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Body size and metabolic differences in Maine Coon cats with and without hypertrophic cardiomyopathy

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Abstract

An interplay between growth, glucose regulation and hypertrophic cardiomyopathy (HCM) may exist, but has not been studied in detail. The purpose of this study was to characterize morphometric features, insulin-like growth factor-1 (IGF-1) and glucose metabolism in Maine Coon cats with HCM. Body weight, body condition score (BCS), head length and width, and abdominal circumference were measured in Maine Coon cats >2 years of age. Echocardiography and thoracic radiography (for measurement of humerus length, and fourth and twelfth vertebrae length) were also performed. Blood was collected for biochemistry profile, DNA testing, insulin and IGF-1. Sixteen of 63 cats had HCM [myosin binding protein C (MYBPC)+, n = 3 and MYBPC–, n = 13] and 47/63 were echocardiographically normal (MYBPC+, n = 17 and MYBPC–, n = 30). There were no significant differences in any measured parameter between MYBPC+ and MYBPC– cats. Cats with HCM were significantly older (P <0.001), heavier (P = 0.006), more obese (P = 0.008), and had longer humeri (P = 0.02) compared with the HCM– group. Cats with HCM also had higher serum glucose (P = 0.01), homeostasis model assessment (HOMA) and IGF-1 (P = 0.01) concentrations, were from smaller litters (P = 0.04), and were larger at 6 months (P = 0.02) and at 1 year of age (P = 0.03). Multivariate analysis revealed that age (P <0.001), BCS (P = 0.03) and HOMA (P = 0.047) remained significantly associated with HCM. These results support the hypothesis that early growth and nutrition, larger body size and obesity may be environmental modifiers of genetic predisposition to HCM. Further studies are warranted to evaluate the effects of early nutrition on the phenotypic expression of HCM.

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Introduction

In humans, hypertrophic cardiomyopathy (HCM) is considered '… a disease entity caused by autosomal dominant mutations in genes encoding protein components of the sarcomere …' and over 1400 mutations have been identified.[1] Mutations in myosin binding protein C (MYBPC) have been described in Maine Coon and Ragdoll cats with HCM,[2–4] but genetic mutations have not been found for most cats with HCM. Nonetheless, the phenotypic expression of the disease is highly variable in both Maine Coon cats and other cats with HCM.[5,6] This phenotypic variation is also seen in humans with HCM in which there can be a wide variation in the clinical appearance of the disease in family members with the same genetic mutation: some have mild myocardial hypertrophy and others have severe hypertrophy and advanced clinical signs.[7] The cause of this phenotypic disparity is unknown, but may be the result of modifier genes or environmental factors.[8,9] Nutrition is one factor that may have significant effects on cardiovascular phenotype.

Nutrient deficiencies and excesses can play an important role in cardiovascular diseases during the in utero and early postnatal period. Human studies have shown that low birth weight is associated with an increased incidence of coronary heart disease and hypertension in later

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life.[10–12] Of particular concern is when there is nutrient restriction in utero, resulting in a low birth weight, followed by rapid early growth (ie, catch-up growth).[10–12] Restricted fetal growth is adaptive when nutrient availability is suboptimal, but when nutrients are sufficient or excessive, these adaptations become detrimental. Therefore, the environment in which a fetus develops and subsequent growth rate influences long-term health, particularly in the cardiovascular system. This idea of 'fetal programming' suggests that the phenotype of HCM may be modifiable depending upon early nutrition or other environmental factors.

Whilst most research on fetal programming and later cardiovascular disease has focused on coronary heart disease and hypertension, there is also evidence that in utero and early postnatal nutrition can impact myocardial hypertrophy. Studies in sheep have shown that maternal nutrient restriction results in fetal left ventricular hypertrophy, insulin resistance, increased myocardial insulin-like growth factor-1 (IGF-1) and upregulation of myocardial genes whose mutations have been associated with HCM (eg, alpha-cardiac actin, caveolin-1 and titin).[13–15] Insulin resistance may play an important role in the pathogenesis of myocardial hypertrophy that is induced via in utero and early nutrient alterations affecting growth. Insulin resistance can occur in humans with heart failure because the heart reverts to fetal metabolic pathways in which glucose becomes the major fuel for myocytes, yet capacity for glucose utilization is limited.[16,17] However, insulin resistance is also present in humans with HCM, even without heart failure, as a result of alterations in glucose transporters.[18]

