Echocardiographic Evidence for Myocardial Failure Induced by Taurine Deficiency in Domestic Cats

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ABSTRACT

Dietary taurine-deficiency is a cause of dilated cardiomyopathy (DCM) in cats. While the incidence of clinical cases of feline DCM has markedly decreased since the association between DCM and taurine-deficiency was first recognized, not all cats maintained on taurine-deficient diets develop DCM. The objective was to temporally evaluate left ventricular (LV) function using M-mode echocardiography in 23 cats maintained on a taurine-deficient diet; 20 time-matched, taurine-supplemented cats served as controls. The duration of feeding trials ranged from 6–15 months. No diminution of myocardial function was recorded in a small number of taurine-deficient cats whereas cardiac performance in some taurine-deficient cats diminished to levels characteristic of DCM. Of the taurine-deficient cats, 17 (74%) experienced a greater than 25% reduction in fractional shortening and 21 (91%) had a greater than 25% increase in LV end-systolic short-axis diameter. On average, LV end-systolic short-axis diameter increased by 70% and fractional shortening decreased by 37% in taurine-deficient cats. Mean velocity of circumferential fiber shortening was similarly reduced in taurine-deficient cats. The greatest rate of change in M-mode echocardiographic variables occurred during the first four months on the taurine-deficient diet. Dietary taurine deficiency leads to a spectrum of changes in myocardial function in domestic cats. While DCM is observed in some cats, decreased systolic pump function and increased LV end-systolic short-axis diameter are more consistent findings.

RÉSUMÉ

Une déficience alimentaire en taurine est une cause de cardiomyopathie dilatée (CMD) chez le chat. Alors que l'incidence de cas cliniques de CMD féline a nettement diminué depuis que l'association entre la CMD et la déficience en taurine a été reconnue pour la première fois, les chats maintenus sur des diètes déficientes en taurine ne développent pas tous une CMD. L'objectif de cette étude était d'évaluer l'évolution de la fonction ventriculaire gauche (VG) en utilisant l'échocardiographie en mode M chez : 1° 23 chats maintenus sur une diète déficiente en taurine; 2° 20 chats avec diète supplémentée en taurine et assortie en fonction du temps. La durée des essais alimentaires s'étalait de 6 à 15 mois. Chez les chats déficients en taurine, la fonction myocardique restait stable pour un faible nombre d'animaux alors que, chez d'autres, elle diminuait à des niveaux caractéristiques d'une CMD. Parmi les chats déficients en taurine, 17 (74 %) présentaient une réduction de plus de 25 % de la fraction de raccourcissement et 21 (91 %) avaient une augmentation de plus de 25 % du diamètre télé-systolique du VG mesuré dans le petit axe. En moyenne, le diamètre télé-systolique du VG en petit axe augmentait de 70 % et la fraction de raccourcissement diminuait de 37 % chez les chats déficients en taurine. La vitesse de raccourcissement de la circonférence du VG était diminuée de façon similaire chez les chats déficients en taurine. La majeure partie des changements échographiques en mode M s'est produite pendant les quatre premiers mois de la diète déficiente en taurine. Les déficiences nutritionnelles en taurine entraînent un ensemble de changements de la fonction myocardique chez les chats domestiques. Bien qu'une CMD soit observée chez certains chats, une diminution de la fonction d'éjection systolique et une diminution du diamètre télé-systolique du VG en petit axe sont les signes les plus constants. (*Traduit par Dr Phillipe Pibarot*)

INTRODUCTION

Dietary taurine deficiency is associated with the occurrence of dilated cardiomyopathy (DCM) in domestic cats (1–4). Conclusions that taurine deficiency results in DCM are based chiefly on clinical studies demonstrating a strong relationship between low plasma taurine concentrations and echocardiographic findings supportive of DCM. Cats were fed a variety of commercially-prepared feline diets that for unknown reasons failed to support adequate plasma taurine concentrations. Since the first report of an association between low plasma taurine concentration and DCM in cats, the incidence of feline DCM has apparently decreased (5). Taurine

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supplementation reverses echocardiographic signs of DCM (1,2). Interestingly, Pion *et al* (1) reported that only 2 of 11 research cats maintained for four years on a purified diet containing a marginal concentration of taurine had echocardiographic evidence of dilated cardiomyopathy (fractional shortening <35%; left ventricular end-systolic short-axis diameter >12 mm). In another study in which cats were maintained on taurine-deficient diets for 280 to 320 days prior to recording echocardiograms, clearly less than half of the cats met echocardiographic criteria for DCM (3). It would appear from these studies that dietary taurine deficiency does not consistently result in DCM.

