



The presence of thymus detectable at necropsy in adult cats with hypertrophic cardiomyopathy

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INTRODUCTION

The thymus undergoes age-associated atrophy (thymic involution) and is no longer detectable at 1 year in most cats. Otherwise, thymic tissue remains plastic and retains potent regenerative capacity. The hyperplastic or persistent/residual thymus in adults may be associated with hyperthyroidism or autoimmune disorders. Hypertrophic cardiomyopathy (HCM) is a life-threatening feline cardiac disease. However, the mechanism underlying these conditions is not fully understood. The purpose of the present study was to investigate the relationship between HCM and the presence of thymus detectable at necropsy in adult cats.

MATERIALS and METHODS

Necropsy and histopathology records of 153 cats submitted to the Department of Pathology and Veterinary Diagnostics, SGGW between 2016 and March 2023 were retrospectively reviewed. Inclusion criteria were age ≥ 2 years, complete demographic data, and information on the presence/absence of thymus at necropsy. 87 cats were males (63 [72.4%] neutered) and 66 females (39 [59.1%] spayed). 100 cats were domestic shorthair (DSH; 65.4%) and 53 cats (34.6%) belonged to 17 breeds of which most common were British Shorthair (n=11), Maine Coon (n=9), and Russian Blue (n=7). Histopathology: haematoxylin and eosin (HE) and for selected cases Masson's trichrome stains were performed. Statistical analysis was performed using TIBCO Statistica 13.3.0 (TIBCO Statistics Inc., Palo Alto, CA, USA). The numerical variables were presented as the median, interquartile range (IQR), and range, and compared between groups using the Mann-Whitney U test. Categorical variables were presented as counts and percentages. The 95% confidence intervals were calculated using Wilson score method and the difference between proportions was calculated using Newcombe's method (Altman et al. 2000). The variables in which the univariable analysis yielded p-value < 0.2 were entered into the multivariable analysis. The analysis was performed using the multiple logistic regression according to the backward stepwise procedure. Magnitude of the relationship between variables was measured using odds ratios (OR) with CI 95%. The Hosmer-Lemeshow (H&L) test and Nagelkerke's R² coefficient were used to assess the goodness of fit of the logistic model (Hosmer & Lemeshow, 2000). The significance level (α) was set at 0.05, except the univariable analysis where $\alpha=0.2$. All statistical tests were two-tailed.

RESULTS

Characteristics	HCM (n=72)	Non-HCM (n=81)	p-value	Difference between proportions (CI 95%)	OR (CI 95%)
Thymus present	20 (27.8%; 18.8% – 39.0%)	3 (3.7%; 1.3% – 10.3%)	<0.001	24.1% (12.9% – 35.6%)	10.0 (2.8 – 35.4)

- Thymic tissue was detected in 23 cats, without evidence of thymic neoplasm.
- Thymus was detectable at necropsy in significantly higher percentage of cats with hypertrophic cardiomyopathy (HCM) compared to cats without HCM (non-HCM) ($p < 0.001$).
- 3 cats that had thymus detectable in the gross examination and did not die of HCM died of: circulatory and respiratory failure caused by chronic multiorgan damage (n=1), circulatory and respiratory failure (n=1), and meningoencephalitis (n=1).

Demographic characteristics	detectable at necropsy (n=23)	undetectable at necropsy (n=130)	p-value	OR (CI 95%)
Males ^a	16 (69.6%)	71 (54.6%)	0.176	-
Castrated ^a	21 (91.3%)	81 (62.3%)	0.003	6.4 (1.4 – 28.3)
Pedigree ^a	15 (65.2%)	38 (29.2%)	0.001	4.5 (1.8 – 11.6)
Age [years] ^{a,c}	4.0, 3.0 – 7.0 (2.5 – 13.8)	6.0, 4.0 – 10.0 (2.0 – 25)	0.018	-
Body weight [kg] [data for 110 cats] ^{b,c}	6.0, 3.8 – 7.1 (1.9 – 10.0)	4.0, 3.0 – 5.3 (1.5 – 10.0)	0.012	-

^a included in the multivariable analysis due to $p < 0.2$, ^b could not be included in the multivariable analysis due to missing data in 43 cats, ^c presented as the median, IQR, and range in parentheses;

- Cats with thymus detectable at necropsy were significantly more often castrated ($p=0.003$), significantly more often were pedigree ($p=0.001$), younger ($p=0.018$) and heavier cats ($p=0.012$).

