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Factors associated with sudden death versus congestive heart failure or arterial thromboembolism in cats with hypertrophic cardiomyopathy

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Keywords

- HCM

23 - sudden death

24 - CHF

25 - ATE

26

27 Abbreviations:

28 ATE – Arterial Thromboembolism

29 CHF – Congestive Heart Failure

30 E/A – ratio of mitral inflow peak early filling (E) to late filling (A) velocities

31 FS% – Left ventricular fractional shortening

32 HCM – Hypertrophic cardiomyopathy

33 LA – Left atrial

34 LA:Ao – short axis ratio of diastolic left atrial diameter to aortic root diameter

35 LAD – the diameter of the left atrium measured parallel with the mitral annulus in the last frame before

36 mitral valve opening

37 LA-EF% – Left atrial emptying fraction

38 LA-FS% – Left atrial fractional shortening

39 LV – Left ventricle

40 LVWd – end-diastolic left ventricular septal or free wall thickness

41 MR – Mitral regurgitation

42 QMHA – Queen Mother Hospital for Animals

43 SAM – Systolic Anterior Motion of the mitral valve

44 SEC – Spontaneous echo-contrast

45

46 Conflict of Interest

47 The authors have no conflict of interest to declare with regard to this study.

48

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50

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53 owners, referring vets and QMHA clinicians involved in the care of these cats.

54

55

56 **Abstract**

57 **Objectives**

58 To evaluate differences in risk factors associated with death due to congestive heart failure (CHF),
59 arterial thromboembolism (ATE) or sudden death in cats with hypertrophic cardiomyopathy (HCM)

60 **Animals**

61 255 cats with HCM referred to a veterinary teaching hospital.

62 **Methods**

63 Retrospective study. Cats with HCM were identified that had either died within 2 years of diagnosis or
64 were known to be alive 2 years after initial examination. Signalment, physical exam,
65 electrocardiographic and echocardiographic data were analyzed separately for association with death
66 due to congestive heart failure (CHF) vs. aortic thromboembolism (ATE) vs. sudden death. Results:

67 **Results**

68 Within 2 years of follow-up, 23/255 (9.0%) cats had died with ATE, 44/255 (17.3%) cats had died with
69 CHF and 12/255 (4.7%) cats had experienced a sudden death, with 141/255 (55.3%) cats still alive at the
70 end of 2 years. Presence of CHF at presentation and reduced left ventricular fractional shortening (FS%)
71 were independently associated with a CHF death within 2 years of diagnosis. Presence of ATE and
72 reduced left atrial fractional shortening (LA-FS%) were independently associated with dying with ATE
73 within 2 years. No multivariable models were generated for risks of dying a sudden death owing to the
74 low event rate, but syncope at presentation and arrhythmias on auscultation were associated with
75 sudden death on univariable analysis.

76 **Conclusions**

77 Asymptomatic cats have a reduced risk of all three types of death. Reduced FS% and a history of CHF
78 independently predict CHF death, and reduced LAFS% and history of ATE independently predict ATE
79 death. Sudden death is less commonly reported but is associated with syncope.

80 Hypertrophic cardiomyopathy (HCM) is defined as a hypertrophied, non-dilated left ventricle (LV) in the
81 absence of other systemic or cardiac disease capable of producing a similar degree of hypertrophy.¹ It is
82 the most common human familial heart disease^{2,3} and the most commonly diagnosed feline myocardial
83 disease.⁴ HCM is a heterogeneous disease, both in terms of presentation and outcome. Affected cats
84 may be asymptomatic, or may show signs associated with congestive heart failure (CHF), arterial
85 thromboembolism (ATE), syncope or sudden death. Some cats will die of their cardiac disease but
86 others may have long survival times and die of non-cardiac causes.⁵⁻¹⁰ Previous studies have reported
87 clinical features at presentation in cats that have subsequently died with cardiomyopathy and CHF, ATE
88 or sudden death. These features include presence of clinical signs, left atrial (LA) enlargement, the
89 absence of systolic anterior motion of the mitral valve (SAM), increasing age and breed.^{6-8, 11-13} We have
90 previously reported reduced LA fractional shortening, left ventricular (LV) fractional shortening and
91 extreme LV hypertrophy as independent predictors of cardiac mortality in 282 cats with HCM.

92 Studies evaluating the risk factors for specific types of cardiac death (such as sudden death vs. CHF
93 death or ATE death) are lacking in cats. An association between LA enlargement and ATE was noted in
94 one study, and a breed predisposition noted for sudden death in another study, but in general our
95 understanding is poor of the risk factors predicting death due to CHF instead of ATE or sudden death.

96 We hypothesized that the risk factors in cats with HCM would be different for death due to CHF
97 compared with thromboembolic death or sudden cardiac death. The aim of this study was to conduct a
98 sub-analysis of a previously reported population of cats with HCM to investigate risk factors for different
99 mortality end-points (CHF death, ATE death and sudden cardiac death).