We have previously reported decreased left ventricular (LV) contractility in Langendorff-perfused hearts from cats maintained on a taurine-deficient diet for six to eight months (6). This was in agreement with a report by Lake *et al* (7), who observed diminished contractility of LV preparations isolated from rats after consuming the taurine transport inhibitor guinidinoethane sulfonate (GES), which depletes myocardial taurine. We also reported that upon perfusion with 10 mM taurine, inotropic indices significantly improved in hearts isolated from taurine-deficient cats (6).

To our knowledge, there have been no published accounts of the changes in echocardiographic LV performance variables in response to dietary taurine deficiency from controlled studies in cats. The purpose of the present study was to assess changes in echocardiographic variables in cats maintained on a taurine-deficient diet as well as changes in relation to variables recorded from time-matched, taurine-replacement groups of cats. Current findings provide additional support for diminished LV function stemming from dietary taurine deficiency in cats.

MATERIALS AND METHODS

EXPERIMENTAL ANIMALS AND DEVELOPMENT OF TAURINE DEFICIENCY

Twenty-three adult domestic cats (17 females and 6 males) were maintained on a purified, taurine-deficient feline diet (<0.005% taurine; Results Brand Diet #F1470, Bioserv, Frenchtown, New Jersey) for 6 to 15 months. Six cats were mix-breed female cats of random-source and the nutritional status of these cats prior to arrival in the animal care facility was unknown. The remaining 17 subjects were colony-source, domestic shorthair cats that had been maintained on dietary formulations that supported adequate plasma taurine concentrations prior to the study. An additional 20 cats served as taurine-supplemented controls in these experiments. Controls consisted of six mix-breed female cats of random-source maintained on the identical taurine-deficient dietary formulation, however these cats received 1000 mg crystalline taurine (Sigma, St. Louis, Missouri) orally once daily throughout the duration of the study. The remaining 14 control animals were colony-source, domestic shorthair cats that had been maintained on commercial diets that supported adequate plasma taurine concentrations prior to the study. During the study these cats were maintained on the purified diet supplemented with taurine at 0.10% (Results Brand Diet #F2483, Bioserv). The taurine-supplemented diet differed from the taurine-deficient diet only in the percentage of taurine. Both the 0.10% taurine diet and 1000 mg of crystalline taurine given once daily supported plasma taurine concentrations greater than that which places cats at risk for developing taurine deficieny (8).

The random source, taurine-deficient and taurine-supplemented cats were studied for six to eight months. Results of *in vitro* isolated, perfused heart studies of intrinsic LV contractility in the 12 random-source cats have been previously reported (6). The colony-source cats were maintained on respective taurine-deficient and taurine-supplemented diets for 12–15 months. All experiments were conducted according to guidelines of the "Guide to the Care and Use of Experimental Animals", Volumes 1 and 2 of the Canadian Council on Animal Care.

Prior to the onset of the feeding trials, normal cardiac function was determined through thoracic auscultation, electrocardiography, thoracic radiography, and echocardiography. Blood samples were collected in heparin at the onset of the study and at points during the study. Plasma samples were harvested and stored at −20°C until measurement of plasma taurine concentrations.

ANALYSIS OF PLASMA TAURINE CONCENTRATIONS

Plasma taurine concentrations in cats studied for six to eight months were measured as previously described (6) using an automatic amino acid analyzer (Beckman Model 119 CL, Beckman Instruments, Irvine, California). Plasma samples from cats studied for 12–15 months were analyzed by high performance liquid chromatography techniques described by Einarsson *et al* (9). Plasma was deproteinized using 10% sulfosalicylic acid (Sigma) and precipitated protein was removed by centrifugation. The supernatant was harvested and the pH was adjusted to 8–10 with NaOH. Taurine was extracted with 9-fluorenylmethyl chloroformate (Aldrich Chemical Co., Milwaukee, Wisconsin). Taurine concentrations were determined using an HPLC system (Gilson 714, Gilson Medical Electronics, Middleton, Wisconsin) with a 250 × 4.6 mm ID, C-18, 5 μm Hypersil reverse phase column (Phenomenex, Torrance, California). A fluorescence detector (Model RF-535, Shimadzu, Kyoto, Japan) was used with the excitation wavelength at 265 nm and the emission wavelength at 305 nm. Dehydrokanic acid (Sigma) served as the internal standard. The sensitivity of the assay was approximately 0.5 nmol/mL.