Demographic characteristics	HCM (n=72)	Non-HCM (n=81)	p-value	OR (CI 95%)
Male gender ^a	48 (66.7%)	39 (48.2%)	0.020	2.15 (1.12 – 4.15)
Castration ^a	56 (77.8%)	46 (56.8%)	0.006	2.66 (1.31 – 5.41)
Pedigree ^a	40 (55.6%)	13 (16.1%)	<0.001	6.54 (3.08 – 14.9)
Age [years] ^c	5.0, 4.0 – 9.5 (2.0 – 16.0)	6.0, 4.5 – 10.5 (2.0 – 25.0)	0.265	-
Body weight [kg] [data for 110 cats] ^{b,c}	5.7, 4.0 – 6.5 (1.9 – 10.0) [53 cats]	3.6, 2.5 – 4.3 (1.5 – 10.0) [57 cats]	<0.001	-

^a included in the multivariable analysis due to $p < 0.2$, ^b could not be included in the multivariable analysis due to missing data in 43 cats, ^c presented as the median, IQR, and range in parentheses;

- In the univariable analysis the presence of HCM was significantly positively associated with male gender ($p=0.020$), castration ($p=0.006$), and being a pedigree cat ($p < 0.001$). Moreover, in the univariable analysis cats with HCM were significantly heavier than non-HCM cats ($p < 0.001$).

Variables	Regression coefficient (SE)	Wald's statistic	p-value	OR (CI 95%)
Intercept	-1.73 (0.54)	-	-	-
Thymus	1.79 (0.69)	6.67	0.010	5.97 (1.54 – 23.19)
Confounders:				
Sex	0.76 (0.39)	3.82	0.051	2.14 (1.00 – 4.59)
Neuter status	0.48 (0.41)	1.36	0.244	1.62 (0.72 – 3.62)
Pedigree	1.71 (0.42)	16.78	<0.001	5.50 (2.43 – 12.44)
Age	0.01 (0.04)	0.03	0.872	1.01 (0.92 – 1.10)

H&L $\chi^2=4.23$, $p=0.836$, Nagelkerke's pseudo-R² coefficient = 0.335

- Thymus detectable at necropsy proved to be independently significantly positively associated with HCM ($p=0.010$).

Variables	Regression coefficient (SE)	Wald's statistic	p-value	OR (CI 95%)
Intercept	-1.40 (0.34)	-	-	-
Male gender	0.81 (0.39)	4.40	0.036	2.25 (1.06 – 4.78)
Pedigree	1.75 (0.41)	18.24	<0.001	5.76 (2.58 – 12.88)
Thymus	1.88 (0.68)	7.67	0.006	6.58 (1.74 – 24.98)
Variables dropped from the model:				
Neuter status	0.48 (0.41)	1.37	0.242	1.62 (0.72 – 3.62)
Age	0.01 (0.04)	0.03	0.872	1.01 (0.92 – 1.10)

