Original Article

Survival time and prognosis factors in hypertrophic cardiomyopathy cats with congestive heart failure

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Abstract

Hypertrophic cardiomyopathy (HCM) is a common myocardial disease in cats. Nowadays, there is no study determining the survival time of cats affected with HCM in Thailand. This study aimed to evaluate the survival time in HCM cats with congestive heart failure (CHF) in Thailand and to determine the factors associating with survival time. A retrospective study was performed in 47 HCM cats to analyze survival time and the association of survival time and factors including sex, age, breeds, weight, physical findings, the presence of complications, medication and echocardiographic findings. The data was analyzed by the Log-Rank test and displayed with the Kaplan-Meier curve. The results reveal that the median survival time of HCM cats with CHF was 283 days and factors associating with a lesser survival time were the presence of aortic thromboembolism (ATE), a decrease in left ventricular internal dimension at end-diastole (LVIDd) < 10.8 mm and the use of other cardiovascular drugs besides the combination of angiotensin converting enzyme inhibitors (ACEi) and furosemide. The data of this study is valuable for prognosis and for the future management of HCM cats with CHF.

Keywords: cat, congestive heart failure, hypertrophic cardiomyopathy, survival time

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Introduction

Hypertrophic cardiomyopathy (HCM), the most common heart disease in cats, is caused by an abnormality of myocardium related to myocardial dysfunction. Hypertophic cardiomyopathy is commonly found in Thailand but its prevalence has not been published. This disease is usually diagnosed in the middle-age of cats (median age 6.2 years with a range of 0.75 to 17.4 years) (Payne et al., 2013). Male cats are more prone to the disease (Payne et al., 2013). Hypertrophic cardiomyopathy is commonly found in domestic short hair (DSH) and purebred cats such as Ragdoll, Maine Coon, Himalayan, Burmese, Sphynx, Persian, and Devon Rex.

Hypertrophic cardiomyopathy primarily affects the left ventricular myocardium and can cause left-sided congestive heart failure (CHF) in the late stage of the disease. Intracardiac thrombi and aortic thromboembolism (ATE) may develop in HCM cats with a severely enlarged atrium (White, 2015).

There have been several studies reporting the survival time in HCM cats (Atkins et al., 1992; Rush et al., 2002; Payne et al., 2010). However, there has been no report in Thailand. Previous studies indicate that the prognosis of cats with HCM is highly variable depending on variations in diagnosis and treatment protocols, clinician opinions, the financial constraints of the owner and owner compliance. Payne et al. (2013) showed that cats presented with an extreme left ventricular hypertrophy (≥9 mm), left ventricular fractional shortening ≤30%, and decreasing in the left atrium to %fractional shortening had a poor prognosis.

As mentioned previously, HCM is a life-threatening disease in cats. The purpose of the study reporting here is to determine the survival time and prognostic indicators of HCM cats with CHF in Thailand. The results of this study will be valuable information for veterinarians to provide a prognosis to cat owners in Thailand.

Materials and Methods

A retrospective study was performed. Electronic medical records of the Small Animal Teaching Hospital, Faculty of Veterinary Science, Chulalongkorn University from March 2014 to March 2017 were retrieved to identify cats diagnosed with HCM. The day of the echocardiographic examination was defined as the first day of a visit. Information on cats including sex, age, breed, body weight, heart sound, radiographic findings, echocardiographic findings, systolic blood pressure, manifestation of CHF, the presence of arterial thromboembolism (ATE), the presence of concurrent chronic kidney disease (CKD), cardiac medical treatments, duration of treatment, live status, and date of death was recorded. The criteria for CHF diagnosis were clinical signs including respiratory distress or rapid breathing and radiographic findings including pulmonary edema, pleural effusion, and/or ascites. In the case of cats that did not have a death-alive-status or date of death at the end of the study in March 2017, the death-alive-status was confirmed by telephone interviewing with the owners. If the death-alive status could not be confirmed, these cats were excluded from the study. Data of cats dying from other causes than cardiac death was not included.