100 **Animals, Materials and Methods**

101 These data were originally collected to investigate overall survival for this population and as such, the
102 methods used have been described previously.⁹ In brief, cases of feline HCM diagnosed by a board-
103 certified cardiologist or a cardiology resident supervised by a board-certified cardiologist at the Royal
104 Veterinary College, Queen Mother Hospital for Animals (QMHA) on the basis of 2D and/or M-mode
105 echocardiography^a between June 2004 and August 2009 were included in this study. Cats were
106 excluded from the study if they had a concurrent diagnosis of hyperthyroidism or hypertension, defined
107 as either systolic blood pressure ≥ 180 mmHg; systolic blood pressure ≥ 160 mmHg with retinal changes
108 suggestive of hypertension; medically controlled hypertension; or where renal disease was present and
109 blood pressure had not been determined. Cats were also excluded if they were still alive with less than
110 2 years of follow-up.

111 The medical records for each cat were reviewed for signalment data, physical exam findings, systolic
112 arterial blood pressure assessment, serum total thyroxine concentrations, ECG findings, clinical status
113 and echocardiographic findings. Clinical status at presentation was recorded and grouped into
114 asymptomatic, syncope, exertional dyspnea, CHF and ATE. Congestive heart failure was defined as
115 present based on previous radiographic evidence of pulmonary edema, ultrasonographic evidence of
116 pleural or pericardial effusion, or severe tachypnea responsive to furosemide. Cats presented to our
117 center without congestive signs were designated as having CHF if there was prior evidence of CHF at
118 either our hospital or the referring practice. Aortic thromboembolism was defined as either sudden
119 onset painful pulseless limb paresis; central nervous system signs associated with magnetic resonance
120 imaging findings of a well-demarcated brain lesion, hyperintense on a T2-weighted image; or a history of

^a Vivid 7, GE Medical Systems Ltd, Hatfield, Hertfordshire, UK

121 acute onset abdominal pain, high creatine kinase levels, and echocardiographic evidence of SEC in the
122 LA for mesenteric thromboembolism. For the original study, all echocardiographic examinations were
123 reviewed and remeasured by one board-certified cardiologist (VLF) or a cardiology resident (KB). Details
124 of echocardiographic measurements are listed in Table 1. Left ventricular hypertrophy was defined as LV
125 septal or free wall end-diastolic thickness ≥ 6 mm⁷ in 2D or M-mode measurements.

126 M-mode images were used to obtain LV fractional shortening (FS%) values whilst 2D images were used
127 to record maximal LV end-diastolic wall thickness from either the septum or free wall (LVWd). The
128 presence of any left ventricular regional wall hypokinesis, subjectively assessed based on 2D images, was
129 noted. Presence of systolic anterior motion of the mitral valve (SAM) or mitral regurgitation (MR) was
130 recorded.

131 Mortality was determined by reviewing QMHA medical records and contacting referring veterinarians.
132 Date of death, whether the cat died naturally or due to euthanasia, and whether death was related to
133 cardiac disease (sudden death, CHF, ATE) or non-cardiac causes was recorded. Where insufficient
134 evidence was available, owners were contacted and asked to complete a questionnaire. Sudden death
135 was defined as being found dead without obvious cause at home or as a witnessed event where the cat
136 had been apparently well in the preceding 24 hours, and was assumed to be cardiac. CHF death was
137 defined as dying with dyspnea, crackles, cyanosis, fluid pouring out of mouth and/or euthanasia due to
138 becoming refractory to CHF medication. ATE death was defined as death or euthanasia following a new
139 episode of ATE or worsening of a current ATE. If a cat was alive 2 years after diagnosis it was classified
140 as alive, irrespective of whether or not further long term follow up was available.

141 Statistical analysis was performed using commercially available software^b and values are reported as
142 mean \pm standard deviation (normally distributed data) and median (interquartile range (IQR)) for non-
143 normally distributed data. Cats reaching a specific end point (sudden cardiac death, CHF death or ATE
144 death), were compared to a composite of cats that had either died of the other two end points or a non-
145 cardiac death within 2 years of diagnosis or were still alive 2 years after diagnosis (irrespective of their
146 ultimate outcome). Univariable analyses on continuous data were performed using t-tests or Mann
147 Whitney U test as appropriate and for proportions using Chi-squared or Fisher's exact as appropriate.
148 Multivariable analysis was performed using binary logistic regression for the outcomes that had at least
149 20 cats. Overall model fit was assessed using the Hosmer-Lemeshow test, positive and negative
150 predictive values from classification tables and assessment of DFBeta and deviance residuals. A value of
151 $p < 0.05$ was considered statistically significant.

