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RESEARCH ARTICLE

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Prevalence of cardiomyopathy and cardiac mortality in a colony of non-purebred cats in New Zealand

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ABSTRACT

Aims: To evaluate the prevalence of subclinical cardiomyopathy and cardiac mortality in a research colony of non-purebred cats, established as a model of the wider cat population in New Zealand.

Methods: All apparently healthy, compliant, non-pregnant, non-neonatal cats in the colony at the Centre for Feline Nutrition (Massey University, Palmerston North, NZ) underwent physical examination and echocardiography using a 4.4–6.2-MHz probe by a board-certified veterinary cardiologist. Cardiac phenotype was classified following current guidelines. Hypertrophic cardiomyopathy (HCM) phenotype was defined as an end-diastolic left ventricular wall thickness ≥ 6 mm. Colony mortality data from February 2012 to February 2022 was reviewed to determine cardiac mortality.

Results: Cats (n = 132; 65 females and 67 males) included in the study had a median age of 4.1 (IQR 3.0–8.0) years. Thirty-two (24%) cats had a heart murmur, and three (2%) cats had an arrhythmia. Echocardiography revealed heart disease in 24 (18.2%) cats, including 23 with an HCM phenotype and one with a restrictive cardiomyopathy phenotype. Of the cats with the HCM phenotype, 3/23 had systemic hypertension or hyperthyroidism or both, and these cats were excluded from the final diagnosis of HCM (20/132; 15.2 (95% CI = 9.5–22.4)%).

Between 2012 and 2022, 168 colony cats died, with 132 undergoing post-mortem examination. Heart disease was considered the cause of death in 7/132 (5.3%; 95% CI = 2.2–10.6%) cats; five had HCM, one a congenital heart defect, and one myocarditis. The overall prevalence of death related to HCM in the colony during this period was 3.8% (95% CI = 1.2–8.6%). Three cats with HCM and the cat with a congenital heart defect died unexpectedly without prior clinical signs, while congestive heart failure was observed prior to death in two cats with HCM and the cat with myocarditis. Additionally, 30/132 (22.7%) cats had cardiac abnormalities but died for non-cardiac reasons.

Conclusions: Subclinical cardiomyopathy, specifically HCM, was common in cats in the colony. Given that the colony originated as a convenience selection of non-purebred cats in New Zealand, the true prevalence of HCM in the wider New Zealand population is likely to fall within the 95% CI (9.5–22%). The proportion of deaths of colony cats due to HCM was lower (3.8%) supporting the conclusion that subclinical cardiomyopathy may not progress to clinical disease causing death.

Clinical relevance: Veterinarians should be aware of the high prevalence of subclinical HCM when treating cats.

Abbreviations: CAM: Systolic anterior motion of the chordae tendineae; CFN: Centre for Feline Nutrition; HCM: Hypertrophic cardiomyopathy; LA/Ao: Left atrial to aortic ratio; LV FS: Left ventricular fractional shortening; LVIDd: Left ventricular internal diameters in end-diastole; LVIDs: Left ventricular internal diameter in end-systole; LVWT: Max Maximum left ventricular wall thickness; SAM: Systolic anterior motion of the mitral valve; 2D: Two-dimensional

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Hypertrophic cardiomyopathy; heart murmur; feline; cardiomyopathies; cardiac screening; sudden death

Introduction

Cardiomyopathy is a primary myocardial disorder that changes the structure and function of the heart muscle in the absence of other disease sufficient to cause the observed myocardial abnormality. Currently, there are no studies evaluating the prevalence of cardiomyopathy in cats in New Zealand. However, studies of cats in the UK and USA suggest that approximately 15% of clinically healthy cats in the general population have cardiomyopathy that is detectable using echocardiography (Paige *et al.* 2009; Payne *et al.* 2015). Several types of cardiomyopathy have been described in cats (Luis

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Fuentes *et al.* 2020). Of these, hypertrophic cardiomyopathy (HCM) is most common, constituting > 94% of apparently healthy cats diagnosed with cardiomyopathy (Paige *et al.* 2009; Payne *et al.* 2015).

The clinical definition of HCM is left ventricular concentric hypertrophy caused by a genetic abnormality or an unknown aetiology (Fox *et al.* 1995; Luis Fuentes *et al.* 2020). Therefore, HCM is diagnosed by ruling out other diseases such as hyperthyroidism and systemic hypertension, which can mimic HCM (termed "HCM phenotype"; Luis Fuentes *et al.* 2020). Cats with HCM can remain asymptomatic for years (i.e. have subclinical disease) after diagnosis and may live a normal lifespan (Fox *et al.* 2018). However, the disease may progress in some cats and result in congestive heart failure, aortic thromboembolism, myocardial infarction, and sudden death (Fox *et al.* 2018; Luis Fuentes *et al.* 2020; Novo Matos *et al.* 2023).

