Speckle tracking echocardiography in cats with arterial thromboembolism

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ABSTRACT

Two-dimensional speckle tracking echocardiography (2D-STE) is a new approach developed for cardiac imaging that provides a better assessment of regional and global myocardial abnormalities than standard echocardiography techniques. The study's goal was to evaluate regional radial strain variables in the left ventricle using 2D-STE in cats with ATE. The research included ten clinically healthy cats (the control group) and ten cats with ATE (the study group). Cats with ATE which diagnosed with hypertrophic cardiomyopathy (HCM) were divided into both intraventricular septum (IVS) and left vetricular (LV) hypertrophy (IVS-HCM, n:5) and only LV free wall hypertrophy (LV-HCM, n:5) groups. Compared to the control group, cats in the LV-HCM and IVS-HCM groups had a thicker IVSd. LVPWd were considerably higher in the LV-HCM group than in both the IVS-HCM and the control group (8.04 ± 0.93, 4.9 ± 0.4, and 3.91 ± 0.17, respectively, P<0.001). Mid-posterior (MP) strain values in cats with IVS and LV hypertrophy were significantly lower than in the control group (both P<0.05). Values from mid-lateral (ML) were significantly lower than in the control group (both P<0.05). Our results showed that MP strain values decreased in the LV. Increased IVS and LVPW wall thickness is associated with a depressed MP strain in cats with HCM. Increased IVS wall thickness is related to low MP and strain values in cats with HCM.

Introduction

Feline arterial thromboembolism, which is linked to a high mortality rate, is a serious complication of myocardial disease (4, 5). ATE is strongly associated with a prominent prevalence of cardiac disease, and all forms of cardiomyopathy pose a risk for ATE (25). Some cats do not show any clinical signs of cardiac disease and have a normal lifespan (22). An impressive number of cardiomyopathies show not typical echocardiographic changes that are considered 'unclassified' cardiomyopathy (UCM) characterized by ATE and sudden death (4). Recent research has shown that a significant number of asymptomatic and mildly symptomatic HCM patients exhibit varied amounts of patchy myocardial fibrosis in the left ventricular myocardium, even in the context of preserved ejection fraction (EF) (9). In HCM, there are uncontrolled cellular changes and growth at the site of hypertrophy, which is characterized by cell loss, a typical pattern disorder, and irregular replacement fibrosis (11, 17). Less is known about the pattern of myocyte disarray and fibrosis, as well as its clinical and pathophysiologic relevance (1, 15, 16).

Two-dimensional speckle tracking echocardiography (2D-STE) is a recently developed approach to cardiac imaging designed to assess myocardial deformation and velocity parameters such as strain (St) and strain rate (StR). No angle-dependence 2D-STE provides an assessment of all segments of the heart. In addition, this technique allows improved measurement of localized and global cardiac deformations compared to conventional echocardiography techniques (3). 2D-STE has been reported for the evaluation of cardiac function in humans with HCM (6, 7, 12), dogs (8, 31), and cats with HCM (27). The latest studies have demonstrated that asymptomatic and mildly symptomatic patients with hypertrophic cardiomyopathy have variable areas of

patchy myocardial fibrosis in the left ventricular myocardium. However, no previous studies in cats with feline arterial thromboembolism (ATE) have used 2D-STE to assess myocardial function. The objective of the study was to evaluate the regional radial strain characteristics of the left ventricle (LV) in cats with ATE utilizing 2D-STE.

Materials and Methods

Animals: The study groups included 10 client-owned cats with ATE. Ten clinically healthy cats (the control group) were presented to the Small Animal Hospital, Veterinary Faculty, Ankara. The most common breed was the tabby cat (12/20), followed by mixed breed (5/20), and siamese (3/20). Cats with HCM were further divided into IVS hypertrophy without LV free wall hypertrophy (IVS-HCM, n:5) and only LV free wall hypertrophy (LV-HCM, n:5) groups. Cats in the control group were determined to be clinically healthy based on history, auscultation, thoracic radiographs, physical examination, echocardiographic examination, CBC, and serum biochemical profiles.