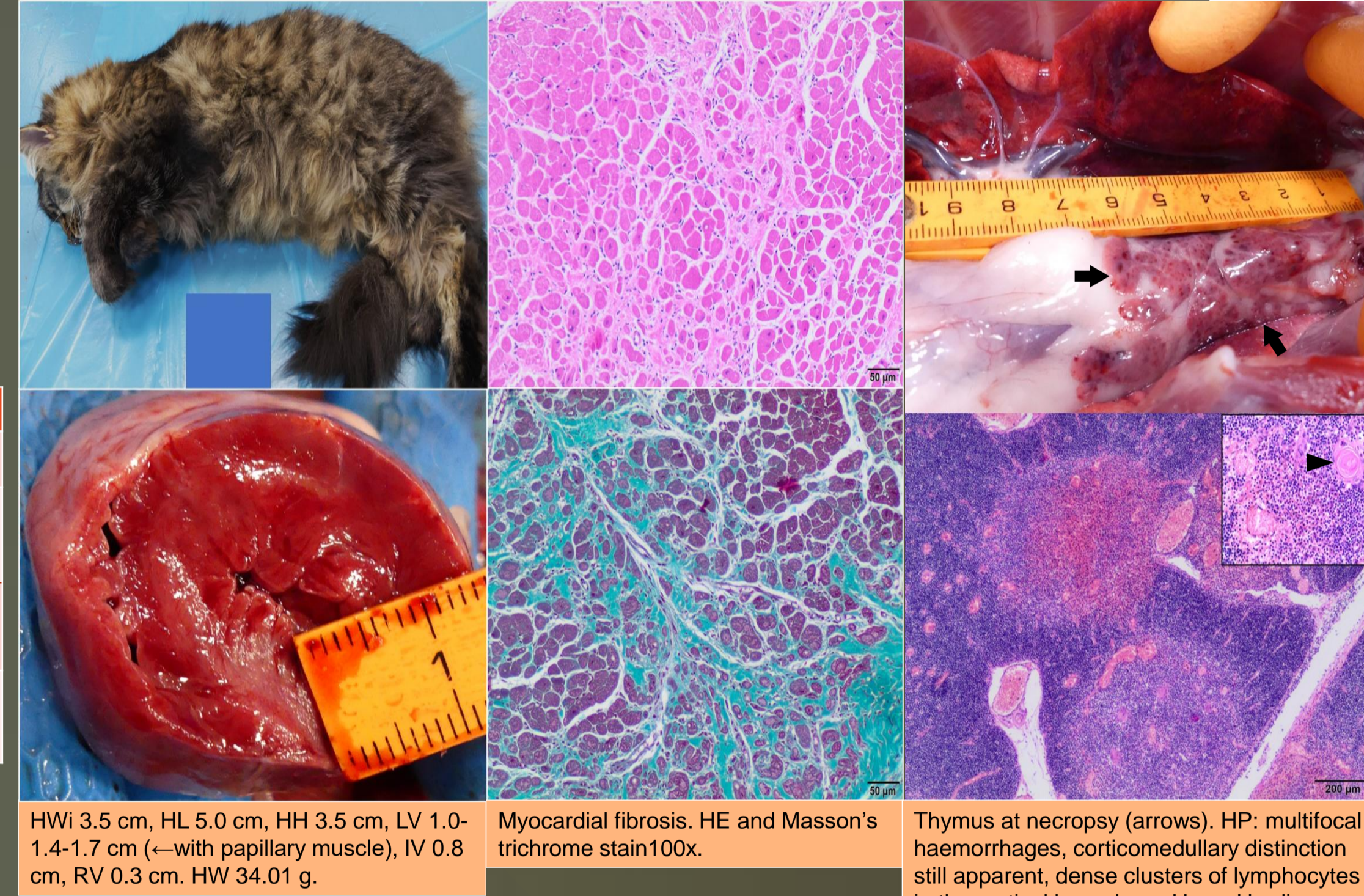
H&L $\chi^2=1.39$, $p=0.709$, Nagelkerke's pseudo-R² coefficient = 0.326

- Male gender, being a pedigree cat turned out to be demographic characteristics of cats significantly associated with HCM. Thymus detectable at necropsy was significantly associated with the presence of HCM.

