Journal of Veterinary Cardiology (2023) **50**, 51—62

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Journal of Veterinary Cardiology
ESVC

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Transient myocardial thickening: a retrospective analysis on etiological, clinical, laboratory, therapeutic, and outcome findings in 27 cats

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Received 29 April 2023; received in revised form 7 September 2023; accepted 15 September 2023

KEYWORDS
Cardiac troponin I;
Congestive heart failure;
Transthoracic echocardiography;
Left atrial dilation;
Myocardial injury

Abstract *Introduction/objective:* Transient myocardial thickening (TMT) in cats is a poorly characterized clinical entity. Therefore, this study aimed to provide descriptions of additional cats diagnosed with this clinical phenomenon.
Animals, materials, and methods: For this multicenter observational retrospective study, cats diagnosed with TMT were searched in three medical databases. TMT was defined for cats with at least two echocardiograms showing an increased end-diastolic left ventricular wall thickness (LVWTd; i.e. $\geq$6 mm) at presentation and subsequent echocardiographic normalization (i.e. LVWTd $<$5.5 mm). Signalment, history, clinical, laboratory, therapeutic, and outcome data were retrieved.
Results: Twenty seven cats were included. The median age was 3 years. In 9/27 cats, an antecedent event was documented. At admission, 27/27 cats had evidence of myocardial injury (median value of cardiac troponin I 5.5 ng/mL), 25/27 cats had congestive heart failure, 13/27 cats had hypothermia, 8/27 cats had systemic hypotension, 7/27 cats had bradycardia, and 7/27 cats had electrocardiographic evidence of an arrhythmia. The median LVWTd was 6.4 mm. A potential cause of myocardial injury was identified in 14/27 cats. The median time from diagnosis

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https://doi.org/10.1016/j.jvc.2023.09.001

to a significant reduction in LVWTd was 43 days.
Discussion: TMT can be diagnosed in a wide range of cats, including young subjects. An antecedent predisposing event and/or a possible causative trigger can be identified in some. The reduction in LVWTd that defines this phenomenon usually occurs over a variable time frame.
Conclusions: This study represents the largest investigation of TMT in cats and provides additional information on this uncommon clinical entity.

Abbreviations

ATE	arterial thromboembolism
CAM	systolic anterior motion of mitral valve chordae tendinae
CBC	complete blood count
CHF	congestive heart failure
cTnI	cardiac troponin I
FIV	feline immunodeficiency virus
HCM	hypertrophic cardiomyopathy
IVSd	end-diastolic thickness of the interventricular septum
LA	left atrial
LA:Ao ratio	left atrial to aortic root ratio
LAD	left atrial anteroposterior diameter
LAFS	left atrial fractional shortening
LVFS	left ventricular fractional shortening
LVFWd	end-diastolic thickness of the left ventricular free wall
LVWT	left ventricular wall thickening
PCR	polymerase chain reaction
SAM	systolic anterior motion of mitral valve
SEC	spontaneous echocardiographic contrast
TMT	transient myocardial thickening
Vmax-Lau	peak velocity of the left atrial auricle blood flow
2D	two-dimensional

Introduction

In feline medicine, the term 'transient myocardial thickening' (TMT) was formally introduced in 2018 to define a clinical entity that typically affects young cats, is characterized by reversible left ventricular wall thickening (LVWT), and initially mimics hypertrophic cardiomyopathy (HCM) [1]. According to that report, cats with TMT often show concurrent transient left atrial (LA) dilation and dysfunction, congestive heart failure (CHF), and increased circulating concentration of cardiac troponin I (cTnI) [1], indicating ongoing myocardial injury [2]. Although the mechanism of this condition remains to be elucidated in this species, transient interstitial edema due to myocarditis (i.e. an inflammatory myocardial infiltration associated with cardiomyocyte damage of non-ischemic origin [3]) represents the main etiology of reverse remodeling of TMT in humans [4—7]. In cats, both infectious and non-infectious diseases have been documented as possible causes of myocarditis and TMT [1,3,8]. To date, only a few infective agents associated with feline myocarditis and/or TMT have been described, namely *Bartonella henselae*, *Streptococcus canis*, feline immunodeficiency virus (FIV), panleukopenia virus, feline coronavirus, *Sarcocystis felis*, *Hepatozoon silvestris* and *Toxoplasma gondii* [9—16]. Moreover, it should be noted that, currently, only a single original study has been published on feline TMT [1], whereas the remaining available data are based on sparse case reports [11,14] and a small case series [16]. This inevitably limits our current knowledge of the etiological, epidemiological, and clinical features of TMT in cats, and our therapeutic and prognostic considerations in affected cats.

Therefore, the aim of this study was to retrospectively evaluate a population of cats with TMT, and to provide a detailed description of selected historical, clinical, diagnostic, therapeutic, and outcome data.