A retrospective multicentre study of 1,730 cats with HCM reported the incidence rate of all cardiovascular deaths in cats with HCM as 63.4 per 1,000 cat-years (Fox *et al.* 2018). Therefore, HCM is a serious health concern in cats. The prevalence of subclinical HCM in New Zealand has not previously been investigated. If the prevalence of HCM in New Zealand is similar to that of other countries, approximately 180,000 of the estimated 1.2 million pet cats in NZ (CANZ 2020) may have subclinical HCM. Furthermore, approximately 11,400 cats may die due to HCM in the next 5 years.

The Centre for Feline Nutrition (CFN) at Massey University (Palmerston North, NZ) was created in 1992 by breeding 10 cats obtained from rehoming centres in NZ. Since then, a population of 130–150 cats has been maintained by introducing four new breeding cats from rehoming centres every 5 years to maintain genetic diversity. The aim of the CFN is to represent the non-purebred feline population in NZ for nutritional studies. In the CFN, each large pen houses an average of eight cats. Cats in each pen interact with staff members daily and receive weekly enrichment time in a playroom where cats are played with one-on-one, weighed, groomed, and undergo a health check. Cats are given water *ad libitum* and fed a varied combination of canned and dry cat foods that are approved by the Association of American Feed Control Officials.

The aim of this study was to use the CFN colony cats as a convenience sample of non-purebred cats in New Zealand to estimate the prevalence of cardiomyopathy in this population. The secondary aim was to estimate the proportions of cats in New Zealand that die due to cardiomyopathy and that die with subclinical HCM by comparing the rates of cardiomyopathy to the causes of death of cats within the colony.

Materials and methods

Study design

The first part of this study (describing the prevalence of HCM in New Zealand) was prospective and observational in design. The second part (describing cardiac mortality) was a retrospective study. Ethics approval was provided by Massey University Animal Ethics Committee (MUAEC protocol 21/47).

Part 1 – prevalence of cardiomyopathy

Animals

A convenience sample of cats from the CFN was prospectively screened for the presence of cardiomyopathy. Inclusion criteria were all cats at the CFN (n = 149). Exclusion criteria were neonates, queens that were nursing, clinically unwell cats, and cats that were unable to be examined due to their behaviour. All enrolled cats underwent physical examination and then echocardiography by a board-certified veterinary cardiologist (JS). Oral treats were provided to keep the cats still during data collection. No cats were sedated.

Medical histories from the CFN records and CFN staff were also reviewed. Information on age, sex, neuter status, current body weight, and current medications were retrieved from the CFN records. From the physical examination, body condition score (scale 1–9), heart rate, and presence of a heart murmur, gallop sound, or arrhythmias were recorded. When present, the heart murmur intensity was graded on a scale of 1–6.

Echocardiography

Right parasternal two-dimensional (2D) echocardiography was performed using a general ultrasound machine (Xario 200; Toshiba, Tochigi, Japan) equipped with a sector array probe (6S3, frequency 4.4–6.2 MHz) as previously described (Thomas *et al.* 1993). All images were then analysed using image processing software (TOMTEC Imaging Systems, Unterschleissheim, Germany). The presence of systolic anterior motion of the mitral valve (SAM) or chordae tendineae (CAM) were examined subjectively using 2D imaging (Schober and Todd 2010; Seo *et al.* 2020). Each echocardiographic variable of interest was measured over three consecutive cardiac cycles and averaged.

The maximum left atrial diameter was measured using a right parasternal, long-axis, four-chamber view by bisecting the left atrium parallel to the mitral annulus, one frame before the mitral valve opening. The left atrial to aortic ratio (LA/Ao) was measured using a right parasternal, short-axis view at the level of the aortic valve, one frame after the aortic valve closing. The thickest sections of the interventricular

septum and left ventricular free wall were measured at end-diastole in three views: right parasternal, long-axis, four-chamber view; right parasternal, long-axis, five-chamber view; and short-axis view at the level of papillary muscles in end-diastole. The greatest value from the measurements in all three views was recorded as maximum left ventricular wall thickness (LVWT Max). Descriptive data on which segment of the left ventricular wall was thickened was not collected. The left ventricular internal diameters in end-diastole (LVIDd) and end-systole (LVIDs) were recorded by bisecting the left ventricle using the right parasternal short-axis view at the level of the papillary muscles.

