

ORIGINAL ARTICLE

Occurrences of heart disease in apparently healthy cats in Klang Valley, Malaysia

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ABSTRACT

Objective: Annual health screening inclusive of heart workup is recommended for the detection of heart diseases, especially in asymptomatic patients (no clinical signs). This study determined the occurrences of the common heart disease and the risk factors in apparently healthy cats.

Material and methods: This prospective study that screened 59 healthy cats and the status of the heart were evaluated based on a combination of findings from physical examination, electrocardiography, blood pressure measurement, routine blood test, urinalysis, and total thyroid level.

Results: Approximately 40.7% ($n = 24/59$) of the apparently healthy cats were diagnosed with heart disease hypertrophic cardiomyopathy (62.5%) remains to be the most commonly diagnosed. The mean age was 4.9-year old (age range, 7-month-old to 19-year-old). The prevalence was higher in males (45.0%; $n = 17/38$) cats, especially the domestic shorthairs (46.0%; $n = 11/24$). Among the healthy cats with vertebral heart scale (VHS) > 8.0 , only 52% ($n = 12/23$) of them were diagnosed with cardiomyopathy. However, 33% ($n = 12/36$) of the cats with normal VHS ≤ 7.9 were diagnosed with heart disease. Consistently, all healthy cats with abnormal heart sounds were diagnosed with heart disease. About 31.4% ($n = 16/51$) of these cats with typical heart sound had cardiomyopathy too.

Conclusion: The occurrence of cardiomyopathy in apparently healthy cats has no association with the patient's age, sex, and VHS, except for the heart sound. Echocardiography remains the best diagnostic tool, as normal heart size and normal heart sound do not exclude cardiomyopathy in this group of apparently healthy cats.

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Introduction

Cats diagnosed with heart disease are often associated with congestive heart failure (CHF) due to combinations of abnormal structure and function of the cardiac muscles, chambers, and valve. Feline cardiomyopathy can be grouped into three categories, which are congenital heart disease, acquired heart disease, and other forms of structural heart disease [1]. There are four main classifications of acquired cardiomyopathy in cats, namely, hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy (DCM), restrictive cardiomyopathy (RCM), and unclassified cardiomyopathy. HCM remains the most prevalent heart disorder in cats [1,2]. Based on the retrospective study by Khor et al. [3], the overall prevalence of heart disease cat patients diagnosed in University Veterinary Hospital (UVH), Universiti Putra Malaysia (UPM) from the year 2013

to 2015 was 1% ($n = 155/15,493$). About 0.99% of the cats diagnosed with heart disease acquired heart disease, while the remaining 0.01% was diagnosed with congenital heart disease. The males cats appeared more frequently diagnosed with cardiomyopathy than in females [3].

Cats with cardiac disease may appear to remain asymptomatic throughout their life, and clinical signs often observed as a sequela of CHF or feline aortic thromboembolism (FATE), leading to death [2,4]. According to the New York Heart Association Classification [5], these asymptomatic cats are categorized as Class I, where heart disease is present in the affected cats that do not shows clinical signs even with exercise. Khor et al. [3] reported that out of 155 heart disease patients presented, 10 of these cats ($n = 10/155$) were asymptomatic, and heart disease was diagnosed only during annual health screening

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or pre-anesthetic health screening. Otherwise, these cats seemed healthy upon presentation. Paige et al. [6] showed that 16 out of 103 cats that appeared healthy had heart disease. Out of the 16 cats, the murmur was not detected in 11 cats with heart disease. Most of the cats appeared and had no signs of cardiomyopathy, perhaps due to the sedentary nature of cats [6].

To date, none to our knowledge had observed cardiomyopathy among the healthy cohorts of cats in Malaysia. This study determined the prevalence and the common type of heart disease in apparently healthy cats. Other associated factors such as sex, breed, age, heart sound, and vertebral heart scale (VHS) that may be potential risk factors of cardiomyopathy in apparently healthy cats were investigated.

Materials and Methods

Ethical approval

Before the recruitment of their pet cat into the study on screening for heart disease, consent was obtained from the cat owner. Any cat that was non-compliant to routine restraining during the consult was allowed to withdraw from the study to avoid unnecessary stress imposed on their cat. This study obtained approval from the Institutional Animal Care and Use Committee (UPM/IACUC/AUP: R087/2014).

