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Comparative Echocardiographic and Clinical Features of Hypertrophic Cardiomyopathy in 5 Breeds of Cats: A Retrospective Analysis of 344 Cases (2001–2011)

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Background: Primary hypertrophic cardiomyopathy (HCM) is the most common feline heart disease and has been demonstrated to be inherited in some breeds. However, few studies have compared HCM phenotypes and survival according to breed.

Objectives: To compare epidemiological characteristics, clinical findings, left ventricular (LV) geometric patterns, and survival in several breeds of cats with HCM.

Animals: Three hundred and forty-four cats from 5 different breeds (Persian, Domestic Shorthair [DS], Sphynx, Maine coon [MC], and Chartreux) with primary HCM diagnosed by conventional echocardiography.

Methods: Retrospective study. Cats were classified according to breed and clinical status.

Results: Age at the time of diagnosis was lower ($P < .001$) in MC (median age, 2.5 years) and Sphynx (3.5 years) than in other breeds (OB), ie, 8.0, 8.0, and 11.0 years for DS, Chartreux, and Persians, respectively. The prevalence of LV outflow tract obstruction was higher ($P < .001$) in Persians (23/41; 56%) than in OB (115/303; 38%). Age at the first cardiac event was lower ($P < .01$) in MC (median age, 2.5 years) than in OB (7.0 years). All cats surviving > 15 years of age were DS, Persians, or Chartreux. Sudden death (representing 24% of all cardiac deaths) was observed only in 3 breeds (DS, MC, and Sphynx).

Conclusion and Clinical Importance: As in humans, feline HCM is characterized by marked phenotypic variability with several breed-dependent features regarding epidemiology, LV geometric patterns, and clinical course (ie, age at diagnosis, 1st cardiac event, and cause of death).

Key words: Cat; Echocardiography; Doppler; Heart; Myocardium.

Hypertrophic cardiomyopathy (HCM) is the most common feline heart disease. It remains a major cause of morbidity and mortality and is associated with risk of sudden death.[1,2] This primary myocardial disorder is characterized by a hypertrophied nondilated left ventricle (LV) in the absence of an obvious cause of LV hypertrophy, such as systemic hypertension or hyperthyroidism.[3] The phenotypic expression of HCM is highly variable, including diffuse symmetric or asymmetric LV hypertrophy with predominant thickening of the interventricular septum (IVS) or the LV free wall (LVFW). Feline HCM also may result in segmental LV hypertrophy, such as basal hypertrophy of the subaortic IVS, which can be either focal or associated with the latter LV geometric patterns, and which can lead to LV outflow tract obstruction (LVOTO).[4–6]

Some evidence exists of HCM being inherited in numerous breeds, such as Maine coons (MC), Persians, British Shorthairs, and Ragdolls, among others.[a,b,c,d,7–9]

Abbreviations:

ACEI	angiotensin-converting enzyme inhibitors
Ao	aorta
ATE	aortic thromboembolism
CHF	congestive heart failure
DS	Domestic Shorthair
HCM	hypertrophic cardiomyopathy
IVS	interventricular septum
IVSd	end-diastolic interventricular septum
IVSs	end-systolic interventricular septum
IVRT	isovolumic relaxation time
LA	left atrium
LA/Ao	left atrium-to-aorta ratio
LV	left ventricle
LVFW	left ventricular free wall
LVFWd	end-diastolic left ventricular free wall
LVFWs	end-systolic left ventricular free wall
LVOTO	left ventricular outflow tract obstruction
MC	Maine coon
SA-IVS	subaortic interventricular septum
SABP	systolic arterial blood pressure
%SF	shortening fraction

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Most recent studies have focused on the genetic aspects of HCM in some of these specific breeds (eg, MC, Ragdoll) with the identification of mutations in the cardiac Myosin Binding Protein C sarcomeric gene.[10–12] Population characteristics and survival also have been assessed in several retrospective studies.[4,5,13–15]

However, little is known about the comparative expression of feline HCM (eg, clinical signs, epidemiological characteristics, LV hypertrophic patterns) or the disease course (eg, age at 1st cardiac event, type of cardiac event, cause of death, survival rate) according to the breed.

The aim of this retrospective study therefore was to compare epidemiological characteristics, clinical findings, LV geometric patterns, and clinical course of HCM in several breeds of cats.

Material and Methods

Animals

The case records of client-owned cats from 5 different breeds (Chartreux, Domestic Shorthair [DS], MC, Persian, and Sphynx) subjected to conventional echocardiographic and Doppler examination and leading to the diagnosis of HCM between September 2001 and February 2011 at the Cardiology Unit of Alfort (National Veterinary School of Alfort, France) were retrospectively reviewed.

Confirmation of HCM Phenotype and Genotype. The LV hypertrophic pattern was diagnosed by conventional echocardiography by 2-dimensional (2D) and M-modes.[4,5,16,17] In cats with an LV hypertrophic pattern, primary HCM was diagnosed after excluding both systemic arterial hypertension (systolic arterial blood pressure [SABP] > 160 mmHg in unstressed animals[18]) and hyperthyroidism in cats > 8 years old (total serum thyroxine concentration [T4] reference interval, 10–50 nmol/L). In addition, MC cats were divided into 3 groups (homozygous mutated, heterozygous, or homozygous wild-type) according to their genotype (respectively, presence or absence of the MyBPC3-A31P mutation based on direct DNA sequence analysis).[10] Mutational analysis was performed in a single laboratory,[c] as previously described.[17]

Systemic Arterial Blood Pressure Measurement

Systolic arterial blood pressure was measured indirectly on the tail in awake cats by the same trained observers by the standard Doppler method[d] according to the ACVIM consensus statement,[18] as previously described.[16,17]

Echocardiography and Doppler Examination

Standard M-mode, 2D, and Doppler blood flow measurements were performed with continuous ECG monitoring by trained observers (CCS, CM, ET, VC, VG) in awake standing cats by use of 2 ultrasonographic units[e] equipped with 7.5–10 MHz phased-array transducers, as previously described and validated.[19]

Data from the original echocardiographic reports were collected. All echocardiographic measurements were directly performed on the screen freeze-frame images, and then averaged (3 measurements for each value). Left ventricular end-diastolic and end-systolic diameters, LVFW and IVS thicknesses in diastole and in systole were measured by use of the 2D-guided M-mode,[20,21] and the LV shortening fraction (%SF) then was calculated. Pathologic hypertrophy was defined as a diastolic LVFW (LVFWd) or IVS (IVSd) thickness $\geq$ 6 mm or both.[4,16,17]

Hypertrophy was considered as symmetric if the IVSd/LVFWd ratio was 0.7–1.3 or asymmetric with predominant IVS or LVFW thickening if IVSd/LVFWd was > 1.3 or < 0.7, respectively.[22]

The subaortic interventricular septal (SA-IVS) thickness also was measured at end-diastole by 2D mode from the right parasternal 5-chamber view at the mitral valve-chordae tendinae interface,[5] and SA-IVS hypertrophy was subclassified as focal or associated with another M-mode form of HCM.

