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Sarah J Silverman, Joshua A Stern and Kathryn M Meurs

*Journal of Feline Medicine and Surgery* 2012 14: 246 originally published online 16 January 2012

DOI: 10.1177/1098612X11435040

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# Hypertrophic cardiomyopathy in the Sphynx cat: A retrospective evaluation of clinical presentation and heritable etiology

Journal of Feline Medicine and Surgery  
 14(4) 246–249  
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 sagepub.co.uk/journalsPermissions.nav  
 DOI: 10.1177/1098612X11435040  
 jfms.com  
 SAGE

Sarah J Silverman<sup>\*</sup>, Joshua A Stern<sup>†</sup> and Kathryn M Meurs<sup>†</sup>

## Abstract

Hypertrophic cardiomyopathy is an inherited disease in some feline breeds including the Maine Coon and Ragdoll. In these breeds, distinct causative genetic mutations have been identified. The two breeds appear to have slightly different clinical presentations, including age of diagnosis. The observation that these two breeds may have different clinical presentations, as well as different genetic mutations, suggests that hypertrophic cardiomyopathy is a diverse disease in the cat. Hypertrophic cardiomyopathy is poorly described in the Sphynx. The objective of this study was to phenotypically characterize Sphynx hypertrophic cardiomyopathy and to evaluate for a familial etiology. Records of 18 affected cats (11 female, seven male) were evaluated. Age of affected cats ranged from 0.5 to 7 years (median, 2 years). Four affected cats were from a single family and included an affected cat in each of four generations (three females, one male). Further studies are warranted to evaluate for a causative mutation and better classify the phenotypic expression.

**Accepted:** 12 December 2011

## Introduction

Hypertrophic cardiomyopathy is the most common form of heart disease in the cat.<sup>1,2</sup> It is an adult onset disease with a reported age of diagnosis of 5–6 years (range of 3 months to 17 years).<sup>2–4</sup> Although the disease is classically characterized by interventricular septal and/or left ventricular posterior wall hypertrophy, variations can be observed, including hypertrophy of the papillary muscles<sup>5–7</sup> and the presence of dynamic left ventricular outflow tract obstruction associated with systolic anterior motion of the mitral valve (SAM).<sup>8</sup> These clinical variations could suggest the presence of multiple forms of hypertrophic cardiomyopathy in the cat.

Hypertrophic cardiomyopathy is an inherited disease in human beings and in some breeds of cats including the Maine Coon and Ragdoll.<sup>9–12</sup> An autosomal dominant pattern of inheritance is reported most commonly in both human beings and the Maine Coon.<sup>9,13</sup> In the Maine Coon and the Ragdoll breed, distinct genetic mutations for hypertrophic cardiomyopathy have been identified.<sup>12,14,15</sup> In both breeds, the genetic mutation has been identified in the cardiac myosin binding protein C gene but the unique nucleotide change and the location of the mutation within the gene appears to be breed specific. Additionally, the two breeds appear to have slightly

different clinical presentations, including age of diagnosis. Ragdoll cats have been reported to have a mean age of diagnosis as young as 15 months, while the Maine Coon has a mean age of diagnosis of 2.6 years, although large studies are lacking.<sup>10,11</sup> The observation that these two breeds may have different ages of onset, as well as the fact that they have two different genetic mutations, may support the theory that hypertrophic cardiomyopathy is a diverse disease in the cat.<sup>16</sup>

The Sphynx breed has been reported to have a predisposition for development of hypertrophic cardiomyopathy that may suggest a heritable nature.<sup>17</sup> The Sphynx is