All cats had echocardiography performed by one investigator. The diagnostic criteria for HCM consisted of a thickened left ventricular wall (≥6 mm) and a decreased left ventricular chamber size. Echocardiographic data including types of hypertrophy (symmetry/asymmetry), left ventricular internal dimension at end-diastole (LVIDd), fractional shortening, the presence of spontaneous contrast in the left atrium, left atrial dimension at end-diastole (LA), the ratio of left atrial dimension to the aortic annulus dimension (LA:Ao) and the ratio of peak velocity of early diastolic to late diastolic transmitral flow of mitral valve (E:A) were recorded (Boon, 2017).

Data analysis was performed by a commercial statistical program (IBM SPSS 22, USA). Descriptive statistical analysis was used to identify the population characteristics. The univariable Cox-regression was analyzed for the hazard of death. The survival time analysis was performed by the Kaplan-Meier survival curve. The difference of the survival curves was compared by the Log-rank test. $P < 0.05$ was considered to be of statistical significance. The survival time was presented as median and 95% confident interval (CI). The data from live cats at the end of the study was censored.

Results

Data from 47 HCM cats with CHF was retrieved. The median survival time of 47 HCM cats with CHF was 283; 95% CI 1-596 days.

Breeds of HCM cats in this study included DSH (48%, 23/47), Persian (40.4%, 19/47), American Shorthair (4.26%, 2/47), Maine Coon (2.12%, 1/47), Scottish Fold (2.12%, 1/47), and Exotic Shorthair (2.12%, 1/47). There were 51.1% males (24/47), seventeen intact and seven neutered male cats, and 48.9% female (23/47), six intact and seventeen spayed female cats. The descriptive data of cats recruited to the study is presented in Table 1. Twenty-six cats had cardiomegaly with pulmonary edema. Thirteen cats had pleural effusion, and four cats had pleural effusion and ascites. Four cats had both pulmonary edema and pleural effusion. Twenty-five cats died during the study period and twenty-two cats were alive at the end of the study.

The result from the Cox-regression analysis is summarized in Table 2. Hypertrophic cardiomyopathy cats with the presence of ATE and a decrease in LVIDd had an increased hazard of death compare to those without these conditions (Table 2). In addition, HCM cats treated with ACEi and furosemide had a decreased hazard of death compared with those treated with other cardiovascular drugs (Table 2).

A comparison of survival times of HCM cats depending on different categories is summarized in Table 3. The presence of ATE, a decrease of LVIDd, and the use of ACEi and furosemide affected the survival time of HCM cats with CHF (Table 3). The survival time was not different when analyzed with other parameters including age, breed, sex, heart sound, systolic blood pressure, % fractional shortening, types

of hypertrophy, LA, LA:Ao, E:A, and the presence of spontaneous contrast.

The survival time between HCM cats with ATE and without ATE was distinctly different (p < 0.0001) (Figure 1, Table 5). Cats with LVIDd <10.8 mm had a shorter survival time than those with LVIDd >10.8 mm (p = 0.009) (Figure 2, Table 5). According to the treatment protocol, cats treated with ACEi and furosemide had a longer survival time than cats treated with other cardiovascular drugs besides ACEi and furosemide including diltiazem, pimobendan, or atenolol (p = 0.019) (Figure 3, Table 5).

There were thirteen cats presented with CKD. The median survival time of 17 cats with CKD (339; 95% CI 60-617 days) and without CKD (230; 95% CI 96-363 days) (p=0.657) was no different. A sub-analysis from data of HCM cats without CKD was performed. The comparison of survival time of HCM cats without CKD depending on different categories is summarized in Tables 4 and 5.