^b GraphPad Prism 5, GraphPad Software, 2007 and PASW Statistics 20, 2011

152 Results

153 Between June 2004 and August 2009, 282 cats were diagnosed with HCM. Of those, 255 had either died
154 within 2 years of diagnosis or were known to be still alive 2 years after diagnosis. The other 27 cats
155 were known to be still alive at the last point of contact but had less than 2 years of follow up and were
156 therefore excluded. Most cats were male (75.3%) and neutered (94.5%), and 81.2% were nonpedigree.
157 Mean body weight was 4.69 +/- 1.09 kg. The study population were not different in terms of sex
158 ($p=1.000$), neutering status ($p=0.375$), breed ($p=0.442$) or weight ($p=0.477$) to the 27 excluded cats. The
159 study population was significantly older (7.0 [3.1-10.0] years) than the excluded 27 cats (3.6 [2.2-7.5]
160 years, $p=0.016$). On presentation, the majority (139, 54.5%) of cats were asymptomatic, but 84 (32.9%)
161 had CHF, 16 (6.3%) had ATE, 13 (5.1%) were presented for syncope and 3 (1.2%) had exertional dyspnea
162 (Table 2). Of the 16 cats presenting with ATE, four also had CHF but were classed as ATE. Four of the cats
163 presenting with ATE also had a history of ATE. A minority of cats designated as having CHF (10/84 with
164 CHF and 2/4 with ATE and CHF) had a history of CHF but were not showing overt signs of congestive
165 failure at presentation on the visit used in this study. At the initial visit, antithrombotic treatment was
166 started in 44 (17.3%) cats. Antithrombotic treatment included aspirin ($n=40$), clopidogrel ($n=2$), or
167 both aspirin and clopidogrel ($n=2$). Of those started on antithrombotic treatment, 15 (34.1%)
168 subsequently presented with ATE, and 25 (56.8%) presented with CHF. Within 2 years of diagnosis,
169 79/255 cats had died of their heart disease (31%). Death was associated with CHF in 44 of the 255
170 (17.3%) cats, ATE in 23 (9.0%) cats, and sudden death in 12 (4.7%) cats. Sixteen (6.3%) cats did not
171 survive to discharge; eight (50%) cats were euthanized because of noncardiac disease, five (31.3%) were
172 euthanized because of CHF, two (12.5%) died suddenly and one (6.3%) was euthanized because of ATE.
173 Of the eight cats euthanized in hospital because of noncardiac disease, seven (87.5%) were classified as
174 asymptomatic and one cat (12.5%) developed CHF during investigations for neoplastic disease and was

175 euthanized because of the neoplastic disease but was classified as having CHF. One of the cats that died
176 suddenly was witnessed to develop ventricular fibrillation and resuscitation was unsuccessful. Of the 44
177 deaths due to CHF, 37 (84.1%) were euthanized and seven (15.9%) died spontaneously. Of the 23 deaths
178 due to ATE, nine (39.1%) also had CHF at the time of death, though they were classed as ATE deaths.
179 Seventeen (73.9%) of the cats that died because of ATE were euthanized and six (26.1%) died
180 spontaneously. Other than the two sudden deaths that occurred during the original visit, all sudden
181 deaths occurred at home. For all the cats that died at home, the primary veterinarian was unaware of
182 their death and information was gained from the owners. Death was due to noncardiac disease in 35
183 (13.7%) cats, and 141 (55.3%) cats were still alive 2 years after diagnosis.

184 **CHF death**

185 Cats that died because of CHF were compared to a composite of cats that died suddenly, died because
186 of ATE, died a noncardiac death or were still alive 2 years after diagnosis. On univariable analysis, the
187 hazard of a CHF death (Fig. 1) increased with increasing age, presence of an arrhythmia, presenting with
188 CHF, decreasing left ventricular fractional shortening (FS%), increasing LA size (LA:Ao and LAD),
189 decreasing left atrial emptying fraction (LA-EF%) and left atrial fractional shortening (LA-FS%), increasing
190 maximal 2D LVWd, presence of regional wall hypokinesis, presence of SEC/thrombus, and having a
191 restrictive filling pattern. The hazard of a CHF death was decreased in cats with a murmur, cats that
192 were asymptomatic at presentation, and cats with SAM.

193 **ATE death**

194 Cats that died because of ATE were compared to a composite of cats that died suddenly, died because
195 of CHF, died a noncardiac death or were still alive 2 years after diagnosis. The hazard of an ATE death
196 (Fig. 2) was increased in male cats, cats with a gallop sound, presenting with an ATE, increasing LA size

197 (LA:Ao and LAD), decreasing LA-EF% and LA-FS %, increasing maximal 2D LVWd, presence of SEC/
198 thrombus and cats with a restrictive filling pattern. The hazard of an ATE death was decreased in cats
199 that were asymptomatic at presentation.

200 **Sudden death**

201 Cats that died suddenly were compared to a composite of cats that died because of an ATE, died
202 because of CHF, died a noncardiac death or were still alive 2 years after diagnosis. The hazard of sudden
203 death (Fig. 3) was increased in cats with an arrhythmia, those with syncope, decreasing FS %, increasing
204 LA size (LA:Ao and LAD), decreasing LA-EF%, presence of regional wall hypokinesis and presence of
205 SEC/thrombus. The hazard of sudden death was decreased in cats that were asymptomatic at
206 presentation. Separate multivariable models were generated for predicting either a CHF death (Table 3)
207 or an ATE death (Table 4) within 2 years of diagnosis. Presence of CHF at diagnosis and decreasing LV
208 FS% predicted a CHF death while presence of an ATE at presentation and decreasing LA-FS% predicted
209 an ATE death. Owing to low numbers of sudden deaths, a multivariable model could not be generated.
210 Model fit for the CHF model (HosmerLemeshow χ^2 0.329, positive predictive value χ^2 82.4%, negative
211 predictive value χ^2 90.1%, correctly classified χ^2 89.5%) and for the ATE model (HosmerLemeshow χ^2
212 0.895, positive predictive value χ^2 88.9%, negative predictive value χ^2 93.7%, correctly classified χ^2 93.5%)
213 were both considered good. Analysis of the residuals for each model showed good model fit.