In utero or postnatal modifications in nutrient supply and growth patterns may also alter phenotype through alterations in growth hormone or IGF-1 production. Growth hormone, whose actions are mediated via IGF-1, is related intimately to many aspects of growth, from overall body growth (eg, stature) down to the cellular level (eg, protein synthesis in myocytes). IGF-1 regulates cardiomyocyte maturation in utero, as well as postnatal hypertrophic responses, so is an important determinant of ventricular growth responses. IGF-1 overproduction increases myocardial protein synthesis and causes left ventricular hypertrophy.[19–21] IGF-1 is regulated by many factors, including growth hormone, nutrients (eg, protein, certain amino acids), left ventricular pressure overload, angiotensin II and IGF binding proteins.[19,22,23] Studies have shown that myocardial IGF-1 and circulating IGF-1 concentrations are elevated in humans with HCM.[24,25]

One study showed that cats with HCM were significantly larger (ie, body weight, head length and width, and humeral and vertebral length), but not more obese than healthy controls.[26] However, it is not yet known if these same morphometric alterations occur in Maine Coon cats with HCM, or if there is a relationship between body size and the MYBPC mutation found in some cats of this breed. The larger size of cats with HCM may be associated with increased growth hormone and IGF-1 production. One study found elevated growth hormone concentrations in cats with HCM,[27] but interpretation is difficult as growth hormone concentrations fluctuate dramatically throughout the day. In a previous study of cats with HCM, IGF-1 concentrations were not significantly different between cats with HCM and controls.[26] However, IGF-1 concentrations were correlated significantly with body weight, and vertebral and humeral length.[26] These data suggest a relationship between body size and the growth hormone–IGF axis, but it is not yet definitively known if IGF-1 is altered in cats with HCM.

Thus, a possible interplay between glucose dysregulation, fast or excessive growth, and HCM may exist, but has not been studied in detail. Therefore, the purpose of this study was to characterize morphometric features, IGF-1 and glucose metabolism in Maine Coon cats with HCM. We hypothesized that morphometric features, glucose metabolism and IGF-1 are abnormal in cats with HCM and that these alterations may contribute to the phenotypic expression of the disease.

Materials and methods

Maine Coon cats of at least 2 years of age and without other major diseases were eligible for the study. Cats with congestive heart failure were excluded. Historical information, if available, was collected from the owner on litter size, size at 6 and 12 months, and early feeding method. For size at 1 year, owners were asked for the cat's body weight, but size at 6 months it was assessed using a subjective assessment (ie, very small, somewhat small, average size, somewhat large or very large). Feeding method was assessed by asking owners if the kittens were meal-fed or fed free-choice. Cats were fasted for at least 8 h prior to the evaluation. Body weight, body condition score (BCS) (using a nine-point scale),[28] head length and width,[26] and abdominal circumference[26] were measured. BCS was assigned in all cats by a single investigator (LF).

Echocardiography [two-dimensional (2D), M-mode, and color flow, spectral and tissue Doppler (Vivid 7 Dimension, General Electric Healthcare)] and blood pressure measurements (Doppler technique with >170 mmHg considered hypertensive) were performed on all cats without sedation. For echocardiography, 2D right parasternal long- and short-axis, 2D left parasternal and M-mode right parasternal short axis views were obtained. Left ventricular, left atrial and aortic M-mode dimensions were measured in right parasternal short axis views using 2D guidance in accordance with the guidelines established by the American Society of Echocardiography.[29] The 2D left atrial and aortic

dimensions were obtained in the right parasternal short axis view in diastole,[30] and the 2D interventricular septum and left ventricular free wall measurements were obtained in the right parasternal short or long axis view of the left ventricle in end-diastole. Mitral inflow E and A wave velocities were evaluated using pulsed wave Doppler in the left apical view by placing a 2 mm sample volume at the tips of the mitral valve leaflets and the ratio of mitral E wave to A wave velocity (mitral E:A) was calculated. Pulsed wave tissue Doppler E′ and A′ velocities were recorded from the lateral and septal mitral annulus. The ratios of mitral E wave velocity to lateral and septal E′ velocities (E/E′ LVW and E/E′ IVS) were calculated. To be classified as normal, cats had to have both an interventricular septal thickness in diastole (IVSd) and left ventricular free wall thickness in diastole (LVWd) <0.6 cm on M-mode, short axis and long axis 2D measures; a subjectively normal left atrial size; no systolic anterior motion of the mitral valve; and an aortic velocity ≤1.5 m/sec, with no subjective evidence of LV hypertrophy or papillary muscle hypertrophy. Cats were diagnosed with HCM if they had either an IVSd or LVFWd >0.6 cm, measured by 2D and/or M-mode echo, and concurrent findings indicative of HCM (ie, some combination of diffuse or focal concentric hypertrophy of the left ventricle, systolic anterior motion of the mitral valve, left atrial enlargement or increased aortic velocity). Cats that did not fit into the HCM or normal categories were excluded from the study. All echocardiograms were performed by a board-certified veterinary cardiologist (JR, BB or SC) and in any case where the diagnosis of normal or HCM was in question, the echocardiogram was reviewed by a second board-certified veterinary cardiologist (JR, BB or SC).