Study design

This prospective study was conducted in a veterinary hospital that accepts both primary and referral cases. The case file of apparently healthy cats with no clinical signs associated with any diseases was retrieved. Often these cats were presented at UVH for either an annual vaccination for health screening and/or pre-anesthetic screening. The cat owners were contacted and offered a full cardiac examination for their cats. Only one apparent healthy cat will be selected if the cat came from a multi-cat household.

Health screening and inclusion criteria of the healthy cat

Information such as cat's signalment (i.e., age, gender, breed, and body weight) was obtained. Cats were recruited as healthy based on the following criteria: (1) unremarkable findings from physical examination with 3–5/5 body condition score [7], (2) thoracic auscultation identified a typical lung sound (3) normal sinus rhythm or sinus tachycardia with a mean electrical axis between -10 and $+140$ based from the six-lead electrocardiogram (ECG) [8], (4) normal blood pressure measurement [9], (4) has a normal parameter of the blood hemogram and serum biochemistry, (5) normal urinalysis findings and (6) normal serum total T4 (IDEXX SNAP® Total T4 Test Kits).

Heart and lung auscultation of the healthy cats recruited

The information on physical examination, specifically of the heart and lung auscultation of the healthy cats, were recorded. Five heart rate measurements were recorded, averaged, and further categorized as normal bradycardia and tachycardia. The heart sounds noted described as either as normal, murmur (of Grade I to Grade IV), and gallop rhythm. Five respiratory rate measurements were recorded and averaged.

Radiography

Thoracic radiography of lateral and dorsal-ventral views was obtained for each cat. The VHS of the heart of each cat was measured by comparing the sum of the cardiac long (CLA) and short (CSA) axis to the length of the thoracic vertebrae, starting from the 4th thoracic vertebrae (at the cranial edge of T4). The measurement from the ventral border of the largest bronchi main stem from the tracheal bifurcation to the apex of the heart was referred to as CLA. At the same time, the CSA was measured perpendicularly to the CLA, suggested as the maximum heart width [10]. According to Guglielmini et al. [10], a VHS of more than eight was referred to as cardiomegaly.

Echocardiography

All the healthy cats were subjected to echocardiography imaging. Echocardiographic examination using Esaote MyLab™ ClassC (Genova, Italy) was performed with the cat being gently restrained on right lateral recumbency on a well-padded custom-made built table (Medical Plus Pte. Ltd, Singapore). The placement of the transducer probe (12 MHz) was on the right thorax. During the examination, a simultaneous lead II ECG was recorded. All the echocardiography were obtained by a single echocardiographer (KKH).

Using the two-dimension (2-D) short-axis and M-mode images, the measurements of the left ventricle (LV) made from a right parasternal short-axis view at the level of the papillary muscles were obtained [11]. Using the leading-edge method [12], a measurement obtained were as follows: (i) the thickness of the LV in both diastole and systole phase [which consists of Interventricular septum at diastole (IVSd), Left ventricular free wall at diastole (LVFWd), Interventricular septum at systole (IVSs), and Left ventricular free wall at systole (LVFWs)] and (ii) the internal diameter of the LV in diastole and systole [Left ventricular internal diameter at diastole (LVIDd) and Left ventricular internal diameter at systole (LVIDs), respectively] phase. Using a modified described technique [13] and adopting the right parasternal 2-D short-axis view at the heart base, the left atrium (LA) and aortic root (Ao) dimensions were measured. A measured line placed along the commissure between the

non-coronary and the remaining coronary aortic valve cusps through the Ao and LA. These measurements were recorded during atrial systole at the onset of the P wave [14]. All the valves and the outflow tracts were assessed using color-flow and pulsed-wave Doppler to identify valvular insufficiencies or any outflow obstruction suggestive of non-HCM cardiac disease. The peak of LV outflow tract velocity was quantified when the systolic anterior motion (SAM) of the mitral valve was observed with HCM. Five measurements were obtained from four to five different images and averaged.

Data analysis

All the information and data collected from the case files of apparently healthy cats were tabulated in Microsoft® Office Excel 2010. Data were tested for normality, and descriptive analysis was done using IBM SPSS version 23 (IBM, USA). Statistical analysis was conducted with cross-tabulation, Pearson Chi-square test, risk estimate test, and Cramer's V test. A *p*-value of < 0.05 was considered to be significant.

Results

Seventy apparently healthy cats were recruited, of which 11 cats withdrawn from the study as these cats were either non-compliant cats (*n* = 5) to minimal handling during the procedure of blood collection, blood pressure monitoring, and examination using electrocardiography, or were not healthy. Five cats were diagnosed with kidney disease, and one cat had hyperthyroidism.

