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RESEARCH ARTICLE

Role and Importance of Cardiac Biomarkers in Diagnosis and Prognosis of Feline Arterial Thromboembolism

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Abstract

Feline arterial thromboembolism (FATE) is a common complication of myocardial disease, often having poor prognosis. The purpose of this study is to evaluate the diagnostic and prognostic value of serum levels of cardiac biomarkers (N-terminal prohormone of brain natriuretic peptide [NT- proBNP], creatine kinase isoenzyme-MB [CK-MB], and cardiac troponins [cTnI and cTnT] in cats with hypertrophic cardiomyopathy (HCM) that was complicated by FATE. Two groups were constituted in the study. Cats with a diagnosis of HCM were included in group I (n=10) and cats with HCM having acute episodes of FATE were included in group II (n=10). Results of cardiac biomarkers and echocardiographic measurements of left ventricle related parameters were compared between groups. The ratio of left atrium to aorta ($P<0.05$), fractional shortening ($P<0.05$), left ventricular dimensions ($P<0.05$), and stroke volume ($P<0.01$) were found statistically significant between groups. Serum CK-MB and cTnI levels in group II were higher ($P<0.001$ and $P<0.05$ respectively)) than those in group I. Serum levels of cTnI and cTnT were found respectively under 3.0 ng/mL and 0.1 ng/mL in the cats (n=3) which have survived. Our data demonstrate that remarkably elevated serum levels of cardiac biomarkers could be associated with the diagnosis of HCM with acute onset of FATE in cats, however cTnI and CK_MB might have a role in the risk assessment.

Keywords: *Cardiac troponins, CK-MB, Feline arterial thromboembolism, Hypertrophic cardiomyopathy, NT-proBNP*

Feline Arteriyel Tromboembolizm Tanısı ve Prognozunda Kardiyak Biyobelirteçlerin Rolü ve Önemi

Öz

Feline arteriyel tromboembolizm (FATE), miyokardiyal hastalıkların en sık görülen ve genellikle kötü bir prognoza sahip olan bir komplikasyonudur. Bu çalışmanın amacı, FATE gelişmiş kedilerde, N-terminal prohormon beyin natriüretik peptid (NT-proBNP), kreatinin kinaz (CK_MB) ve cTnI, cTnT serum seviyelerinin diyagnostik ve prognostik önemini belirlemektir. Çalışma için iki grup (I ve II) oluşturuldu. HCM teşhisi almış kediler grup I'e (n=10) dahil edildi. Akut FATE gelişimi olan HCM'li kediler ise grup II'e (n=10) dahil edildi. cTnI, cTnT, NT-proBNP, CK-MB seviyeleri tüm grupta analiz edildi ve kardiyak belirteçlerin sonuçları ile sol ventrikül ölçümleri gruplar arasında Mann-Whitney U non-parametrik test ile karşılaştırıldı. Kardiyak belirteçlerin seviyesi, ekokardiyografik ölçümler ve yaşam süreleri Pearson korrelasyon testi ile karşılştırıldı. Gruplar arasında sol atriyum çapı ($P<0,05$), sol atriyum aorta oranında ($P<0.05$), fraksiyonel kısalma ($P<0.001$), sol ventrikül çapı ($P<0.01$) ve atım hacmi ($P<0.01$) ölçümlerinde istatistiksel farklılık saptandı. Grup II'e ait CK-MB ($P<0.001$), ve cTnI ($P<0.05$) ölçümlerinde anlamlı artış bulundu. Yaşamakta olan kedilerde (n=3), cTnI ve cTnT seviyeleri sırasıyla 3.0 ng/mL ve 0.1 ng/mL'nin altında bulundu. Çalışma verileri, belirgin şekilde artış gösteren kardiyak belirteçlerin akut olarak FATE gelişen HCM'li kedilerin tanısında önemli olduğunu göstermektedir. FATE için kardiyak biyobelirteçlerin diagnostik faydası bulunmaktadır, bununla birlikte cTnI ve CK_MB FATE'ye bağlı risk değerlendirilmesinde önemli bir role sahip olabilir.