ECHOCARDIOGRAPHIC METHODS

Quantitative M-mode echocardiography was performed with an ultrasound system (Ultramark 8, Advanced Technology Laboratories, Markham, Ontario) using 7.5 MHz and 10 MHz mechanical sector transducers. Cats were sedated with ketamine hydrochloride (Ketalean, MTC Pharmaceuticals, Cambridge, Ontario; 2–2.5 mg/kg of body weight, IV) and positioned in right lateral recumbency over a raised sheet of plexiglas having a rectangular opening for transducer placement in the right parasternal position. The transducer was directed to obtain short-axis echocardiograms as previously described (10–13).

TABLE I. Plasma taurine concentrations in taurine-supplemented and taurine-deficient cats (nmol/mL)

	Supplemented	Deficient
Baseline	201 ± 27	227 ± 25
Four months	128 ± 8	12 ± 2[a,b]
End	181 ± 28	7 ± 1[a,b]

Each value is the mean ± SEM of data from 20 taurine-supplemented cats and 23 taurine-deficient cats

[a]Significantly different than within group baseline values

[b]Significantly different than time-matched, taurine-supplemented group at $p < 0.05$; ANOVA and Bonferroni *t*-test

TABLE II. M-mode fractional shortening values (%) from taurine-supplemented and taurine-deficient cats at the beginning and end of the feeding trials

Duration (months)	Supplemented			Deficient		
	Baseline	End	% Change	Baseline	End	% Change
6	43.4	39.0	−10.1	33.0	9.0	−72.7
8	33.7	40.5	+20.2	35.8	21.1	−41.1
8	33.7	39.8	+18.1	33.0	18.4	−44.2
8	36.0	35.6	−1.1	33.7	18.2	−46.0
8	43.6	36.9	−15.4	46.7	20.9	−55.2
8	44.3	37.0	−16.5	32.0	8.1	−74.6
Mean	38.3	38.0		36.2	17.3[a,b]	
SEM	2.4	0.9		2.7	2.4	
12	38.4	44.1	+14.8	38.2	31.8	−16.8
12	38.4	44.0	+14.6	50.2	40.1	−20.1
12	40.3	42.6	+5.7	40.8	31.4	−23.0
12	39.6	40.4	+2.0	42.9	30.7	−28.4
12	44.5	44.2	−0.7	38.7	26.8	−30.7
12	49.5	48.4	−2.2	39.7	26.1	−34.2
12	43.4	38.6	−11.0	40.6	25.4	−37.4
12	39.1	34.2	−12.5	48.7	25.4	−47.8
12	48.8	36.8	−24.6	47.0	17.7	−62.3
12				36.5	7.9	−78.4
Mean	42.4	41.5		42.3	26.3[a,b]	
SEM	1.4	1.5		1.5	2.8	
15	35.9	34.0	−5.3	39.8	40.3	+1.2
15	42.2	39.7	−5.9	40.4	38.9	−3.7
15	33.6	30.8	−8.3	47.5	40.1	−15.6
15	41.5	38.0	−8.4	45.8	32.7	−28.6
15	37.2	32.9	−11.6	37.8	27.0	−28.6
15				40.8	27.6	−32.4
15				41.9	26.7	−36.4
Mean	38.1	35.1		42.0	33.3[a]	
SEM	1.6	1.6		1.3	2.4	
Grand mean	40.4	38.9	−2.9	40.5	25.8	−37.2
SEM	1.05	0.98	2.75	1.10	2.02	4.41

[a]Significantly different than within group baseline values

[b]Significantly different than time-matched, taurine-supplemented group at $p < 0.05$; ANOVA and Bonferroni *t*-test

Images considered essential to the study included the short-axis image of the LV chamber and the LV outflow tract. The leading edge method was used to measure left ventricular dimensions (14); each dimension was measured for three representative cardiac cycles and results were averaged.

From echocardiograms, LV end-systolic and end-diastolic short-axis internal diameters (LVESD and LVEDD) were measured. The LV ejection time (LVET) was measured as the time from the opening of the aortic valve to closure of the valve (12,15). The LV systolic function was assessed from M-mode echocardiograms by calculating the ejection phase variables, fractional shortening (FS) and mean velocity of circumferential fiber shortening (Vcf).

