to cardiovascular death (67%) such as CHF, ATE and SD while 33 cats did not survive due to non-cardiovascular death (33%) such as kidney failure, cancer, bacteria pneumonia, feline infectious peritonitis (FIP), accident and liver disease (refer Table 3)

Table 3: Common cause of death in cause diagnosed with hypertrophic cardiomyopathy (*n*=101)

Common cause of death	**Number of animal**	**Percentage, %**
Cardiovascular death:	68	67
Congestive Heart Failure	46	
Atrial Thromboembolism	13	
Sudden Death	9	
Non-cardiovascular death:	33	33
Kidney disease	18	
Cancer	4	
Feline Infectious peritonitis	5	
Accident	4	
Bacteria pneumonia	1	
Liver disease	1	

4.7 SURVIVABILITY OF FELINE HYPERTROPHIC CARDIOMYOPATHY

4.7.1 Survivability of HCM Cats Based On Stage

Only 147 cats with known status of survival was recruited for survivability analysis based the stage of the disease, namely Stage B, Stage C and Stage D.

The median survival time for all 147 HCM cats were 608 days and it was significant different between the three different stage (p=0.001). The median survival time for HCM cats in Stage B was 1518 days (n=11), Stage C was 1253 days (n=88) and Stage D was 30 days (n=48). Between Stage B and C, the medial survival time did not show significant different (p=0.344) but in Stage D, it did show significant different in median survival time compare to both Stage B and C (p=0.001).

4.7.2 Survivability of HCM Cats Based On Treatment Compliance

Only stage C and D HCM cats required long term treatment and therefore only these two groups were analysed for treatment compliance. The median survival time of both group of cats (n=136) with owners who were compliance (n=97, 507 days) to treatment versus non-compliance (n=39, 918 days) did not significant prolonged (p=0.135) the survivability despite that there was an extended 411 survival days in cats with compliance to treatment.

When analysed in detail based on the staging, the median survival time for cats with Stage C HCM with compliance treatment (n=62, 1207 days) and non-compliance treatment (n=26, 1515 days) showed no significant difference (p=0.382). For Stage D

HCM cats, the median survival time with compliance treatment (n=35, 45 days) and non-compliance treatment (n=13, 30 days) also showed no significant different (p=0.289).

4.7.3 Survivability of HCM Cats Based On Presence of Concurrent Disease

The median survival time for cats with concurrent disease (n=83, 458 days) versus no concurrent disease (n=64, 1155 days) showed no significant different (p=0.056). However, when analysing in detail, the median survival time for cats with Stage C HCM with concurrent disease was 918 days (n=49) while without concurrent disease was 1439 days (n=39) which showed significant difference between each other (p=0.008). However, the medial survival time for Stage B HCM cats with concurrent disease (n=6, N/A) and without concurrent disease (n=5, 1518 days) showed no significant different (p=0.857). The median survival time for cats with Stage D HCM with concurrent disease (n=28, 46 days) and without concurrent disease (n=20, 16 days) also showed no significant difference (p=0.087).

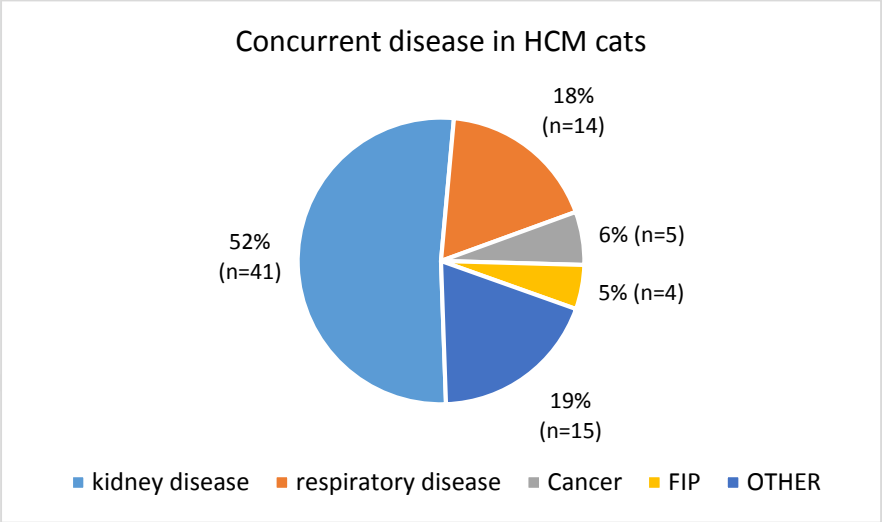
Table 4: Median survival time for cats diagnosed with HCM based on stage, treatment compliance and presence of concurrent disease (n=147)