A basic assessment of left atrial and left ventricular systolic function was performed by calculating the fractional shortening as follows:

$$\textit{Fractional shortening} = \frac{(\textit{Maximum diameter} - \textit{Minimum diameter})}{\textit{Maximum diameter}} * 100$$

The maximum and minimum left atrial diameter was measured using the same view as LA/Ao in end-systole and end-diastole. The maximum and minimum left ventricular diameter was already measured as LVIDd and LVIDs.

Echocardiographic classification of cardiomyopathy

Cardiomyopathy was classified based on the current consensus guidelines from the American College of Veterinary Internal Medicine (Luis Fuentes *et al.* 2020). Arbitrary cut-offs were used in this study when objective cut-offs were unavailable or inconsistently used in the literature. Briefly, an HCM phenotype was defined as LVWT Max $\geq$ 6 mm (Fox *et al.* 1995). To reach the diagnosis of HCM, other differentials of an HCM phenotype were excluded. In cats that were < 6 years old, careful physical examination and review of the CFN record were used to exclude the differentials of an HCM phenotype. In comparison, cats that were $\geq$ 6 years underwent blood pressure measurements using the Doppler technique, with systemic hypertension defined as systolic arterial blood pressure > 160 mmHg (Acierno *et al.* 2018). To avoid inadvertently missing clinical signs of hyperthyroidism and hypersomatotropism in cats of any age, CFN staff performed weekly assessment of appetite, thirst, and weight checks as part of the colony protocol; any significant changes in the 2 years following echocardiography were flagged to the investigator, and appropriate blood tests were performed.

For this study, a restrictive cardiomyopathy phenotype was defined as left or biatrial enlargement (LA/Ao > 1.6 and maximal left atrial diameter in long-axis > 16 mm, right atrial enlargement on subjective assessment) with either normal or equivocal left ventricular thickening (LVWT Max < 6 mm) or the presence of a fibromuscular band crossing the left ventricle. A dilated cardiomyopathy phenotype was defined as an increased LVIDd (> 18 mm) and reduced left ventricular fractional shortening (LV FS)% (< 30%). An arrhythmogenic cardiomyopathy phenotype was defined as right atrial and right ventricular enlargement on subjective assessment in the absence of features of pulmonary hypertension. Lastly, cats were categorised as having non-specific cardiomyopathy if the features of cardiomyopathy did not meet any of the above criteria.

Part 2 – prevalence of cardiac mortality

The 10-year mortality data was collected by reviewing the records of the CFN and the Pathology Database of the School of Veterinary Science (Massey University) between February 2012 and February 2022. From these records, the sex of the cat, age at death, reason for euthanasia (if applicable), post-mortem findings, and the recorded cause of death were extracted. In this study, cardiac death was defined by the presence of congestive heart failure, aortic thromboembolism, or sudden death with gross or histologic evidence of cardiac disease without any other explainable cause. In the pathologist's report, the left ventricle was assessed to be grossly thickened if the left ventricular wall thickness was more than three times the right ventricular free wall thickness (Wilkie *et al.* 2015). The heart was considered enlarged if it weighed > 20 g, or if the relative heart-weight to bodyweight ratio was > 4 g/kg (Kittleson and Côté 2021). The presence of congenital heart defects was assessed subjectively. Histology of the heart was routinely performed.

Statistical analysis

SPSS Statistics (v 26, IBM; Armonk, NY, USA) was used for statistical analysis. Graphs were produced in GraphPad Prism (v 8.4.2; GraphPad, Boston, MA, USA). Normality of data was tested by visual assessment and the Shapiro–Wilk test. Normally distributed data was presented as mean (SD) and non-normally distributed data was presented as median (IQR). Categorical variables were presented as proportions (percentage). The proportions or summary means or medians that apply only to the sample are presented without CI. The prevalence of cardiomyopathy and cardiac mortality is intended to estimate that of the wider population so 95% CI are also reported.

All comparisons were unadjusted for the presence of potential confounders. Cats from the echocardiographic study were divided into groups based on the presence or absence of cardiomyopathy. Unadjusted comparisons of continuous variables were made using an independent t-test or a Mann–Whitney test depending on the distribution, and unadjusted

comparisons of categorical variables were made by Pearson's χ^2, or Fisher's exact test when the cell count was < 5. For contingency tables larger than 2 × 2, Fisher's exact test was used. Significance was considered where $p < 0.05$.