Materials and methods

Study population

For this multicenter observational retrospective study, we collected data from the internal databases of three veterinary centers. Cats were included in the study if they underwent cardiac diagnostic evaluation that led to a final diagnosis of TMT between January 2014 and March 2023. To be considered affected by TMT, cats had to meet the following criteria: (1) an initial echocardiographic examination showing an end-diastolic thickness of the interventricular septum (IVSd) and/or left ventricular free wall (LVFWd) $\geq$ 6 mm [17,18]; (2) a concurrent demonstration of elevated circulating cTnI (>0.2 ng/mL)[d]; (3) an echocardiographic follow-up demonstrating a subsequent reduction of IVSd and LVFWd below 5.5 mm [1]; and (4) a concurrent reduction of cTnI compared to the first examination. Cats with other acquired or congenital heart diseases and those that required sedation for echocardiographic acquisition were excluded. Additionally, the presence of diseases and/or the administration of drugs capable of inducing an increase in LVWT (e.g. hyperthyroidism, hypersomatotropism, systemic hypertension), CHF (e.g. corticosteroids), or arterial thromboembolism (ATE) were considered additional exclusion criteria [18–20]. Moreover, since pseudohypertrophy from volume depletion represents a further differential in the diagnosis of LVWT in cats [18,21], cats with clinical signs of overt dehydration (e.g. dry mucous membranes, decreased skin turgor [22]) at the time of LVWT diagnosis were also excluded regardless the cause (i.e. spontaneous dehydration or drug-induced dehydration, such as in cats already receiving diuretic therapy).

Historical and clinical data

Historical data that were gathered at baseline included the presence of antecedent events (e.g. general anesthesia or traumatic incidents occurring within 14 days before presentation and diagnosis of TMT) [1] and information about the cat's lifestyle (i.e. indoor, outdoor, mixed). Vaccination history was not included. Clinical data collected at the time of first presentation included: signalment (i.e. sex, breed, age, body weight); physical findings (details below); thoracic radiographic and/or ultrasonographic findings (i.e. presence of pulmonary edema, pleural effusion, pericardial effusion, and/or ascites); and electrocardiographic findings (i.e. presence of arrhythmia and type of electrocardiographic changes observed over $\leq$2 min in unsedated cats manually restrained in the right lateral recumbency, according to the standard technique [23]).

Regarding physical examination, particular attention was paid to the following findings/parameters: presence of heart murmur; rectal temperature (considering cats hypothermic when rectal temperature was <37 °C [24,25]); heart rate (considering cats bradycardic when heart rate was <140 beats/minute [26]); systolic arterial blood pressure measured by a high-definition oscillometric device[e] according to the guidelines of the American College of Veterinary Internal Medicine [27] (considering cats hypotensive when systolic blood pressure was <90 mmHg [28]); and presence and type of shock. For the purpose of this study, shock was classified as early decompensatory shock, which is commonly characterized by relative bradycardia, pallor, prolonged capillary refill time, a weak pulse, low-normal arterial blood pressure, hypothermia, and depressed mentation; and late decompensatory shock, which is commonly characterized by marked bradycardia, muddy mucous membranes, markedly prolonged capillary refill time, hypothermia, stupor/coma, and extremely low arterial blood pressure, if it can even be measured [22,29].

Laboratory data

Laboratory data included findings from complete blood count (CBC), serum chemistry, serum cTnI, and tests aimed at documenting possible infective conditions. These included serology for *T. gondii* (IgM and IgG titers measured by indirect immunofluorescence assay [30]); serology (IgM and IgG titers measured by direct immunofluorescence assay [1,31]) and/or polymerase chain reaction (PCR) (without Bartonella alpha Proteobacteria growth medium enrichment [32]) for *B. henselae;* FIV/feline leukemia virus serological test; cytology; and blood and urine culture. The number and type of laboratory tests performed varied

[d] IMMULITE 2000, Siemens, Erlangen, Germany.

[e] petMAPTM graphic, Ramsey Medical, Inc., Tampa, U.S.A.

according to each cat's historical and clinical findings and the veterinarian's judgment.

Echocardiographic data

All echocardiographic video loops from cats with TMT included in the study (before and after resolution of LVWT) were reviewed by experienced operators (i.e. a board-certified cardiologist [G.R] and a veterinarian with more than 20 years of cardiology experience [C.G.]) to ensure that inclusion criteria were met. Specifically, the thickness of the left ventricular free wall and interventricular septum was measured using a leading edge-to-leading edge technique from a two-dimensional (2D) right parasternal long-axis four-chamber view and a short-axis view at the papillary muscle level, as the average of the thickest end-diastolic segment on three different cardiac cycles in each view. End-diastolic frames were defined as the first frame after mitral valve closure in the long-axis view and as the time point in the cardiac cycle with the largest left ventricular internal diameter in the short-axis view. The maximum averaged end-diastolic wall thickness from both interventricular septum and left ventricular free wall in these two views was recorded, and the highest value was used for the final data analysis, defined as the maximum thickness of the left ventricular walls [33]. For the purpose of this study, in addition to IVSd and LVFWd thickness, further selected echocardiographic parameters were evaluated. These included: left ventricular fractional shortening (LVFS); left atrium-to-aorta ratio (LA:Ao ratio); LA anteroposterior diameter (LAD); LA fractional shortening (LAFS); presence of spontaneous echocontrast (SEC) or thrombus; peak velocity of the left auricle blood flow (Vmax-Lau); presence of systolic anterior motion of the mitral valve (SAM); and presence of systolic anterior motion of mitral valve chordae tendinae (CAM).