Radiography was performed by use of a digital radiography system for measurement of length of the humerus, and fourth and twelfth vertebrae from a lateral radiograph in which the left front leg was positioned to be visible in its entirety on the radiograph. All measurements of the humeri and vertebrae were performed by a single investigator (LF). Blood was collected for a biochemistry profile, T_4 (if >7 years), insulin (radioimmunoassay: Human Insulin Specific; Millipore) and IGF-1 (high performance liquid chromatography; Endocrine Section, Diagnostic Center for Population and Animal Health, Michigan University). The homeostasis model assessment (HOMA) — a calculation that has been used as an estimate of insulin sensitivity in cats — was calculated using the formula: HOMA = (insulin × glucose)/22.5.[31] The biochemistry profile and T_4 were performed immediately, and serum for all other analyses was stored at -80°C until batch analysis. DNA testing (blood) for the MYBPC A31P mutation was performed at the Veterinary Cardiac Genetics Laboratory at Washington State University College of Veterinary Medicine.[2] The study was approved by the Tufts Cummings School of Veterinary Medicine Clinical Studies Review Committee and all owners signed an informed consent form before enrolling cats in the study.

All data are presented as median (range) and skewed data were transformed prior to analysis. Categorical variables were compared between groups using χ^2 analyses. Continuous data were compared between groups using independent *t*-tests. Correlation between continuous variables was performed using Pearson correlation tests. Any variables found to be P <0.10 on univariate analysis also were analyzed using logistic regression analysis to assess the independent effects of these variables. All analyses were performed with commercial statistical software (Systat 12.0, SPSS) and P <0.05 was considered statistically significant.

Results

Eighty-five Maine Coon cats were screened for the study between July 2010 and April 2011. Of these, two cats were excluded for congestive heart failure (chronic: n = 1, acute: n = 1), the echocardiogram was equivocal (ie, the heart could not be clearly classified as either normal or HCM) in 16 cats and four cats had other cardiac abnormalities (ie, tricuspid valve dysplasia, n = 2; ventricular septal defect, n = 1; unexplained left ventricular dilation, n = 1). These 22 cats were excluded from further evaluation. Therefore, 63 cats qualified for the study: 16 had echocardiographic evidence of HCM [hereafter designated as HCM+ (MYBPC+, n = 3 and MYBPC–, n = 13)] and 47 were echocardiographically normal [HCM– (MYBPC+, n = 17 and MYBPC–, n = 30)]. Echocardiographic measurements for the HCM- group were similar to those found in a previous study of healthy Maine Coon cats.[32] There were no significant differences between MYBPC+ and MYBPC– cats in any measured parameter. Therefore, all further comparisons are made between HCM+ and HCM– cats. Most cats (52/63; 83%) were owned by breeders. Two cats were receiving cardiac medication (both in the HCM+ group and both were MYBPC–); enalapril, n = 1; atenolol, n = 1; aspirin, n = 1). Cats with HCM were significantly older (median = 9.1 years, range = 4.1–11.4 years) compared with cats without HCM (median = 3.2 years, range = 2.0–10.9 years; P <0.001). Gender of the HCM+ group (12 males, one female) was not significantly different from the HCM– group (25 males, 22 females; P = 0.13). However, a significantly greater proportion of the HCM+ group was neutered (15/16) compared with the HCM– group (10/47; P <.001). Neuter age was not significantly different between the two groups (HCM+: median = 8 months, range 5–90 months; HCM–: median = 6 months, range 5–72 months; P = 0.79).