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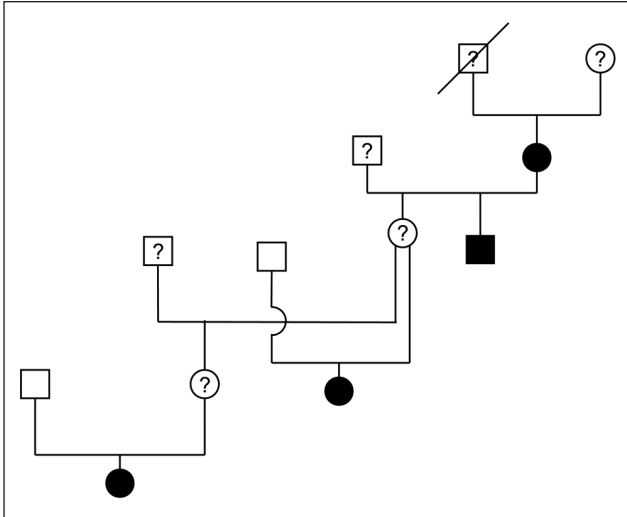
Department of Veterinary Clinical Sciences, College of Veterinary Medicine, Washington State University, USA

<sup>\*</sup>Current address: University of California-Davis School of Veterinary Medicine, Davis, CA, USA

<sup>†</sup>Current address: North Carolina State University College of Veterinary Medicine, Raleigh, NC, USA

## Corresponding author:

Kathryn M Meurs DVM, PhD, Diplomate ACVIM (cardiology), North Carolina State University College of Veterinary Medicine, Raleigh, NC, USA  
 Email: Kate\_meurs@ncsu.edu



**Figure 1** Family of Sphynx cats with hypertrophic cardiomyopathy. Four affected cats were from the same family and an affected cat was observed in each of four generations. Two of the affected cats had one parent that had been documented as unaffected. The male proband (represented by square symbol with a line across) of this family died suddenly before 8 years of age but a necropsy was not performed and cause of death is unknown. Circles represent females, square represent males. Solid black symbols represent cats with hypertrophic cardiomyopathy; solid white symbols represent unaffected cats; symbols with a question mark represent cats that were not available for evaluation

a fairly new breed with most of the breed expansion occurring after the 1960s. The identification of hypertrophic cardiomyopathy in this breed is fairly recent and specific aspects of the disease in this breed are not well described.<sup>18</sup> The objective of this study was to phenotypically characterize Sphynx hypertrophic cardiomyopathy and to evaluate for a possible familial etiology.

## Materials and methods

The records of Sphynx cats that had a minimum of a screening echocardiogram (ECG) at Washington State University College of Veterinary Medicine were evaluated, as well as the reported ECG examinations of Sphynx cats performed by an American College of Veterinary Internal Medicine (ACVIM) board-certified cardiologist that were provided by Sphynx owners for study. Three generation pedigrees were obtained when available.

### Phenotypic characterization

Medical records were evaluated and information was retrieved including age, gender and standard ECG measurements including interventricular (IVS) and left ventricular posterior wall (LVPW) thicknesses at systole (IVSS, LVPWS) and diastole (IVSD, LVPWD) and the left atrial to aortic ratio by M-mode.<sup>19</sup> When available, wall

thickness was taken as the average of three measurements; however, some examiners provided only a maximum measurement for the IVS and the LVPW. Cats were classified as affected as defined by an IVSD or LVPWD measurement greater than 6.0 mm. ECG examinations were further evaluated for the presence of systolic anterior motion of the mitral valve and/or papillary muscle hypertrophy.

### Familial evaluation

Pedigrees were evaluated with respect to presence of clearly defined unaffected or affected cats. Unaffected status was defined by an IVSD and/or LVWD measurement <5.5 mm at 9 years of age. Affected status was defined as stated above. Cats with a LVPWD and/or IVSD measurements between 5.51 and 5.99 mm were considered equivocal and not included in pedigree analysis. Pedigrees were analyzed with Pedigree Viewer (<http://www-personal.une.edu.au/~bkinghor/pedigree.htm>) to evaluate for a possible mode of inheritance.

## Results

Eighteen cats met the criteria for affected. Eleven cats (seven intact, four spayed) were female and seven were male (four intact, three castrated). The age of the affected cats ranged from 0.5 to 7 years, with a median of 2 years.