The left atrium-to-aorta ratio (LA/Ao) was obtained by a 2D method from the right parasternal short axis view as previously described and validated,[19] and LA enlargement was defined as a LA/Ao > 1.2 (upper cut-off obtained from a population of 100 prospectively recruited healthy cats).[23] Pulsed-wave Doppler parameters included maximal systolic aortic as well as early and late diastolic mitral flow velocities and the isovolumic relaxation time (IVRT).[23] Continuous-wave Doppler was used to measure the maximal systolic aortic flow velocity and to confirm a LVOTO characterized by turbulent aortic flow of high velocity (> 2 m/s).[23] The presence of systolic anterior motion (SAM) of the mitral valve, defined as a motion of the anterior mitral valve leaflet toward the LVOT, was assessed by both 2D and M-modes.[24]

Radiography

In case of dyspnea or cough, thoracic radiographs (lateral and ventrodorsal views) also were obtained to confirm radiographic signs of congestive heart failure (CHF).

Follow-Up

Survival times were obtained by reviewing the electronic patient records of the Alfort University Veterinary Hospital. Owners of cats for which the outcome could not be found in the database were contacted by telephone, mail, or e-mail to determine the current status of their animals: alive (asymptomatic or symptomatic) or dead (date and cause of death). Asymptomatic cats at the time of diagnosis were classified as stable if they still were asymptomatic or decompensated if they had undergone at least 1 cardiac event including sudden death or clinical signs attributed to HCM (eg, CHF, aortic thromboembolism [ATE], syncope). Sudden deaths included sudden witnessed deaths and suspected sudden deaths (cats found dead without an obvious cause and completely asymptomatic in the preceding 12 hours). Cats for which the outcome could not be obtained at the time of writing were considered lost to follow-up and consequently were excluded from subsequent analysis.

Statistical Analysis

Statistical analyses were performed by computer software.[f] Data are presented as percentage or mean ± SD except for ages (ages at the time of diagnosis, at decompensation, and at death), which were expressed as median, and compared among groups by the Log-Rank test. The proportion of cats with the different patterns of HCM, LVOTO, SAM, LA enlargement or clinical signs was compared among breeds by a chi-square test. Body weight, rectal temperature, heart rate, SABP as well as echocardiographic variables were compared among breeds by a Student *t*-test. To avoid multiple comparisons, post hoc analyses were compared only between each breed and the pooled population of all the other breeds (OB). Those variables also were compared between asymptomatic and symptomatic cats by means of a Student *t*-test, and also between cats with and

without a LVOTO. The level of significance was set at $P < .05$.

Results

Characteristics of the Study Population

The study population consisted of 344 cats with HCM (Table 1), including 239 DS, 41 Persians, 22 Sphynx, 28 MC, and 14 Chartreux with a majority of males (70.3%). Thirty-eight of the 344 cats (11.0%), including 20 MC and 18 Sphynx, were seen for screening purposes, 64/344 (18.6%) came for a cardiovascular evaluation before anesthesia, and 164/344 (47.7%) were referred for an echocardiographic examination because of abnormal cardiac auscultation (eg, heart murmur, gallop rhythm). The other 78/344 cats (22.7%) were referred for clinical signs related to HCM.

For the entire study population, median age was 7.0 (0.5–19) years, with most cats (220/344, 64.0%) aged < 10 years, 107/344 (31.1%) between 10 and 15 years, and 17/344 (4.9%) > 15 years. The latter (10 males and 7 females) included 14/17 DS (9 asymptomatic and 5 symptomatic), 2/17 asymptomatic Persians, and 1 asymptomatic Chartreux. As shown in Figure 1, age at the time of diagnosis differed among breeds ($P < .001$), with MC and Sphynx being younger than OB. Genetic status regarding the MyBPC3-A31P mutation was obtained for 19/28 MC cats: 6/19 were homozygous mutated (median, 2.5 years; 1.0–4.5), 7/19 were heterozygous (median, 4.0 years; 2.5–5.0), and 6/19 were wild-type (median, 1.1 years; 0.8–1.8).

Clinical Findings at the Time of Diagnosis

Clinical findings are presented in Table 2. Most of the cats (266/344, 77.3%) were asymptomatic. Among the 19 MC cats with available genetic status, 14 (4 homozygous, 6 heterozygous, and 4 wild-type) were

Table 1. Epidemiologic characteristics at inclusion of the whole HCM study population (n = 344) and of each tested breed (Domestic Shorthair, Persian, Sphynx, Maine coon, and Chartreux).

	Whole Study Population (n = 344)	Domestic Shorthair (n = 239)	Persian (n = 41)	Sphynx (n = 22)	Maine coon (n = 28)	Chartreux (n = 14)
Sex						
Male	242 (70.3%)	174 (72.8%)	25 (61%)	13 (59%)	21 (75%)	9 (64%)
Female	102 (29.7%)	65 (27.2%)	16 (39%)	9 (41%)	7 (25%)	5 (36%)
Body weight (kg) (mean ± SD, [minimum-maximum])	4.9 ± 1.4 [2.0–9.5]	4.8 ± 1.3 [2.5–9.3]	3.9 ± 0.9 [2.0–5.5][a]	4.8 ± 1.3 [3.0–7.6]	6.3 ± 1.3 [4.4–9.5][a]	5.5 ± 1.0 [4.0–7.0]

HCM, primary hypertrophic cardiomyopathy.
[a]Significantly different from other breeds ($P < .001$).