Results

Part 1 – prevalence of cardiomyopathy

The outcome of the study is summarised in Figure 1. Of 149 cats in the CFN colony, 17 were excluded due to being neonates (n = 11), queens that were nursing (n = 2), clinically unwell (n = 2), or non-compliant (n = 2), leaving 132 cats that underwent cardiac examination. Five (3.8%) cats were from rehoming centres and 127/132 (96.2%) cats were born in the colony. The median age was 4.1 (IQR 3.0–8.0) years (Figure 2). There were 65 (49.2%) female cats and 67 (50.8%) male cats. Many female cats were intact (42 intact *vs.* 23 neutered) whereas most male cats were neutered (3 intact *vs.* 64 neutered). The median body weight was 3.5 (IQR 2.9–4.1) kg. Eleven (8.3%) cats had co-morbidities. These were two cats each with chronic diarrhoea, controlled hyperthyroidism, dental disease, and lameness, and one cat each with an abdominal mass, skin mass, or nasal mass. The cats with controlled hyperthyroidism were receiving carbimazole (Vidalta; MSD Animal Health, Wellington, NZ). The cats with dental disease, lameness, and the nasal mass were

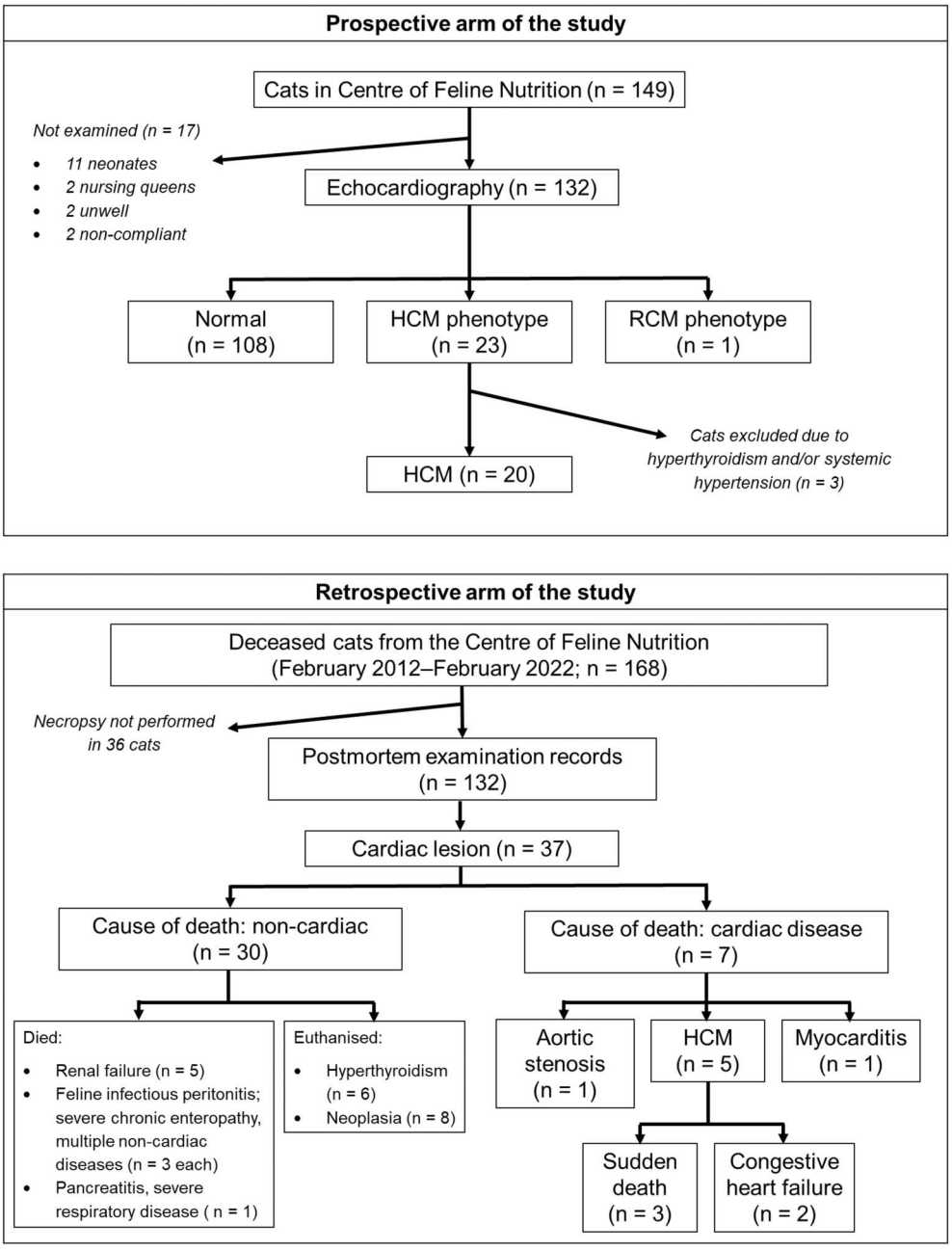

Figure 1. Flow chart summarising the design of a study to evaluate the prevalence of subclinical hypertrophic cardiomyopathy (HCM) and cardiac mortality in a colony of non-purebred cats. HCM = hypertrophic cardiomyopathy; RCM = restrictive cardiomyopathy.