Table 1 Descriptive data of hypertrophic cardiomyopathy cats recruited in the study

Category	Median	Interquartile range
Age (years)	8	3.8-12
Weight (kg)	3.8	3.0-4.8
Blood pressure (mmHg)	140	115-170
Echocardiography		
Fractional shortening (%)	58.13	47.19-67.47
LVIDd (mm)	13.4	12.2-15.6
LA (mm)	15.6	12.6-17.4
LA:Ao	1.8	1.35-2.31
E:A	1.18	0.86-2.24

LVIDd, left ventricular internal dimension at end-diastole; LA, left atrium; LA:Ao, the ratio of left atrial dimension to the aortic annulus dimension; E:A, the ratio of peak velocity of early diastolic to late diastolic transmitral flow of mitral valve

Table 2 The result of the Cox-regression analysis for the hazard of death

Parameters	Category	Hazard ratio	95% CI	P value
Age (years)	<7 and >7	0.665	0.284-1.559	0.348
Breed	DSH and others	1.4	0.635-3.09	0.405
	Persian and others	0.972	0.436-2.168	0.944
	DSH and persian	1.195	0.529-2.696	0.668
Sex	Male and female	0.573	0.259-1.269	0.170
Heart sound	Normal and abnormal	1.430	0.622-3.287	0.400
Blood pressure (mmHg)	<160 and >160	1.262	0.443-3.591	0.663
ATE	Presence and absence	5.169	1.932-13.834	0.001
CKD	Presence and absence	1.230	0.491-3.085	0.658
Echocardiography				
Fractional shortening (%)	<40, 40-60 and >60	0.872	0.248-3.069	0.831
Types of hypertrophy	Asymmetry and symmetry	1.145	0.520-2.523	0.737
LVIDd (mm)	<10.8 and >10.8	3.257	1.274-8.327	0.014
LA (mm)	<16 and >16	1.277	0.579-2.816	0.544
LA:Ao	<2 and >2	0.614	0.280-1.347	0.224
E:A	<1: impaired 1-2: pseudonormalized >2: restrictive	0.304	0.080-1.150	0.080
Spontaneous contrast	Presence and absence	1.027	0.407-2.594	0.955
Medication				
ACEi and Furosemide	With and without	0.377	0.161-0.881	0.024

ACEi, angiotension converting enzyme inhibitor; ATE, aortic thromboembolism; CI, confident interval; CKD, chronic kidney disease; DSH, domestic short hair; LVIDd, left ventricular internal dimension at end-diastole; LA, left atrium; LA:Ao, the ratio of left atrial dimension to the aortic annulus dimension; E:A, the ratio of peak velocity of early diastolic to late diastolic transmitral flow of mitral valve

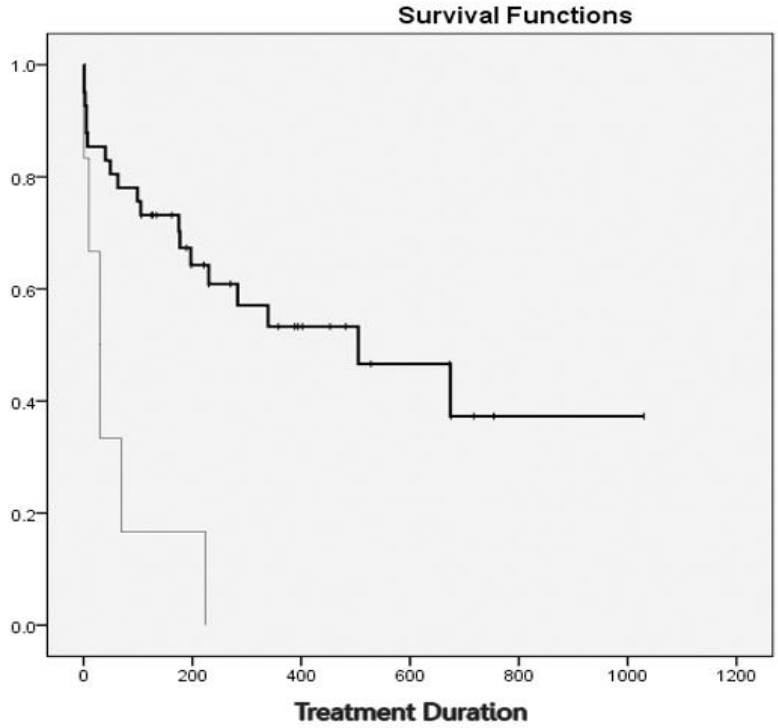

Figure 1 Kaplan-Meier survival curves for hypertrophic cardiomyopathy cats with arterial embolism (ATE) (regular line) and without ATE (bold line). The two curves differ significantly ($p < 0.0001$). Hypertrophic cardiomyopathy cats with ATE had a shorter survival time.