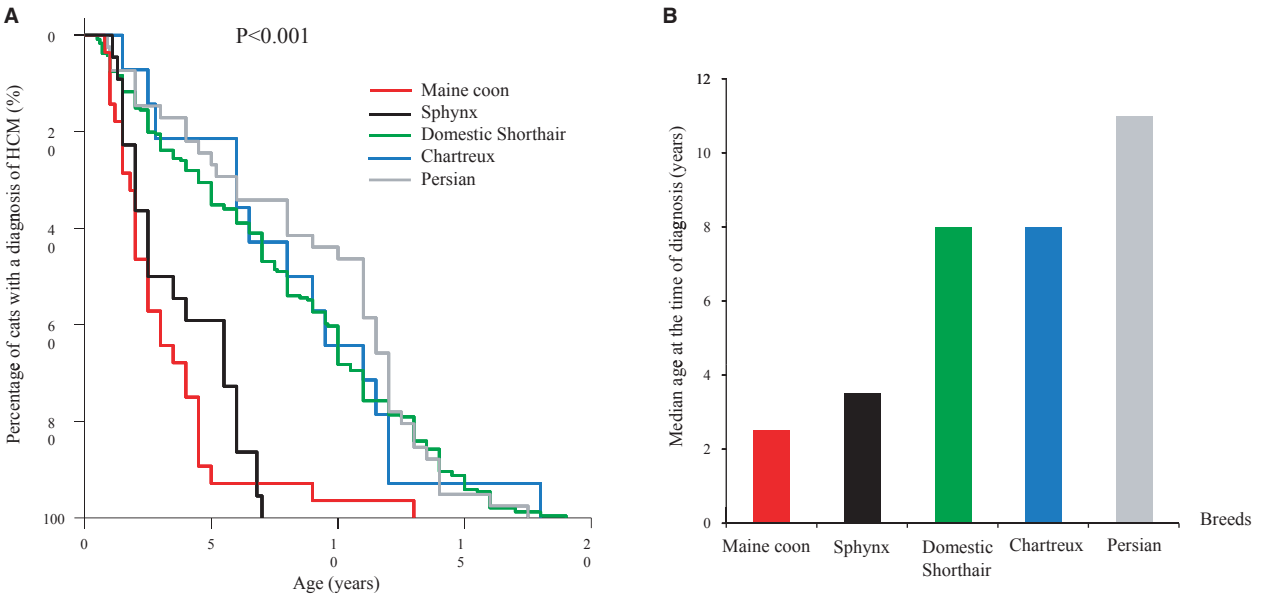

Fig 1. Age at the time of diagnosis of primary hypertrophic cardiomyopathy (HCM) in a population of 344 cats affected by HCM, including 239 Domestic Shorthairs, 41 Persians, 22 Sphynx, 28 Maine coons, and 14 Chartreux. **(A)** Kaplan–Meier curves showing the percentages of cats with a diagnosis of HCM according to the age. **(B)** Bar graph illustrating the median age at the time of diagnosis. Median ages at the time of diagnosis were 2.5 [0.8–13.0], 3.5 [1.1–7.0], 8.0 [0.5–19.0], 8.0 [1.5–18.0], and 11.0 [0.9–17.5] years for Maine coons, Sphynx, Domestic Shorthairs, Chartreux, and Persians, respectively.

Table 2. Clinical findings at inclusion of the whole HCM study population (n = 344) and of each recruited breed (Domestic Shorthair, Persian, Sphynx, Maine Coon, and Chartreux).

Clinical Status	Whole Study Population (n = 344)	Domestic Shorthair (n = 239)	Persian (n = 41)	Sphynx (n = 22)	Maine coon (n = 28)	Chartreux (n = 14)
Asymptomatic	n = 266 (77.3%)	n = 171 (71.5%)[b]	n = 39 (95%)[b]	n = 21 (96%)[b]	n = 21 (75%)	n = 14 (100%)[b]
Auscultation						
Heart rate (bpm, mean ± SD, [minimum-maximum])[a]	189 ± 30 [100–270]	191 ± 30 [100–270]	180 ± 24 [110–211]	203 ± 31 [160–260][b]	167 ± 21 [135–200]	188 ± 10 [180–200]
Normal auscultation	18/266 (6.8%)	11/171 (6.4%)	2/39 (5.1%)	1/21 (4.8%)	4/21 (19.0%)[b]	0/14 (0%)
Murmur	245/266 (92.1%)	157/171 (91.8%)	37/39 (94.9%)	20/21 (95.2%)	17/21 (81.0%)[b]	14/14 (100%)
Gallop rhythm	12/266 (4.5%)	11/171 (6.4%)[b]	1/39 (2.6%)	0/21 (0%)	0/21 (0%)	0/14 (0%)
Arrhythmia	10/266 (3.8%)	6/171 (3.5%)	2/39 (5.1%)	0/21 (0%)	2/21 (9.5%)	0/14 (0%)
Symptomatic	n = 78 (22.7%)	n = 68 (28.5%)[b]	n = 2 (5%)[b]	n = 1 (4%)[b]	n = 7 (25%)	n = 0 (0%)[b]
Auscultation						
Heart rate (bpm, mean ± SD, [minimum-maximum])[a]	173 ± 32 [100–240]	173 ± 33 [100–240]	180 ± 0 [180–180]	ND	173 ± 39 [145–200]	ND
Normal auscultation	11/78 (14.1%)	11/68 (16.2%)	0/2 (0%)	0/1 (0%)	0/7 (0%)	ND
Murmur	60/78 (76.9%)	53/68 (77.9%)	2/2 (100%)	0/1 (0%)	5/7 (71.4%)	ND
Gallop rhythm	11/78 (14.1%)	8/68 (11.8%)	0/2 (0%)	0/1 (0%)	3/7 (42.9%)[b]	ND
Arrhythmia	9/78 (11.5%)	5/68 (7.4%)[b]	0/2 (0%)	1/1 (100%)	3/7 (42.9%)[b]	ND
Dyspnea because of CHF (pulmonary edema and/or pleural effusion)	63/78 (80.8%)	55/68 (80.9%)	2/2 (100%)	0/1 (0%)	6/7 (85.7%)	ND
Ascites	2/78 (2.6%)	2/68 (2.9%)	0/2 (0%)	0/1 (0%)	0/7 (0%)	ND
Aortic thrombo-embolism	14/78 (17.9%)	13/68 (19.1%)	1/2 (50.0%)	0/1 (0%)	0/7 (0%)	ND
Syncope	3/78 (3.8%)	2/68 (2.9%)	0/2 (0%)	1/1 (100%)	0/7 (0%)	ND
Weakness attributed to ventricular arrhythmia	1/78 (1.3%)	0/68 (0%)	0/2 (0%)	0/1 (0%)	1/7 (14.3%)	ND

CHF, congestive heart failure; HCM, primary hypertrophic cardiomyopathy.
[a]Heart rate was assessed during M-mode examination by concomitant ECG tracing.
[b]Significantly different from other breeds ($P < .05$). ND = not determined.