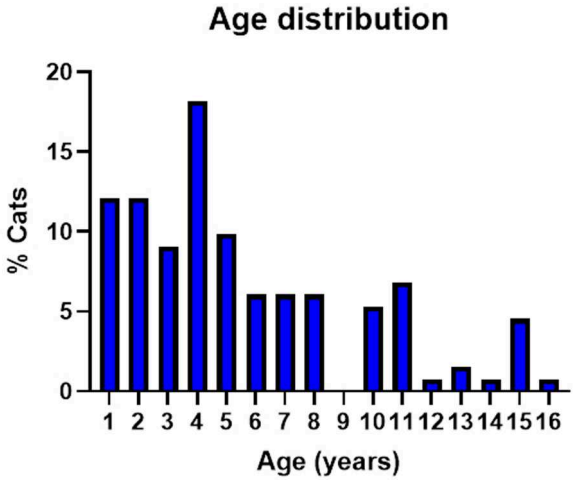

Figure 2. Age of cats (n = 132) prospectively enrolled in a study to evaluate the prevalence of subclinical hypertrophic cardiomyopathy in a colony of non-purebred cats using echocardiography.

receiving meloxicam (Metacam; Boehringer Ingelheim Animal Health NZ Ltd., Auckland, NZ).

Thirty-two of the 132 (24.2%) cats had a heart murmur, and 3/132 (2.3%) cats had an audible arrhythmia on auscultation. No cats had a gallop sound. Twenty-four of the 132 (18.2%) cats had an abnormal echocardiogram (Figure 1). Of these, 23/132 (17.4%; 95% CI = 11.4–25.0%) cats had an HCM phenotype and 1/24 (0.8%; 95% CI = 0.0–4.1%) cats had a restrictive cardiomyopathy phenotype. Seven of the 23 cats with an HCM phenotype were older than 6 years old. Systemic hypertension was diagnosed in three of these cats, and one of these three also had hyperthyroidism. These three cats were excluded from the final HCM diagnosis. The final number of cats with HCM was 20/132 (15.2%; 95% CI = 9.5–22.4%). The cat with a restrictive cardiomyopathy phenotype also had hyperthyroidism.

The results of statistical comparison between normal cats and cats with HCM is summarised in Tables 1 and 2. Of the 20 cats with HCM detected by echocardiography, 8 (40%) cats had a murmur detected on physical examination while 12 (60%) did not have a detectable murmur. Conversely, of the 108 normal cats that did not have evidence of heart wall changes detected on echocardiography, 23 (21.3%) had a murmur detected on physical examination. Five of the 20 (25%) cats with HCM had SAM, and 3/20 (15%) had CAM without SAM. None of the cats with a normal echocardiogram had SAM or CAM. The proportion of cats that had a moderate-to-loud heart murmur was greater in cats with HCM (4/20; 20%) than in cats with a normal echocardiogram (3/108; 2.8%; p = 0.038). Similarly, the proportion of cats receiving medication was greater among cats with HCM (3/20 (15%) receiving meloxicam) than those with a normal echocardiogram (3/108 (2.8%) receiving meloxicam or carbimazole; p = 0.048). In female cats, HCM was positively associated with neutered status (p = 0.042). Cats with HCM had a lower LVIDd and LVIDs, greater LV FS%, and greater LVWT Max than normal cats.

Table 1. Categorical variables compared between cats with a normal echocardiogram and those diagnosed with hypertrophic cardiomyopathy (HCM)[a] in a study to evaluate the prevalence of subclinical HCM in a colony of non-purebred cats (n = 132) using echocardiography.