Anahtar sözcükler: *CK-MB, Feline arteriyel tromboembolizm, Hipertrofik kardiyomiyopati, Kardiyak troponinler, NT-proBNP*

INTRODUCTION

Hypertrophic cardiomyopathy (HCM) is the most commonly diagnosed disease of the cardiac sarcomere and is diagnostically and therapeutically challenging for veterinarians [1,2]. It is reported that feline arterial thromboembolism (FATE) is a common complication of myocardial disease, often having poor prognosis [2]. Besides there is more interest in

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feline HCM, as it constitutes a model for study of human HCM [1,3].

For detection of myocardial damage, the cardiac biomarkers are useful parameters. Cardiac troponin I and T (cTnI and cTnT, respectively) are also highly sensitive and specific for myocardial damage [2,4-8]. It was shown that especially an increase in cTnI was also a reliable method for differentiating cats with moderate to severe HCM from normal cats with a sensitivity of 85% and specificity of 97% [2]. In another study it was reported that cTnI has a sensitivity of 62.0% and specificity of 100% when used to distinguish healthy cats from asymptomatic cats with HCM but without left atrial dilatation and high sensitivity and specifity (95% and 77.8%, respectively) for assessing heart failure [9]. It was determined that NT-proBNP is reliable on differentiating cardiac and respiratory causes of respiratory distress but it appears to be inadequate when it comes to prognostic information [6]. Also, it is known that creatine kinase isoenzyme-MB (CK-MB) is a useful cardiac biomarker to detect myocardial injury in cats although it is less sensitive than cTnI [2]. However, diagnostic and prognostic utility of troponin, NT-proBNP and CK-MB measurements in FATE remains unknown. Therefore, the purpose of this study was to evaluate the diagnostic and prognostic values of serum levels of cardiac biomarkers; N-terminal prohormone of brain natriuretic peptide (NT-proBNP), CK-MB, cTnI and cTnT in cats with HCM that was complicated by FATE. Although there are other cardiac biomarkers suitable for assessing myocardial status, this study focused on these biomarkers which are the most common and accessible cardiac biomarkers to evaluate myocardial stress and injury.

Material and Methods

Ethical Statement

Ethical approval of this study was obtained from Istanbul University-Cerrahpasa Faculty of Veterinary Ethical Committee (2021/17). The animals were treated in compliance with ethical standards.

Animal Selection and Groups

Two groups (I and II) were constituted in the study; cats with HCM (n=9) in group I, and that was complicated by acute episodes of FATE (n=24) in group II. Average age of group I was 6.9 and group II was 5.5. Approximately 70% of both groups were male cats. A diagnosis of HCM was established based on echocardiographic examination. Cats have an end-diastolic left ventricular wall (LVWd) thickness ≥6 mm, considered as HCM. Cats in group I were subclinical and classified as cardiomyopathy stage B1 and group II were classified as cardiomyopathy stage C according to ACVIM classification criteria [10]. The cats in group I were classified as stage B1 according to their LA size. All the cats that included in group I had normal or mild LA dilatation with ≥6 mm LVWd [10] *(Table 1)*.

All the cats have been evaluated for some other diseases or conditions that can cause a HCM phenotype such as anemia, systemic hypertension, hyperthyroidism, viral diseases, hydration status, kidney and liver function, blood glucose level, and recently used medications. Cats that have abnormal or inadmissible data in terms of these diseases and conditions have been excluded from this study.

Diagnosis of FATE was based on the presence of dysfunction in one or two limbs and clinical evidence of decreased perfusion (paresis, coldness, lack of palpable arterial pulses, pallor of the nail beds) in the affected limb(s). Cats with FATE were accepted in case they were brought to clinic within 12 h after the start of the episode. Presence of dilated, restrictive or unclassified cardiomyopathy and FATE diagnosis more than 12 h later constituted the exclusion criteria of the study. Survival time and affected limbs were recorded.

