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Comparison of echocardiography, biomarkers and taurine concentrations in cats eating high- or low-pulse diets

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Abstract

Objectives There are ongoing investigations into diet-associated dilated cardiomyopathy in dogs, but there has been minimal investigation into possible diet-associated dilated cardiomyopathy in cats. The objective of this study was to compare cardiac size and function, cardiac biomarkers and taurine concentrations in healthy cats eating high- vs low-pulse diets. We hypothesized that cats eating high-pulse diets would have larger hearts, lower systolic function and higher biomarker concentrations than cats eating low-pulse diets and that there would be no difference in taurine concentrations between the diet groups.

Methods Echocardiographic measurements, cardiac biomarkers, and plasma and whole-blood taurine concentrations were compared between cats eating high- and low-pulse commercial dry diets in a cross-sectional study.

Results There were no differences between the high- (n = 21) and low-pulse (n = 31) diet groups with regard to age, sex and breed, but more cats in the high-pulse group were overweight or obese (67% vs 39%; $P = 0.05$). Diet duration was not different in the groups, but the range was wide (6–120 months). No differences were found between the diet groups for key cardiac measurements, biomarker concentrations, or plasma or whole-blood taurine concentrations. However, there were significant negative correlations between diet duration and measures of left ventricular wall thickness in the high-pulse, but not the low-pulse, diet group.

Conclusions and relevance This study did not detect significant associations between high-pulse diets and cardiac size, function and biomarkers, but the secondary observation of significant negative correlations between time on high-pulse diets and left ventricular wall thickness warrants further evaluation.

Keywords: Cardiomyopathy; heart disease; grain-free; pulses; cardiology; nutrition

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Introduction

The US Food and Drug Administration (FDA) and researchers have been investigating a secondary dilated cardiomyopathy (DCM) in pets that appears to be associated with grain-free diets and diets high in pulses (eg, peas, lentils and chickpeas) and, to a lesser extent, potatoes or sweet potatoes.[1–10] As of July 2020, more than 1100 dogs with DCM have been reported to the FDA.[11] In addition to overt DCM, these diets have also been associated with earlier, subclinical abnormalities in cardiac size and function or elevated cardiac biomarkers.[12–17] Although the

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cause of this diet-associated DCM (daDCM) is unknown, it is speculated that it could be due to a deficiency or toxicity resulting from ingredients in these diets. In contrast to primary DCM, which is typically a progressive disease, many dogs with daDCM have improvements in cardiac size and function, or even resolution of heart disease after a diet change; dogs whose diets are changed also have a longer survival time than dogs with primary DCM.[3–6,8,10,11]

While the majority of cases reported to the FDA have been dogs, more than 20 cats with suspected daDCM had also been reported as of July 2020.[3,11] DCM was one of the most common heart diseases affecting cats until the discovery in 1987 of the link between taurine deficiency and this disease.[18–21] Subsequent increases in taurine levels in commercial cat diets have dramatically reduced taurine deficiency-induced DCM in cats.[22] However, a recent survey identified that 15% of veterinary cardiologists surveyed perceived an increase in the number of cats being diagnosed with DCM between 2018 and 2020, and that some of these cats improved with a diet change, despite normal taurine concentrations.[23] Additionally, a retrospective, multicenter study of 37 cats with DCM found that 38% of cats for which diet could be determined were eating high-pulse diets and that taurine deficiency was uncommon.[23] An additional finding was that cats eating high-pulse diets that changed diet ($n = 8$) had a longer survival time than cats eating high-pulse diets that did not change diet ($n = 6$) or cats eating low-pulse diets ($n = 20$).[23] While much additional research is needed to be able to substantiate a possible association between diet and feline DCM, these results support the hypothesis that cats with DCM eating high-pulse diets might have a secondary daDCM unrelated to taurine deficiency which might improve with diet change, similar to what has been seen in dogs.

Considering that pulses appear to be common ingredients for both cat and dog foods in both grain-free and grain-containing diets, it is important to determine whether high-pulse diets could be associated with subclinical cardiac changes in cats. Therefore, the purpose of this study was to compare cardiac size and function, cardiac biomarkers and taurine concentrations in apparently healthy cats eating high- vs low-pulse diets. We hypothesized that cats eating high-pulse diets would have higher biomarker concentrations, larger hearts and lower contractile function than cats eating low-pulse diets but that there would be no difference in taurine levels between diet groups.