	Normal (n = 108)	HCM (n = 20)	*P*-value
Sex: n female (%)	57 (52.8%)	7 (35%)	0.223
Proportion neutered (%)			
Female	17/57 (29.8%)	5/7 (71.4%)	0.042
Male	49/51 (96.1%)	12/13 (92.3%)	0.500
BCS (scale: 1–9)			
1	0	0	0.062
2	2	0	
3	0	0	
4	19	2	
5	71	10	
6	16	8	
7	0	0	
8	0	0	
9	0	0	
Heart murmur (n; %)	23 (21.3%)	8 (40.0%)	0.090
Soft: moderate–loud	18:5	4:4	0.038
Arrhythmia	1 (0.9%)	2 (8.7%)	0.063
Co-morbidities[b]	7 (6.5%)	3 (15.0%)	0.190
Medications[c]	3 (2.8%)	3 (15.0%)	0.048

[a]Diagnosed after excluding other differentials for an HCM phenotype.
[b]Co-morbidities for normal cats were chronic diarrhoea (2), and abdominal mass, cutaneous mass, hyperthyroidism, lameness, and dental disease (1 each). Co-morbidities for cats with HCM were nasal mass, lameness, and dental disease (1 each).
[c]Normal cats: meloxicam (2 cats) and carbimazole (1 cat). HCM group: meloxicam (3 cats).
BCS = body condition score.

Part 2 – prevalence of cardiac mortality

A total of 168 cats from the CFN died between February 2012 and February 2022, with 132 cats subject to

Table 2. Continuous variables[a] compared between cats with a normal echocardiogram and those diagnosed with hypertrophic cardiomyopathy (HCM)[b] in a study to evaluate the prevalence of subclinical HCM in a colony of non-purebred cats (n = 132) using echocardiography.

	Normal (n = 108)	HCM (n = 20)	*P*-value
Age (years)	4.5 (2.1–8.0)	4.0 (3.2–5.3)	0.728
Body weight (kg)	3.42 (2.9–4.1)	3.80 (3.1–4.3)	0.152
LAD Max (mm)	13.1 (± 1.3) (n = 105)	12.8 (± 1.4)	0.276
LA/Ao	1.2 (1.1–1.3)	1.2 (1.1–1.2)	0.165
LVIDd (mm)	13.6 (± 1.8) (n = 107)	12.1 (± 2.0)	0.001
LVIDs (mm)	6.6 (± 1.3) (n = 107)	5.2 (± 1.1)	< 0.001
LV FS (%)	51.0 (± 7.8)	56.3 (± 8.8)	0.007
LVWT Max (mm)	4.7 (4.4–5.1)	6.3 (6.2–6.6)	–

[a]Normally distributed data are presented as mean (± SD) and non-normally distributed data are presented as median (IQR). Where data was not available for all members of a group, the number of cats for which the variable was available is shown in brackets.
[b]Diagnosed after excluding other differentials of an HCM phenotype.
LA/Ao = left atrial to aortic ratio; LAD Max = maximal left atrial size; LV FS = left ventricular fractional shortening; LVIDd = left ventricular internal diameter in end-diastole; LVIDs = left ventricular internal diameter in end-systole; LVWT Max = left ventricular maximal thickness.

full post-mortem examination (Figure 1). The median lifespan of the cats was 11.3 (IQR 9.5–12.8) years. There were 55 females and 73 males, with sex not documented in four neonatal kittens. Eighteen of 132 (13.6%) cats were from rehoming centres and 114/132 (86.4%) were born in the colony.

Thirty-seven of the 132 (28%; 95% CI = 17.2–32.5%) cats were reported to have cardiac abnormalities on either gross examination or histology. Of these 37 cats, 28 were reported to have hearts that were grossly thickened or enlarged on quantitative or subjective assessments, suggestive of cardiomyopathy. One of these 37 cats was diagnosed with congenital aortic stenosis, and another cat was diagnosed with myocarditis on gross examination and histology. Seven of the 37 cats had cardiac lesions that were only detected by routine histology. These included 5/7 cats with left ventricular fibrosis and 2/7 with fatty infiltrates in the left and right ventricles.

While gross evidence of cardiac abnormality was common, only 7/132 (5.3%; 95% CI = 2.2–10.6%) cats were considered to have died of heart disease. Three of these seven cats (42.9%) died suddenly and the only post-mortem findings were a grossly thickened left ventricle and histological lesions suggestive of HCM (myocardial hypertrophy, myofibre disarray, and interstitial fibrosis). Two of the seven (28.6%) cats that died of heart disease had clinical evidence of congestive heart disease prior to death and gross and histological lesions of HCM. Therefore, the total number of cats that died probably due to HCM during the study period was 5/132 (3.8%; 95% CI = 1.2–8.6%). Of the remaining two cats with a cause of death of heart disease, one cat was considered to have suffered arrhythmogenic sudden death due to aortic stenosis, and the other had myocarditis and pulmonary oedema. No cats died due to aortic thromboembolism.