Table 3 The percentage of hypertrophic cardiomyopathy cats categorized in comparison to survival time

Parameters	Category	Numbers (%)	*P* -value
Age (years)	>7 and <7	27 (57.4) and 19 (40.4)	0.343
Breed	DSH and others	23 (48.9) and 24 (51.1)	0.401
	Persian and others	19 (40.4) and 28 (56.6)	0.944
	DSH and Persian	23 (48.9) and 19 (40.4)	0.667
Sex	Male and Female	24 (51.1) and 23 (48.9)	0.163
Heart sound	Normal and abnormal	17 (36.2) and 30 (63.8)	0.396
Blood pressure (mmHg)	<160 and >160	27 (57.4) and 10 (21.3)	0.662
ATE	Presence and absence	6 (12.8) and 41 (87.2)	<0.0001
CKD	Presence and absence	13 (27.7) and 34 (72.3)	0.657
Echocardiography			
Fractional shortening (%)	<40	6 (12.8)	0.976
	40-60	18 (38.3)	
	>60	23 (48.9)	
Types of hypertrophy	Asymmetry and symmetry	27 (57.4) and 20 (42.6)	0.736
LVIDd (mm)	<10.8 and >10.8	7 (14.9) and 40 (85.1)	0.009
LA (mm)	<16 and >16	23 (48.9) and 24 (51.1)	0.542
LA:Ao	<2 and >2	27 (57.4) and 19 (40.4)	0.217
E:A	<1	17 (36.2)	0.086
	1-2	13 (27.7)	
	>2	13 (27.7)	
Spontaneous contrast	Presence and absence	13 (27.7) and 34 (72.3)	0.954
Medication			
ACEi and Furosemide	With and without	23 (57.5) and 17 (42.5)	0.019

P<0.05 indicates statistically significant

ACEi, angiotensin converting enzyme inhibitor; ATE, aortic thromboembolism; CKD, chronic kidney disease; DSH, domestic short hair; LVIDd, left ventricular internal dimension at end-diastole; LA, left atrium; LA:Ao, the ratio of left atrial dimension to the aortic annulus dimension; E:A, the ratio of peak velocity of early diastolic to late diastolic transmitral flow of mitral valve