Materials and methods

This study was approved by the Tufts University Institutional Animal Care and Use Committee (protocol #G2021-06). Cats were recruited from hospital staff, students and clients, and from area practices via email, elists, websites, flyers and social media. Information to determine eligibility was gathered via an electronic screening survey (Qualtrics; SAP), which was available for completion from 6 May 2021 to 6 May 2022. A survey was considered complete and evaluable if the respondent had answered all of the questions. Cats were considered eligible for inclusion if they were between 2 and 15 years old; were overtly healthy and not taking medications other than flea, tick or heartworm preventatives; were not taking dietary supplements clinically relevant to the heart (eg, taurine and omega-3 fatty acids); and were eating dry commercial cat food as their major source (⩾70%) of calories. Cats had to be eating the diet for at least 6 months and the diet had to meet study criteria for categorization as either high- or low-pulse. If cats were eating more than one diet (eg, mixing two diets, or rotating back and forth between two diets), they were considered eligible as long as both diets could be categorized into the same pulse grouping.

For this study, high-pulse was defined as at least one pulse in the top-five ingredients or at least two pulses in the top-10 ingredients on the diet's ingredients list; low-pulse was defined as pulses present below the 25th ingredient on the list or not present at all. Vitamin or mineral premixes were counted as a single ingredient, and compounds used to preserve fats or oils were not counted as an ingredient. Diet pulse and pulse/potato scores for each cat were calculated as previously described.[8,16] If a cat was eating more than one diet, the diet with the highest pulse score was used for that cat's diet pulse score.

Exclusion criteria included pre-existing heart disease or known heart murmurs, hypertension (systolic blood pressure >180 mmHg), hyperthyroidism or significant systemic illness (eg, diabetes or cancer). If a cat's inclusion status could not be determined based on their survey alone, owners or primary care veterinarians were contacted for further information.

All cats were evaluated by one of two board-certified veterinary cardiologists (JER and ETK) who were blinded to the cats' diets. Each cat underwent a physical examination and M-mode, two-dimensional and color Doppler echocardiography using standard procedures.[24] M-mode left ventricular (LV) dimensions in systole and diastole were measured, along with two-dimensional ratio of the left atrial:aortic (LA:Ao) dimensions.[25] Simpson's method of disc measurements were performed on a right parasternal long-axis four-chamber view. LV volumes and ejection fraction were automatically calculated by the ultrasound machine. An electrocardiogram was recorded concurrently during the echocardiogram to monitor for arrhythmias. If a cat was found to have a cardiac murmur during the examination, the cat's data were included in the analysis, although cats identified to have hypertrophic cardiomyopathy were excluded from data analysis.

Blood was collected by jugular or medial saphenous venipuncture using minimal restraint. Samples for high-sensitivity cardiac troponin I (cTnI, serum; Gastrointestinal

Laboratory Texas A&M College of Veterinary Medicine), N-terminal pro B-type natriuretic peptide (NT-proBNP, EDTA plasma; IDEXX Laboratories), and plasma and whole-blood taurine concentrations (heparinized plasma and whole blood; Amino Acid Laboratory, University of California Davis) were stored at –80°C until analysis; batches were sent out monthly. Packed cell volume (whole blood), biochemistry profile (serum) and thyroxine (T4, serum) concentration (for cats ⩾7 years of age) were analyzed immediately (Clinical Pathology Laboratory, Cummings School of Veterinary Medicine at Tufts University).

Descriptive statistics were summarized and stratified by diet group using medians and ranges for continuous variables (many variables were skewed) and frequencies and percentages for non-continuous variables. Demographic variables (eg, age and sex), and all laboratory testing and echocardiographic measurements were compared between the two diet groups using χ^2 analysis for categorical variables (Fisher's exact tests were utilized if expected cell counts were <5) and Wilcoxon rank sum tests for continuous variables. Multiple linear regression models were used to determine if diet group was associated with echocardiographic measurements or laboratory results. Outcomes that did not follow a normal distribution were transformed using the natural log or cubic root transformation so that the assumptions of the linear regression model were met. All models were adjusted for body condition score (BCS), age and duration cats had been on the diet ('diet duration'). Interactions between diet group and BCS were assessed by incorporating interaction terms in the multiple linear regression models. Spearman correlation coefficients were used to compare diet duration to M-mode echocardiographic measurements, stratified by diet group. P values ⩽0.05 were considered to be statistically significant. Statistical tests were performed using commercial statistical software (SPSS 25.0 [IBM] and RStudio Team 2021).