Table 3. Echocardiographic and Doppler variables assessed in the whole HCM study population (n = 344) and in each recruited breed (Domestic Shorthair, Persian, Sphynx, Maine coon, and Chartreux). Data expressed as mean ± SD, and ranges as minimum-maximum values (Min-Max).

	Whole Study Population (n = 344)		Domestic Shorthair (n = 239)		Persian (n = 41)		Sphynx (n = 22)		Maine coon (n = 28)		Chartreux (n = 14)	
	Mean ± SD	Min-Max	Mean ± SD	Min-Max	Mean ± SD	Min-Max	Mean ± SD	Min-Max	Mean ± SD	Min-Max	Mean±SD	Min-Max
M-mode echocardiographic variables												
LVFWd (mm)	6.2 ± 1.6	2.2–12.1	6.3 ± 1.6[a]	2.6–12.1	5.5 ± 1.6[a]	2.2–9.4	5.9 ± 0.9	4.6–8.0	6.7 ± 1.9	3.9–11.8	5.6 ± 1.4	3.6–8.4
IVSd (mm)	6.2 ± 1.3	3.4–13.0	6.3 ± 1.3	3.4–13.0	6.1 ± 1.3	4.1–8.8	6.3 ± 1.0	4.4–8.7	6.2 ± 1.4	4.1–10.0	5.6 ± 1.4	3.9–9.4
LVFWd/IVSd	1.06 ± 0.28	0.41–2.07	1.04 ± 0.27	0.41–1.91	1.18 ± 0.33[a]	0.68–2.07	1.09 ± 0.25	0.55–1.71	0.97 ± 0.26	0.50–1.46	1.05 ± 0.33	0.58–1.58
%SF	54.4 ± 9.9	23.8–84.0	54.1 ± 9.9	23.8–84.0	52.9 ± 9.9	35.0–75.0	60.8 ± 9.3[a]	41.0–78.0	55.5 ± 8.5	39.4–72.0	51.9 ± 11.1	30.3–69.7
Two-dimensional echocardiographic variables												
SA-IVS	6.7 ± 1.6	2.4–11.1	6.8 ± 1.5	3.2–11.1	7.3 ± 1.4[a]	4.5–11.1	5.5 ± 1.3[a]	3.5–8.6	5.9 ± 1.7[a]	2.4–10.1	6.8 ± 1.6	4.0–9.6
LA/Ao	1.25 ± 0.52	0.63–3.72	1.30 ± 0.52[a]	0.64–3.72	1.19 ± 0.51	0.65–2.90	1.00 ± 0.30[a]	0.77–2.19	1.21 ± 0.70	0.63–3.51	1.01 ± 0.22	0.76–1.54
Conventional Doppler variables												
Peak aortic flow velocity (m/s)	2.2 ± 1.6	0.5–7.3	2.2 ± 1.6	0.6–7.3	2.7 ± 1.8[a]	0.85–6.71	2.4 ± 1.4	1.1–5.8	1.46 ± 0.83[a]	0.53–4.96	2.61 ± 1.62	0.72–6.63
Peak mitral E/A ratio	1.16 ± 0.61	0.32–4.88	1.14 ± 0.55	0.32–2.86	1.01 ± 0.49	0.52–3.18	1.07 ± 0.53	0.49–2.77	1.48 ± 0.95	0.56–4.88	0.98 ± 0.41	0.74–1.45
IVRT (ms)	61.2 ± 20.6	17.0–170.0	61.7 ± 19.6	17.0–129.0	64.4 ± 28.5	33.0–170.0	49.8 ± 12.9[a]	33.0–84.0	62.8 ± 19.3	30.0–107.0	61.5 ± 22.3	29.0–100.0

HCM, primary hypertrophic cardiomyopathy; IVRT, isovolumic relaxation time; IVSd, end-diastolic interventricular septum; LA/Ao, left atrium-to-aorta ratio; LVFWd, end-diastolic left ventricular free wall; SA-IVS, end-diastolic subaortic interventricular septum;%SF, shortening fraction.

[a]Significantly different from other breeds ($P < .05$).

asymptomatic and 5 (2 homozygous mutated, 1 heterozygous, and 2 wild-type) symptomatic.

Eighteen of the 266 asymptomatic cats (6.8%) were receiving 1 or more treatments, including angiotensin-converting enzyme inhibitors (ACEI), such as benazepril, imidapril, or enalapril (n = 9, 50%), diltiazem (n = 7, 39%), furosemide (n = 2, 11%), or aspirin (n = 1, 6%). Twenty-one of the 78 symptomatic cats (27%) were receiving 1 or more treatments, including furosemide (n = 15, 71%), ACEI such as benazepril or ramipril (n = 12, 57%), diltiazem (n = 3, 14%), spironolactone (n = 3, 14%), aspirin (n = 2, 10%), or heparin (n = 2, 10%).