In random-source taurine-deficient cats, echocardiograms were performed at the beginning (baseline) and the end (six or eight months) of the feeding trial. Colony-source cats, who were studied for 12–15 months, had echocardiograms performed at the baseline, four months, eight months, and the end (12 or 15 months) of the feeding trial.

STATISTICAL ANALYSIS

Data are reported as means (SEM). Statistical analyses were performed using analysis of variance and the Bonferroni *t*-test (16). Spearman rank correlation coefficients were computed to test the degree of correlation between plasma taurine concentrations and echocardiographic variables of LV performance at the endpoint of the feeding trials. Probability (p) values less than 0.05 were considered significant. A statistical software computer program was used to assist in data analysis (Instat, Graphpad, San Diego, California).

RESULTS

RESPONSE TO DIETARY TAURINE DEFICIENCY

At four months following the onset of the study, plasma taurine concentrations in all cats receiving the taurine-deficient diet were ≤ 40 nmol/mL and significantly less than the corresponding prestudy, baseline values (Table I). Plasma taurine concentrations in the deficient group were reduced even further at the end point, with values ranging from nondetectable (<1 nmol/mL) to 17 nmol/mL. Cats receiving 1000 mg of taurine daily or the taurine-supplemented diet (0.10%) had plasma concentrations that remained at or above (range 73–595 nmol/mL) established normal plasma values for cats (8).

No overt clinical signs of heart failure developed in any of the cats during the study. From the taurine-deficient group, five cats developed gallop rhythms, four cats developed systolic murmurs, and one developed both a gallop rhythm and a murmur starting between five and eight months on the taurine-deficient diet. One member of the taurine-deficient group developed cardiomegaly and pulmonary edema detected by thoracic radiography by six months. This cat, along with one cat from the taurine-supplemented group, was removed from the feeding trial at this time as previously described (6). All other cats were maintained on the dietary program for 8–15 months.

ECHOCARDIOGRAPHIC DATA

The most frequently reported echocardiographic estimates of LV function in cats are M-mode fractional shortening and LV end-systolic short-axis diameter (1,2,4). Listed in Table II are the values for FS measured in taurine-supplemented and taurine-deficient cats at the beginning and end of the feeding trials. Data are listed in order of duration each cat was maintained in the feeding trial and by percent change of FS in response to taurine replacement or taurine depletion. Seventeen of 23 (74%) taurine-deficient cats experienced greater than 25% reductions in FS values in response to dietary taurine deficiency. The overall average reduction of FS in response to taurine deficiency was 37%.

Listed in Table III are values for LVESD measured at the beginning and end of the feeding trials. Twenty-one of 23 (91%) of the taurine-deficient cats had increases greater than 25% in response to taurine-deficiency. On average, the percent increase in LVESD was approximately 70% in taurine-deficient cats, whereas the percent increase in LVEDD (data not shown) was approximately 30%.

Shown in Table IV are data from the 31 colony-source cats whose echocardiographic variables were recorded at the beginning, four months, eight months and end (12 or 15 months) of the feeding trials. The greatest rate of change in M-mode echocardiographic dimension and ejection phase variables occurred during the first four months in the taurine-deficient group. Beyond four months LVESD continued to increase and FS and Vcf continued to decline in response to taurine deficiency, however at a lower rate of change.

Spearman rank correlation coefficient values computed from plasma taurine concentrations and echocardiographic variables demonstrate moderate and significant positive correlations between taurine concentration and FS and Vcf (Table V). A similar, but negative, correlation existed between plasma taurine and LVESD.