Thirty cats had gross or histological evidence of heart disease, but these changes were not considered to have contributed to the death of the cat. Fourteen of these cats were euthanised (eight due to neoplasia and six due to uncontrolled hyperthyroidism) and 16 died from the following causes: renal failure (n = 5), feline infectious peritonitis (n = 3), chronic severe enteropathy (n = 3), multiple non-cardiac diseases (n = 3), pancreatitis (n = 1) and respiratory disease (n = 1).

Discussion

In the present study, 15% of cats in the colony had cardiomyopathy, specifically HCM, that was detected by echocardiography. Less than half of these cats had either a murmur or arrhythmia detectable on physical examination. Conversely, a murmur or arrhythmia was detected in cats that did not have cardiomyopathy. The lack of consistent association between findings of the physical examination and the presence of cardiomyopathy have been reported previously and highlight the need for echocardiography to diagnose cardiomyopathy (Paige *et al.* 2009; Payne *et al.* 2015).

The detection of subclinical cardiomyopathy in cats, specifically HCM, is important because this condition may increase the risks associated with sedation, general anaesthesia, fluid therapy, or steroid medication. For example, many anaesthetic agents affect cardiovascular function, and the presence of cardiac disease can alter the anaesthetic plan (Clark *et al.* 2020). Additionally, fluid therapy and steroid medication may increase blood volume, resulting in congestive heart failure in cats affected by HCM (Ployngam *et al.* 2006; Ostroski *et al.* 2017; Block and Oyama 2020). Furthermore, HCM can be progressive and can predispose cats to aortic thromboembolism and congestive heart failure (Fox *et al.* 2018; Novo Matos *et al.* 2022). Therapies such as clopidogrel can be used in cats with moderate to severe heart enlargement to reduce the risk of aortic thromboembolism and cardiac death (Hogan *et al.* 2015).

Not all cats with subclinical HCM will subsequently die of this disease, with previous studies reporting an incidence rate for all cardiovascular deaths in cats with HCM of 63.4 per 1,000 cat-years (Fox *et al.* 2018). The probability that many cats with subclinical HCM will die of an unrelated cause was supported in the present study by the observation that only 3.8% of cats in the colony died due to HCM while 15% of cats in the colony were identified as having subclinical HCM. These two populations cannot be directly compared due to the difference in the method of data collection and age of the cats. However, if cardiac mortality represented 4% of deaths in the CFN during the period under study and assuming a 15% prevalence of HCM based on echocardiography, this would correspond to 25.3% of the cats with HCM dying of the disease. This is consistent with the literature (Fox *et al.* 2018; Novo Matos *et al.* 2022). Further evidence that HCM can remain subclinical over the lifetime of a cat was derived from the observation that 23 cats in our study died of non-cardiac causes but were found to have gross lesions consistent with HCM at necropsy. The increase in frequency of HCM diagnosis on post-mortem examination compared to echocardiography is likely due to the difference in age between two study populations, as the frequency and severity of HCM increases with age (Payne *et al.* 2015; Novo Matos *et al.* 2022). As the median age of cats at death in this study was 11.3 years, more cats would be expected to be diagnosed with HCM in this group than in the group that underwent echocardiography (median age 4.1 years). Other than genetics, it is largely unknown why some cases of HCM progress faster than others (Borgeat *et al.* 2015; Fox *et al.* 2018, Novo Matos *et al.* 2022). It is possible that the current criteria used to diagnose HCM on echocardiography

or by post-mortem examination are not narrow enough, and a wide range of diseases are inadvertently grouped into a single disease entity. Further studies are needed to evaluate factors associated with the progression of HCM and disease classification.

The median age of the colony cats (4.1 years) is similar to cat populations used to investigate subclinical HCM in the UK and USA (Paige *et al.* 2009; Payne *et al.* 2015). However, a recent survey showed the median age of cats in New Zealand may be closer to 7 years old (CANZ 2020). As the prevalence of HCM increases with age (Payne *et al.* 2015), the true proportion of cats with subclinical HCM in New Zealand may be higher than the 15% detected in the cat colony.