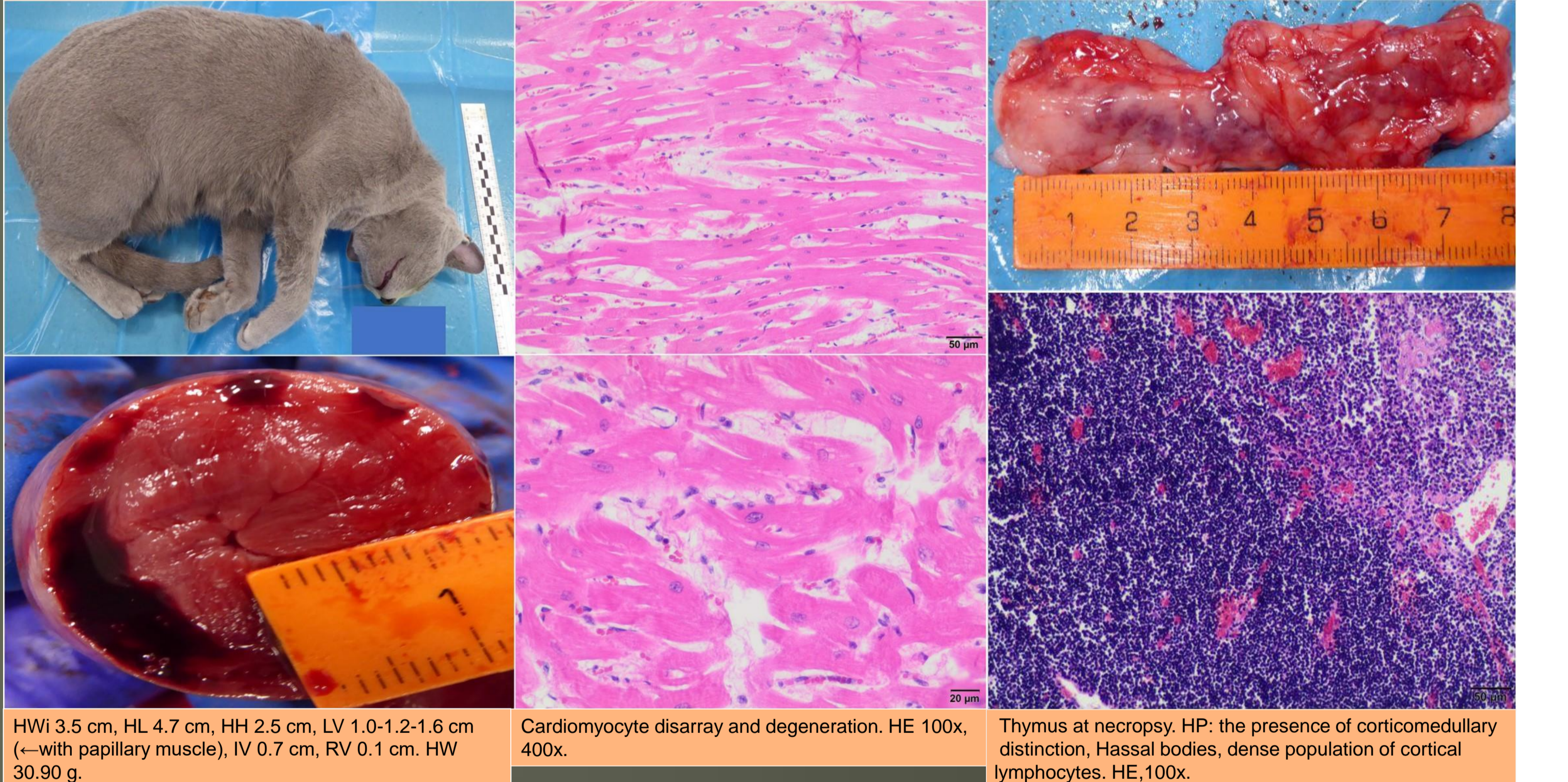
Seventy-two cats died of HCM. Presence of HCM was ($p=0.001$) significantly positively associated with sudden unexpected death and hydropericardium ($p=0.020$) compared to non-HCM cats.

	HCM		Non-HCM		p-value
	n	median, IQR (range)	n	median, IQR (range)	
Thymus length [cm]	12	4.3, 2.8 – 8.0 (1.0 – 10.0)	0	-	-
Thymus width [cm]	11	1.5, 1.0 – 1.5 (0.5 – 4.5)	0	-	-

Representative patients: Male, neutered, 2 1/2 years old, Maine Coon, 9.70 kg. Sudden death.