ECG findings included a mean IVSD of 6.0 mm (range 3.9–8.0), a mean IVSS of 8.5 mm (6.7–10.5), a LVPWD of 6.6 mm (5.0–9.2) and a LVPWS of 9.0 mm (7.5–10.4). Four cats were considered affected based on an interventricular septum greater than 6.0 mm, eight cats based on a left ventricular posterior wall measurement greater than 6.0 mm and four cats based on hypertrophy of both walls. In two affected cats only, a value for the LVPWD (6.3 mm) or IVSD (6.0 mm) was recorded.

Eight cats had systolic anterior motion of the mitral valve and four were noted to have subjectively prominent papillary muscles. Two affected cats had notations of prominent moderator bands.

### Pedigree analysis

Pedigrees were available on nine of the affected cats. Four affected cats were from the same family (Figure 1). The male proband of this family died suddenly before 8 years of age but a necropsy was not performed and cause of death is unknown. An affected cat was observed in each of four generations within this family and included three females and one male cat. Two of the affected cats had one parent that was classified as unaffected. With an affected cat in each generation, both males and female cats affected, and the presence of an unaffected parent in at least some cases, the inheritance is suggestive of an autosomal dominant mode of inheritance; however, this can not be conclusively determined at this time.

## Discussion

Sphynx cats appear to have a form of hypertrophic cardiomyopathy similar to that described in other breeds with systolic anterior motion of the mitral valve and prominent papillary muscles. The disease appears to be a familial disease, at least in some cases, based on the presence of multiple affected cats within a family. Although the mode of inheritance is consistent with an autosomal dominant mode of inheritance as is observed in the Maine Coon cat and in human beings,<sup>9,13</sup> a prospective breeding study would be required to further classify the exact mode of inheritance. Further studies are warranted to investigate a causative mutation amongst the affected population, as previous studies involving affected Sphynx cats did not identify either the Maine Coon or Ragdoll mutation.<sup>15</sup>

Similar to the general population, the results of this study have shown that, at the time of diagnosis, the severity of hypertrophic cardiomyopathy in Sphynx cats varies from mild to severe. Sphynx cats in this study, however, were diagnosed with hypertrophic cardiomyopathy at a younger age than what has been previously reported for the general feline population with a median age at the time of diagnosis of 2.0 years, compared with 5–6 years.<sup>2,3</sup>

The retrospective nature of this study resulted in some limitations, but still provides useful information regarding hypertrophic cardiomyopathy in Sphynx cats. Despite using measurements from accepted ECG views, examinations were performed by several ACVIM board-certified cardiologists making it difficult to standardize subjective findings. Many of the included cats were found during breeder evaluations and it is possible that the age of onset may be biased by early screening. Breeders typically evaluate asymptomatic cats regularly; the general pet-owning population will not typically request an ECG for their cat unless advised by a veterinarian because clinical signs are seen or a murmur is ausculted. An additional limitation is that only initial ECG examinations were evaluated and follow-up examinations may have shown further changes in the measurements of affected cats, as well as shown any progression of equivocal or normal cats to affected which could help clarify the mode of inheritance. For that reason, any equivocal cats were excluded from the pedigree evaluation and cats were not classified as unaffected until they were at least 9 years of age — 2 years older than the oldest affected cat in our study. Finally, pedigrees were not available for every cat included and, consequently, there were sires and dams whose ECG status was not known.

Hypertrophic cardiomyopathy appears to be a familial disease in the Sphynx cat. The age of onset in this breed may be younger than that seen in the general cat population. This observation, as well as the previously

noted finding that Sphynx cats with hypertrophic cardiomyopathy do not have the Maine Coon or Ragdoll mutation,<sup>15</sup> supports the consideration of Sphynx hypertrophic cardiomyopathy as a unique form of this disease. Further studies are warranted to evaluate for a causative mutation and better classify the phenotypic expression.

**Funding** This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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

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