Auscultation was normal in 29/344 cats (8.4%), with a greater proportion of symptomatic than asymptomatic cats having normal auscultation ($P < .05$). Asymptomatic MC cats were more likely ($P < .05$) to have a normal auscultation than OB (19.0% versus 5.7%, respectively). A systolic heart murmur detected in 305/344 cats (88.7%) was more common ($P < .001$) in asymptomatic than in symptomatic cats. However, asymptomatic MC cats were less likely ($P < .05$) to be presented with a heart murmur than were the other asymptomatic cats. Conversely, gallop rhythms (23/344, 6.7%) and arrhythmias (19/344, 5.5%) were more common ($P < .01$) in symptomatic cats than in asymptomatic cats. ECG tracings (concurrent with echocardiographic examinations) were recorded in 192/344 cats: 127/239 DS (53%), 22/28 MC (79%), 19/41 Persians (46%), 21/22 Sphynx (95%), and 3/14 Chartreux (21%). Arrhythmias (n = 19 cats) included mostly left ventricular premature complexes (12/19; single ventricular premature complexes in 9/12 cats [5 DS, 3 MC, and 1 Persian] and characterized by bigeminy in 3/12 cats [2 MC and 1 Sphynx]). Three cats presented with single right ventricular premature complexes (DS), 1 with atrial fibrillation (DS), 2 with atrio-ventricular dissociation (including 1 MC of the 15 cats with left ventricular premature complexes and 1 Persian), and 2 with supraventricular premature complexes (DS).

Most symptomatic animals showed clinical signs of CHF (pulmonary edema, pleural effusion, ascites or some combination of these). Other symptomatic cats were presented with ATE, syncope, and weakness attributed to arrhythmia (collapse without loss of consciousness and with ventricular premature complexes detected on electrocardiogram). Among the 78 symptomatic cats, an antecedent event, which may have precipitated decompensation, was recorded in 11 cases (14%), including recent anesthesia or surgery (n = 9), recent corticosteroid administration (n = 1), and trauma (n = 1).

Rectal temperature was lower ($P < .001$) in symptomatic cats (37.4 ± 1.0°C [35.2–39.7]) than in asymptomatic cats (38.2 ± 1.0°C [35.2–40.2]).

The mean SABP of HCM cats was 139 ± 17 mmHg (80–160 mmHg), with no difference between asymptomatic and symptomatic cats (137 ± 20 mmHg [80–160] versus 139 ± 17 mmHg [90–160], respectively) or between cats with and without LVOTO (137 ± 17 mmHg [90–160] versus 140 ± 17 mmHg [80–160], respectively).

Echocardiography and Doppler Examination

Echocardiographic variables are presented in Table 3. Persians had thicker SA-IVS than OB cats ($P < .05$). As a result, HCM with SA-IVS hypertrophy (focal or associated with diffuse LV hypertrophy), as well as the dynamic form of the disease, were more common ($P < .001$ and $P < .05$, respectively) in Persian cats than in OB (39/41 (95%) versus 212/303 (70.0%), and 23/41 (56%) versus 115/303 (38.0%), respectively).

Regarding the LV geometric patterns, a significant difference ($P < .05$) was observed among breeds (Fig 2), with Persians and Chartreux cats presenting with more focal basal IVS hypertrophy (24/55, 44%) than OB (52/289, 18.0%, $P < .0001$). Almost half of the MC cats showed diffuse symmetric LV hypertrophy, which was a more common LV geometric pattern in this breed than in Persians ($P < .05$).

Heart rate (184 ± 31 bpm [100–270]), assessed during M-mode examination by a concurrent ECG tracing (Table 2), was higher in Sphynx ($P < .05$) than in the OB cats. Sphynx also had a higher %SF ($P < .01$) and a shorter IVRT ($P < .05$) than OB cats.

A SAM was detected in 97/344 cats (28.2%). Most of these cats were asymptomatic at the time of diagnosis (72/97, 74%). Chartreux cats had SAM more commonly ($P < .05$) than OB cats (8/14 [57%] versus 89/330 [27.0%], respectively).

At the time of inclusion, 121/344 (35.2%) cats were presented with LA enlargement. Almost half of them (57/121, 47.1%) were asymptomatic. Left atrial enlargement was detected less commonly in Sphynx ($P < .05$) than in OB (3/22 [14%] versus 118/322 [36.6%], respectively).

Cardiac Events and Survival

Follow-up data were available for 217 of the 344 cats of the study (127 were lost to follow-up and therefore were excluded from subsequent statistical analyses).

Age at end of follow-up was < 10 years for 125/217 (57.6%) cats, between 10 and 15 years for 63/217 (29.0%) cats, and > 15 years for 29/217 (13.4%) cats. Among the latter (19 males and 10 females), 20/29 (69%) were DS (17 [85%] asymptomatic and 3 [15%] symptomatic at inclusion), 6/29 (21%) were asymptomatic Persians, and 3/29 (10%) were asymptomatic Chartreux. Median age at the time of diagnosis for these 29 old cats was 14.0 (10.0–19.0) years.

Among the 217 cats for which follow-up was available, 169 and 48 cats were asymptomatic and symptomatic at inclusion, respectively. Data concerning the treatments prescribed after the initial diagnosis of HCM were available for 136/169 and 40/48 asymptomatic and symptomatic cats, respectively. All 40 symptomatic cats received 1 or more treatments after the initial HCM diagnosis, which included furosemide (n = 29, 73%), an ACEI (benazepril, n = 26, 65%), spironolactone (n = 16, 40%), aspirin (n = 13, 33%), heparin (n = 4, 10%), diltiazem (n = 2, 5%), atenolol (n = 2, 5%), or flunarizine (n = 2, 5%). Similarly, 119/136 (87.5%) of the asymptomatic cats received 1 or more treatments after the initial HCM diagnosis including an ACEI, such as benazepril or imidapril (n = 91, 76.5%), diltiazem (n = 29, 24.4%), furosemide (n = 5, 4.2%), spironolactone (n = 1, 0.8%), or aspirin (n = 1, 0.8%).