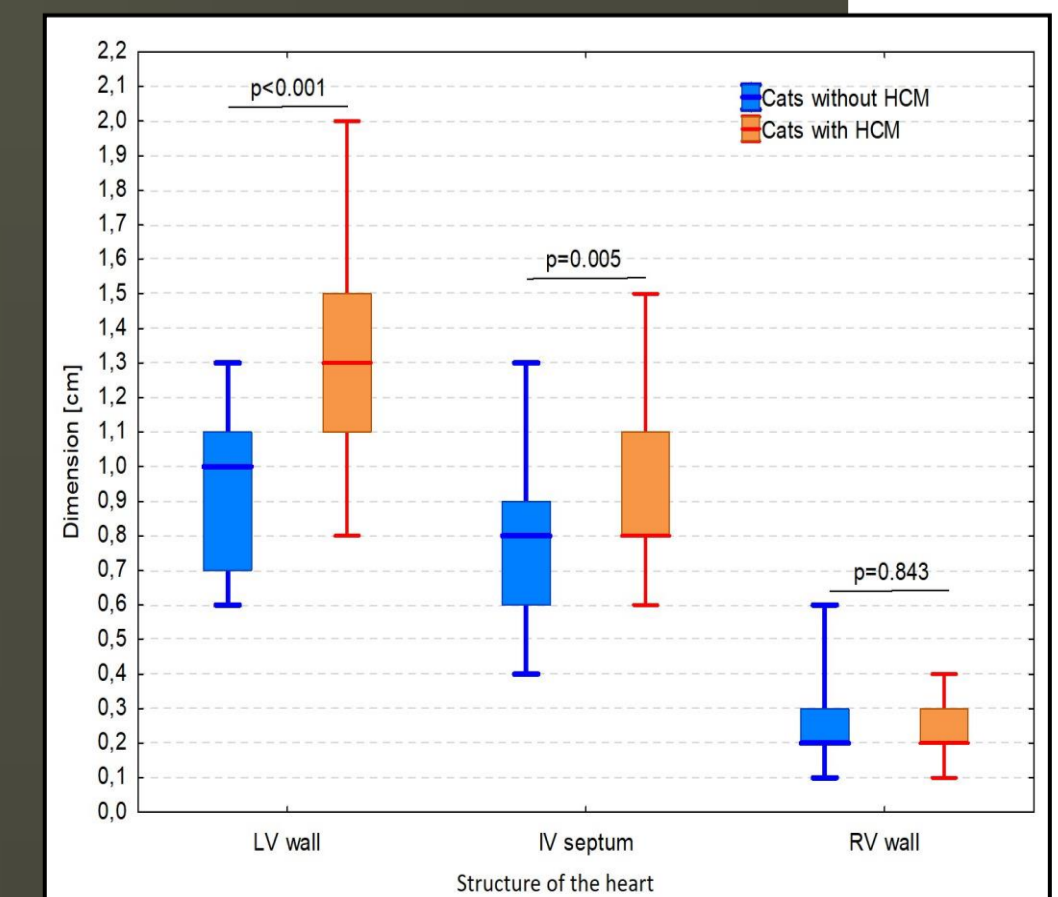


Male, neutered 4 years old, Russian Blue, 6.05 kg. Sudden death.



	HCM		Non-HCM		p-value
	n	median, IQR (range)	n	median, IQR (range)	
Heart width, HWi [cm]	50	3.5, 3.3 – 4.0 (2.8 – 5.0)	47	3.5, 3.1 – 3.8 (2.5 – 4.4)	0.115
Heart length, HL [cm]	50	4.5, 4.0 – 4.7 (3.0 – 5.6)	48	4.0, 3.5 – 4.5 (2.4 – 6.5)	0.007
Heart height, HH [cm]	25	2.2, 2.0 – 2.5 (1.2 – 3.5)	18	2.0, 1.7 – 2.5 (0.9 – 3.5)	0.226
Heart weight, HW [g]	29	22.6, 19.7 – 30.0 (12.4 – 43.0)	14	16.0, 14.0 – 18.4 (12.1 – 24.1)	<0.001
Heart-to-body weight ratio [g/kg]	26	3.7, 3.1 – 5.4 (2.8 – 9.2)	9	3.9, 3.5 – 4.8 (3.2 – 8.0)	0.485
Left ventricular wall thickness, LV [cm]	51	1.3, 1.1 – 1.5 (0.8 – 2.0)	40	1.0, 0.7 – 1.1 (0.6 – 1.3)	<0.001
Interventricular septal thickness, IV [cm]	47	0.8, 0.8 – 1.1 (0.6 – 1.5)	38	0.8, 0.6 – 0.9 (0.4 – 1.3)	0.005
Right ventricular thickness, RV [cm]	47	0.2, 0.2 – 0.3 (0.1 – 0.4)	37	0.2, 0.2 – 0.3 (0.1 – 0.6)	0.843

- Cats with HCM had significantly longer ($p=0.007$) and heavier heart ($p < 0.001$). Cats with HCM had significantly thicker LV ($p < 0.001$) and IV septum ($p=0.005$) but not RV ($p=0.843$) (look also at the graph).



CONCLUSIONS

We report for the first time the significant association between the presence of thymus detectable at necropsy and the presence of feline HCM. The results showed that adult cats which have died from HCM often have remnant thymic tissue. The presence of thymus detectable at necropsy in these cats may be loosely interpreted as a result of delayed thymic involution. Further studies are necessary to better understand the potential link between thymic involution and HCM in cats.

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