TABLE III. The LV end-systolic short-axis diameter values (mm) from taurine-supplemented and taurine-deficient cats at the beginning and end of the feeding trials

Duration (months)	Supplemented			Deficient		
	Baseline	End	% Change	Baseline	End	% Change
6	4.3	5.2	+20.9	5.2	16.9	+225.0
8	5.4	4.0	−25.9	6.1	6.1	0.0
8	5.7	5.7	0.0	6.1	9.1	+49.2
8	5.0	5.1	+2.0	5.7	10.3	+80.7
8	4.4	4.9	+11.4	4.9	11.0	+124.5
8	6.3	7.2	+14.3	6.6	17.4	+163.6
Mean	5.4	5.4		5.9	10.8[a,b]	
SEM	0.32	0.53		0.28	1.8	
12	7.0	5.7	−18.6	6.0	7.3	+21.7
12	6.1	5.8	−4.9	6.6	8.4	+27.3
12	7.5	7.2	−4.0	8.0	10.2	+27.5
12	8.7	8.4	−3.4	6.1	7.9	+29.5
12	7.2	7.7	+6.9	7.9	11.6	+46.8
12	7.1	7.6	+7.0	4.5	6.9	+53.3
12	5.4	5.8	+7.4	6.3	10.1	+60.3
12	6.6	7.5	+13.6	4.6	8.9	+93.5
12	4.9	5.8	+18.4	9.0	19.0	+111.1
12				5.0	12.4	+150.0
Mean	6.7	6.8		6.4	10.3[a,b]	
SEM	0.38	0.35		0.48	1.12	
15	6.1	6.6	+8.2	5.3	6.8	+28.3
15	6.4	7.1	+10.9	5.8	7.5	+29.3
15	6.0	6.7	+11.7	5.3	7.6	+43.4
15	5.4	6.2	+14.8	5.3	7.8	+47.2
15	5.1	6.3	+23.5	4.6	7.3	+58.7
15				5.5	8.9	+61.8
15				3.5	5.9	+68.6
Mean	5.8	6.6		5.0	7.4[a]	
SEM	0.25	0.16		0.29	0.35	
Grand mean	6.0	6.3	+5.7	5.8	9.8	+69.6
SEM	0.25	0.25	2.80	0.26	0.75	11.2

[a]Significantly different than within group baseline values
[b]Significantly different than time-matched, taurine-supplemented groups at $p < 0.05$; ANOVA and Bonferroni *t*-test

TABLE IV. Echocardiographic variables from taurine-deficient and taurine-supplemented colony-source cats studied for 12-15 months

	Baseline	4 Months	8 Months	End
LV End-diastolic diameter (mm)				
Supplemented (n = 14)	10.8 ± 0.5	11.3 ± 0.3	10.5 ± 0.3	11.2 ± 0.4
Deficient (n = 17)	10.3 ± 0.5	12.8 ± 0.6[a]	12.2 ± 0.5[a]	12.6 ± 0.6[a]
LV End-systolic diameter (mm)				
Supplemented (n = 14)	6.4 ± 0.3	6.8 ± 0.3	6.4 ± 0.3	6.7 ± 0.2
Deficient (n = 17)	5.8 ± 0.3	8.6 ± 0.6[a,b]	8.5 ± 0.5[a,b]	9.1 ± 0.7[a,b]
Fractional shortening (%)				
Supplemented (n = 14)	40.9 ± 1.2	40.2 ± 1.6	40.0 ± 1.3	39.2 ± 1.4
Deficient (n = 17)	42.2 ± 1.0	33.6 ± 1.8[a,b]	30.7 ± 1.8[a,b]	29.2 ± 2.0[a,b]
Vcf (circ/s)				
Supplemented (n = 14)	3.71 ± 0.16	3.54 ± 0.20	3.33 ± 0.27	3.43 ± 0.16
Deficient (n = 17)	3.71 ± 0.16	2.79 ± 0.20[a,b]	2.50 ± 0.16[a,b]	2.58 ± 0.21[a,b]

Each value in the mean ± SEM of data. Vcf, mean velocity of circumferential fiber shortening
[a]Significantly different than within group baseline values
[b]Significantly different than time-matched, taurine-supplemented group at $p < 0.05$; ANOVA and Bonferroni *t*-test

DISCUSSION

In the present study, M-mode echocardiographic techniques were used to assess changes in LV short-axis internal diameters and ejection phase variables of LV performance in response to dietary taurine deficiency in cats. Systolic dysfunction of the left ventricle is an important pathophysiological feature of taurine deficiency in this species and our experimental findings are in agreement with clinical observations of Pion *et al* (1,3,4) and Sisson *et al* (2), who arrived at similar conclusions based on spontaneous cases of feline dilated cardiomyopathy associated with low plasma taurine concentrations. In