214

215 Discussion

216 Numerous studies have reported factors associated with a cardiac death in cats with HCM,^{4, 6-9, 12, 13}
217 including our previous report of the population included in this study,¹¹ but the risk factors have not
218 been reported separately for CHF vs. ATE or sudden death. If risk factors vary for different forms of
219 cardiac death, this could have important implications for design of therapeutic trials and the prevention
220 of these complications of HCM. Although no treatment is known to prevent the onset of CHF in cats with
221 HCM, antithrombotic treatment is commonly recommended for cats believed to be at risk of ATE, even
222 though risk factors for ATE have largely been presumed based on clinical experience and anecdotal
223 evidence.¹⁶ Our previous analysis of the cohort of cats with HCM reported here yielded multiple
224 echocardiographic risk factors for cardiac death, but no attempt was made to link these risk factors with
225 specific types of mortality end-point.¹¹ We reanalyzed the data from the previous study to evaluate the
226 specific risk factors for different cardiac mortality end-points: death due to CHF; death due to ATE; and
227 death due to sudden death. We found that initial clinical presentation remained an important predictor
228 for all three types of cardiac death, with asymptomatic cats at lower risk of all forms of cardiac
229 mortality. Multivariable analysis showed CHF on presentation and LV systolic dysfunction to be
230 independent predictors of CHF death, and ATE on presentation and reduced LA-FS% as independent
231 predictors of ATE death. Univariable analysis demonstrated an increased risk for sudden death in cats
232 with a history of syncope, or arrhythmias. In the current population, cardiac mortality was most
233 commonly associated with CHF (55.7%), then ATE (29.1%) and least commonly sudden death (15.2%). In
234 the 2002 study by Rush et al.,⁶ ATE was the most common cause of cardiac death, followed by CHF and
235 then sudden death. Where type of cardiac death has been reported in survival studies in cats with HCM,
236 sudden death is usually the least common type of death, but data on prevalence of sudden cardiac
237 death in cats with HCM are generally scarce. The proportion of sudden deaths reported by owners to

238 their own veterinarian is not known. In our cohort, none of the primary veterinarians of the cats that
239 experienced sudden death at home were aware that the cat had died, supporting the notion of under-
240 reporting. One cat in this study developed ventricular fibrillation, but the cause of sudden death in the
241 other cats was not known. Alternative possible causes include bradyarrhythmias, coronary or central
242 nervous systemic thromboembolic events or a thrombus within the LV outflow tract. In people, sudden
243 cardiac deaths appear to be more common in young adults, with CHF related deaths more common in
244 middle-aged people, and embolic related deaths more likely to occur in the elderly.^{10, 44} In the study by
245 Trehou-Sechi et al., Maine Coons that died suddenly were younger than other breeds with sudden
246 death. In our population of cats, CHF deaths within 2 years of diagnosis occurred in older cats than in
247 those who did not experience a CHF death, but age was not associated with either ATE deaths or sudden
248 deaths.

249 Factors previously associated with ATE in the literature include LA enlargement, increased LV diameter,
250 and SEC. All the LA variables (LA:Ao, LAD, LA-FS%, LA-EF%) were also associated with ATE risk in our
251 study, as well as SEC or presence of a thrombus, increasing LV wall thickness, presence of a gallop, and
252 restrictive diastolic filling, but not LV systolic dysfunction or regional wall motion abnormalities. The
253 multivariable model showed that a history of ATE and reduced LA-FS% were independent predictors.
254 The initial clinical presentation of the cat was an important predictor of specific mortality endpoints.
255 Cats presenting with CHF were at increased risk of dying with CHF but not of ATE, and cats presenting
256 with ATE were at increased risk of dying with ATE but not of CHF. Cats with syncope were more likely to
257 experience sudden death, although this was only explored at the univariable level because of a low
258 event rate. Syncope is an important risk factor for sudden death in people and our data suggest this may
259 also be true in cats. Left atrial variables were predictive of CHF deaths and ATE deaths. Cats with CHF
260 have been reported to have worse LA function than healthy controls. Left atrial enlargement has

261 consistently been one of the most important risk factors reported for cardiac mortality in previous
262 studies and reduced LA-FS% was an independent predictor of cardiac mortality in the previous overall
263 survival analysis of the cats in the present study.¹¹ It is therefore likely that a large, poorly contractile
264 left atrium increases the risk of death due to both CHF and ATE. In human cardiovascular disease, the
265 presence of SEC has been associated with embolic events and it has been assumed that this is also the
266 case in cats with HCM.¹⁶ In these results, however, SEC appears to predict any type of cardiac end-point
267 rather than being specific for ATE. Given the previously reported association with SEC and left auricular
268 appendage velocities, it is likely that SEC is a surrogate marker for LA dysfunction and as such can
269 predict a CHF or ATE death. At the univariable level LA:Ao, LAD and LA-EF% were predictive of sudden
270 death. However, it is more difficult to assess the predictive value for sudden death because of low
271 numbers.