Blood pressure was not significantly different between groups (HCM+: median = 140 mmHg, range 109–167 mmHg;

Table 1 Echocardiographic measurements for cats without (HCM–; n = 47) and with hypertrophic cardiomyopathy (HCM+; n = 16). Data are presented as median (range)

	HCM–	HCM+	*P*
M-mode			
IVSd (cm)	0.47 (0.38–0.59)	0.61 (0.41–0.84)	<0.001
LVIDd (cm)	1.67 (1.43–2.15)	1.52 (1.27–2.08)	0.07
LVWd (cm)	0.46 (0.29–0.57)	0.63 (0.42–0.89)	<0.001
IVSs (cm)	0.71 (0.49–0.96)	0.92 (0.71–1.17)	<0.001
LVIDs (cm)	0.97 (0.45–1.31)	0.67 (0.41–0.95)	<0.001
LVWs (cm)	0.74 (0.62–0.89)	0.96 (0.77–1.30)	<0.001
Aorta (cm)	1.11 (0.88–1.42)	1.25 (0.99–1.44)	0.11
Left atrium (cm)	1.37 (0.98–1.73)	1.50 (1.14–1.92)	0.02
Two-dimensional (2D)			
IVSd 2D (cm)	0.51 (0.37–0.60)	0.68 (0.36–0.92)	<0.001
LVWd 2D (cm)	0.49 (0.33–0.60)	0.64 (0.58–0.93)	<0.001
Aorta 2D (cm)	1.08 (0.88–1.32)	1.12 (0.87–1.70)	0.07
Left atrium 2D (cm)	1.35 (0.98–1.92)	1.56 (1.24–1.90)	0.007
Doppler			
Aortic velocity (m/s)	0.98 (0.69–1.50)	1.31 (0.57–3.11)	<0.001
E (m/s)	0.66 (0.49–0.94)	0.64 (0.51–0.89)	0.42
A (m/s)	0.58 (0.30–0.87)	0.70 (0.44–0.89)	0.03
E:A	1.17 (0.80–2.60)	0.95 (0.65–1.50)	0.02
E′ LVW (m/s)	0.11 (0.06–0.19)	0.09 (0.05–0.15)	0.02
A′ LVW (m/s)	0.07 (0.04–0.13)	0.08 (0.06–0.16)	0.11
E′ IVS (m/s)	0.08 (0.06–0.15)	0.06 (0.03–0.11)	0.001
A′ IVS (m/s)	0.08 (0.02–0.18)	0.09 (0.05–0.19)	0.77
E/E′ LVW	6.18 (3.72–13.00)	8.86 (4.23–12.40)	0.01
E/E′ IVS	8.13 (4.00–14.83)	11.00 (6.38–19.33)	0.007
E′/A′ LVW	1.71 (0.67–3.00)	0.96 (0.59–2.00)	0.001
E′/A′ IVS	1.00 (0.50–4.00)	0.69 (0.30–2.20)	0.02
Isovolumetric relaxation time (ms)	59.77 (25.88–92.40)	53.92 (35.74–92.40)	0.28

IVSd/s = interventricular septal thickness in diastole/systole, LVIDd/s = left ventricular internal dimension in diastole/systole, LVWd/s = left ventricular free wall thickness in diastole/systole, E = early diastolic velocity of mitral inflow, A = late diastolic velocity of mitral inflow, E′ = early peak diastolic myocardial velocity, A′ = late diastolic myocardial velocity

HCM–: median = 141 mmHg, range 100–170 mmHg; P = 0.84). Cats with HCM had a significantly higher median murmur grade (median = 2, range 0–4) compared with controls (median = 0, range 0–2; P <0.001). On M-mode echocardiography, cats with HCM had significantly thicker IVSd/s and LVWd/s measurements (all P <0.001) and significantly smaller left ventricular internal dimension in diastole/systole (LVID) in systole (P <0.001; Table 1). The IVSd and LVWd measured by 2D echocardiography were also significantly thicker in the HCM+ group (both P <0.001). All measures of left atrial size were significantly larger in the HCM+ group compared with the HCM– group [M-mode left atrial diameter (P = 0.02) and 2D left atrial diameter (P = 0.007)]. Systolic anterior motion of the mitral valve was present in 4/16 HCM+ cats and 0/47 HCM– cats (P <0.001). Cats with HCM had significantly higher aortic velocity (P <0.001), A wave (P = 0.03), E/E′ LVW (P = 0.01) and E/E′ IVS (P = 0.007; Table 1) compared with controls. Cats with HCM had significantly lower E/A (P = 0.02), E′ LVW (P = 0.02), E′ IVS (P = 0.001), E′/A′ LVW (P = 0.001) and E′/A′ IVS (P = 0.02).