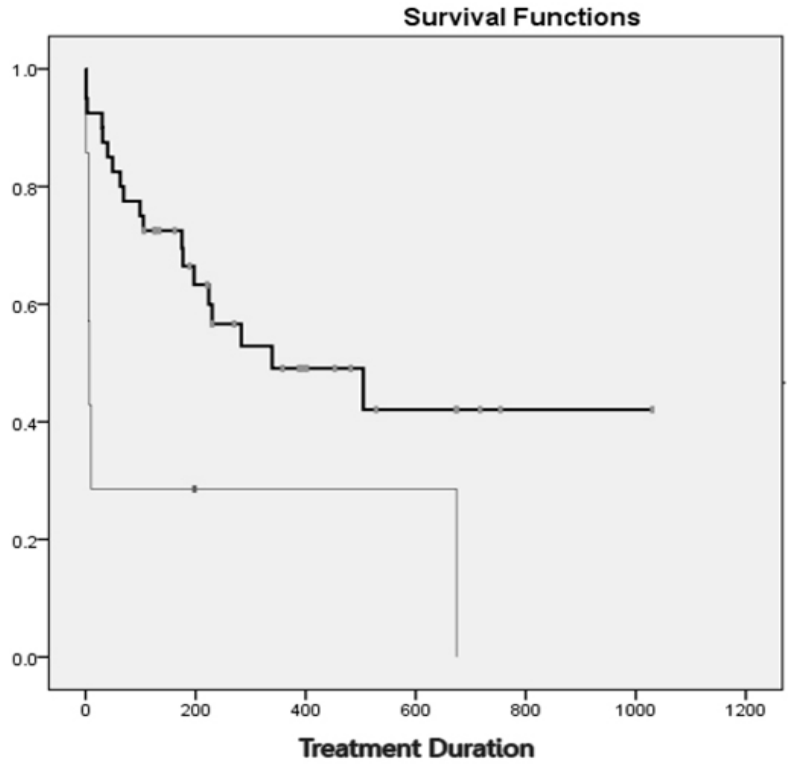

Figure 2 Kaplan-Meier survival curves for the group of cats with normal left ventricular internal dimension at end-diastole (LVIDd) >10.8 mm (bold line) and <10.8 mm (regular line). The two curves differ significantly (p = 0.009). Cats with LVIDd >10.8 mm had a longer survival time.

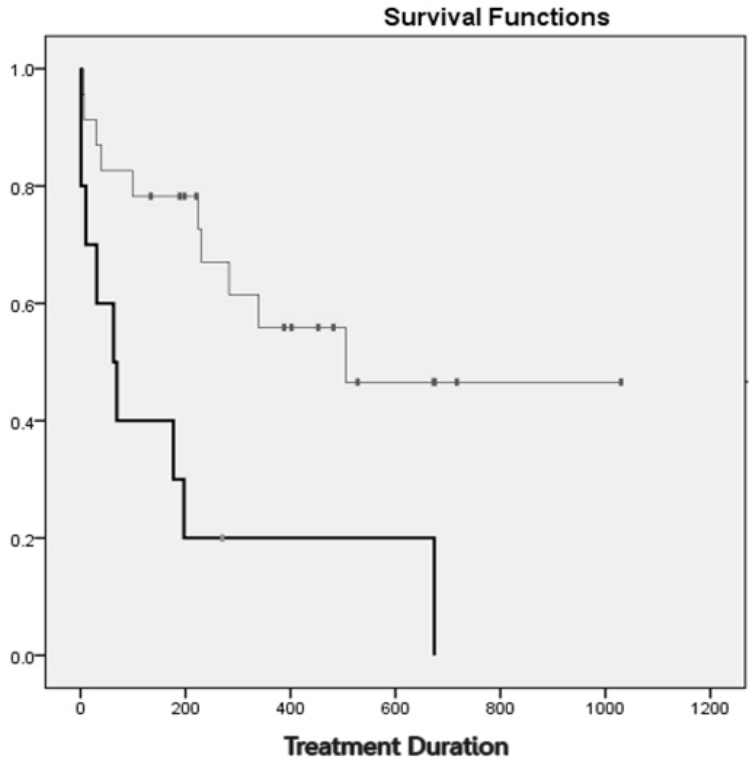

Figure 3 Kaplan-Meier survival curves for cats treated with angiotensin converting enzyme inhibitor (ACEi) and furosemide (regular line) and cats treated with other cardiovascular drugs (bold line). The two curves differ significantly (p = 0.019). Cats treated with ACEi and furosemide had a longer survival time.

Table 4 The percentage of hypertrophic cardiomyopathy cats without chronic kidney disease categorized in comparison to survival time

Parameters	Category	Numbers (%)	*P* -value
Age (years)	>7 and <7	14 (41.18) and 19 (55.88)	0.227
Breed	DSH and others	17 (50) and 17 (50)	0.375
	Persian and others	13 (38.24) and 21 (61.76)	0.906
	DSH and Persian	17 (50) and 13 (38.24)	0.652
Sex	Male and female	18 (52.94) and 16 (47.06)	0.270
Heart sound	Normal and abnormal	16 (47.06) and 18 (52.94)	0.757
Blood pressure (mmHg)	<160 and >160	21 (61.76) and 3 (8.82)	0.746
ATE	Presence and absence	6 (17.65) and 28 (82.35)	0.001
Echocardiography			
Fractional shortening (%)	<40	6 (17.65)	0.925
	40-60	12 (35.29)	
	>60	16 (47.06)	
Types of hypertrophy	Asymmetry and symmetry	15 (44.12) and 19 (55.88)	0.562
LVIDd (mm)	<10.8 and >10.8	6 (17.65) and 28 (82.35)	0.001
LA (mm)	<16 and >16	14 (41.18) and 20 (58.82)	0.195
LA:Ao	<2 and >2	17 (50) and 16 (47.06)	0.506
E:A	<1	10 (29.41)	0.057
	1-2	12 (35.29)	
	>2	10 (29.41)	
Spontaneous contrast	Presence and absence	12 (35.29) and 22 (64.71)	0.954
Medication			
ACEi and Furosemide	With and without	5 (50) and 5 (50)	0.696