The diagnosis of ATE was based on history and clinical signs of limb paralysis of acute onset (<24 hours from the onset of clinical signs) with at least four of the clinical symptoms listed below: Sudden onset of lameness, plegia, or paralysis in the afflicted limbs; absence of dorsal pedal pulse verified by absence of doppler signal; paleness or cyanosis of the foot pads or nail bed in the affected limb(s); low rectal temperature (<37 °C); and reduced motor neuron symptoms in at least one limb (18).

Exclusion criteria included no evidence of pulmoner neoplasia on radiography, the presence of hyperthroidizm, clinical evidence of bleeding, hypoalbunemia, a platelet count <50,000/ml, and a history of chronic paresis or paralysis. At the time of recruitment, none of the cats in the study were getting any medication.

Echocardiographic Examination: Standard 2D, M-mode, and doppler blood flow measurements were performed on restrained, laterally recumbent cats using an ultrasound (Hitachi, Arietta V60) unit equipped with 5.5–7.5 MHz phased-array transducers as previously described and validated (19).

End-diastolic dimension (IVSd) of the interventricular septum, end-diastolic inside diameter of the left ventricle (LVIDd), left ventricular free (posterior) end-diastolic thickness, end-systolic thickness of the interventricular septum (IVSs), end-systolic diameter of the left ventricle (LVIDs), left ventricular free (posterior) end-systolic thickness (LVPWs), heart rate (HR), end-diastolic volume (EDV), end-systolic volume (ESV), stroke volume (SV), cardiac output (CO), and ejection fraction (EF) were measured in the standard right parasternal short-axis view at the level of the chordae tendineae. Then the LV shortening fraction (FS) was calculated using M-Mode.

An M-mode echocardiographic examination was used to detect HCM in cats with an IVSd and/or LVFWd of 6 mm or above.

Statistical Analysis: For each variable, descriptive statistics were computed. As parametric test assumptions, variables were assessed with the Shapiro-Wilk test for normality and the Levene test for variance homogeneity prior to hypothesis testing. The Kruskal-Wallis test was used to test the difference between IVS-HCM, LV-HCM, and control groups since the variables violated the assumptions associated with parametric distribution. A Dunn-Bonferroni post hoc test was performed after any significant difference. The Fisher-Freeman-Halton test was used to test the frequency distribution of gender among groups. The level of significance was set at $P<0.05$. All statistical analyses were calculated using SPSS 21 statistical software.

Results

The clinical features of the twenty cats that enrolled in the study were presented in Table 1. Age, sex and body weight showed no significant differences among the groups.

Cats in the LV-HCM and IVS-HCM groups had thicker IVSd in comparison with control group. LVPWd were significantly higher in LV-HCM group than in both IVS-HCM and control group (8.04 ± 0.93, 4.9 ± 0.4, 3.91 ± 0.17 respectively, $P<0.001$). EF values were not statistically significant between the groups. Echocardiographic values of both groups are summarized in Table 2.

Table 1. Characteristic of IVS-HCM, LV-HCM and control groups.

Parameters		IVS-HCM (n:5)	LV-HCM (n:5)	Control (n:10)	*P*
Gender (female/male)	*(n/n)*	(3/2)	(2/3)	(4/6)	0.85
Age (mounts)	*Mean ± SEM*	49.2±5.54	56,5±3.78	53.2 ±3.12	0.713
	Median (Q1-Q3)	48 (46-54)	55 (54-60)	53.5 (47.5-59.3)	
Body weight (kg)	*Mean ± SEM*	4.02±0,25	3.96 ±0,27	3.98 ±0.25	0.996
	Median (Q1-Q3)	4.2 (3.7-4.3)	4 (3.6-4.2)	4.05 (3.8-4.2)	

SEM: Standard Error of mean, Q1: 25th percentage, Q3: 75th percentage.