Morphometric measurements of the cats revealed significantly higher median body weight (P = 0.006), BCS (P = 0.008) and abdominal circumference (P = 0.004) in the HCM+ group compared with the HCM– group (Table 2). Cats in the HCM+ group also had significantly longer humeri (P = 0.02). The median length of the fourth and twelfth vertebra was not significantly different between groups (P = 0.07 and P = 0.22, respectively).

The HCM+ group had higher serum glucose (P = 0.01) and HOMA (P <0.001), although insulin and insulin/glucose ratios were not significantly different between groups (Table 3). IGF-1 concentrations were higher in the HCM+ cats (P = 0.01; Table 3). Cholesterol and triglyceride concentrations were not significantly different in the HCM+ cats compared with the HCM– cats (both P = 0.32).

Table 2 Morphometric measurements for cats without (HCM–; n = 47) and with hypertrophic cardiomyopathy (HCM+; n = 16). Data are presented as median (range)

	HCM–	HCM+	*P*
Body weight (kg)	5.6 (2.3–8.2)	7.8 (4.1–10.2)	0.006
Body condition score (1–9)	5 (4–8)	7 (5–8)	0.008
Abdomen (cm)	37.0 (23.0–52.0)	47.8 (27.0–62.0)	0.004
Head length (cm)	12.0 (7.4–14.0)	12.3 (9.7–13.2)	0.46
Head width (cm)	8.2 (5.2–11.4)	8.5 (6.7–10.1)	0.43
Humerus length (cm)	11.0 (9.6–14.7)	12.0 (10.0–12.9)	0.02
Fourth vertebra length (cm)	1.1 (0.9–1.4)	1.2 (1.0–1.3)	0.07
Twelfth vertebra length (cm)	1.6 (1.4–1.9)	1.7 (1.4–2.0)	0.22

Table 3 Laboratory analyses in cats without (HCM–; n = 47) and with hypertrophic cardiomyopathy (HCM+; n = 16). Data are presented as median (range)

	HCM–	HCM+	*P*
Glucose (mg/dl)	100 (66–152)	120 (88–195)	0.01
Insulin (pmol/l)	87 (45–189)	92 (64–168)	0.37
Insulin/glucose ratio	0.9 (0.3–1.6)	0.8 (0.4–1.6)	0.42
Homeostasis model assessment	21.3 (11.0–58.9)	26.6 (15.7–80.8)	<0.001
Cholesterol (mg/dl)	124 (73–259)	138 (80–212)	0.32
Triglycerides (mg/dl)	26 (13–90)	32 (17–108)	0.32
Insulin-like growth factor-1 (nmol/l)	40 (16–172)	68 (28–124)	0.01

Historical data could be obtained from some cat owners [size at 6 months, n = 57 (88% were breeders); litter size, n = 55 (86% were breeders); feeding method for kittens, n = 54 (85% were breeders); weight at 1 year, n = 42 (86% were breeders)]. Litters from which the HCM+ cats were born were significantly smaller (median = 4, range 2–6) compared with those of the HCM– cats (median = 5, range 2–8; $P = 0.04$). HCM+ cats were also judged subjectively by their owners/breeders to be larger at 6 months of age ($P = 0.02$) and weighed more at 1 year of age (HCM+: 6.1 kg, range 3.2–8.6 kg; HCM–: median = 5.5 kg, range 3.6–7.5 kg; $P = 0.03$). The percentage of cats fed ad libitum as kittens (HCM–: 37/41 vs HCM+: 11/13; $P = 0.57$) and adults (HCM–: 41/44 vs HCM+: 10/13; $P = 0.09$) was not significantly different between groups.

As cats in the HCM+ group were significantly older than cats in the HCM– group, multivariate analysis was performed and age ($P < 0.001$), BCS ($P = 0.03$) and HOMA ($P = 0.047$) remained significantly associated with HCM.