P<0.05 indicates statistically significant

ACEi, angiotensin converting enzyme inhibitor; ATE, aortic thromboembolism; CKD, chronic kidney disease; DSH, domestic short hair; LVIDd, left ventricular internal dimension at end-diastole; LA, left atrium; LA:Ao, the ratio of left atrial dimension to the aortic annulus dimension; E:A, the ratio of peak velocity of early diastolic to late diastolic transmitral flow of mitral valve

Table 5 Different median survival time in hypertrophic cardiomyopathy cats with different categories

Parameters	Category	Median	95% CI
All HCM cats			
ATE	Presence	30	5-55
	Absence	505	125-885
LVIDd)mm(	<10.8	7	2-12
	>10.8	339	14-664
ACEi and Furosemide	With	505	156-854
	Without	69	1-274
HCM cats without CKD			
ATE	Presence	30	5-55
	Absence	674	16-1332
LVIDd)mm(	<10.8	5	1-10
	>10.8	222	134-373
ACEi and Furosemide	With	267	162-453
	Without	63	1-127

ACEi, angiotensin converting enzyme inhibitor; ATE, aortic thromboembolism; CI, confident interval; CKD, chronic kidney disease; HCM, hypertrophic cardiomyopathy; LVIDd, left ventricular internal dimension at end-diastole

Discussion

A previous study demonstrated that Ragdoll and Main Coon cats have more chance to develop HCM (Payne et al., 2010). Moreover, the survival time of these breeds was shorter than other breeds. However, Ragdoll and Main Coon cats are rare in Thailand. The popular cat breeds in Thailand are DSH and Persian, which are also the major population of HCM cats in this study. The median age of HCM cats in this study was eight years (range 3.8-12.0 years). This result is in agreement with a previous study suggesting that HCM usually develops in aging cats (Wess et al., 2010; Visser et al., 2017). However, breed and age did not affect the survival time based on the result of this study.

63.8 % of cats in this study had abnormal heart sound. Other studies found that 78-88.2% of cats with HCM presented with abnormal heart sound (Payne et al., 2010; Rush et al., 2002). A previous study showed that the presence of a galloping heart sound was related to a worse survival time (Payne et al., 2013). However, the characteristics of heart sound did not affect the survival time in the group of cats in this study.

There were variations in survival time in HCM cats reported previously including 1276 days in

England (Payne et al., 2010) and 732 days in the United States (Atkins et al., 1992). However, the inclusion criteria for cats in each study were different. The stage of the disease, the treatment protocol and owner compliance might affect the survival time. Therefore, the survival time of cats from each study may not be comparable.

There was a study reporting that up to 21% of cats with HCM develop ATE (Fuentes, 2012). 12.8% of cats in the present study had ATE. These ATE cats had a shorter survival time and a higher risk of death than those cats without ATE. This result suggests that signs of ATE are a good indicator for a poorer prognosis in cats affected with HCM.

A decrease of LVIDd was significantly associated with decreased survival time in the group of cats in this study. This result is in agreement with the result of a prior study (Sugimoto et al., 2015). The smaller the left ventricular chamber, the less blood volume fills up the ventricle resulting in a decrease in cardiac output. Eventually, the left atrium will become enlarged and left-sided congestive heart failure will develop. From these consequences, a decrease in LVIDd can increase the risk of cardiac death in HCM cats. This presumption supports the result of this study that found a higher risk of death of approximately three times in cats with a small ventricular chamber size than those with a normal ventricular chamber size.