Table 2. Results of M-Mode echocardiograpy indices in IVS-HCM, LV-HCM, and control group.

Parameters	IVS-HCM (n:5)		LV-HCM (n:5)		Healthy (n:10)		P
	Mean + SEM	Median (Q1 - Q3)	Mean + SEM	Median (Q1 - Q3)	Mean + SEM	Median (Q1 - Q3)	
IVSD (mm)	6.18 ± 1.05	6.2 (3.3 - 9) ab	6.74 ± 0.48	6.6 (5.2 - 8) a	4.59 ± 0.7	4.05 (2.8 - 10.6) b	0.049
LVIDd (mm)	13.98 ± 1.26	14.3 (10.8 - 17)	12.8 ± 1.74	14.1 (6 - 15.8)	13.4 ± 0.37	13.4 (11.1 - 15.2)	0.742
LVPWd (mm)	4.9 ± 0.4	5 (3.5 - 5.8)b	8.04 ± 0.93	7.8 (6.1 - 11.5)a	3.91 ± 0.17	3.95 (3.1 - 4.9)b	<0.001
IVSs (mm)	6.98 ± 0.19	6.9 (6.4 - 7.4)	7.9 ± 0.53	8.1 (5.9 - 8.9)	6.47 ± 0.55	5.85 (4.7 - 10.8)	0.067
LVIDs (mm)	7.64 ± 1.35	7.8 (4.1 - 11.2)	5.04 ± 1.04	5 (1.9 - 7.8)	6.9 ± 0.5	6.6 (5.3 - 10.5)	0.173
LVPWs(mm)	6.7 ± 0.23	6.8 (5.9 - 7.3)b	10.26 ± 1.27	8.5 (8 - 14.1)a	6.9 ± 0.41	6.65 (5.6 - 10)b	0.004
HR (BPM)	184.8 ± 8.84	183 (158 - 206)	192.2 ± 10.59	191 (169 - 220)	187.5 ± 17.19	169.5 (140 - 318)	0.961
EDV (ml)	5.36 ± 1.19	5.4 (2.5 - 8.4)	4.54 ± 1.08	5.1 (0.5 - 6.9)	4.58 ± 0.32	4.55 (2.8 - 6.3)	0.723
ESV (ml)	1.26 ± 0.5	1 (0.2 - 2.8)	0.42 ± 0.19	0.3 (0 - 1)	0.85 ± 0.19	0.65 (0.4 - 2.4)	0.265
SV (ml)	4.1 ± 0.96	2.6 (2.4 - 6.5)	4.12 ± 1.08	4.5 (0.4 - 6.9)	3.75 ± 0.22	3.85 (2.4 - 4.7)	0.799
CO (l/m)	0.76 ± 0.19	0.54 (0.41 - 1.29)	0.75 ± 0.18	0.86 (0.08 - 1.17)	0.71 ± 0.09	0.72 (0.38 - 1.37)	0.962
EF (%)	78.46 ± 8.01	86.2 (48.4 - 93.1)	86.34 ± 4.98	86.8 (73.3 - 99.7)	82.73 ± 2.79	86.4 (62.4 - 91)	0.704
FS (%)	46.42 ± 6.89	52.2 (22 - 61.8)	57.1 ± 9.1	52.6 (37.2 - 87.9)	48.81 ± 2.7	51.8 (30.8 - 58.5)	0.442

a,b: Different letters in the same row represents statistical significance (P<0.05).