272 Cats with LV systolic dysfunction (FS% <30%) or regional wall hypokinesis were at increased risk of a CHF
273 death or sudden death at the univariable level, with FS% <30% being an independent predictor of a CHF
274 death. Human HCM patients that have an end-stage phenotype (LV systolic dysfunction, defined as a
275 left ventricular ejection fraction <50%) are more likely to progress to advanced CHF than those without
276 systolic dysfunction^{20, 24, 25} and FS% <30% been reported to be associated with increased risk of
277 cardiovascular mortality in people.⁴⁶ The end-stage phenotype of HCM has been suggested as a
278 predictor of sudden death in people.^{24, 25} LV systolic function appears to have similar predictive value in
279 cats as in people, although further work investigating the role in sudden death is required.

280 In our original survival analysis of this population, LV hypertrophy was an independent predictor of
281 cardiac mortality and this sub-analysis suggests the increased risk is primarily associated with death due

282 to CHF or ATE, which contrasts with findings in people where extreme hypertrophy is associated with an
283 increased risk of sudden death.

284 Auscultation findings showed some predictive value at the univariable level, with the presence of a
285 murmur significantly associated with freedom from a CHF death within 2 years of diagnosis. The
286 presence of a murmur is often due to the presence of SAM causing dynamic left ventricular outflow tract
287 obstruction (LVOTO),⁸ and SAM was also associated with freedom from a CHF death. A number of feline
288 studies have reported a similar association between a favorable outcome and a murmur or dynamic
289 LVOTO. It could be speculated that cats with SAM are detected earlier in their disease course than cats
290 without SAM because diagnostic investigations are undertaken following detection of a murmur rather
291 than demonstration of clinical signs, which might explain the apparent survival benefit of both a murmur
292 and SAM in cats in the short term. There are no studies in cats to evaluate the long term effect of
293 dynamic LVOTO on cardiac mortality, so it is not clear if cats genuinely differ from people with HCM, in
294 whom the presence of LVOTO is associated with progression to severe heart failure.²² Neither the
295 presence of a murmur nor the presence of SAM was associated with a risk of an ATE death or sudden
296 death. Gallop sounds were associated with an ATE death but not with a CHF death. Arrhythmias (both
297 on auscultation and on electrocardiography) were associated with an increased risk of a CHF death or a
298 sudden death, but it was not possible to analyze individual arrhythmia types because of low numbers.

299 This is a retrospective study conducted in a referral environment and as such, there are limitations.
300 Blood pressure was not recorded in every cat, so that it is possible that hypertensive cats were included,
301 although efforts were made to exclude cats without a blood pressure measurement if they had factors
302 predisposing to hypertension, such as renal disease. Serum thyroxine concentrations were not routinely
303 measured unless clinically indicated and so it is possible that some hyperthyroid cats may have been

304 included. Each cat only had 1 echocardiographic examination measured and used for the study. As
305 HCM is a disease that progresses at a variable rate, some cats may have died a cardiac death within two
306 years of diagnosis without any of the risk factors being obvious at the point of examination. Therefore
307 the absence of these risk factors does not exclude the potential for a cat dying within two years of
308 diagnosis. At the time of admission some cats were showing signs of CHF and so did not receive a full
309 echocardiographic examination until stabilized. Some echocardiographic measurements (eg left atrial
310 size or function) are likely to have changed during stabilization. Equally, some cats were already
311 receiving treatment at admission, which may have affected their echocardiographic measurements. Not
312 all echocardiographic measurements were available for every cat, either due to clinician preference,
313 patient stability or temperament. Owner descriptions and clinical records of referring practices were
314 used to determine the outcome for the cats. It is possible that some deaths were missed, particularly as
315 27 cats could not be included due to lack of follow up data. Reliance was placed on owner description
316 for deciding what type of death the cat had experienced. There were only low numbers of sudden
317 deaths and ATE deaths within 2 years of diagnosis, limiting the ability to generate meaningful
318 multivariable models. Veterinary survival studies are always confounded by variability in selection of
319 timing for euthanasia versus survival attributable to spontaneous death, and this is also true of our
320 study.

321 In conclusion, the most important predictor of the type of cardiac death appears to be symptomatic
322 status at first presentation, with those presenting with either CHF or an ATE most likely to die of the
323 same complication within 2 years, and those presenting with syncope are at higher risk of sudden death.
324 The variables LA:Ao, LAD and LA-EF% were all associated with an increased risk for all three types of
325 cardiac death. Left atrial fractional shortening was associated with an increased risk for CHF and ATE
326 deaths.