The LVFS was calculated by M-Mode from a right parasternal short-axis at the level of the papillary muscles using the formula ([end-diastolic left ventricular diameter − end-systolic left ventricular diameter]/end-diastolic left ventricular diameter × 100%), and was considered reduced if <28% [34].

The LA:Ao ratio was measured using a 2D inner edge-to-inner edge technique from a right parasternal short-axis view at the heart base, in the frame after aortic valve closure (end-ventricular systole), and was considered increased if ≥1.6 [35,36].

The LAD was obtained from the right parasternal long-axis four-chamber view by measuring in 2D the widest distance, parallel to the mitral valve annulus, from the inner wall of the middle of the interatrial septum to the inner wall of the posterior free wall at end systole [36,37], and was considered increased if ≥16 mm [36].

The LAFS was calculated by M-Mode from a right parasternal short-axis at the heart base using the formula ([maximal LA diameter − minimal LA diameter]/maximal LA diameter × 100%), and was considered reduced if <21% [38].

The presence of SEC or thrombus was assessed on 2D examination from both the right parasternal long-axis four-chamber view and the short-axis view at the heart base as well as from the left parasternal apical four-chamber view and the oblique long-axis view optimized for left auricle visualization [39].

The Vmax-Lau was measured by pulsed-wave Doppler from a right parasternal short-axis view at the heart base optimized for left auricle visualization or from a left parasternal long-axis oblique view optimized for left auricle visualization, and was considered reduced if ≤20 cm/s [39].

The presence of SAM was diagnosed if the tip of the anterior mitral valve leaflet bent, with the distal tip of the leaflet approaching or contacting the intraventricular septum, on 2D examination from the right parasternal long-axis five-chamber view, with concomitant color Doppler evidence of a turbulent jet at the level of the left ventricular outflow tract and a jet of eccentric mitral valve regurgitation [40].

The presence of CAM was diagnosed on 2D examination if chordae that could be visualized and followed from their origin at the head of the respective papillary muscle to their insertion into the mitral valve leaflets protruded into the outflow tract in systole [40].

Final diagnosis, treatment, and outcome data

The medical records were also reviewed for a suspected cause of myocardial injury associated with LVWT, duration of hospitalization, and cardiovascular treatment at the time of TMT diagnosis. Outcome data included: the number of relapses of CHF and/or ATE; the time from diagnosis to LVWT resolution; and clinical, laboratory, echocardiographic, and therapeutic data at the time of the final echocardiographic evaluation.

Statistical analysis

After testing for normality using the Shapiro–Wilk test and visual inspection, normally or not normally distributed continuous variables were reported as mean and standard deviation and median (25th–75th quartile), respectively. Statistical analysis involved the utilization of both paired samples t-test and Wilcoxon signed-rank test, depending on the distribution of the variables. These tests were employed to compare the paired data, specifically the time of the first presentation and the time of the LVWT resolution. A significance level of $P<0.05$ was used to determine statistical significance.

Results

Study population and clinical data

The study population included 27 cats, 16 males (59.3%) and 11 females (40.7%). The median age was 3 years (2–8 years), with 19/27 cats (70.4%) and 14/27 (51.9%) cats being ≤5 and ≤4 years, respectively. The median body weight was 4.4 kg (3.7–5.2 kg). These cats belonged to seven breeds, with the mixed-breed cats being the most frequently presented (18/27 [66.7%]), followed by Scottish Fold (4/27 [14.8%]), and Burmese, Chartreux, Maine Coon, Persian, and Ragdoll (1/27 [3.7%] each). The cats' lifestyle was predominantly indoor in 12/27 (44.5%) cases, mixed (i.e. equally indoor and outdoor) in 6/27 (22.2%) cases, and predominantly outdoor in 4/27 (14.8%) cases; whereas data on lifestyle were not available for the remaining 5/27 (18.5%) cats. In 9/27 (33.3%) cats, an antecedent event was documented within a median of 5 days (3–6 days) before presentation, including spaying/neutering (7/9 [77.8%]) and abscess formation/rupture (2/9 [22.2%]). The main clinical findings, including electrocardiographic abnormalities, documented at the time of arrival are reported in Table 1. In all 10 cats with a heart murmur, a parasternal left-sided murmur with an intensity ≤3/6 was audible. The median rectal temperature in the nine hypothermic cats was 36.3 °C (34.7–36.7 °C). The median heart rate of the five bradycardic cats was 100 beats/minute (85–125 beats/min). Systolic blood pressure was too low to be measurable in two cats. Collectively, 5/27 (18.5%) cats met the clinical criteria of decompensatory shock, with 3/27 (11.1%) cats and 2/27 (7.4%) cats showing signs of early and late decompensatory shock, respectively.