Twenty of the 169 (11.8%) asymptomatic cats with an available follow-up decompensated (ie, encountered at least 1 cardiac event). Considering these cats and those that were already symptomatic at inclusion (n = 78), a total of 98/344 (28.5%) HCM cats presented with clinical signs attributed to HCM, with a significantly different prevalence according to breed ($P < .01$): 11/28 (39%) in MC, 79/239 (33.1%) in DS, 5/41 (12%) in Persians, 2/22 (9%) in Sphynx, and 1/14 (7%) in Chartreux cats. The type of first cardiac event also differed significantly ($P < .05$) according to breed (Fig 3): the most common type was CHF (66/98, 67%), but this was not observed in any Sphynx, followed by ATE (16/98, 16%), which was only observed

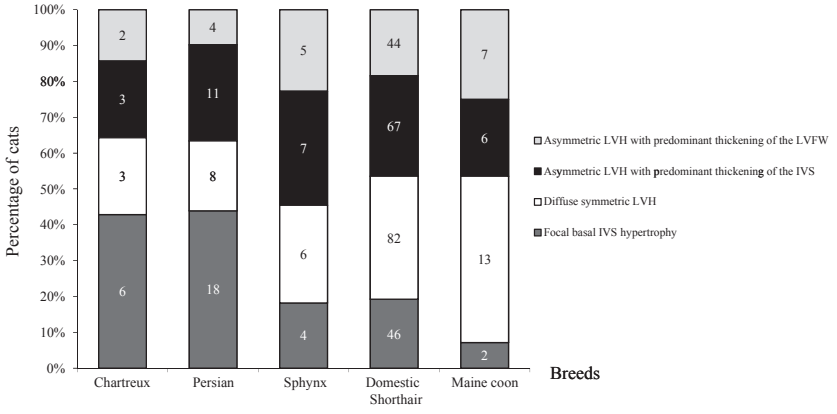

Fig 2. Histograms representing the distribution of the left ventricular geometric patterns assessed by echocardiography for each tested breed, in a population of 344 cats affected by primary hypertrophic cardiomyopathy, including 239 Domestic Shorthairs, 41 Persians, 22 Sphynx, 28 Maine coons, and 14 Chartreux (values on the bars represent the number of cats). IVS: interventricular septum; LVFW: left ventricular free wall; LVH: left ventricular hypertrophy.

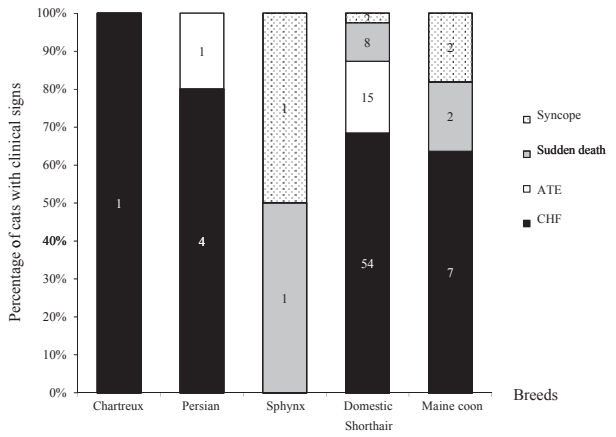

Fig 3. Histograms representing the distribution of 1st cardiac events for each tested breed, in a population of 98 cats affected by primary hypertrophic cardiomyopathy, including 79 Domestic Shorthairs, 11 Maine coons, 5 Persians, 2 Sphynx, and 1 Chartreux (values on the bars represent the number of cats). ATE: aortic thromboembolism; CHF: congestive heart failure.

in 2 breeds (ie, 15 DS and 1 Persian). Aortic thromboembolism was the 1st clinical sign in 16 cats (including 2 that decompensated during the study) and the 2nd clinical sign in 2 cats that had CHF at inclusion (6 and 12 months after inclusion, respectively). As shown in Figure 4, the age at the 1st cardiac event was significantly lower in MC than in OB cats ($P < .01$), with a median age of 2.5 years versus 7.0 years (6.8, 7.0, 9.0, 13.0 years for Sphynx, DS, Persians, and Chartreux, respectively).

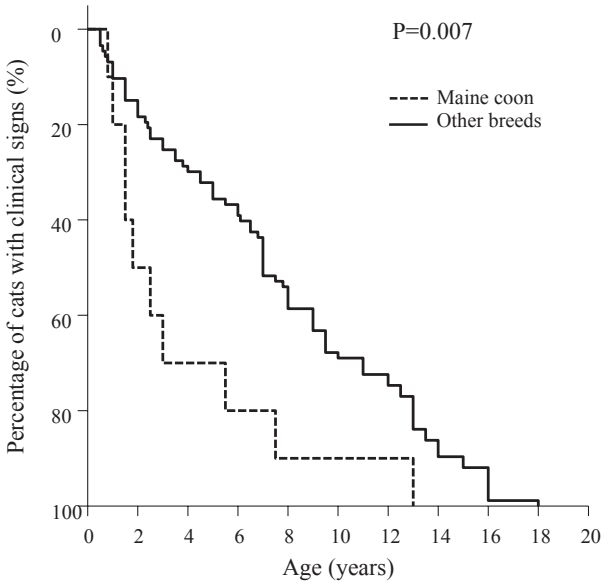

Fig 4. Kaplan–Meier curves illustrating the age at decompensation (ie, percentages of animals eliciting clinical signs according to the age) in Maine coon cats (n = 11) and other breeds including Domestic Shorthair (n = 79), Persian (n = 5), Sphynx (n = 2), and Chartreux (n = 1) with a diagnosis of primary hypertrophic cardiomyopathy. Median ages at the time of decompensation were 2.5 [0.8–13.0] and 7.0 [0.5–18.0] years for Maine coons (n = 11) and other breed cats (n = 87), respectively.

Among the 217 cats with available follow-up, 93 were still alive and 124 (including 89 asymptomatic cats and 35 symptomatic cats at inclusion) had died or been euthanized (all cause mortality) at median ages of 8.0 (1.0–18.5) and 10.0 (0.7–23.0) years, respectively.

Of the 124 cats that had died, 46 (37.1%) died for a cardiac reason (spontaneous death or euthanasia because of nonresponsive cardiovascular clinical signs and sudden death, n = 35/46 [76%] and 11/46 [24%], respectively) at a median age of 7.9 years (1.0–23.0), and 78 (62.9%) died for noncardiac related reasons (eg, cancer [n = 15], nephrologic and urologic [n = 15], gastrointestinal [n = 5], respiratory [n = 5], neurological [n = 5], endocrine [n = 4], and viral diseases [n = 3], postoperative complications [n = 2], pyometra [n = 1], road traffic accident [n = 1], and unknown [n = 22]) at a median age of 11.2 years (0.7–20.0). Most cats that were asymptomatic at inclusion (71/89, 80%) died for noncardiac reasons, whereas most of those that were symptomatic (28/35, 80%) died for cardiac reasons. Considering both death from all causes and cardiac-related death (Fig 5), asymptomatic cats at inclusion died at an older age than symptomatic ones. However, age at sudden death was not statistically different between the 2 groups.