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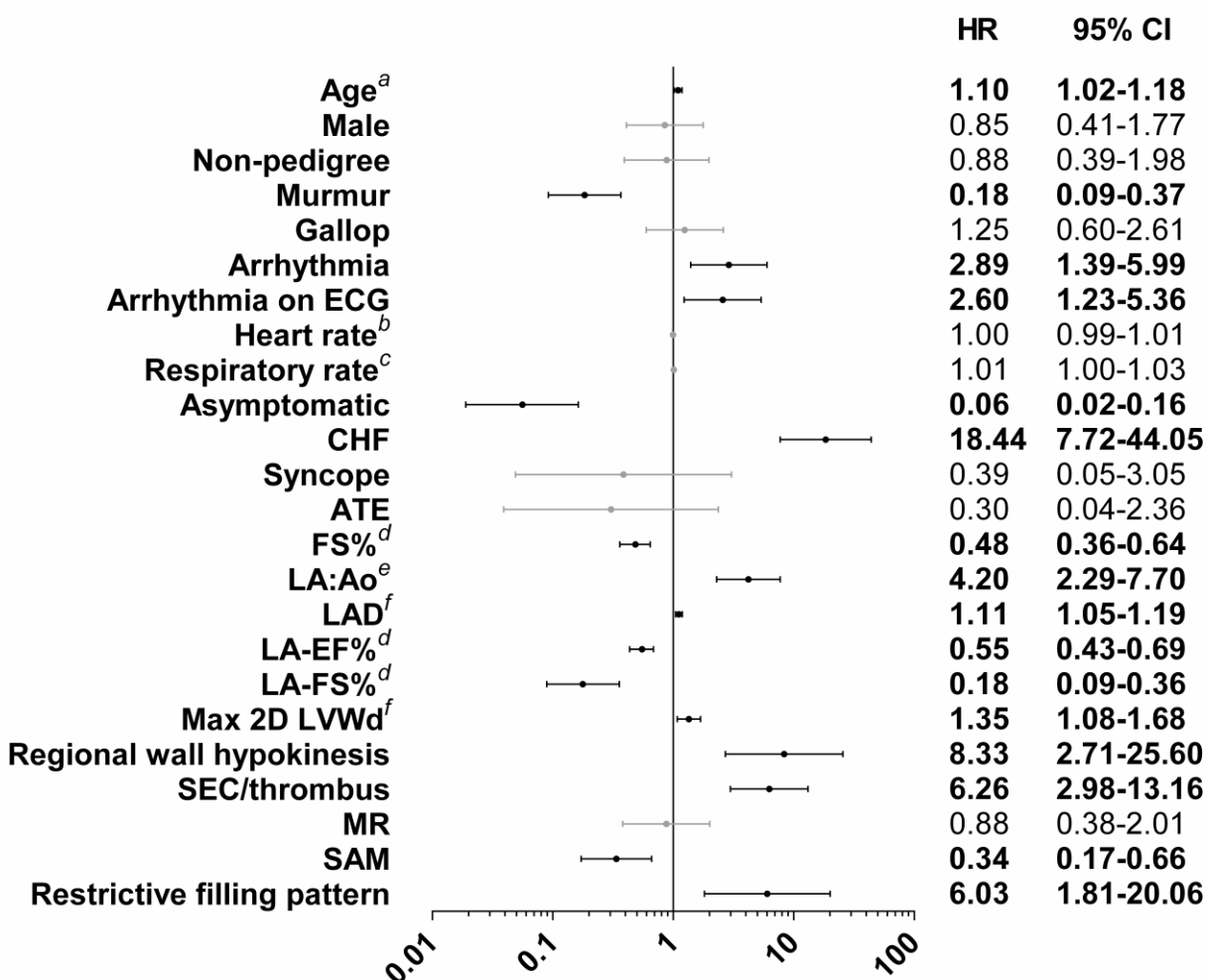


Figure 1 – Risk of death due to congestive heart failure (CHF); univariable hazard ratios of physical exam and echocardiographic findings at presentation between cats that did and did not suffer a CHF death within 2 years of diagnosis. CHF – congestive heart failure, ATE – arterial thromboembolism, FS% - Left ventricular fractional shortening, LA:Ao - short axis ratio of diastolic left atrial diameter to aortic root diameter, LAD – the diameter of the left atrium measured parallel with the mitral annulus in the last frame before mitral valve opening, LA-EF% – left atrial emptying fraction, LA-FS% – left atrial fractional shortening, Max 2D LVWd – maximum end-diastolic left ventricular septal or free wall thickness measured on a 2D image, SEC – spontaneous echo contrast, MR – mitral regurgitation, SAM – systolic anterior motion of the mitral valve, *a* – for a unit change of 1 year, *b* – for a unit change of 1 beat per minute, *c* – for a unit change of 1 breath per minute, *d* – for a unit change of 10%, *e* – for a unit change of 1, *f* – for a unit change of 1 mm