The CFN is considered to contain cats that are representative of non-purebred cats in New Zealand. However, CFN is not a randomly selected population, and the genetic diversity in the colony has not been assessed. Given that HCM is likely to have a genetic basis, we acknowledge that there is some uncertainty in how representative the colony data is to the wider New Zealand cat population. A recent survey suggested that 20% of pet cats in New Zealand are purebred (CANZ 2020). As there are genetic differences between breeds and non-purebred cats, the findings of this study may not be applicable to the New Zealand population if purebred cats are included. The prevalence of HCM and cardiac death in purebred cats in New Zealand is currently unknown. Furthermore, only 23/65 (35.4%) female cats in the colony were neutered, which may differ from the wider NZ population. Therefore, a 95% CI was provided, which suggests 95% certainty that the true prevalence of subclinical HCM lies between 9.5% and 22.4%.

The proportion of cats that died due to heart disease in the present study was similar to that observed in a study of cats presenting to first opinion veterinary clinics in the UK (4.2%; O'Neill *et al.* 2015). Cardiac deaths were not further classified into sudden death, congestive heart failure, or aortic thromboembolism in that study. However, congestive heart failure and aortic thromboembolism are the most common causes of cardiac death in cats with HCM (Fox *et al.* 2018; Novo Matos *et al.* 2022). In contrast, sudden death was the most common cause of cardiac death in the present study at post-mortem examination. The reason for this difference is uncertain, although it may have been due to chance considering the relatively small sample size and the small number of cats dying due to HCM in the present study. Furthermore, post-mortem diagnosis of other causes of sudden death, including asthma, neurological causes, anaphylaxis, and pulmonary embolism can be challenging. Due to the high prevalence of cardiomyopathy, pathologists may inadvertently attribute the cause of sudden death to subclinical cardiomyopathy. Alternatively, not all cases of sudden death may have been recorded in previous studies, as they rely on owners to provide the data. In humans with HCM, sudden death is the most common cause of death, and is also more common in young patients (McKenna *et al.* 1981; McKenna and Behr 2002). It is possible that the incidence of sudden death in cats with HCM is higher than previously described.

Loud heart murmurs, neutering in female cats, and receiving medications were associated with the detection of HCM using echocardiography in the present study. A loud heart murmur was previously shown to predict diagnosis of HCM (Payne *et al.* 2015). In the present study, neutered female cats had higher rates of HCM than intact female cats. While male cats have been previously reported to be at risk for HCM, to the authors' knowledge no predisposition in neutered female cats has previously been reported. While this association may have been due to random chance, it is possible that oestrogen could provide some protection against HCM. It is possible that previous studies did not observe a reduced rate of HCM in intact females as cats in the UK and USA are typically spayed and therefore surveys may have contained few intact queens. The present study also showed that cats receiving medication had higher rates of HCM than cats not receiving medications. Medications may predispose to HCM either directly (certain non-steroidal anti-inflammatory drugs may cause systemic hypertension in humans; Grosser *et al.* 2005) or the stress of being medicated may increase blood pressure. Alternatively, concurrent illnesses that require medication may predispose cats to HCM, perhaps by increasing blood pressure. Due to the small number of cats receiving medications in this study, further statistical analysis of the effect of individual medication was not possible.

There are some limitations in this study. First, the general sonographic machine used to perform echocardiography was not a cardiac-specific machine. This was adequate in quality but limited the cardiac assessment of the cats to 2D imaging. Second, not all differentials of an HCM phenotype were ruled out using blood tests. However, each cat in the colony unit undergoes a yearly veterinary examination and weekly evaluation of appetite, thirst and body weight. It is possible some cats may have had early hyperthyroidism or hypersomatotropism. However, none of the cats in the HCM group developed any symptoms in the 2 years following the data collection, making this unlikely. Third, the echocardiographic prevalence of cardiomyopathy was assessed by a single cardiologist at a single time point. Although cardiac measurements from 2D imaging are considered highly repeatable among cardiologists, the objective criteria used to define types of feline

cardiomyopathy can vary among cardiologists. Lastly, the 10-year mortality data from the CFN was collected retrospectively, and many pathologists were involved in the post-mortem examinations. There may therefore be some unaccounted variation in approaches to assessing cardiac abnormalities post-mortem in this study. A prospective study would be required to test repeatability and standardise the post-mortem diagnosis of cardiac abnormalities among veterinary pathologists.

In summary, the results of this study suggest that around 15% (95% CI = 9.5–22.4%) of non-purebred cats in NZ may have HCM without clinical signs of disease. This is important for clinicians to be aware of because subclinical HCM may complicate anaesthesia and increase the risks associated with IV fluid therapy and corticosteroid therapy. Additionally, if subclinical HCM is identified in cats, preventative treatments can be started that may prolong their lifespan. Many cats in this study died of non-cardiac diseases despite having evidence of HCM on post-mortem examination. This suggests that subclinical HCM may have a more favourable prognosis in cats than has previously been believed.

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