Table 1 Selected clinical and electrocardiographic findings at initial presentation in 27 cats with transient myocardial thickening.

Sign	N. of cats (%)
Heart murmur	10/27 (37%)
Intensity 2/6	5/10 (50%)
Intensity 3/6	5/10 (50%)
Hypothermia	9/27 (33.3%)
Bradycardia	5/27 (18.5%)
Hypotension	5/27 (18.5%)
CHF	25/27 (92.6%)
LE	10/25 (40%)
LE and PlE	8/25 (32%)
PE	3/25 (12%)
LE, PlE and PE	2/25 (8%)
LE and PE	1/25 (4%)
LE and A	1/25 (4%)
Electrocardiographic abnormalities	7/27 (25.9%)
Complete RBBB	2/7 (28.6%)
LAFB	1/7 (14.3%)
LBBB	1/7 (14.3%)
AS	1/7 (14.3%)
IAVD	1/7 (14.3%)
VPCs	1/7 (14.3%)

A: ascites; AS: atrial standstill; CHF: congestive heart failure; IAVD: isorhythmic atrioventricular dissociation; LAFB: left anterior fascicular block; LBBB: left bundle branch block; LE: lung edema; PE: pericardial effusion; PlE: pleural effusion; RBBB: right bundle branch block; VPCs: ventricular premature complexes.

Laboratory data

At admission, serum chemistry (including cTnI measurement) and CBC were performed on all cats; the main laboratory changes are reported in Table 2. According to inclusion criteria, at admission, all cats had increased cardiac troponin I (median value 5.5 ng/mL [3.1–11.9 ng/mL]). Among 8/27 cats with leukocytosis (29.6%), 5/8 cats (62.5%) cats, 2/8 (25%) cats, and 1/8 (12.5%) cat had a neutrophilic, neutrophilic and monocytic, and neutrophilic and lymphocytic leukocytosis, respectively. Among 6/27 (22.2%) cats with anemia, all had a normocytic, normochromic, and nonregenerative type. Seventeen (63%) cats underwent a FIV/feline leukemia virus serological test; all subjects tested negative. Fifteen (55.6%) cats underwent a serological test for *T. gondii*; three subjects tested positive (i.e. in two cases, IgM and IgG titers 1:80 and 1:1,280, respectively; in the remaining case, IgM and IgG titers 1:80 and 1:640, respectively). Nine (33.3%) cats underwent a PCR for *B. henselae*; one subject tested positive. Five (18.5%) cats underwent a blood culture; all subjects tested negative. Two (7.4%) cats

Table 2 Laboratory changes documented on complete blood cell count and serum biochemical panel at initial presentation (T0) and at the time of resolution of left ventricular wall thickening (T1) in 27 cats with transient myocardial thickening.

Parameter	N. of cats (%) at T0	Value at T0	N. of cats (%) at T1	Value at T1	HRI
Serum chemistry					
Increased cTnI (ng/mL)	27/27 (100%)	5.5 (3.1–11.9)	3/27 (11.1%)	0.33 ± 0.12	≤0.2
Increased AST (U/L)	16/27 (59.3%)	72 (65–130)	1/27 (3.7%)	43	9–40
Increased urea (mg/dL)	13/27 (48.2%)	107 (78–126)	5/27 (18.5%)	85.7 ± 20	30–65
Increased SAA (μg/mL)	10/27 (37%)	56 (26–77)	0/27 (0%)	–	0–5
Increased ALT (U/L)	8/27 (29.6%)	102 (83–174)	1/27 (3.7%)	97	20–72
Hypochloremia (mEq/L)	7/27 (25.9%)	107 (94–108)	0/27 (0%)	–	110–123
Increased creatinine (mg/dL)	6/27 (22.2%)	2 (1.8–2.6)	3/27 (11.1%)	2.1 ± 0.22	0.8–1.8
Hyponatremia (mEq/L)	6/27 (22.2%)	142 ± 1	0/27 (0%)	–	145–155
Increased CK (IU/L)	5/27 (18.5%)	1,151 (784–1,443)	0/27 (0%)	–	91–326
Hyperkalemia (mEq/L)	1/27 (3.7%)	6.1	1/27 (3.7%)	5.3	3.4–5.1
Hypernatremia (mEq/L)	0/27 (0%)	–	3/27 (11.1%)	157 ± 1	145–155
Hypokalemia (mEq/L)	0/27 (0%)	–	1/27 (3.7%)	3.3	3.4–5.1
Complete blood cell count					
Leukocytosis (WBC/μL)	8/27 (29.6%)	19,960 (19,260–20,435)	1/27 (3.7%)	16,870	4,800–14,930
Reduced Hct (%)	6/27 (22.2%)	27.5 ± 2.3	2/27 (7.4%)	29 and 29.4	32–48
Leukopenia (WBC/μL)	2/27 (7.4%)	2,930 and 4,740	0/27 (0%)	–	4,800–14,930