Category	Median survival time (days)		Significant difference (p)
All cats (n=147)	608		0.001
Stage B (n=11)	1518		
Stage C (n=88)	1253		
Stage D (n=48)	30		
	Treatment compliance	No treatment compliance	
All (n=136)	507 (n=97)	918 (n=39)	0.135
C (n=88)	1207 (n=62)	1515 (n=26)	0.382
D (n=48)	45 (n=35)	30 (n=13)	0.289
	Concurrent disease	No concurrent disease	
All (n=147)	458 (n=83)	1155 (n=64)	0.056
B (n=11)	N/A (n=6)	1518 (n=5)	0.857
C (n=88)	918 (n=49)	1439 (n=39)	0.008
D (n=48)	46 (n=28)	16 (n=20)	0.087

4.8 CONCURRENT DISEASE

Among 184 cats with HCM, 79 cats had concurrent with other diseases (43%). Among those concurrent diseases, kidney disease was the most frequently diagnosed at 52% followed by other disease at 19% and some had respiratory disease at 18%. A smaller groups of cats diagnosed with HCM cats had concurrent with cancer and feline infectious peritonitis (FIP) at 6% and 5%, respectively. Other disease included liver disease, skin disease, stomatitis, parasitism, fracture bone and feline leukaemia virus disease (FeLV) (refer Figure 13).

Figure 8: Concurrent disease in cats diagnosed with hypertrophic cardiomyopathy (n=79)



CHAPTER 5.0

DISCUSSION

This retrospective study determined the survival time and clinical outcome of cats diagnosed with HCM from 2013-2019 in University Veterinary Hospital, Universiti Putra Malaysia, which is a primary veterinary healthcare. The mean age of cats diagnosed with HCM were 6.7 years old (age range 4-month to 20-year-old). Similar observation was reported by Payne *et al.* (2013) and Fox *et al.* (2018) where the mean age of HCM cats in their study 6.2 years old and 6.5 years old, respectively. It should also be noted that the disease can occur in any life stage of cats. Studies had shown that male especially castrated male were most commonly presented with HCM (Payne *et al.*, 2013, Fox *et al.*, 2018) and similarly was observed in this cohort of cats recruited. The role of gender behind this prevalence were still remains unclear and merit further investigation.

The domestic shorthair cats were often presented with HCM, followed by Persian cats in this study. Similarly as reported by other investigators (Ferasin *et al.*, 2003, Fox *et al.*, 2018) and it could agree upon that there could have been an over-presentation of this two breeds. Moreover, perhaps more cat owners favoured domestic shorthair cats as pets compare to other breed (Spalla *et al.*, 2016), but this fact could not be ascertained locally. Persian breed was considered predisposed to HCM but there is still no HCM-associated mutation been identified in this breed as well as in domestic shorthair cats (Granström *et*

al., 2011). Although Maine Coon had gene mutation of MYBPC3 (Meur *et al.*, 2005), there was only 5% of cats diagnosed with HCM were Maine Coon in this study.