Results

Study population

Using data from canine studies,[8,12,13] sample size calculations showed that 28 cats per diet group would provide adequate statistical power (80% power, alpha = 0.05). To allow for larger than anticipated variability in cats vs dogs, the goal was a sample size of 32 cats per group. From 588 screening surveys, 21 cats eating high-pulse diets and 31 cats eating low-pulse diets were included in the final analysis (Figure 1).

Demographics and physical examination findings

There were no differences in age, sex or breed between the diet groups (Table 1). The range in diet duration for the entire population was very broad, from 6 months to 10 years; however, both diet groups had a median diet duration of approximately 2 years and there was no statistically significant difference between the diet groups (high-pulse diet median 22 months [range 8–96] and low-pulse diet median 24 months [range 6–120]; *P* = 0.96).

While there was no significant difference in body weight between diet groups, cats in the high-pulse group had a statistically significantly higher BCS (*P* = 0.02). Twenty-six of 52 cats (50%) were overweight (high-pulse, n = 14/21 [67%]; low-pulse, n = 12/31 [39%]; *P* = 0.05). Nineteen of 52 cats had a cardiac murmur (high-pulse, n = 7/21 [33%]; low-pulse, n = 12/31 [39%]; *P* = 0.83), 2/21 (10%) high-pulse cats had a cardiac gallop (*P* = 0.08) and one cat in each diet group had an arrhythmia (1/21 [5%] cats in the high pulse group had atrial premature complexes; 1/31 [3%] cats in the low-pulse group had bradycardia [*P* = 1.00]).

Laboratory results

No significant differences were identified between the diet groups for NT-proBNP, cTnI, or plasma or whole-blood taurine concentrations (Table 1). In the high-pulse group, 15/21 cats (71%) were in the laboratory's normal range (300–600 nmol/ml), while 6/21 (29%) were in the laboratory's 'no known risk of deficiency' range (200–300 nmol/ml). In the low-pulse group, 17/31 cats (55%) were in the laboratory's normal range, while 13/31 (42%) were in the laboratory's range of 'no known risk for deficiency' and 1/31 (3%) had a whole-blood taurine concentration below this range (whole-blood taurine 199 nmol/ml; plasma taurine 166 nmol/ml). Median phosphorus concentration was statistically significantly higher in the high-pulse group compared with the low-pulse group (*P* = 0.05), but there were no other significant differences in packed cell volume or relevant biochemistry profile results (data not shown). None of the 20 cats ⩾7 years of age (high-pulse, n = 7/21; low-pulse, n = 13/31) had elevated T4 concentrations. Regression analysis showed no significant interaction between diet group and diet duration, and no significant differences in NT-proBNP, cTnI or taurine concentrations between diet groups after adjusting for BCS, age and diet duration.

Echocardiographic evaluation

There were no significant differences found between diet groups for any echocardiographic measurements (Table 2). Regression analysis showed no significant interaction between diet group and diet duration and no significant differences in echocardiographic measurements between diet groups after adjusting for BCS, age and diet duration.

Given the wide variation in diet duration in both diet groups identified during data analysis, diet duration was compared in post-hoc analysis to M-mode echocardiographic measurements separately between the two diet groups (Table 3). In the high-pulse group, diet