In total, 59 healthy cats with an averaged body weight of 4.3 kg (body weight range, 1.8–6.8 kg) were recruited. Thirty-five out of 59 cats (59%) were diagnosed to be healthy, while 41% (*n* = 24/59) of them were found to have cardiomyopathy (Fig. 1). The majority of the healthy cat was diagnosed with HCM and followed by RCM. The remaining three healthy cats were diagnosed with inter-ventricular septal defect (IVSD), left ventricular outflow tract obstruction (LVOTO), and SAM of the mitral valve, respectively (Fig. 1). Table 1 shows the number of genders (male vs. female) affected in each type of cardiomyopathy diagnosed.

The mean age of apparently healthy cats recruited in this study was 5-year old (age range, 7-month-old to 19-year-old). The cats were further categorized into two groups (Table 2). There was no association (*p* = 0.940) between age group and cardiomyopathy in the apparent healthy cats even though cats of less than 5-years old appeared to be more likely to be affected.

In this study, the majority of the apparent healthy cats recruited were male (64%) compared to female cats (Table 2). There was no association (*p* = 0.390) between gender group and cardiomyopathy in the apparent healthy cats. Out of these 21 healthy female cats, 33% (*n* = 7/21) of these cats was diagnosed with cardiomyopathy, while for the male cats, 45% (*n* = 17/38) of the cats were found to have cardiomyopathy. HCM appeared frequently diagnosed in both female (*n* = 4/7) and male (*n* = 11/17) healthy cats,

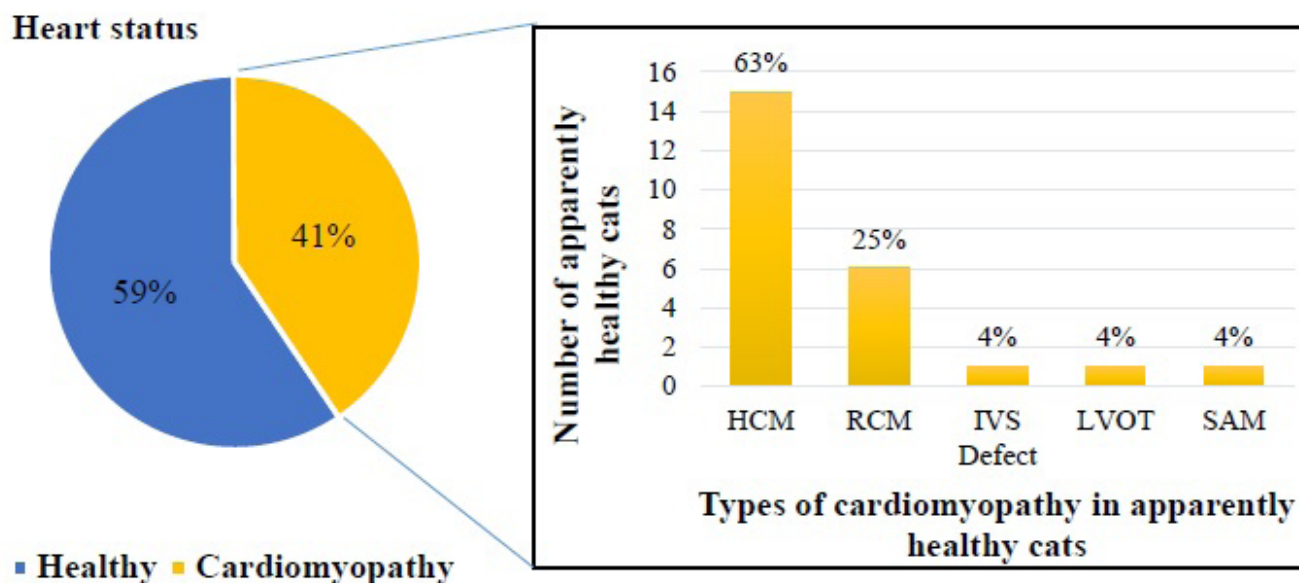


Figure 1. (Left) Heart status of the healthy cats presented (*n* = 59) and (Right) types of cardiomyopathy diagnosed in apparently healthy cats (*n* = 59).