Discussion

Maine Coon cats with echocardiographic evidence of HCM (HCM+) were older, more likely to be neutered, heavier and more obese, and had longer humeri compared with cats without HCM. This is similar to findings from a study of cats of breeds other than Maine Coons, in which cats with HCM also were heavier and had longer humeri.[26] However, the current results of higher abdominal circumference and BCS in HCM+ cats differ from the results of this previous study.[26] The reason for the differences in obesity in these two studies is not clear but may be related to the age difference between groups in the current study, which was not present in the study by Yang et al. Although not evaluated in the current study, distribution of adipose tissue (ie, central vs peripheral adiposity) can confer different metabolic effects in humans;[33] this would be interesting to evaluate in future studies. Morphometric differences have not been studied in humans with HCM so it is unknown whether this is a species-specific finding. In addition, the current study did not find differences in head width or length, in contrast to the previous study by Yang et al[26] in which cats with HCM had significantly longer and wider heads compared with healthy controls. This difference between studies may be related to the single breed (Maine Coon cats) in the current study compared with the previous study, which specifically excluded Maine Coon cats.

Cats with HCM in the current study also had higher serum glucose and IGF-1 concentrations, and a higher HOMA compared with HCM– cats, although this could be related to differences in age between groups. Glucose and IGF-1 concentrations were not significantly different between cats with HCM and healthy controls in a previous study, which included only breeds other than Maine Coon cats,[26] so this finding may be specific to Maine Coon cats. The higher median glucose concentration and HOMA in the current study may also be related to the

fact that HCM+ cats had a higher median BCS than HCM– cats, as obese cats have been shown to be more insulin resistant than lean cats.[34] The previous study by Yang et al did not evaluate HOMA, so it is unknown whether this calculated estimate of insulin sensitivity would have differed in breeds other than Maine Coon. The use of HOMA is not well studied in cats so future studies of HCM should not only include assessment of insulin, glucose and HOMA, but also of other, more specific measurements of insulin resistance which also take into account more than just a single time point. The lack of difference in IGF-1 concentrations in the previous study by Yang et al compared with the differences found in IGF-1 in the current study may be a breed-specific finding, or may be related to growth and overall size differences. In the current study, HCM+ cats came from smaller litters and were already larger than HCM– cats at 6 months and 1 year of age. Whether these historical factors contributed to higher glucose, IGF-1 concentrations and obesity, or were independent factors is not known. Further prospective investigation is needed to better understand these findings.

The higher percentage of neutered cats in the HCM+ cats compared with HCM– cats could also play a role in the greater risk of obesity in this group, as neutering is known to significantly reduce the energy requirements of cats.[35–38] The percentages of cats fed ad libitum during growth and as adults was not different between the HCM+ and HCM– groups, but was very high overall (89% during growth, 90% as adults). The high percentage of cats in this study that were overweight suggests that enhanced owner education regarding optimal body condition is needed.

There are a number of limitations to this study. One is the significant difference in age between the HCM+ and HCM– cats. Although body weight and HOMA concentrations were determined to be associated independently with HCM in the multivariate statistical analysis, it would have been desirable to have age-matched groups. This proved to be difficult in the current study in order to enroll as large a population as possible. However, this should be a goal of future studies.

The difference in age also raises the question of whether younger cats in the HCM– group would remain free of HCM later in life, as this was a cross-sectional study. In the article by Kittleson et al on HCM in Maine Coon cats, the age at which left ventricular hypertrophy became moderate-to-severe was 24 ± 13 months.[6] Therefore, it would be likely that Maine Coon cats >2 years of age would show some echocardiographic signs of HCM. However, longitudinal studies are needed to determine the proportion of MYBPC+ and MYBPC– Maine Coon cats that will ultimately develop HCM over the course of their lifetimes.

Another limitation is that historical information on cats was not available for all cats and some of it was subjective (eg, 67% could provide the cat's weight at 1 year of age and 91% were able to provide a subjective assessment of the cat's size at 6 months of age). For the subjective question on size at 6 months, 88% of the respondents were breeders (and some of the others who were not breeders obtained the information from the cat's breeder). Cat breeders may be more likely than the average cat owner to be able to assess size, but this question was still subjective. Prospective studies of Maine Coon cats during growth would provide valuable information on the role of early nutrition and growth on the phenotype of HCM. The population enrolled in the study may have been biased as many cats were owned by breeders. Therefore, some were from related lines and owners with cats already determined to be MYBPC+ or to have HCM may have been more or less likely to have volunteered for the study. Finally, the genotype and phenotype of cats in this population reflects cats from the Northeast and mid-Atlantic regions, and may be different from cats in other parts of the country and the world.

Conclusions

These data support the hypothesis that early growth and nutrition, larger body size and obesity may be environmental modifiers of genetic predisposition to HCM. Further studies are warranted to evaluate the effects of early nutrition and growth on the phenotypic expression of HCM.

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Conflict of interest The authors do not have any potential conflicts of interest to declare.

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