TABLE V. Spearman rank correlation coefficient values computed from plasma taurine concentrations and echocardiographic variables at the end of the feeding trials

	r_s	p
LV End-diastolic short-axis diameter	−0.2981	0.0522
LV End-systolic short-axis diameter	−0.5543	0.0001
Fractional shortening	0.6510	< 0.0001
Vcf	0.4947	0.0007

r_s, Spearman rank correlation coefficient. Vcf, mean velocity of circumferential fiber shortening

those studies, decreased FS and increased LV end-systolic and end-diastolic internal diameters, in relation to a population of clinically normal cats, were the chief criteria used to determine the presence of dilated cardiomyopathy. In a study where reference was made to taurine-supplemented control groups of cats, cardiac performance was not evaluated (17). An advantage of the current study was the use of time-matched, taurine-supplemented, control groups of cats maintained on the identical dietary preparation or the identical dietary preparation containing 0.10% taurine.

The dietary manipulations employed in this study did lead to taurine depletion in cats maintained on the taurine-deficient diet, while taurine-replacement supported plasma taurine concentrations at or above that considered normal for the species (8). Sturman *et al* (18) reported a plasma taurine concentration of 5.6 ± 3.1 nmol/mL (mean ± SD) in adult female cats fed for up to 24 months a similar taurine-deficient dietary formulation as used in the current study. The formulation fortified with 0.05% taurine supported a plasma concentration of 126 ± 12 nmol/L. Plasma taurine concentrations measured in taurine-deficient cats from the current study are in agreement with values from Sturman *et al* (18). Further, Sturman *et al* (18) and Fox and Sturman (17) reported that the taurine-deficient diet resulted in myocardial taurine concentrations of 1.40 ± 0.70 and 1.07 ± 0.48 μmol/g (mean ± SD) of wet weight tissue, respectively. When supplemented with taurine at 0.05%, myocardial taurine concentrations were 12.6 ± 3.1 and 12.0 ± 2.3 μmol/g of wet weight, or approximately tenfold higher than deficient hearts.

Myocardial function did correlate with plasma taurine concentration in this study as indicated by significant positive (FS and Vcf) and negative (LVESD) Spearman rank correlation coefficients determined between echocardiographic variables and plasma taurine concentration. The strength of the correlations however is moderate, which might be predicted from the data (Tables II and III). While all taurine-deficient cats underwent marked reduction in plasma taurine concentrations (≤17 nmol/mL), a spectrum of changes in echocardiographic variables was observed. In addition, other factors as discussed below may have contributed to taurine-deficient myocardial failure. Additional evidence for an association between taurine and myocardial function in cats includes the apparent reduction in the number of clinical cases of feline DCM in the 1990s following increased taurine supplementation of commercial cat foods. Recently Fox *et al* (19) reported a significant association between low plasma taurine concentration and DCM in cats.

Qualitative echocardiographic criteria for diagnosis of dilated cardiomyopathy in cats include increased LV chamber dimensions, left atrial enlargement, normal or decreased ventricular free-wall and septal thickness, and decreased ejection phase indices of LV systolic function (20). However, specific quantitative criteria seem to vary between laboratories and even within the same laboratory (2,10–12,21). The most comprehensive set of M-mode echocardiographic data was reported by Sisson *et al* (2) from a multicenter study of DCM diagnosed clinically in cats. In this study M-mode fractional shortening <35%, along with other clinical manifestations of heart failure, in nonsedated cats was considered indicative of DCM. Pion *et al* (1), who first published findings linking DCM in cats to taurine deficiency, listed M-mode FS <35% and LVESD >12 mm as diagnostic criteria for DCM in cats without evidence of any other congenital or acquired heart disease. At the onset of the current study several cats had FS values between 30 and 35%, however none had LVESD >12 mm. Since FS can be affected by sedation (2,20), these lower FS values could be attributed to ketamine sedation and are consistent with values reported by Fox *et al* (12) who reported a range of 30–60% as normal for FS in cats sedated with ketamine (1.5–2.5 mg/kg, IV) in a manner similar to that in the current study. All taurine-supplemented cats in the current study maintained FS values greater than 30% while 15 of 23 (65%) taurine-deficient cats had FS less than 30% at the end of the feeding trials. In a later report, Pion *et al* (4) described criteria for DCM associated with taurine deficiency as M-mode FS ≤28% and LVESD >14 mm. These values were measured in nonsedated cats. If the later criteria are considered characterisitic features of DCM in cats, only three taurine-deficient cats in the current study met these criteria for DCM. In the three cats FS was <9.0% and LVESD was ≥16.9 mm, which clearly support an echocardiographic diagnosis of DCM.