Hypertrophic cardiomyopathy cats treated with ACEi and furosemide stayed longer than those treated with other cardiovascular drugs besides ACEi and furosemide. Furosemide helps HCM cats by reducing excess extravasation fluid in peripheral tissues. Angiotensin converting enzyme inhibitor inhibits renin angiotensin aldosterone system (RAAS) and has benefits to HCM cats by reducing preload and afterload increasing the amount of blood being pumped by the heart (Gordon and Coˆt e, 2015). For these reasons, the combination use of these two drugs, furosemide and ACEi would provide benefits by increasing survival time particularly in HCM cats with CHF.

Although the study was carefully prepared, data from some cats was missed due to the limitation in gathering the information of cats from the owners. This limitation resulted from the retrospective design of the study. Because the missing data was varied in each parameter, the multivariate regression analysis could not be performed.

In conclusion, this study showed that the presence of ATE and the size of the left ventricular chamber during diastole are related to shorter survival time in HCM cats with CHF. These parameters should be included in the diagnostic investigation and the prognosis of the disease. Treating HCM cats with CHF by ACEi and furosemide helps cats stay longer than treating by other cardiovascular drugs besides ACEi and furosemide. Lastly, this study reports an estimated survival time of HCM cats with CHF in Thailand.

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บทคัดย่อ

ระยะเวลาการอยู่รอด และปัจจัยในการพยากรณ์โรคกล้ามเนื้อหัวใจผิดปกติในแมวที่มีภาวะหัวใจล้มเหลว

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โรคกล้ามเนื้อหัวใจหนาผิดปกติเป็นโรคกล้ามเนื้อหัวใจที่พบได้บ่อยในแมว ปัจจุบันยังไม่มีการศึกษาถึงระยะเวลาการอยู่รอดของแมวที่เป็นโรคกล้ามเนื้อหัวใจหนาผิดปกติในประเทศไทย การศึกษานี้มีวัตถุประสงค์เพื่อหาระยะเวลาการรอดชีวิต และปัจจัยที่มีผลต่อระยะเวลาการรอดชีวิตในแมวที่เป็นโรคกล้ามเนื้อหัวใจหนาผิดปกติร่วมกับภาวะหัวใจล้มเหลว การศึกษานี้เป็นการศึกษาข้อมูลย้อนหลังในแมวทั้งหมด 47 ตัว เพื่อวิเคราะห์หาระยะเวลาการรอดชีวิต และความสัมพันธ์ของระยะเวลาการรอดชีวิตกับปัจจัยต่างๆ ได้แก่ เพศ อายุ พันธุ์ น้ำหนัก ผลการตรวจร่างกาย การปรากฏของโรคภาวะแทรกซ้อน การรักษาทางยา และผลการตรวจหัวใจด้วยคลื่นสียงสะท้อนความถี่สูง นำข้อมูลมาวิเคราะห์ทางสถิติ โดยใช้ Log-rank test และแสดงผลในรูปแบบของกราฟ Kaplan-Meier โดยผลการศึกษาพบว่าแมวที่เป็นโรคกล้ามเนื้อหัวใจหนาผิดปกติและมีภาวะหัวใจล้มเหลวมีระยะเวลาการรอดชีวิต 283 วัน และปัจจัยที่ทำให้ระยะเวลาการรอดชีวิตสั้นลงคือ การปรากฏของภาวะลิ่มเลือดอุดตันในหลอดเลือดแดงเอออร์ตา ขนาดของหัวใจห้องล่างซ้ายขณะคลายตัวสุดที่น้อยกว่า 10.8 มิลลิเมตร และการใช้ยารักษาโรคหัวใจชนิดอื่นนอกจากการใช้ยากลุ่มยับยั้งเอนไซม์แองจิโอเทนซินคอนเวอร์ตติ้งร่วมกับยาฟูโรซีไมด์ ข้อมูลจากการศึกษานี้มีประโยชน์ต่อการพยากรณ์โรคและการวางแผนการจัดการในแมวที่เป็นโรคกล้ามเนื้อหัวใจหนาผิดปกติ

คำสำคัญ: แมว ภาวะหัวใจล้มเหลว โรคกล้ามเนื้อหัวใจหนาตัวผิดปกติ ระยะเวลาการรอดชีวิต

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