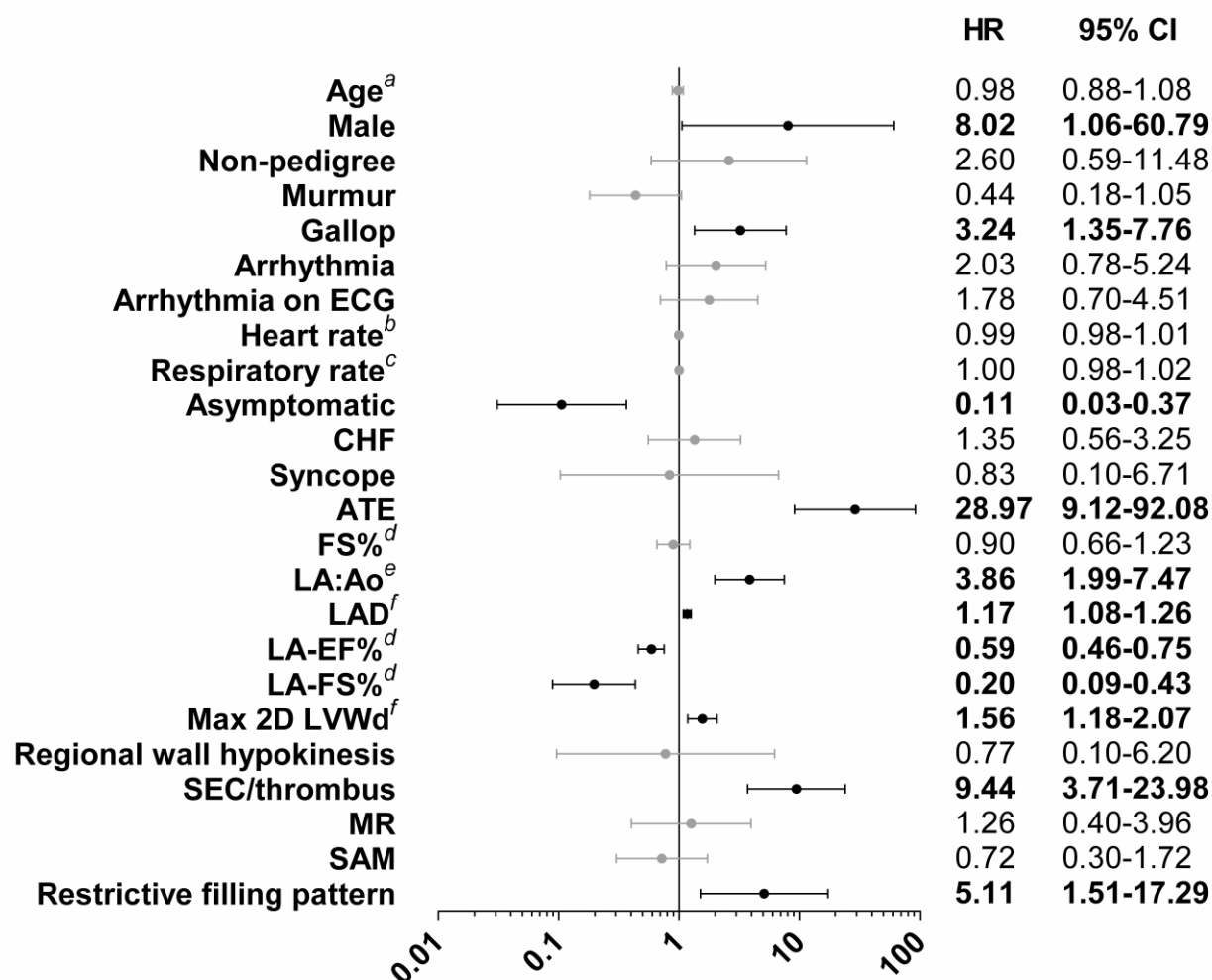


Figure 2 - Risk of death due to arterial thromboembolism (ATE); univariable hazard ratios of physical exam and echocardiographic findings at presentation between cats that did and did not suffer an ATE death within 2 years of diagnosis. CHF – congestive heart failure, ATE – arterial thromboembolism, FS% – Left ventricular fractional shortening, LA:Ao – short axis ratio of diastolic left atrial diameter to aortic root diameter, LAD – the diameter of the left atrium measured parallel with the mitral annulus in the last frame before mitral valve opening, LA-EF% – left atrial emptying fraction, LA-FS% – left atrial fractional shortening, Max 2D LVWd – maximum end-diastolic left ventricular septal or free wall thickness measured on a 2D image, SEC – spontaneous echo contrast, MR – mitral regurgitation, SAM – systolic anterior motion of the mitral valve, *a* – for a unit change of 1 year, *b* – for a unit change of 1 beat per minute, *c* – for a unit change of 1 breath per minute, *d* – for a unit change of 10%, *e* – for a unit change of 1, *f* – for a unit change of 1 mm