While ejection phase indices of LV systolic function indicate global left ventricular function, FS and Vcf are determined by the contractile state of the heart, preload, afterload, chamber size, and the presence or absence of shunts or valvular insufficiencies. End-systolic dimensions are primarily affected by myocardial contractility and afterload and provide a better assessment of changes in the inotropic state (22,23). The percent change in LVESD in response to taurine-deficiency was approximately twice that observed for LVEDD and FS and supports the hypothesis that taurine-deficiency leads to a decrease in intrinsic myocardial contractility. This observation is in agreement with our previously reported finding of diminished contractility in hearts isolated from taurine-deficient cats (6).

The random-source cats appeared to have a greater propensity to develop myocardial failure in response to taurine-deficiency than colony-source cats (Tables II and III) as a higher percentage of taurine-deficient cats from

this group tended to experience greater changes in FS and LVESD. The reason colony-source cats were more resistant to developing myocardial failure in response to chronic dietary taurine deficiency was not readily apparent. Distinguishing features of random-source cats included: 1) unknown nutritional background prior to housing in the animal care facility; 2) exclusively female cats; and 3) slightly younger at the onset of the feeding trial (estimated average age: 1–1.5 years). Features of colony-source cats included: 1) less genetic variability; 2) nutritional background known to support adequate plasma taurine concentrations; 3) mixture of male and female cats; and 4) an average age at the onset of the feeding trial of 21 months. Sex differences did not appear to account for differences in response to taurine deficiency as proportional numbers of colony-source males and females were distributed along the spectrum of cardiac changes caused by taurine deficiency. Female cats were not more likely to develop taurine-deficient myocardial failure in this study. The explanation for the difference in the magnitude of response to dietary taurine deficiency is more likely a factor of nutritional or genetic background. Perhaps random-source cats were not supplied with an adequate nutritional level of taurine during fetal or neonatal development thereby predisposing this population of cats to development of myocardial failure upon reexposure to a taurine-deficient diet. Taurine is clearly essential for normal development of excitable tissues (18,24). Alternatively, some other nutritional factor prior to the study may have influenced the development of myocardial failure in random-source cats following the onset of the feeding trial with the taurine-deficient diet. For example, Dow *et al* (25) recently reported a possible link between taurine and potassium balance and the occurrence of cardiovascular disease in cats. Potassium balance in the random-source cats was unknown prior to their arrival in the animal care facilities, however, study diets (both taurine-supplemented and taurine-deficient) had identical potassium concentrations (0.9%, dry matter basis).

In the clinical-based studies (1,2,4), many cats presented with clinical signs of severe myocardial failure and occasionally in cardiogenic shock. Only one cat in the current study had any evidence of pulmonary congestion, although several taurine-deficient cats had gallop rhythms and/or murmurs. No cats displayed any overt clinical symptoms of heart failure that are often present in clinical cases of dilated cardiomyopathy in cats (19,26). Cats in the current study were considerably younger than cats clinically diagnosed with DCM associated with taurine deficiency. Had the duration of the study been extended, perhaps more cats would have developed echocardiographic criteria of DCM.

It was interesting that among colony-source cats during the 12–15 months on the taurine-deficient diet, the most rapid changes in FS and LVESD tended to occur early in taurine deficiency, followed by more gradual changes in these variables. It is unknown if myocardial function in clinical cases of taurine-deficient DCM follows a similar pattern. However, such a gradual deterioration of myocardial function over several months or years may be related to the occurrence of DCM in predominately middle-aged to older cats (19) and the inability to consistently induce DCM in experimental studies of taurine-deficiency in cats (3).

In summary, a spectrum of changes in myocardial structure and function was observed in taurine-deficient cats ranging from no diminution in LV performance in a small number of cats to diminished systolic pump function coupled with increased LV chamber size. While taurine deficiency of 6 to 15 months duration did result in cardiac changes consistent with dilated cardiomyopathy in some cats, diminution of systolic pump function and increased LV short-axis diameter were more consistent observations. Current findings complement those of Pion *et al* (1,3,4), who demonstrated improved myocardial function with taurine supplementation in clinical cases of taurine-deficient dilated cardiomyopathy. In addition, present data provide direct evidence for a causal relationship between dietary taurine deficiency and myocardial failure in cats.

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