Table 1. Types of cardiomyopathy diagnosed in apparently healthy heart disease cats ($n = 24/59$) and the affected gender distribution Table 1.

| Types of cardiomyopathy | Healthy cats diagnosed with heart disease | | Gender | |
|-----------------------------------|-------------------------------------------|-----|------------------|--------------------|
| | <i>n</i> | % | Male <i>n</i> | Female <i>n</i> |
| Hypertrophic cardiomyopathy (HCM) | 15 | 63 | 11 | 4 |
| RCM | 6 | 25 | 4 | 2 |
| IVSD | 1 | 4 | 1 | 0 |
| LVOTO | 1 | 4 | 1 | 0 |
| SAM of the mitral valve | 1 | 4 | 0 | 1 |
| Total | 24 | 100 | 17 | 7 |

Table 2. The distribution of the age, gender, and breed of the healthy diagnosed with or without cardiomyopathy.

| Signalment | Healthy cats (<i>n</i> = 59) | Diagnosed with cardiomyopathy | | | | Odd ratio | <i>p</i> -value | |
|------------|----------------------------------|-------------------------------|----|----------|----|-----------|-----------------|-------|
| | | No | | Yes | | | | |
| | | <i>n</i> | % | <i>n</i> | % | | | |
| Age | < than 5-year old | 39 | 23 | 39 | 16 | 27 | 1.04 | 0.940 |
| | 5-year old and above | 20 | 12 | 21 | 8 | 13 | | |
| | Total | 59 | 35 | 60 | 24 | 40 | | |
| Gender | Male | 38 | 21 | 36 | 17 | 29 | 1.63 | 0.390 |
| | Female | 21 | 14 | 24 | 7 | 11 | | |
| | Total | 59 | 35 | 60 | 24 | 40 | | |
| Breed | Domestic Shorthair | 36 | 25 | 42 | 11 | 18 | N/A | |
| | Persian | 10 | 4 | 6 | 6 | 9 | | |
| | Maine Coon | 5 | 2 | 4 | 3 | 5 | | |
| | Bengal | 1 | 1 | 2 | - | - | | |
| | Domestic Longhair | 1 | 1 | 2 | - | - | | |
| | Kinkalow | 1 | - | - | 1 | 2 | | |
| | Siamese | 1 | 1 | 2 | - | - | | |
| | Sphynx | 1 | - | - | 1 | 2 | | |
| | Syberian | 1 | - | - | 1 | 2 | | |
| | Exotic Shorthair cross | 1 | - | - | 1 | 2 | | |
| | Persian cross | 1 | 1 | 2 | - | - | | |
| | Total | 59 | 35 | 60 | 24 | 40 | | |

followed by RCM, IVSD, LVOTO, and SAM of the mitral valve (Table 1).

In this present study, the majority of the healthy cats were Domestic Shorthair cats, followed by Persian cats, and Maine coon cats. As for other breeds like the Bengal, Domestic Longhair, Domestic Shorthair cross, Kinkalow, Persian cross, Siamese, Sphynx, and Siberian, there was only one patient recruited for each breed (Table 1). Out of the 36 domestic shorthairs (DSH) cats, 18% of them were diagnosed with cardiomyopathy, which comprised of HCM ($n = 8/11$), RCM ($n = 2/11$), and SAM of the mitral valve ($n = 1/11$).

For the Persian cats, 6 out of the 10 of them were diagnosed with cardiomyopathy (HCM, $n = 4$, and RCM, $n = 2$, respectively). Three out of five apparently healthy Maine Coon cats were diagnosed with cardiomyopathy (HCM, $n = 2$ and LVOTO, $n = 1$).

Based on the heart auscultation findings, the apparently healthy cats diagnosed with cardiomyopathy were infrequently found to have abnormal heart sound, whereas a substantial number of the healthy cats with typical heart sound were diagnosed with cardiomyopathy (28%; $n = 16/59$) (Table 3).

Table 3. The distribution of the type of heart sound and VHS in the healthy diagnosed with or without cardiomyopathy.

| | | Apparently healthy cats (<i>n</i> = 59) | Diagnosed with cardiomyopathy | | | | Odd ratio | <i>p</i> -value |
|-------------|----------|---------------------------------------------|-------------------------------|----|----------|----|-----------|-----------------|
| | | | No | | Yes | | | |
| | | | <i>n</i> | % | <i>n</i> | % | | |
| Heart sound | Normal | 51 | 35 | 59 | 16 | 28 | N/A | |
| | Abnormal | 8 | - | - | 8 | 13 | | |
| VHS | ≤ 7.9 | 36 | 24 | 41 | 12 | 20 | 2.22 | 0.150 |
| | > 8.0 | 23 | 11 | 19 | 12 | 20 | | |

VHS = Vertebral heart score.