Normally and not normally distributed data are presented as mean ± standard deviation and median (25th–75th quartile), respectively. ALT: alanine aminotransferase; AST: aspartate aminotransferase; CK: creatine kinase; cTnI: cardiac troponin I; Hct: hematocrit; HRI: hospital reference interval; SAA: serum amyloid A; WBC: white blood cells.

underwent a serological test for *B. henselae* (in one case both IgM and IgG titers were measured, whereas in the remaining case, only IgG titer was assessed); one subject tested positive (i.e. IgG titre 1:512). Two (7.4%) cats underwent cytological examination of the fluid collected from an abscess; in both cases, bacteria were identified microscopically. One (3.7%) cat underwent a urine culture, leading to a negative result.

Echocardiographic data

Echocardiographic measurements obtained at the time of presentation are reported in Table 3 (Fig. 1A-B). At admission, only 1/27 (3.7%) cat had a reduction in LVFS, 26/27 (96.3%%) had an increased LA:Ao ratio, 26/27 (96.3%) cats had an increased LAD, 11/27 (40.7%) cats had a decreased LAFS, 4/27 (14.8%) cats had evidence of intracardiac SEC, 1/27 (3.7%) cat had an intracardiac thrombus (inside the left auricle), and 8/27 (29.6%) cats had a decreased Vmax-Lau. Furthermore, 6/27 cats (22.2%) had SAM, and 3/27 (11.1%) cats had CAM.

Final diagnosis, treatment, and outcome data

Based on the combination of historical, clinical, cardiological, and laboratory data, a suspected cause/trigger possibly related to myocardial injury was hypothesized in 14/27 cats (51.9%) and included spaying/neutering or related postoperative complications (e.g. infections) occurring within one week from surgery (7/27 [25.9%]), toxoplasmosis (3/27 [11.1%]), bartonellosis (2/27 [7.43%]), and sepsis (2/27 [7.4%]). In septic cats, sepsis was due to an infected bite wound on the tail followed by abscess formation in one case, and to an infected wound on the tongue followed by abscess formation in the remaining case.

All cats diagnosed with CHF, which accounted for 25 cases, were admitted to the hospital and underwent cardiac treatments. These treatments included furosemide for all cats (25/25 [100%]), pimobendan for 16/25 (64%) cats, clopidogrel for 11/25 (44%) cats, spironolactone for 4/25 (16%) cats, and benazepril, enoxaparin, and sotalol for one cat each (1/25 [4%] each). Additionally, during the initial hours of hospitalization, 12/25 (48%) cats required oxygen supplementation. Cats with infectious diseases were also administered antimicrobial treatment. Specifically, clindamycin was given to cats with toxoplasmosis, a combination of pradofloxacin and doxycycline was prescribed for cats with bartonellosis, one of the two cats with sepsis received a combination of ampicillin/sulbactam and marbofloxacin, and the remaining septic cat was treated with piperacillin/tazobactam. The

Table 3 Selected echocardiographic measurements at initial presentation (T0) and at the time of resolution of left ventricular wall thickening (T1) in 27 cats with transient myocardial thickening.

Parameter	T0	T1	P value
LVWTd (mm)	6.4 (6.2—6.8)	5 (4.7—5.2)	<0.0001
LVFS (%)	52 (48—60)	49 (46—56)	0.49
LA:Ao ratio	1.9 ± 0.24	1.37 ± 0.1	<0.0001
LAD (mm)	18.4 ± 2.2	14.6 ± 1.1	<0.0001
LAFS (%)	15 (14—33)	30 (26—38)	0.03
Vmax-Lau (cm/s)	20 (18—38)	35 (29—45)	0.06

Normally and not normally distributed data are presented as mean ± standard deviation and median (25th—75th quartile), respectively. LA:Ao ratio: left atrium to aortic root ratio; LAD: left atrial anteroposterior diameter; LAFS: left atrial fractional shortening; LVFS: left ventricular fractional shortening; LVWTd: maximal end-diastolic left ventricular wall thickness; Vmax-Lau: peak velocity of the left atrial auricle blood flow.