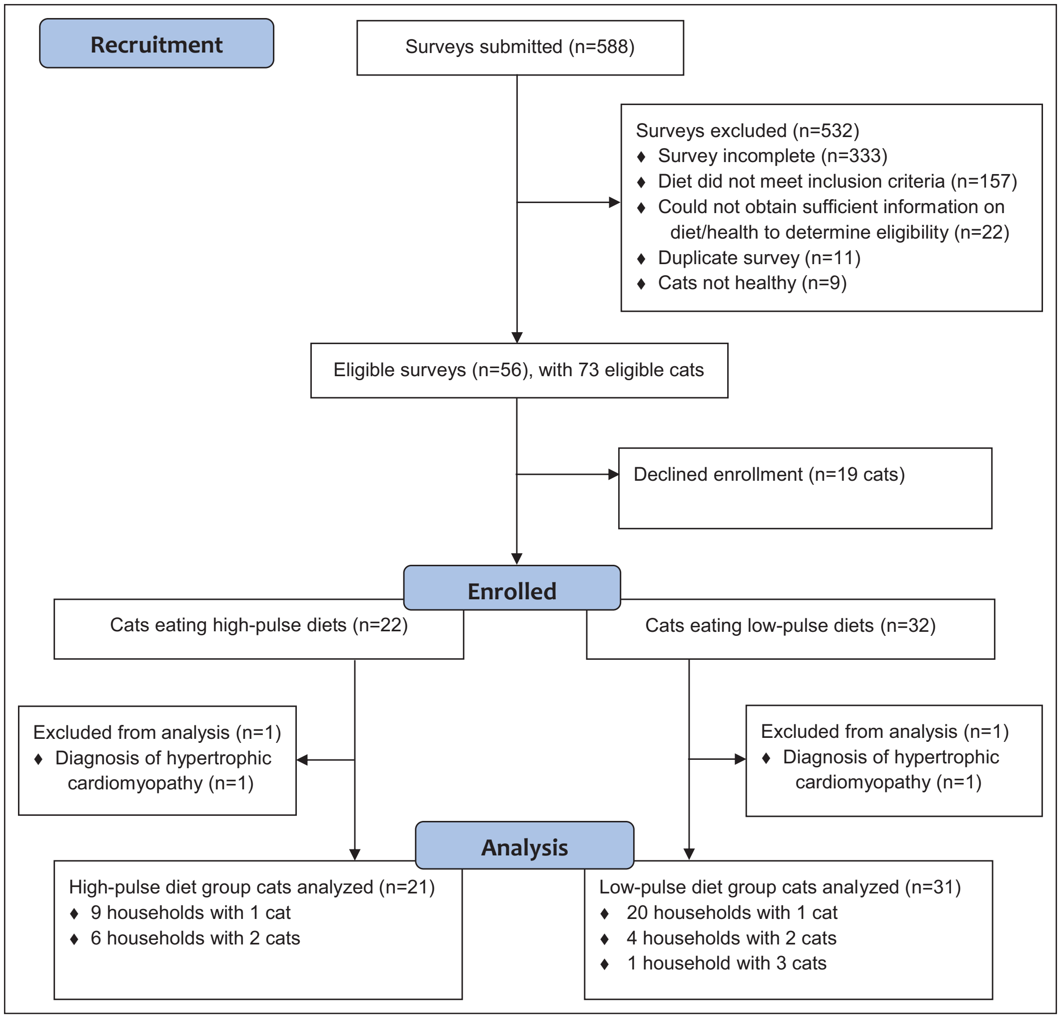

Figure 1 CONSORT flow diagram of the enrollment of cats eating high-pulse or low-pulse diets, reasons for exclusion and number of eligible cats for analysis in this study

duration was significantly negatively correlated with the widths of the interventricular septum (IVS) in diastole ($r = -0.63$; $P = 0.002$), LV posterior wall in diastole ($r = -0.55$; $P = 0.01$), IVS in systole ($r = -0.52$; $P = 0.02$) and LV posterior wall in systole ($r = -0.48$; $P = 0.03$ [Figure 2]). However, in the low-pulse group, diet duration was not significantly associated with any of the M-mode cardiac measurements. Age in the high-pulse group was significantly negatively correlated with the LV internal diameter in diastole ($r = -0.47$; $P = 0.03$), IVS width in systole ($r = -0.51$; $P = 0.02$) and LV posterior wall width in systole ($r = -0.49$; $P = 0.02$). However, in the low-pulse group, the only measurement significantly (negatively) correlated with age was LV posterior wall width in systole ($r = -0.42$; $P = 0.02$).

Discussion

In this study, echocardiographic measurements were not significantly different between diet groups. This lack of significant echocardiographic differences between diet groups opposes our hypothesis, and is in contrast to similar studies performed in apparently healthy dogs, where dogs eating non-traditional/grain-free diets had significantly larger hearts with lower systolic function compared with dogs eating traditional/grain-inclusive diets.[12,17] Definitions for associated diets have varied among studies and have been refined over time as new data have been published on this disease.[1–17,23] High-pulse diets in our study were defined as those having at least one pulse in the top-five ingredients or at least two pulses in the top-10 ingredients on the diet's ingredient list, whereas many of the studies in dogs have defined 'non-traditional' diets as those containing pulses/potatoes in the top-10 ingredients or those classified as 'grain-free'. This definition might require further refinement, and the pulse score may be helpful in the future for defining study groups.