Using 2D-STE, systolic radial strain values from the parasternal short-axis views at the mid-papillary muscle level in ATE and control groups were obtained 2D-STE variables were assessed from 6 separate sections; MAS (mid anteroseptal), MA (mid anterior), ML (mid lateral), MP (mid posterior), MI (mid inferior), MS (mid septal) (Figure 1, Figure 2). The radial 2D-STE exam results among groups are summarised in Table 3. MP value in both LV-HCM and IVS-HCM groups was significantly lower than in the control group (both P<0.05). ML value was statitically lower in both IVS-HCM and LV-HCM group compared to the control group.
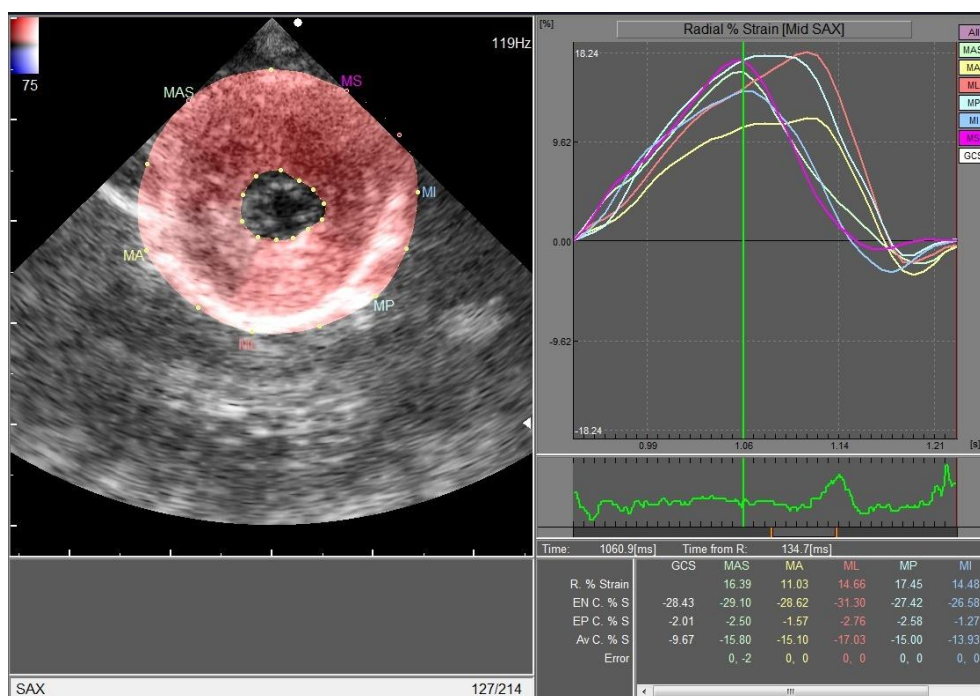

Figure 1. A snapshot of peak systole taken at the short-axis papillary muscle level of one of the control cats. It is understood from the strain data and graph shown in red that contraction is sufficient in 6 different regions; MAS (mid anteroseptal), MA (mid anterior), ML (mid lateral), MP (mid posterior), MI (mid inferior), MS (mid septal).
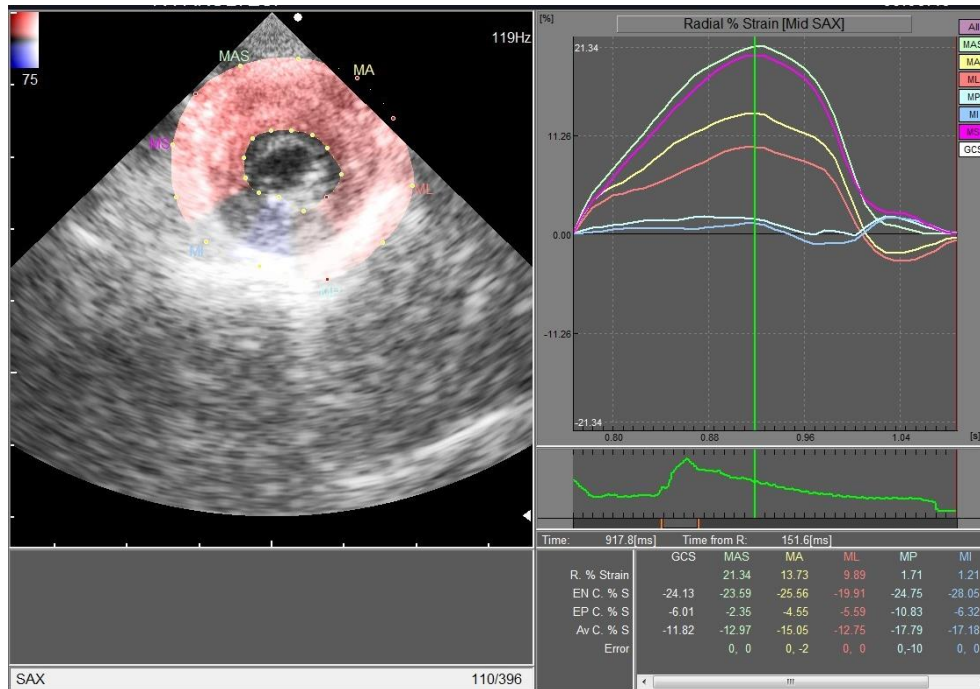
Figure 2. 2-D Speckle tracking echography of left ventricle in a cat with HCM. The color change in the MP and MI regions shows that the strain values are low and the contraction is insufficient in these regions.