About 61% (*n* = 36/59) of the healthy cats had a VHS ≤ 7.9, and 12 out of the 36 cats were diagnosed with cardiomyopathy. The remaining 39% (*n* = 23/59) of the healthy cats had a VHS > 8.0, and 12 of these cats were diagnosed with cardiomyopathy (Table 3). However, there was no association (*p* = 0.150) between VHS and cardiomyopathy in the apparent healthy cats.

Discussion

This prospective study provided information on the occurrences of cardiomyopathy in apparently healthy cats presented in a teaching hospital (UVH, UPM) within 2 years was at 41%. HCM remains to be the most commonly diagnosed, followed by RCM, IVSD, LVOTO, and SAM of the mitral valve. This finding was consistent with a study [6], where HCM was the most commonly diagnosed form of cardiomyopathy among the healthy cats. In comparison to symptomatic cats (with presenting signs of heart disease), HCM remained as the most frequently diagnosed in feline patients with heart disease [2,15–17]. The likelihood of cats diagnosed with HCM could be very high compared to other forms of cardiomyopathy in this species, and therefore, early, or annual screening of the heart is recommended [2,6].

To date, echocardiography remains an essential tool in diagnosing cardiomyopathy in cats [1,16]. It is a non-invasive approach to detect cardiac anatomical and physiological abnormalities [18]. Several techniques have been established for cardiac assessment, such as the motion mode (M-mode), two-dimensional (2D), color and spectral Doppler echocardiography to diagnose and monitor heart disease progression in this species [11]. Recently, a defined technique, namely, focused cardiac ultrasound performed by a trained clinician, has improved the rate of heart disease detection pre-clinical stage, and especially in cats with moderate to severe stage of the disease [19]. Besides on that, a variety of different methods and measurements for assessment has been continuously investigated in both healthy and affected cats [20–22]. Cardiac biomarkers have been used, but negative test results may not rule out, but a

positive test result is a reliable indication of cardiomyopathy [23–25]. Hence, echocardiography remains superior in providing a definitive diagnosis [2,11,20].

Acquired heart disease is known as a cardiomyopathy of an unknown etiological agent associated with cardiomegaly and heart failure [16]. Several forms of acquired cardiomyopathy have been recognized in cats, with the three major types, such as HCM, RCM, and followed by DCM [15]. Other than that, there is also secondary cardiomyopathy caused by underlying diseases which involved systemically (systemic hypertension, systemic infection by virus, bacteria, protozoa, or fungus), metabolic (diabetes mellitus, hyperthyroidism), or nutritional (taurine deficiency) [1]. A study reported that the prevalence of acquired heart disease was at 8% (*n* = 145/1,817) [26], whereas one study locally reported at the prevalence of 1% [3]. Ten out of 155 cats diagnosed with heart disease were asymptomatic, whereas the remaining (145 cats) patients were symptomatic. It is observed that this present study has a higher detection rate probably due to specifically targeted population of apparently heart cats. Hence, it suggested that annual health check inclusive echocardiography is recommended.

In this study, the mean age of the apparently healthy cats recruited was 5-year-old (age range, 7-month-old to 19-year-old), slightly younger than those cats documented in a previous study [15, 27]. Both studies reported a mean age of 7-year old with a slightly different age range of between, 6-month-old to 16-year-old diagnosed with cardiomyopathy [15,27]. It can be suggested that cats can be diagnosed at any life-stage, and that age was not an associated risk. Similarly, Ferasin et al. [15] reported that the age of affected cats was extremely variable at different ages and depending on the progression of cardiac disease development. In this group of apparently health cats, cats of less than 5 years were more frequently diagnosed with heart disease despite having unremarkable findings from the routine physical examination conducted, including auscultation.

In this present study, the healthy male cats seemed to have 1.6 times greater chance of being diagnosed with

cardiomyopathy, but findings found that gender was non associated risk factors probably contributed by the over-presentation of male cats and small sample size. It can be assumed that both gender groups provide similar risk towards disease outcomes of cardiomyopathy in the apparent healthy cats. In contrast, studies have reported that HCM was frequently diagnosed cardiomyopathy among male cats with heart disease [15,26–29]. Surprisingly human studies have shown that hormones, specifically low levels of testosterone undergone testosterone therapy, showed a significant reduction in the occurrence of myocardial infarction and stroke [30], and testosterone treatment was found to improve cardiac function [31]. Further investigation in an association of blood testosterone concentration with evidence of cardiomyopathy in cats may provide a further understanding of pathophysiology and development of heart disease, especially in male cats.