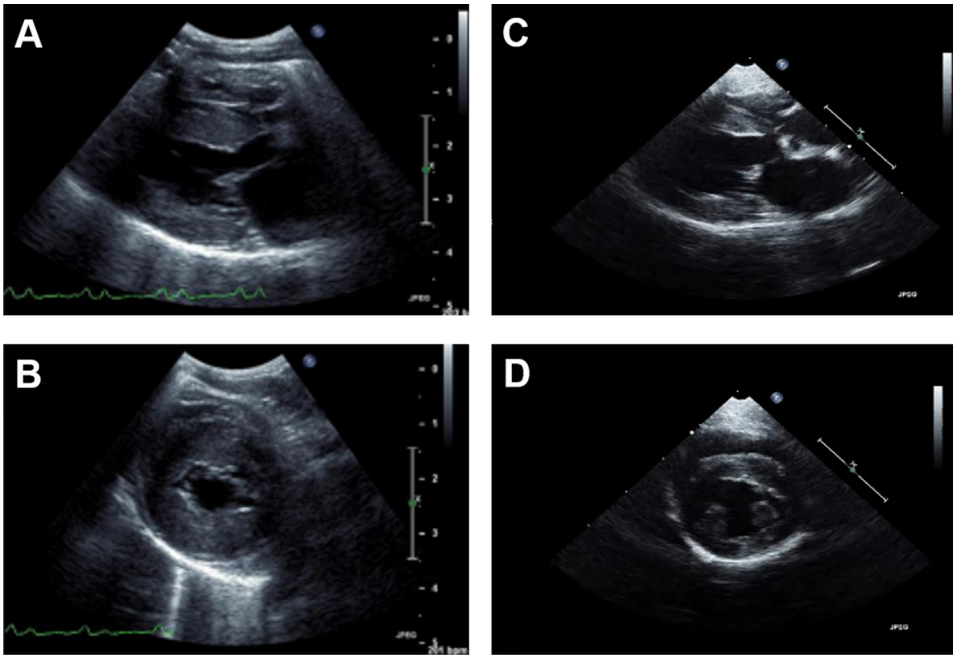

Figure 1 Transthoracic echocardiography obtained in one cat from this study at the time of diagnosis (A and B) and resolution (C and D) of left ventricular wall thickening. A and C. Right parasternal long-axis four-chamber view. B and D. Right parasternal short-axis view at the level of papillary muscles. At the time of presentation, note the left ventricular wall thickening; moreover, multiple B lines associated with lung edema can be noticed (A and B). At that time, an electrocardiogram could be recorded during echocardiography showing a sinus rhythm with a heart rate of 200—210 beats/minute. At the time of echocardiographic control, despite the different setting/probe used, it is possible to note the resolution of left ventricular wall thickening; moreover, no B lines can be identified (C and D). At that time, the cat not tolerated the electrocardiographic clips; therefore, an electrocardiogram could not be recorded during echocardiography.

median duration of hospitalization for these cats was 4 days, ranging from 2 to 9 days.

All cats were regularly rechecked in the following weeks until the resolution of LVWT; the median number of cardiologic rechecks was five (from three to eight). The median time from diagnosis to evidence of echocardiographic resolution of LVWT was 43 days (18—96 days). Over this time lapse, 4/27 (14.8%) cats showed relapses of CHF (one relapse was diagnosed in 2/4 cats, whereas the remaining 2/4 cats experienced two relapses). At the time of LVWT resolution, cats neither showed signs of CHF or ATE nor hypothermia, bradycardia, or hypotension. Moreover, concerning cardiac auscultation, only one cat (3.5%) still had a heart murmur (i.e. a 3/6 left-sided systolic murmur associated with mild mitral regurgitation). On electrocardiographic analysis, no cat showed disturbances of cardiac rhythm. At that time, all cats had a cTnI assessment (Table 2),

showing a statistically significant decrease compared to values obtained at first presentation ($P<0.001$). Specifically, 24/27 (88.9%) cats had a normal cTnI value at the time of resolution of LVWT (0.14 ng/mL [0.07—0.19 ng/mL]). In the remaining 3/27 (11.1%) cats, although the cTnI was still above the upper hospital reference limit, its value was remarkably decreased compared to that measured at initial presentation (i.e. from 3.1 to 0.24 ng/mL in one case, from 5.51 to 0.41 ng/mL in another case, and from 2.98 to 0.34 ng/mL in the remaining case). At the time of LVWT resolution, 24/27 (88.9%) cats had a CBC and/or serum chemistry recheck. In these cats, only a few laboratory changes were documented (Table 2). Among the cases with anemia, both cats (2/2 [100%]) had a normocytic, normochromic, non-regenerative type. In the only case with leukocytosis, a neutrophilic one was documented. In cats with a previous diagnosis of an infectious disease, serological tests and PCR yielded negative results after the completion of the relative antimicrobial protocol in all cases (i.e. toxoplasmosis, bartonellosis, and sepsis were successfully treated in all infected cats). The echocardiographic measurements obtained at the time of the last echocardiographic recheck are reported in Table 3 (Fig. 1C-D). At that time, all cats (27/27 [100%]) had a normal LVFS, LA:Ao ratio, LAFS, and Vmax-Lau. Concerning LAD, it was within the reference range in 26/27 (96.3%) cats, with only one cat (3.7%) showing LAD still above the upper range (i.e. 16.5 mm). Furthermore, no SEC, intracardiac thrombosis, SAM, or CAM were found in any of the cases. In light of the previously mentioned findings, cardiac therapies were gradually tapered down and/or discontinued. Specifically, at the time of the last recheck, drugs were discontinued in 18/27 (66.7%) cats. Among the remaining cases, 5/27 (18.5%) cats still received furosemide and pimobendan (although the dose of furosemide was tapered down compared to initial prescription), and 4/27 (14.8%) cats exclusively received pimobendan. Despite these therapeutic changes, no cat subsequently experienced further episodes of CHF, ATE, or arrhythmias.