As shown in Figure 6, concerning death from all causes, median survival differed significantly ($P < .05$) among breeds, reflecting an overall breed effect, even if no significant difference was found with post hoc analyses. Considering cardiac death, including sudden death, no statistical difference was found between MC and OB cats, but concerning sudden death solely, MC cats died younger ($P < .05$) than OB cats (median survival ages were > 7.5 [3.0–7.5] years and > 16.0 [6.0–16.0] years for MC cats, n = 20, and OB, n = 197, respectively). The cause of death differed by breed ($P < .05$). Half of the MC deaths were attributed to cardiac reasons (4/8, including 2 sudden deaths at 3 and 7.5 years old). Only 1 Sphynx died (sudden death at 7.8 years old). No sudden death was reported in Chartreux and Persian cats, which mostly died from noncardiac reasons (6/7, 86% and 10/13, 77%). More than half of the DS died from noncardiac reasons (58/95, 61%), and less than a quarter of their cardiac-related deaths (8/37, 22%) were sudden deaths (between 5 and 16 years old).

Discussion

To the authors' knowledge, this study is the first to focus on comparative features of HCM in 5 feline breeds. As previously reported,[4,5,13–15] males were overrepresented in the present study (70%), both in the entire study population and in each of the 5 tested breeds. However, unlike the cats in previous studies, most of those in our study were asymptomatic at the time of diagnosis (ie, 77% versus 47% and 33% in the reports by Payne et al and Rush et al, respectively).[14,15] This discrepancy may be explained by the

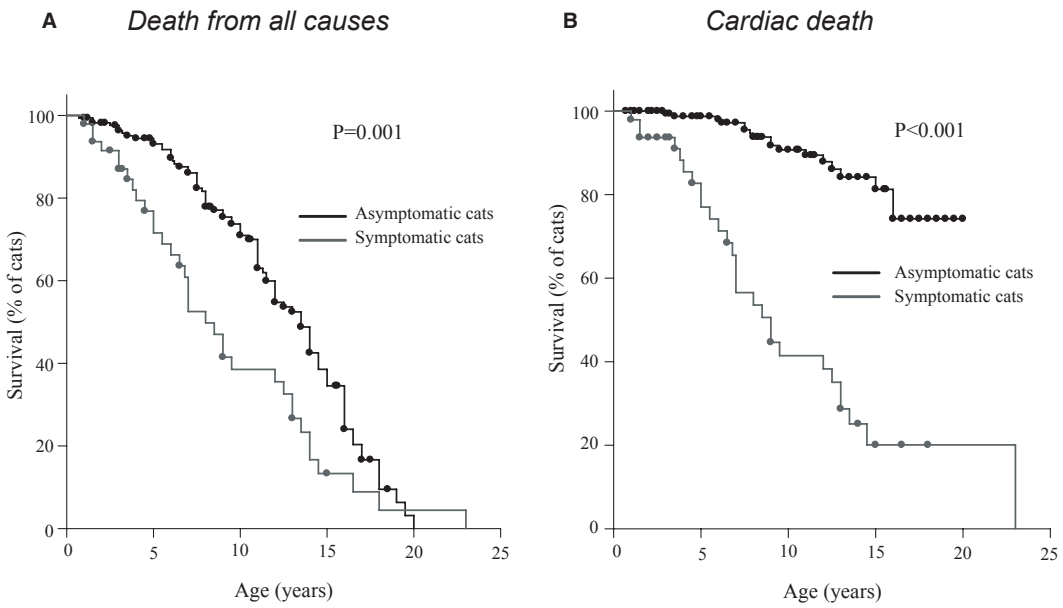

Fig 5. Kaplan–Meier curves of asymptomatic (n = 169) and symptomatic cats (n = 48) at inclusion, with a diagnosis of primary hypertrophic cardiomyopathy and an available follow-up. **(A)** Death from all causes: median survival ages were 13.5 years [0.7–20.0] and 8 years [1.0–23.0] for asymptomatic and symptomatic cats, respectively. (**B**) Cardiac death: median survival ages were > 16 years [3.0–16.0] and 8 years [1.0–23.0] for asymptomatic and symptomatic cats, respectively.

specific recruitment of HCM cats at our cardiology unit (with a predominance of cardiovascular evaluations before mating or before surgery or because of abnormal cardiac auscultation).

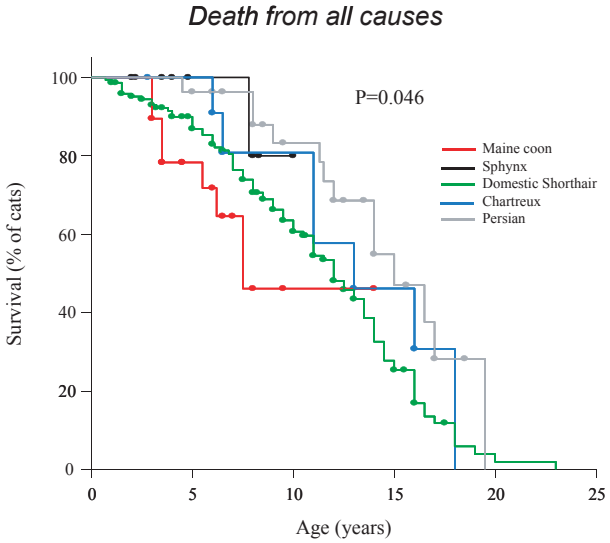

Fig 6. Kaplan–Meier curves of cats illustrating the age at death from all causes in 5 different breeds with a diagnosis of primary hypertrophic cardiomyopathy and an available follow-up (n = 217): Maine coon (n = 20), Sphynx (n = 12), Domestic Shorthair (n = 146), Chartreux (n = 12), and Persian (n = 27) cats. Median survival ages were 7.5 [3.0–7.5], 7.8 (n = 1), 12.0 [0.7–23.0], 13.0 [6.0–18.0], and 15.0 [4.5–19.5] years for Maine coon, Sphynx, Domestic Shorthair, Chartreux, and Persian cats, respectively.