The over-presentation of DSH cats in this study has placed this breed to be commonly diagnosed with cardiomyopathy. Spalla et al. [29] claimed that the DSH cats were the most popular cat breed found in Italy as pets and, similarly, in Malaysia. Both the Persian and Maine coon cats were most often diagnosed with HCM, consistent findings reported by Ferasin et al. [15]. Familial occurrence of HCM has been observed in mix-breed [32], Persian [17], and British Shorthair cats [33], while genetic mutation has been identified in Maine coon cats with HCM [34,35]. This factor has been taken into consideration before the conduct of the study. Therefore, only one cat from a multi-cat household was selected to prevent higher detection of cardiomyopathy among cats that might be due to genetic inheritance.

Studies have shown that the cats with heart disease may remain asymptomatic throughout their life, whereby clinical signs will often appear with severe CHF or FATE with high mortality [2,4]. A local study reported a small cohort of cats patients (10/155) diagnosed with heart diseases were asymptomatic, while the rest of the cats succumb to CHF [3]. Ferasin et al. [15] documented that the approximate incidence of murmur detected during auscultation in cats with cardiomyopathy was 60%, followed by, 30% for tachycardia, 20% for gallop rhythm, 10% for arrhythmia, 6% for bradycardia, and 5% for muffled heart sound. However, in apparently healthy cats, heart auscultation is not a reliable indicator as some cats affected cats may not have appreciable heart murmurs [6]. Paige et al. [6] has shown that 11 out of 16 healthy cats diagnosed with cardiomyopathy did not have heart murmurs.

Similarly, in this study, approximately two-thirds of the healthy cats diagnosed with cardiomyopathy had typical heart sound. Hence, it can be concluded that auscultation murmur is a reliable finding of cardiomyopathy. However, it is to be cautioned that a normal heart sound detected

could not rule out a possibility of cardiomyopathy in these cats. Besides, all the healthy cats were diagnosed with cardiomyopathy upon presentation for annual health screening or pre-anesthetic screening. Therefore, it could be speculated that these cats were in the early stage of the heart disease, and perhaps murmur can only be heard as the heart disease progresses.

Thoracic radiography is useful in diagnosing patients with heart diseases, where the abnormal appearance of the cardiac silhouette and pulmonary vessels can be appreciated. Other radiography findings to support clinical signs of CHF would be pulmonary edema, ascites, or pleural effusion. Determining heart size is crucial as an enlarged heart may indicate any pathological cardiac changes [10], and it was reported that radiographic indices with a cut-off point of VHS ≤ 7.9 were adequate in distinguishing cats with the cardiac disease from healthy cats. This study revealed that healthy cats with VHS > 8.0 had 2.2 times greater chance of being diagnosed with cardiomyopathy, but those cats with the VHS ≤ 7.9 had an equal chance of being cardiomyopathy as well. It can be speculated that the accuracy of using VHS as a criterion for the diagnosis of heart disease in apparently healthy cats may not be reliable and is directly influenced by the different type and clinical stage of the cardiac disease diagnosed. In this case, healthy cats with VHS > 8.0 were found to be at higher risk of being diagnosed with cardiomyopathy. But at the pre-clinical stage of HCM, the maybe insignificant findings of the cardiac silhouette, hence appearing normal in size due to the lack of apparent chamber enlargement [36]. Therefore, echocardiography is a much more superior choice over radiographs in providing a diagnosis.

Conclusion

The occurrences of apparently healthy cats presented to UVH, UPM from the year 2016 to 2017 diagnosed with heart disease, was 41% ($n = 24/59$), with HCM being frequently identified. The occurrence of cardiomyopathy in this group of cats has no association with the patient's age, gender, breed (signalment), VHS (heart size), and heart sound of the affected cat. Physical examination alone is not reliable in diagnosing cardiomyopathy in cats. For ante-mortem diagnosis, echocardiography remains the most reliable and non-invasive diagnostic tool for detection of heart disease in cats. It is recommended that owners are to bring their cats for echocardiography screening annually to check for the heart status of their pets and the progress of the cardiac disorders in them if there is any, especially for breeds that are predisposed to heart disease. Other future research studies can venture into areas like genetic screening and testing for cardiac biomarkers in apparently healthy cats.

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Conflict of interest

Both authors do not have conflicts of interest to declare.

Authors' contribution

KKH organized the study, interpretation of findings, and drafted the manuscript. CMX was involved in the collection of data and statistical analysis and also contributed to manuscript preparation.

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