In contrast to a similar study of apparently healthy dogs of four breeds that found higher cTnI concentrations in dogs eating non-traditional/grain-free diets,[13] we did

Table 1 Clinical variables for 52 cats on high- or low-pulse diets

Variable	High-pulse diet (n = 21)	Low-pulse diet (n = 31)	*P* value
Age (years)	5.2 (3.3–7.9)	4.3 (3.0–9.2)	0.65
Sex			
Male intact	0 (0)	0 (0)	0.78
Male castrated	10 (47.6)	16 (51.6)	
Female intact	1 (4.8)	0 (0)	
Female spayed	10 (47.6)	15 (48.4)	
Breed			
DSH, DMH and DLH	16 (76.2)	28 (90.3)	0.23
American Shorthair	1 (4.8)	2 (6.5)	
Turkish Angora	2 (9.5)	0 (0)	
Persian	1 (4.8)	0 (0)	
Scottish Fold	1 (4.8)	0 (0)	
Tonkinese	0 (0)	1 (3.2)	
Diet duration (months)	22 (13–40)	24 (11–48)	0.96
Pulse score	43 (42–52)	0 (0–0)	<0.001
Pulse/potato score	63 (48–71)	0 (0–0)	<0.001
Diet calorie density (kcal/kg)	410 (389–446)	358 (329–480)	0.06
Received gabapentin prior to evaluation	3 (14.3)	5 (16.1)	0.86
Weight (kg)	5.1 (4.0–6.7)	4.8 (3.8–5.4)	0.14
BCS (1–9)	6 (5–8)	5 (5–6)	0.02
Muscle condition score			
Normal	18 (85.7)	28 (90.3)	0.61
Mild	3 (14.3)	3 (9.7)	
Moderate	0 (0)	0 (0)	
Severe	0 (0)	0 (0)	
Heart rate (bpm)*	180 (164–191)	190 (170–200)	0.10
Murmur grade	0 (0–2)	0 (0–1)	0.83
Gallop	2 (9.5)	0 (0)	0.16
Taurine – plasma (nmol/ml)†	146 (123–184)	137 (109–167)	0.17
Taurine – whole blood (nmol/ml)	348 (273–392)	307 (250–341)	0.09
NT-proBNP (pmol/l)	24 (24–39)	33 (24–46)	0.16
High-sensitivity cTnI (ng/ml)	0.026 (0.010–0.036)	0.018 (0.000–0.052)	0.61
Phosphorus (mg/dl)	4.4 (3.6–4.8)	4.0 (3.6–4.4)	0.05

Continuous data are presented as median (interquartile range) and categorical data are presented as frequency and percentages
*n = 48 (three cats in the high-pulse group and one in the low-pulse group did not have this variable collected and were therefore excluded from this comparison)
†n = 51 (one cat in the low-pulse group had hemolyzed plasma and was therefore excluded from this comparison)
DSH = domestic shorthair; DMH = domestic mediumhair; DLH = domestic longhair; BCS = body condition score; bpm = beats/min; NT-proBNP = N-terminal pro B-type natriuretic peptide; cTnI = cardiac troponin I

not find higher cTnI or NT-proBNP concentrations in the current study of apparently healthy cats. The lack of significant differences between the diet groups in the current study for plasma and whole-blood taurine concentrations was expected, considering that all cats were being fed commercial diets with minimum taurine levels established by the Association of American Feed Control Officials.[26] Two previous studies of apparently healthy dogs found no differences in whole blood or plasma taurine between dogs eating non-traditional/grain-free diets,[13,17] although one study in Golden Retrievers reported significantly lower whole-blood taurine (but not plasma taurine) concentrations in dogs eating non-traditional diets.[12]

The present study showed significantly higher median blood phosphorous concentration in the high-pulse group compared with the low-pulse group, which mirrors findings of increased phosphorous concentrations after feeding a high pea and lentil diet to healthy Labrador Retrievers for 30 days (despite a lower dietary phosphorus level in the high-pulse vs low-pulse diet).[27] The phosphorus content of the diets eaten by cats enrolled in the study was not analyzed, so it is unclear whether the higher phosphorus concentration is due to the concentration or bioavailability of dietary phosphorus, or to unknown pathophysiologic mechanisms – cardiac or otherwise – that occur with exposure to high-pulse diets.

Table 2 Echocardiographic measurements for 52 cats eating a high- or low-pulse diet