Radiography and Echocardiography

Radiographic evaluations were performed in all animals. The heart size was measured by vertebral heart score system in radiographs [11].

Echocardiography was performed in all groups using a micro convex probe running at 7-9.3 mHz. The cats were restrained in right lateral recumbency for echo-cardiographic examination which was performed from right chest wall using the parasternal long and short axis view. Interventricular septal end diastolic dimension (IVSd), interventricular septal end systolic dimension (IVSs), left ventricular diastolic diameter (LVd), left ventricular systolic diameter (LVs), left ventricular posterior wall end-diastolic diameter (LVWd), left ventricular posterior wall end-systolic diameter (LVWs), left atrium (LA), fractional shortening (FS), left ventricular outflow tract (LVOT), the ratio of left atrium to aorta (LA/AO) were measured [12]. HCM was defined in case of left ventricular wall and septal wall thickness with normal or elevated left ventricular fractional shortening. Symmetrical (concentric) or asymmetrical (eccentric) enlargements were noted.

Cardiac Biomarker Analysis

Cardiac biomarkers (cTnI, cTnT, NT-proBNP, and CK-MB) were analyzed in the serum samples of animals of two groups. CK-MB was analyzed by kits from Spinreact (Spain). For determination of cTnI and cTnT, Immulite 2000 Systems (TPI, TPT, Siemens, UK) were used following manufacturer's instructions. NT-proBNP was also measured in plasma lithium heparin using Immulite 2000 (Siemens, UK). Human reagents were used in the assays. Several human immunoassays cross-react to canine and feline samples and have appropriate sensitivity for the diagnosis of heart

diseases common to veterinary medicine. There is a great deal of homology between human and nonhuman cardiac troponin isoforms [13]. It was also reported that the interspecies homology of proANP is much greater than that of proBNP [14,15]. However, while evaluating, the differences among the groups were considered.

Treatment

Atenolol (6.25 mg/cat) was started to two groups. Treatment with enoxaparin sodium (1 mg/kg subcutaneously q6h) was performed in cats of group II. Prothrombin time (PT) and activated partial thromboplastin time (aPTT) were measured weekly. After 10 days of treatment with enoxaparin sodium, low dose aspirin (5 mg/cat q72h) was administered for prophylaxis. For supportive therapy, heat sources, physical therapy, oxygen supplement and analgesics (chlorpromazine hydrochloride with a dose of 0.4 mg/kg intravenously q6h) were also used. Amputation was performed when necrosis and erosions were occurred in those cases.

Statistical Analysis

The results of serum cardiac biomarkers and echocardiographic measurements of left ventricle were compared between the groups by Student's T test. Echocardiographic measurements and serum levels of cardiac biomarkers were compared within a group by Pearson correlation test.

Results

The vertebral heart score was more than 8 vertebral bodies in all animals. Eccentric hypertrophy was found in 2 cats of group I and 7 cats of group II. Concentric hypertrophy was detected in 7 cats of group I and 15 cats of group II and echocardiographic examination couldn't be performed on one of the cats from group II *(Fig. 1)*. The results of echocardiographic measurements and cardiac biomarkers were given in *Table 1*. The ratio of left atrium to aorta ($P<0.05$), fractional shortening ($P<0.001$), left ventricular dimension ($P<0.01$) and left atrium diameter ($P<0.05$) between the groups were found statistically significant. Significant increases were determined in CK-MB ($P<0.001$) and cTnI ($P<0.01$) in group II, compared with those in group I. Difference in cTnT and NT-proBNP levels between two groups was not statistically significant.