Tachypnoea and dyspnoea were the two most common clinical sign observed and these clinical signs were highly associated with CHF (Côté *et al.*, 2011). Slightly different from Ferasin *et al.* (2003) and Spalla *et al.* (2015) which reported that dyspnoea was more commonly noted and followed by coughing. Based on findings from lung auscultation, it was noted that harsh lung was often heard and finding were not consistent with radiographic interpretation of pulmonary oedema (78%, n=124/160), pleural effusion (22%, n=35/160) and pericardial effusion (2%, n=3/160). There were 50% of cats diagnosed with HCM that had normal lung auscultation in this study, but heart failure still could not be rule out. Ferasin *et al.*, (2003) reported that only 8% of HCM cats (n=61) had abnormal lung sound upon auscultation and therefore lung auscultation may not be sensitive tool and should be used in combination of other findings in establishing the diagnosis of cats with HCM. Moreover, more than half of the cats in this study had pulmonary oedema, an indicative sign of CHF (Côté *et al.*, 2011). Lungs sounds of crackles, wheezing and dull were often associated with CHF (Côté *et al.*, 2011) but were not usually described by the clinician findings and it was very consistence with the abnormal lung sound auscultated in this study. This could be due to lung sound auscultation findings may be very subjective and interpretation may vary between clinicians.

Payne *et al.* (2013) found that 73% of cats had heart murmur auscultated while only 23.8% of cats had gallop heart sound. Systolic heart murmur occurred due to mitral regurgitation (Côté *et al.*, 2011) has been highly associated with HCM but murmur still may be heard in apparent healthy cat without heart disease (Fox *et al.*, 2018). Therefore, auscultation should always be routinely repeated at different time and days constantly to avoid misdiagnosis. Gallop sound had been associated with death due to ATE but not with CHF (Payne *et al.*, 2015b). In this study, tachycardia was the most common findings followed by heart murmur and gallop sound. Both the heart murmur and gallop sound was not being frequently auscultated in HCM cats could likely be due to uncooperative cat, noisy environment and dependent on the ability and/ skills of clinician in detecting heart murmur.

In this study, 91 % of cats were diagnosed with HCM while 9 % were HOCM. In contrast, Fox *et al.* (2018) reported higher incidence of HOCM (33%) compared to HCM (25%). Majority of the HCM cats (76%) had symmetric hypertrophy of the LV whereas the remaining were asymmetry. About 18% of the cats were diagnosed with equivocal HCM and 2% with focal HCM. The percentage were almost similar with Granström *et al.* (2011) study where 21% of cats were diagnosed with equivocal HCM, 4 % focal HCM and among those diagnosed with normal HCM, 79% were symmetric HCM. The mean LA:Ao and LA size of cats diagnosed with HCM in this study was 1.73 and 14.2 mm, respectively. This was different from Payne *et al.* (2013) and Granström *et al.* (2011) where LA:Ao was 1.44, LA size was 16.6 and LA:Ao was 1.4, LA size was 12.5 respectively. However, comparison between study should be interpreted with limitation

as it may be influenced by the different sample size, clinical signs and the staging of the heart disease of HCM cats at the point of entry was different as Payne *et al.* (2013) reported that most of the HCM cats were asymptomatic whereas majority of the cats in this study were in symptomatic stage.

In this cohort of cats recruited, two third of the cats with HCM did not survive due to cardiovascular disease (*n*=68/101) and another one third were due to non-cardiovascular disease (33/101). The findings were consistence with a study (Payne et al., 2010) and therefore, cats diagnosed with HCM seems to have a higher chance to experience cardiovascular death than non-cardiovascular death such cancer and kidney disease.

CHF (*n*=46) was the most common cause of cardiovascular death compared to the other two which were ATE and SD. Similarly, few studies reported that the prevalence of ATE was lower in HCM cats which ranged from 12-17% (Rush *et al.*, 2002, Payne *et al.*, 2010, Fox *et al.*, 2018) and that ATE was more commonly seen in restrictive cardiomyopathy (RCM) with prevalence of 56% (Stalis *et al.*, 1995). This fact could not be ascertained in this study as the focus was only among HCM cats.

In the group of HCM cats with non-cardiovascular death, CKD was the most common cause (*n*=18/33), but Fox *et al.* (2018) reported differently where cancer was most commonly diagnosed followed by CKD. Generally, in cats, CKD had been associated with cardiovascular disease due to their similar risk factor such as hypertension, aging and others (Subbiah *et al.*, 2016). In this study, 41 cats had HCM concurrent with

CKD. 19 out of 41 cats had died due to CKD, 15 cats died due to CHF, 1 cat died due to FIP and 6 cats still alive.