Table-3 Peak systolic radial strains assessed by 2-dimensional speckle-tracking echocardiography in IVS-HCM. LV-HCM and control groups.

Parameter	IVS-HCM (n:5)		LV-HCM (n:5)		Healthy (n:10)		P
	Mean + SEM	*Median (Q1 - Q3)*	*Mean + SEM*	*Median (Q1 - Q3)*	*Mean + SEM*	*Median (Q1 - Q3)*	
MAS	13.16 ± 3.64	13.04 (2.51 - 21.34)	16.96 ± 4.22	19.24 (3.59 - 28.88)	15.88 ± 3.49	18.55 (-5.23 - 27.92)	0.754
MA	8.72 ± 3.72	3.57 (2.5 - 21.03)	14.89 ± 3.76	14.46 (7.11 - 27.98)	15.54 ± 3.94	18.58 (-12.29 - 29.37)	0.231
ML	7.83 ± 3.51	9.89 (-0.6 - 16.59)b	9.49 ± 4.49	6.11 (0.73 - 24.56)b	17.99 ± 2.01	17.05 (6.36 - 28.54)a	0.048
MP	9.37 ± 4.32	6.11 (0.01 - 21.87)b	7.17 ± 2.46	5.61 (-0.19 - 13.09)b	19.82 ± 2.73	17.15 (11.38 - 35.23)a	0.031
MI	10.96 ± 4.23	8.59 (1.21 - 24.66)	7.57 ± 4.03	7.51 (-6.28 - 16.42)	15.59 ± 2.82	14.55 (1.47 - 33.4)	0.276
MS	13.41 ± 2.43	13.02 (5.49 - 20.33)	14.23 ± 5.05	19.69 (-3.24 - 24.59)	16.82 ± 1.96	17.15 (6.05 - 24.16)	0.672

a,b: Different letters in the same row represents statistical significance (P<0.05).

Discussion and Conclusion

To our knowledge, this is the first study to measure radial strain of the LV in cats with ATE using 2D-STE. We found that systolic MP strain were significantly lower in cats with ATE than in healthy cats. Also, ML value was statitically lower in IVS-HCM compared to healthy cats.