The cats included in the study were predominantly male (24/33). Only nine cats of group II survived of which two of them were known to be alive for more than one year. The other cats were followed for more than 3 months. Survival time and cardiac biomarker results of group II were given in *Table 2*. Serum levels of cTnI were found under 3.0 ng/mL in the cats (n=9) which have survived and serum levels of cTnT were found under 0.1 ng/mL in 5 survival cats. However, NT-proBNP couldn't be analyzed in two cats of group II and also cTnT couldn't be measured in one cat of

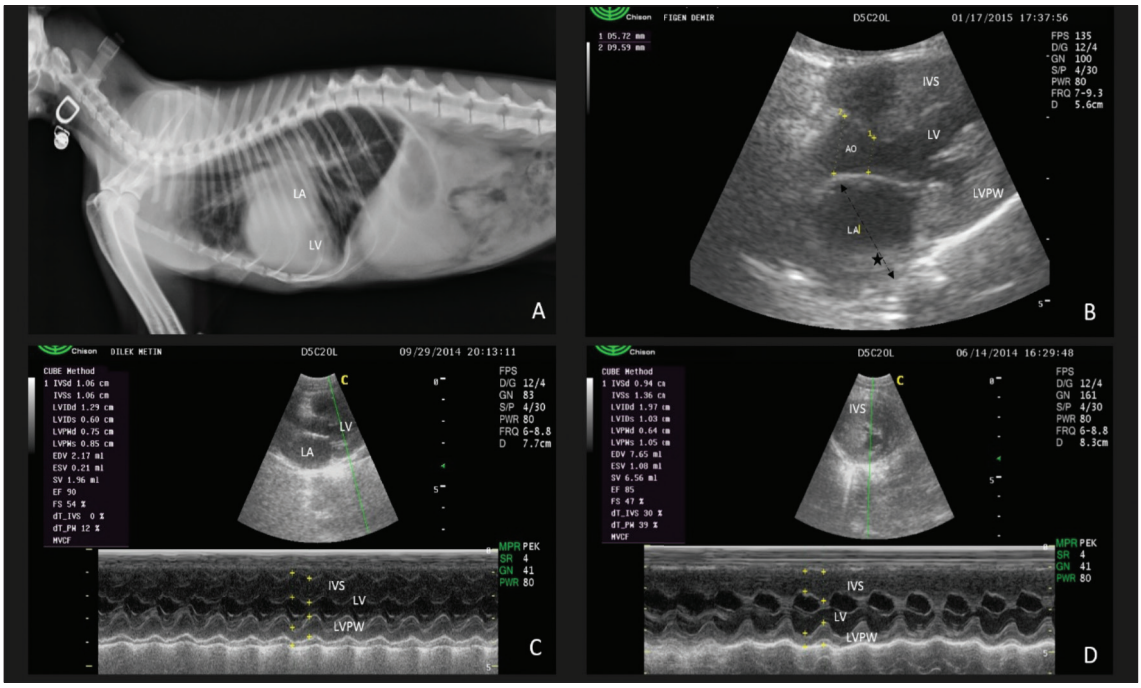

Fig 1. X-ray and echocardiographic images. **A-** Right lateral thoracic radiography of 4 years old short haired cat (case 5) of group II. Generalized cardiomegaly (vertebral heart score >11), peribronchial pattern and pulmonary congestion are present, **B-** Right parasternal long axis view of 3 years old long haired cat (case 7) of group II. Left atrial dilation (18.1 mm) and smoky view of the thrombus (marked by star), left ventricular outflow tract obstruction, hypertrophy in septum and left ventricular posterior wall are visualized, **C-** Right parasternal long axis view of 5 years old cat of group I. Left atrial dilation in 2-D image and concentric hypertrophy in septum and left ventricular posterior wall are seen in M-Mode image, **D-** Right parasternal short axis view of 7 years old short haired cat (case 1) of group II showing eccentric septal hypertrophy in 2-D and M-Mode echocardiogram

Table 1. *Comparison of echocardiographic measurements, cardiac biomarkers and age*