Variable	High-pulse diet (n = 21)	Low-pulse diet (n = 31)	*P* value
M-mode measurements			
IVSd (cm)	0.45 (0.38–0.51)	0.43 (0.38–0.46)	0.36
LVIDd (cm)	1.52 (1.40–1.69)	1.48 (1.36–1.57)	0.47
LV posterior wall in diastole (cm)	0.51 (0.44–0.55)	0.47 (0.44–0.50)	0.12
IVSs (cm)	0.70 (0.62–0.83)	0.72 (0.66–0.79)	0.55
LVIDs (cm)	0.70 (0.62–0.80)	0.68 (0.54–0.77)	0.63
LV posterior wall in systole (cm)	0.78 (0.69–0.88)	0.76 (0.69–0.80)	0.70
FS (%)	52.74 (48.88–58.58)	51.97 (49.09–58.89)	0.85
Two-dimensional measurements			
LAD (cm)	1.29 (1.24–1.41)	1.22 (1.14–1.34)	0.07
Aortic diameter (cm)	0.97 (0.89–1.07)	0.93 (0.87–1.00)	0.14
LA:Ao ratio	1.33 (1.26–1.48)	1.37 (1.24–1.41)	0.85
LVIDd (cm)	1.48 (1.39–1.65)	1.50 (1.40–1.57)	0.77
LVIDs (cm)	0.83 (0.69–0.98)	0.79 (0.70–0.88)	0.33
FS (%)	43.71 (37.87–52.59)	44.92 (41.31–52.69)	0.54
LV end diastolic volume (ml)*	2.62 (2.22–2.79)	2.60 (1.85–3.40)	0.93
LV end systolic volume (ml)†	0.65 (0.51–0.76)	0.57 (0.43–0.79)	0.35
LVEF (%)*	75.23 (70.99–79.66)	75.22 (72.57–80.41)	0.77
LVOT max velocity (ms)‡	1.00 (0.97–1.02)	0.97 (0.85–1.16)	1.00

Data are presented as median (interquartile range)
*n = 51 (one cat in the low-pulse group did not have this data collected and was therefore excluded from this calculation)
†n = 50 (one cat in the low-pulse group did not have these data collected and one cat in the high-pulse group was determined to be an outlier; these cats were therefore excluded from this calculation)
‡n = 24 (14 cats in the high-pulse group and 14 in the low-pulse group did not have these data collected and were therefore excluded from this calculation)
IVSd = interventricular septum in diastole; LVIDd = left ventricular internal diameter in diastole; LV = left ventricle; IVSs = interventricular septum in systole; LVIDs = left ventricular internal diameter in systole; FS = fractional shortening; LAD = left atrial diameter; LA:Ao = ratio of the left atrial:aortic dimension; LVEF = left ventricular ejection fraction; LVOT = left ventricular outflow tract

Table 3 Correlation analyses between diet group and heart measurements with respect to diet duration and age in 52 cats on a high- or low-pulse diet

	IVSd (cm)	LVIDd (cm)	LVPWd (cm)	IVSs (cm)	LVIDs (cm)	LVPWs (cm)	FS (%)	LA:Ao
High-pulse group (n = 21)								
Diet duration	*r* = –0.63; *P* = 0.002	*r* = –0.12; *P* = 0.62	*r* = –0.55; *P* = 0.01	*r* = –0.52; *P* = 0.02	*r* = –0.02; *P* = 0.94	*r* = –0.48; *P* = 0.03	*r* = –0.18; *P* = 0.44	*r* = –0.18; *P* = 0.44
Age	*r* = –0.39; *P* = 0.08	*r* = –0.47; *P* = 0.03	*r* = –0.35; *P* = 0.12	*r* = –0.51; *P* = 0.02	*r* = –0.07; *P* = 0.75	*r* = –0.49; *P* = 0.02	*r* = –0.35; *P* = 0.12	*r* = 0.18; *P* = 0.44
Low-pulse group (n = 31)								
Diet duration	*r* = –0.11; *P* = 0.55	*r* = –0.29; *P* = 0.11	*r* = –0.06; *P* = 0.75	*r* = 0.004; *P* = 0.98	*r* = –0.23; *P* = 0.22	*r* = –0.32; *P* = 0.08	*r* = 0.22; *P* = 0.24	*r* = 0.23; *P* = 0.22
Age	*r* = –0.21; *P* = 0.25	*r* = –0.01; *P* = 0.98	*r* = 0.07; *P* = 0.69	*r* = –0.11; *P* = 0.55	*r* = –0.05; *P* = 0.80	*r* = –0.42; *P* = 0.02	*r* = 0.06; *P* = 0.74	*r* = 0.06; *P* = 0.74

IVSd = M-mode interventricular septum in diastole; LVIDd = M-mode left ventricular internal diameter in diastole; LVPWd = M-mode left ventricular posterior wall in diastole; IVSs = M-mode interventricular septum in systole; LVIDs = M-mode left ventricular internal diameter in systole; LVPWs = M-mode left ventricular posterior wall in systole; FS = M-mode fractional shortening; LA:Ao = two-dimensional ratio of the left atrial:aortic dimensions

However, it does emphasize the importance of considering diet type and ingredients, as well as blood phosphorus and hematocrit, in future studies of feline heart disease.