Earlier 2D-STE investigations of cats have shown that global and segmental longitudinal strain were considerably lower in asymptomatic and symptomatic cats with HCM compared with healthy cats (13, 26, 28). Radial deformations play a significant role on the deterioration pumping function of the heart in both cats and humans with HCM (18, 19, 28, 30) and in subclinical patients with cardiovascular risk factor. Circumferential shortening compensates for LV myocardial contractions that are impaired longitudinally (29). One of the most appealing findings of our study is the differences in regional strain of LV. This can be explained by the fact that in HCM myocardial fibrosis occurs anywhere along the myocardial wall. HCM cases are frequently considered to exhibiting regional heterogeneity of contractility which may be explained by regional variations in strain value (14, 21, 24). Sugimato et al. found that decreased longitudinal strain in cats with both segmental and diffuse hypertrophy (26). The present study showed that STE parameters were low in IVS-HCM and LV-HCM group. An explanation for this phenomenon could be that myofiber disarray (9, 28) and interstitial fibrosis (18, 19, 30), which are mostly located in the mid third of the ventricular wall. Fibrosis affects strain independently of the effects of regional wall thickness. For demonstrating LV wall thickness conventional echocardiography examinations may not reflect myocardial fibrosis, while strain variables indicate the severity of fibrosis in humans with HCM (22, 23).

In this study posterior wall strain was low in cats with ATE. Sasaki et al. showed that grayscale imaging allowing assessment of regional systolic function in the posterior or lateral wall was affected earlier compared with the other segments in human patients (23). The fibers in the inferolateral region pulled by other previously activated myocardial segments may cause further stretching of the fibers before they begin to shorten. The lateral wall with a high regional radius of curvature contributes to increased regional tension. If dystrophin is absent, increased stress may cause earlier muscle damage (2, 10). Further studies are needed to explain regional fibrosis in cats.

Left ventricular thrombus (LVT) forms as a consequence of there factors of Virchow's triad included stasis of flow, hypercoagulability and wall damage (10). A damaged myocardium may trigger all three steps in Virchow's triad, and aggravate the low-flow in the different regions of LV (2). Olsen et. al. found that decreased apical and midventricular strain values are potential risk factors for LVT formation (20). ATE might be explained by decreased strain in left ventricular ML and MP regions in our study.

There were several limitations of this study. The study was included a small number of cats with ATE. Measuring only radial strain was another limitation of this study. It is possible that measurement of circumferential and longitudinal strain will add useful information to the results obtained in this study. We obtained only a parasternal short-axis view in this study. Because, the vast majority of cats with ATE experience severe pain and respiratory distress, which makes any medical procedure and clinical examination difficult including echocardiography. A parasternal short-axis view may be quick guidance to interpret the echocardiographic information and relates it to the clinical context in cats with ATE. These limitations should be overcome in future investigations.

In conclusion, we found that radial peak systolic MP strain value of both HCM groups and MP strain value of IVS-HCM group were significantly lower in cats with ATE than in controls. Our results showed that MP strain values was decreased in the LV, regardless of which wall thickened in HCM cats. The detection of the various regional strain levels may play a significant role in the development of ATE in cats. The therapeutic use of this discovery might help us comprehend the pathophysiology of ATE. Future research with additional animals and strain values from various plains will help us to determine whether LV distribution fibrosis in ATE patients has clinical and pathophysiological importance in cats with HCM. Because LVTs sometimes go unnoticed until symptoms appear or are discovered inadvertently, it is prudent to characterize HCM patients based on the risk of thrombus development using echocardiography. Reduced ML and MP strain can be a useful marker in cats with HCM where the clinician is in doubt whether they will develop a potential LVT.

Ethical Statement
This study was approved by the Ankara University Animal Experiments Local Ethics Committee (Approval No: 2019-15-133).

Conflict of Interest
The authors declared that there is no conflict of interest.

Author Contributions
İB and RE conceived and planned the study. OST, İB and RE carried out the experiments. DÖ did statistics. All authors contributed to the interpretation of the results. İB took the lead in writing the manuscript. All authors provided critical feedback and helped shape the research, analysis and manuscript.

Data Availability Statement
The data supporting this study's findings are available from the corresponding author upon reasonable request.

Animal Welfare
The authors confirm that they have adhered to ARRIVE Guidelines to protect animals used for scientific purposes.

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