Discussion

To the authors' knowledge, this study represents the largest investigation of TMT in cats. Our findings support some previous reports on this myocardial disorder, but also provide additional information to expand our knowledge on this uncommon clinical entity.

Regarding demographic data, our results confirm that affected cats are commonly young animals (median age 3 years), similar to a previous report on 21 cats diagnosed with TMT (median age 1.7 years) [1]. It is also interesting to note that approximately half of the affected cats in this study were <4 years old, different from the majority of cats with HCM showing a median age of 7.4 years with interquartile ranges of 4 and 11 years (according to the results of a study on 430 cats with HCM) [41]. This information is important in clinical practice, as it may help veterinarians consider TMT as a plausible differential diagnosis when LVWT is identified in cats <4 years rather than considering HCM systematically as the most likely diagnosis regardless of the age of the patient.

Another relevant finding not previously underlined was the prevalent lifestyle of affected cats. Interestingly, approximately one-third of our study population had free access to the outdoors (considering both cats that lived predominantly outdoors and cats with a mixed lifestyle). Admittedly a speculative hypothesis, but yet plausible, is that this finding could help explain, at least in part, the relatively high prevalence of infectious triggers of myocardial injury found here. Notably, all cats with infectious diseases had access to the outside, which possibly increased their chances of being infected. This hypothesis is supported by previous studies that have already demonstrated that cats with outdoor access are significantly more likely to be infected with several pathogens (including some of those reported to be associated with feline myocarditis and/or TMT, such as FIV and *T. gondii*) than indoor cats [42,43].

Concerning antecedent events, we could document them in approximately one-third of our cases, different from the around 70% of cases reported by Novo Matos et al., in 2018 [1]. Despite the different prevalence, it is important to note that the types of antecedent events were generally similar, as surgical/anesthetic procedures were the most common in both studies (77.8% and 46.7%, respectively) [1]. Based on the current feline literature, it is challenging to provide a pathophysiological explanation for the development of TMT after a surgical/anesthetic procedure. On the basis of some previous findings from veterinary and human literature, other authors have considered stressful events (such as surgical/anesthetic procedures) potentially leading to catecholamine surges in the list of hypothetical factors eventually associated with the occurrence of myocarditis/TMT in some cats [1]. However, it is important to underline that the aforesaid remains

a hypothesis and further studies are needed to conclusively establish the underlying cause of TMT shown by some cats after surgical/anesthetic procedures.

Regarding clinical findings at presentation, the presence of heart murmur was found in 37% of cases, a prevalence very similar to that found by Novo Matos et al., in 2018 (33%) [1]. In this study, the majority of cats with heart murmurs had functional variants of the mitral valve apparatus (i.e. SAM or CAM) at presentation. Additional and previously not reported physical findings from this report included hypothermia, bradycardia, and reduced systolic blood pressure in approximately one-fifth of cats described here, suggesting the presence of cardiogenic shock at the time of diagnosis. Approximately 93% of the cats in this study had CHF, which manifested predominantly as lung edema, both isolated and associated with cavitary effusion (88% of cases). These results agree with those documented by Novo Matos et al., in 2018, as they reported CHF in 100% of their study population, with lung edema present in 90.5% of cats (counting together cases with isolated lung edema and those with lung edema associated with pleural effusion) [1]. Collectively, these findings suggest that the clinical presentation of feline TMT is typically severe, prompting an emergency approach primarily aimed at managing CHF.

Regarding electrocardiographic findings, we found a higher percentage of abnormalities compared to that reported by Novo Matos et al., in 2018 (i.e. 26% vs. 10% of cases, respectively) [1], with bundle branch blocks being overrepresented. The association between disturbances of intraventricular conduction and myocardial injury has already been described in cats, and has been hypothesized to be the result of myocarditis associated with lymphocytic and plasma cell infiltrates interfering with fiber conduction [44].