Most HCM cats in the present study were middle-aged animals (median age, 7.0 years), confirming the results of previous reports.[14,15] Nevertheless, the age range was wide, thus highlighting the presence of HCM in very young (< 1 year old) but also in very old cats (> 15 years old), as previously described (maximal ages at inclusion of 16.7 and 18.3 years for Payne et al and Rush et al, respectively).[14,15] These findings are in accordance with human HCM characteristics, with up to 25% patients achieving normal longevity ($\geq$ 75 year-old).[25–27] All cats with a follow-up after 15 years of age were DS, Persians, or Chartreux cats, and all of them were diagnosed after the age of 10 years. This may result, at least in part, from an institutional selection bias. However, interestingly, HCM in elderly human patients seems to have a different behavior, based on a different distribution of mutations,[27] with a generally favorable prognosis and even normal life expectancy.[25,26]

As described by Payne et al,[15] a heart murmur was more common in subclinical HCM than in overt forms of the disease. However, the prevalence of heart murmurs may be underestimated in cats with CHF: lung crackles may prevent detection of soft heart murmurs in animals with pulmonary edema, and heart sounds may be muffled in case of pleural effusion. Interestingly, asymptomatic MC cats had normal cardiac auscultation more often than OB, probably reflecting the high rate of cardiovascular screening in this particular breed.

As in the report by Payne et al,[15] in our study a higher proportion of arrhythmias, including ventricular premature complexes and atrial fibrillation, occurred in symptomatic cats than in asymptomatic ones.

Similarly, symptomatic MC cats more commonly were presented with arrhythmias than were OB, perhaps reflecting a more aggressive clinical form of the disease.

The present study confirms the heterogeneity of echocardiographic LV hypertrophic patterns. More focal hypertrophy were detected in Persians than in OB, as well as more dynamic forms of HCM. Nevertheless, no syncope was reported in this particular breed. Interestingly, SABP was similar in cats with or without LVOTO, in contrast to humans with HCM, for whom LVOTO is known to predispose to systemic arterial hypotension.[28] Chartreux cats had a high proportion of focal basal IVS hypertrophy. However, this interesting observation requires more cases to determine whether it is a breed characteristic or results from case bias. In the present study, the clinical expression of HCM was variable with significantly more MC and DS (more than one-third of cases) developing clinical signs than OB (< 15% of cases).

Other studies indicated a longer survival time for cats without clinical signs.[13–15] These findings are consistent with our study, showing a significantly higher survival time of asymptomatic animals both regarding overall and cardiac-related mortality. In the present study, most of the cats (80%) that were asymptomatic at the time of diagnosis died of noncardiac related causes, whereas the same proportion of cats that were symptomatic died for cardiac reasons. However, 88% of these asymptomatic cats were under treatment after the initial diagnosis of HCM, which may have biased the survival results to an unknown extent. Additional prospective studies therefore are needed to assess the value of treatment in subclinical HCM forms and to determine, as in humans,[25] cats at risk for decompensation, which could benefit from medical treatment.

In the study by Payne et al,[15] Ragdoll cats with HCM were significantly younger and had a shorter survival time than other breeds. Unfortunately, the Ragdoll population in our Veterinary Hospital was too small to be taken into account in our study. However, similar findings were observed in the present report with MC (affected younger and with an earlier decompensation than OB). Moreover, half of the MC that died during the time of the study died for a cardiac reason. In addition, MC cats died at a significantly younger age from sudden death than did OB cats. Lastly, almost one-third of the MC cats with known genetic status of this study were wild-type regarding the MyBPC3 mutation. It therefore can be hypothesized, as previously suggested,[17,29] that other mutations in the MyBPC3 gene or in other sarcomeric genes may be responsible for HCM in the MC breed and in other breeds.

This report has several limitations. The retrospective study recorded a wide range of patterns of LV hypertrophy and demographics in 5 breeds of cats that were referred to a single specialty clinic for cardiac consultation. These results therefore are only preliminary data that should be verified by large, multicenter studies including larger numbers of cats per breed. All cases arose from a single study site, which may limit their genetic diversity. In addition, there are relatively small numbers of HCM cases in 2 of the 5 tested breeds (n < 25 for Sphynx and Chartreux breeds) and several breeds of interest could not be included because of the small number of cases (eg, Ragdolls, British Shorthairs). Larger and more representative study populations ideally should have been included to more accurately assess breed-related differences in HCM phenotype. Furthermore, our unit is a referral center. Screening tests therefore represent a large part of the cardiovascular examinations, and the present population may not completely represent a natural population. Other limitations are related to the retrospective nature of the study. Medical treatments were prescribed by several veterinarians. Drugs, doses, and treatment compliance were uncontrolled. The retrospective assessment of a 12-hour window probably was not optimal to accurately distinguish peracute CHF from sudden death. Lastly, when follow-up was unavailable in the electronic database of our hospital, information concerning clinical signs, cause of death, and dates of events was solely based on owners' memories.

In conclusion, similar to human HCM, feline HCM appears to be characterized by marked phenotypic variability with several breed-dependent features with respect to epidemiological characteristics, LV geometric patterns, age at the time of diagnosis, and decompensation, as well as types of cardiac events and cause of death. This may result, at least in part, from marked genotypic variability, although only 2 causative mutations of the MyBPC3 gene have been described. Additional prospective studies are needed to confirm this hypothesis and better analyze the genotype-phenotype relationship according to breed.

Footnotes

[a] Lefbom BK, Rosenthal SI, Tyrell Jr WD, et al. Severe hypertrophic cardiomyopathy in 10 young Ragdoll cats. Presented at the 19th Annual ACVIM Forum, Denver, CO, May 23–26, 2001. J Vet Intern Med 2001;15:308 (abstract)

[b] Meurs KM, Kittleson MD, Towbin J, et al. Familial systolic cranial motion of the mitral valve and/or hypertrophic cardiomyopathy is apparently inherited as an autosomal dominant trait in a family of American Shorthair cats. Presented at the 15th Annual ACVIM Forum, Lake Buena Vista, FL, May 22, 1997. J Vet Intern Med 1997;11:138 (abstract)

[c] Antagene. Veterinary genetic tests (http://www.antagene.com), Limonest, France

[d] 811-BL, Parks Medical Electronics, Inc, Aloha, OR

[e] Vivid 7 dimension and Vivid 7 BT03, General Electric Medical System, Waukesha, WI

[f] Systat, version 10.0, SPSS Inc, Chicago, IL

Acknowledgments

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