The median survival time for cats diagnosed with HCM in this study was 608 days which was much shorter compare to previous study that were 3979 days (Fox *et al.,* 2018) and 1276 days (Payne *et al.,* 2010). The differences could be due to different population size and background, stage of disease and treatment protocol, which were not taken account in this study due to limited sample size. The median survival time for cats diagnosed with HCM showed significant different based on stage but does not different between treatment compliance and presence of concurrent disease. There was no study yet comparing the survival time based on the staging as described by Fuentes *et al.* (2020). Nevertheless, when comparing the similarity criteria of study conducted by Payne *et al.* (2010), the asymptomatic HCM cats (Stage B) had longer survival time than those symptomatic HCM cats. The clinical feature such as first clinical presentation, left atrial size and left ventricular systolic function can become the prognostic factor for HCM cats (Payne *et al.,* 2015b) and those clinical presentations such as CHF or ATE or left atrial size also determine the staging of feline cardiomyopathy as well (Fuentes *et al.,* 2020).

In human, treatment compliance was an important factor affecting the outcome of heart disease (Diaz *et al.,* 2011). However, as to whether the cat owners were compliance or non-compliance to the treatment intended for the heart disease did not show benefit on prolonging the survival time of cats with HCM. This could probably be due ineffective treatment regime available for therapy. Study has described that benazepril did not

improve the survival time of cats with heart disease (King *et al.*, 2019). In contrast, diltiazem (Bright *et al.*, 1991) and pimobendan (Reina-Doreste *et al.*, 2014) was shown to improve the survival time of cats with HCM. Up till now, there are still lack of well-established study with strong evidence to prove the benefit of treatment toward the survival time of cats with HCM.

The survival time did not show significant different in HCM cats with or without concurrent disease in this study. However, further analysis according to stage found that the survival time was shorter in Stage C HCM cats with concurrent disease compared to without concurrent disease but no significant different in Stage D. Similarly, Fox *et al.* (2019) concluded that disease burden contributed by increased cardiovascular death superimposed upon non-cardiovascular death had shorten the survivability of subclinical HCM cats compare to those apparent healthy cats. According to Subbiah *et al.* (2016), one of the consequences of CKD was anemia that may increase cardiovascular burden in heart disease patients and in CKD patient, optimal treatment was underuse due to worrying the negative consequence of ACEi toward kidney. As observed in this study, the most common concurrent disease in HCM cats was kidney disease (especially Stage C) and therefore showed that cats with concurrent disease had shorter survival time. Stage D HCM cats with or without concurrent disease showed not differences in survival time and was speculated due to the natural prognosis of refractory CHF was poor. Thus, the presence of concurrent disease did not show obvious impact toward the survivability of cats.

CHAPTER 6.0

CONCLUSION AND RECOMMENDATIONS

The mean age of cats diagnosed with HCM were 6.7 years old, especially in DSH and male cats. The common cause of death in cats diagnosed with HCM presented were due to cardiovascular death contributed by CHF. The median survival time for HCM cats was 608 days and the survivability of HCM cats were depend on stage of the disease. The owner compliance towards treatment in HCM cats with or without the presence of concurrent disease did not affect the survival time. The median survival time were getting shorter for cats as the stage of the heart disease differs to later stage cardiomyopathy at time of diagnosis, with 1518 days in Stage B, 1253 days in Stage C and 30 days in Stage D. Although the presence of concurrent disease did not show difference in overall, it did show a negative impact towards the survivability in Stage C cats (median survival time without concomitant was 1439 days; with concomitant was 918 days). Thus, early detection of HCM can prolong the life span and early treatment (intervention) may delayed the progression of heart disease and improving the quality of life.

As recommendation, investigate using other prognosis indicator such as left atrial size and left ventricular thickness in HCM cats towards the survivability could be useful. Treatment efficacy for cats with HCM is an interesting topic to be investigated to support the findings of treatment compliance towards survivability of HCM cats in this study.

CHAPTER 7.0

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CHAPTER 8.0

APPENDIX I

Survivability of cats diagnosed with HCM based on stage, treatment compliance and presence of concurrent disease (n=147)