The lack of differences in echocardiographic and cardiac biomarker findings compared with canine studies could be due to species differences, since, both subjectively and based on the number of cases of daDCM reported to the FDA, cats appear to be less susceptible to daDCM than dogs. Another explanation may be diet duration. While diet duration was not significantly different between the high- and low-pulse diet groups in

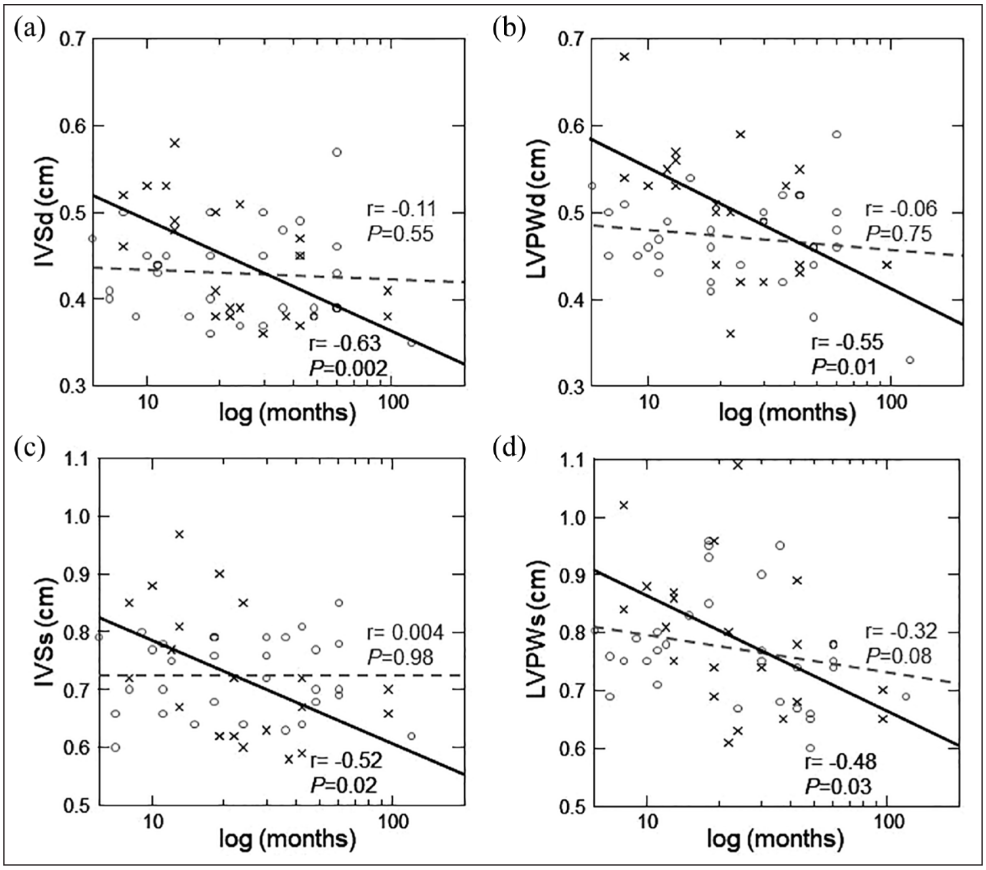

Figure 2 Scatterplots of data from 21 healthy cats eating high-pulse diets (black lines and crosses) and 31 healthy cats eating low-pulse diets (dashed lines and circles). Correlations were significant for the high-pulse diet group for all four echocardiographic measurements, while correlations were not significant for any of the measurements in the low-pulse diet group (*r* and *P* values are indicated on the individual scatterplots). (a) Interventricular septum in diastole (IVSd); (b) left ventricular posterior wall in diastole (LVPWd); (c) interventricular septum in systole (IVSs); (d) left ventricular posterior wall in systole (LVPWs)

the current study, the median duration was only 22 and 24 months, respectively. In a recent prospective study, dogs with overt DCM had been eating non-traditional diets for a median of 48 months, and dogs with subclinical cardiac abnormalities had been eating non-traditional diets for a median of 30 months,[8] while another study of dogs with daDCM found that longer diet duration was associated with shorter survival time.[10] In cats, a significantly negative correlation was found between diet duration and measures of LV thickness, whereas this was not seen in the low-pulse group. This could be consistent with the possibility that a longer duration on high-pulse diets might be necessary for changes to be observed. In two studies of apparently healthy dogs in which echocardiographic or cTnI differences between diet groups were identified, the median diet duration (18 and 21 months, respectively) was similar to that in the current study,[12,13] but if cats are less susceptible to daDCM, longer diet duration or a larger sample size may be needed to identify differences between diet groups.