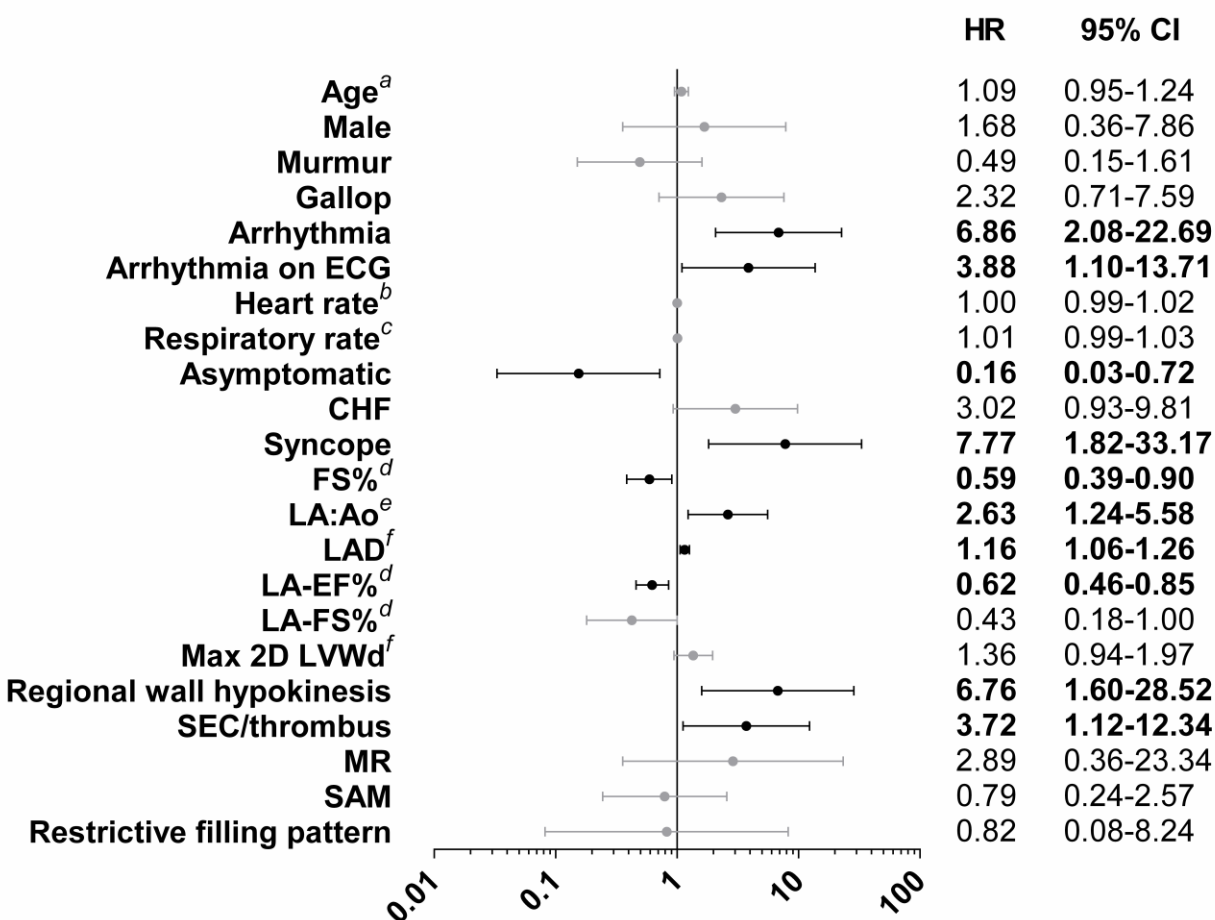


Figure 3 - Risk of death due to sudden death; univariable hazard ratios of physical exam and echocardiographic findings at presentation between cats that did and did not suffer a sudden death within 2 years of diagnosis. Nb No pedigree cat died suddenly so it was not possible to generate hazard ratios, a chi-squared was non-significant ($p=0.130$). No cat that presented with ATE died suddenly so it was not possible to generate hazard ratios, a chi-squared was non-significant ($p=1.000$). CHF – congestive heart failure, ATE – arterial thromboembolism, FS% - Left ventricular fractional shortening, LA:Ao - short axis ratio of diastolic left atrial diameter to aortic root diameter, LAD – the diameter of the left atrium measured parallel with the mitral annulus in the last frame before mitral valve opening, LA-EF% – left atrial emptying fraction, LA-FS% – left atrial fractional shortening, Max 2D LVWd – maximum end-diastolic left ventricular septal or free wall thickness measured on a 2D image, SEC – spontaneous echo contrast, MR – mitral regurgitation, SAM – systolic anterior motion of the mitral valve, *a* – for a unit change of 1 year, *b* – for a unit change of 1 beat per minute, *c* – for a unit change of 1 breath per minute, *d* – for a unit change of 10%, *e* – for a unit change of 1, *f* – for a unit change of 1 mm

	OR (95% CI)	p value
CHF at first presentation	6.318 (1.699 – 23.496)	0.006
LA-FS%	0.892 (0.799 – 0.994)	0.039
FS%	0.965 (0.917 – 0.997)	0.036
Respiratory rate	1.023 (1.001 – 1.045)	0.045

Table 1 - Binary logistic regression model, predicting CHF death within two years of diagnosis, (25 events of 172 cases)

	OR (95% CI)	p value
ATE at first presentation	28.58 (6.05 – 135.03)	<0.001
LA-FS%	0.84 (0.77 – 0.92)	<0.001

Table 2 – Binary logistic regression model, predicting ATE death within two years of diagnosis, (20 events of 200 cases)