Among laboratory data, cTnI represents one of the most important parameters, as it is essential to document ongoing myocardial injury [2]. On the contrary, serum chemistry and CBC do not seem to provide relevant information in the majority of cases, since only some cats had mild changes, usually not clinically relevant. The observed changes were likely the result of systemic hypoperfusion (e.g. increased creatinine and urea) and inflammation (e.g. increased serum amyloid A, leukocytosis, and normocytic, normochromic, nonregenerative anemia), and are similar to those reported in other conditions in which a cardiac compromise is associated with a concomitant inflammatory/infective process (e.g. myocarditis [11,14,44] and endocarditis [45]). Regarding tests aimed at unveiling possible infectious diseases, we identified potential infectious triggers of myocardial injury in approximately 26% of cases, counting together all cats with infectious conditions capable of causing myocardial injury/myocarditis, namely toxoplasmosis [11,16], bartonellosis [14], and sepsis [46]). Interestingly, neither cats with toxoplasmosis nor sepsis were described by Novo Matos et al., in 2018 [1]. Although sepsis is a somewhat unpredictable condition, the fact that we documented cats positive for *T. gondii* may not necessarily be incidental (of note, 2/3 cats testing positive for *T. gondii* have previously been reported in a case series [16]). Indeed, cases of reversible myocardial injury in *T. gondii*-positive dogs have been reported in the same geographical area as the cats from this report [47]. Furthermore, several epidemiological studies conducted in different animal species have documented a relatively wide diffusion of this protozoal disease in Italy [48,49].

The echocardiographic findings of this study are similar to those of previous reports on feline TMT [1,11,14,16], and further confirm that, at the time of diagnosis, this condition does not express itself as a simple LVWT, but is usually associated with LA dilation and LA/left auricular dysfunction (approximately 96—100% and 30—41% of cases, respectively, depending on the type of measurement). Moreover, in some cases, SEC and intracardiac thrombosis can be documented.

Regarding the outcome of cats with TMT in the present study, the median time from diagnosis to echocardiographic evidence of resolution of LVWT was shorter (median 43 days) compared to that previously reported (median 3.3 months) [1]. Conversely, the number of cats experiencing relapses of CHF was higher in this study compared to that documented by Novo Matos et al., in 2018 (i.e. four cats vs one cat, respectively) [1]. This finding highlights the importance of maintaining a conservative approach after discharge of cats with TMT, as complications may occur before LVWT resolution, even after the prescription of appropriate treatments. Regarding the physical findings at the time of resolution of the LVWT, it should be noted that almost all cats were clinically normal (as all physical abnormalities found at presentation had resolved, except one cat showing a mild heart murmur). Furthermore, most of the serum chemistry and CBC changes found at presentation were no longer evident at the last recheck, and the residual abnormalities were not clinically relevant overall. Concomitantly, cTnI decreased in all cats, being completely normalized

in approximately 90% of cases. Lastly, at that time, almost all echocardiographic changes had resolved (with the only exception being a cat with mildly increased LAD [16.5 mm]), as previously described [1]. Collectively, these results indicate that cats with TMT experience not only a reduction of LV wall thickness after successful treatment, but also a decrease in LA size, disappearance of SAM and CAM, and normalization of clinical and laboratory variables.

The results of this study should be interpreted in light of some limitations. First, the retrospective design of our analysis precluded standardization of the timing of diagnostic procedures and type of treatment. Second, the number of cats was relatively small due to the rarity of this clinical entity; therefore, more studies enrolling a larger number of cats are required to confirm and further expand our findings. A third limitation concerns the possible role of the hydration status of cats at the time of study enrollment. Indeed, although we ruled out cats with clinical overt signs of dehydration, the risk of having included some cat with clinically inapparent dehydration potentially associated with some degree of pseudohypertrophy cannot be completely excluded. Moreover, detailed data on the hydration status at each control could not be retrospectively retrieved. Therefore, it is impossible to systematically correlate the echocardiographic findings with hydration status at each time point. Furthermore, we were unable to retrieve complete data on the heart rate of the enrolled cats to explore the possible correlation between this clinical parameter and echocardiographic findings. This lack of data represents a limitation as both dehydration [18,21] and tachycardia [50] can influence echocardiographic measurements, including IVSd and LVFWd. Fourth, advanced echocardiographic modalities (e.g. tissue Doppler imaging, speckle tracking echocardiography), which could have helped to more comprehensively address left ventricular and LA dysfunction, were not systematically assessed in our study population. Finally, no cat underwent an invasive diagnostic procedure to obtain additional information on the nature and extent of myocardial compromise (e.g. cardiac magnetic resonance, endomyocardial biopsy).

Conclusions

This study shows that TMT most commonly occurs in young cats with LA dilation and dysfunction, and increased cTnI associated with CHF. Moreover, clinical signs of shock can be identified at presentation. In some cases, an antecedent event can be identified and in a few an infectious agent may be demonstrated via laboratory tests (e.g. serology, PCR). Proper treatment typically leads to the resolution of clinical, laboratory, and echocardiographic abnormalities in a relatively short period of time.

Funding information

This research did not receive any grants from funding agencies in the public, commercial or not-for-profit sectors.

Conflicts of Interest Statement

The authors do not have any conflicts of interest to disclose.

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