Another possible reason that the current study did not identify a significant difference in echocardiographic measurements between diet groups is that the levels of pulses in various diets may not have been as high as in the recent canine studies that *did* identify differences. The current study's median pulse and pulse/potato scores in the high-pulse group were lower than in previous studies of dogs with DCM or subclinical cardiac abnormalities eating non-traditional/grain-free diets.[8,16] Therefore, the 'dose' of pulses cats were receiving could have been insufficient to be associated with echocardiographic and cardiac biomarker differences.

The cats enrolled in the two diet groups were well matched, with the only significant demographic difference between the two groups being BCS. Overall, 50% of cats in the study were overweight, but more cats in the high-pulse group were overweight (67%) than in the low-pulse group (39%). These numbers are consistent with the fact that 59.5% of pet cats in the USA in 2018 were considered to be overweight or obese.[28] The reason that more cats in the high-pulse group were overweight is unknown, but it could be related to the higher calorie density of these diets (Table 1). While the median age in the two diet groups was not significantly different, there was a significant negative correlation between age and LV internal diameter in diastole in the high-pulse group but not in the low-pulse group. The cause for this correlation is unclear, but there is limited information on structural echocardiographic findings in healthy older cats.

A number of additional limitations to those already noted are important to consider, including the sample size. Sample size calculations based on canine data suggested that 28 cats per group would provide adequate statistical power, and we planned for 32 cats per group to allow for larger variability in cats compared with dogs (although post-hoc analysis showed that a much larger number of cats would have been needed). However, even enrolling the planned 32 cats per group proved to be a challenge. Enrollment efforts were slower than anticipated due to impacts of the COVID-19 pandemic (eg, curbside veterinary appointments, limited face-to-face interactions and schools and businesses working remotely). Ultimately, while we had a substantial response to recruitment efforts (588 submitted screening surveys), the number of eligible cats did not meet the planned 32 cats per group; enrollment for the high-pulse group was more difficult than for the low-pulse group. Rather than keeping the survey open for an extended period to find more cats eligible for inclusion in the high-pulse group and risk unblinding the cardiologists to the cats' diet group, the investigators decided to end the study with a small sample size in the high-pulse group.

Additionally, cats only had one echocardiogram, so this evaluation of cardiac structure and function was a snapshot in time. Thus, it is not known whether some of the echocardiographic measurements could reflect subclinical changes for an individual cat or whether further changes could occur over time. Serial evaluations of cats may be a useful method to consider for subsequent investigations.

Conclusions

Overall, in this study, no significant differences were found in terms of cardiac measurements, biomarker concentrations or plasma or whole-blood taurine concentrations between cats eating high-pulse and low-pulse diets. However, in the high-pulse group, there were significant negative correlations between diet duration and measures of LV wall thickness in diastole and systole that were not identified in cats eating low-pulse diets. This study did not detect significant associations between high-pulse diets and cardiac size, function or biomarkers, but the secondary observation of significant negative correlations between time eating high-pulse diets and LV wall thickness warrants further evaluation in larger populations of cats eating these diets for longer periods of time.

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Conflicts of interest In the last 3 years, Dr Freeman has received research or residency funding from, given sponsored lectures for or provided professional services for Aratana Therapeutics, Elanco, Guiding Stars Licensing Co, Nestlé Purina PetCare, P&G Petcare (now Mars) and Royal Canin. In the last 3 years, Dr Rush has received research funding from, given sponsored lectures for, or provided professional services for Aratana Therapeutics, Boehringer Ingelheim, Elanco, IDEXX, Nestlé Purina PetCare and Royal Canin.

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Ethical approval The work described in this manuscript involved the use of non-experimental (owned or unowned) animals. Established internationally recognized high standards ('best practice') of veterinary clinical care for the individual patient were always followed and/or this work involved the use of cadavers. Ethical approval from a committee was therefore not specifically required for publication in *JFMS*. Although not required, where ethical approval was still obtained, it is stated in the manuscript.

Informed consent Informed consent (verbal or written) was obtained from the owner or legal custodian of all animal(s) described in this work (experimental or non-experimental animals, including cadavers) for all procedure(s) undertaken (prospective or retrospective studies). No animals or people are identifiable within this publication, and therefore additional informed consent for publication was not required.

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