Group I (ACVIM Stage B1) (n=9)		Group II (ACVIM Stage C) (n=20)	
Parameters	**Mean±Std. Error Mean**	**Mean±Std. Error Mean**	**Significance**
Age (years)	6.9±1.206	5.50±0.778	NS
IVSd (cm)	0.775±0.0529	0.904±0.0730	NS
IVSs (cm)	1.218±0.0409	1.321±0.1109	NS
LVd (cm)	0.796±0.0379	1.160±0.1626	P<0.01
LVs (cm)	0.441±0.0308	0.669±0.1043	P<0,05
LVWd (cm)	0.877±0.0582	0.957±0.0786	NS
LVWs (cm)	1.225±0.1041	1.444±0.1149	NS
FS (%)	76.20±3.463	63.10±4.691	P<0.001
LVOT (m/sn)	0.672±0.0434	0.598±0.0459	NS
LA (cm)	1.538±0.0844	1.826±0.1301	P<0,05
LA/AO	1.649±0.12525	2.1278±0.1282	P<0.05
cTnI (ng/mL)	0.559±0.3229	13.860±64.203	P<0.05
cTnT(ng/mL)	0.1505±0.1188	1.695±10.657	NS
CK-MB (U/L)	45.67±7.269	2490.20±1204.601	P<0.001
NT-proBNP (pg/mL)	33.33±10.953	99.13±15.099	NS

NS: *not significant*

Table 2. *Levels of carciac biomarkers, survival time and number of affected limbs in cats of group II*

Cats of Group II	Age (years)	cTnI (ng/mL)	cTnT (ng/mL)	CK-MB (U/L)	NT-proBNP (pg/mL)	Survival Time	Number of Affected Limbs
1	10	9	NA	12310	NA	5 days	2
2	8	8.8	1.3	1202	NA	4 days	2
3	7	1.7	0.092	1020	130	Alive	2
4	3	32.6	0.28	1050	40	3 days	2
5	4	11.8	0.14	1050	58	10 days	2
6	3	0.95	0.057	1050	71	Alive	1
7	4	10	0.25	380	80	7 days	2
8	6	5.9	2.1	990	20	5 days	1
9	3	65	1.2	1510	62	2 days	2
10	7	2.6	0.094	810	32	Alive	1
11	4	1.1	0.86	120	20	Alive	1
12	5	1.3	0.092	277	25	Alive	1
13	13	0.57	0.41	53	10	Alive	1
14	4	0.43	0.075	380	20	6 months	1
15	2	0.87	0.41	159	19	Alive	1
16	3	0.87	0.13	149	29	Alive	1
17	10	0.27	0.044	215	10	Alive	1
18	6	4.3	1.14	470	35	5 days	2
19	4	14.7	0.15	498	34	1.5 days	2
20	7	3.7	0.071	175	18	18 days	2
21	11	2.4	0.12	1245	24	11 months	2
22	5	18	0.17	155	31	1 day	2
23	6	10.3	0.14	1729	28	1 day	2
24	5	175	2	418	37	8 days	2

NA: *not available*

group II. As an adverse effect of enoxaparin sodium, gastric bleeding was occurred in one cat. It was managed by classic treatment and prolonged intervals of enoxaparin sodium treatment. Amputation was performed to 4 cats at 4th, 5th, 11th and 14th days of treatment. Three of them survived. The one amputated at 4th day died at the day after.

Left atrial thrombus was visualized in echocardiographic examinations of 3 cats *(Fig. 1-B)*. According to statistical analysis of all data with Pearson correlation test, positive correlation was found between IVSs and LVWs (P<0.05), FS and IVSs (P<0.01), LVs and LVd (P<0.01), LA and LVd (P<0.05), LVWd and LVWs (P<0.01), LVWs and FS (P<0.01) and negative correlation was found between FS and LVd (P<0.01), LVd and LVWs (P<0.05), LVs and LVWd (P<0.05), LVs and LVWs (P<0.01) FS and LVs (P<0.01), LVWd and LVd (P<0.05), FS and LA (P<0.05). Also, positive correlation was found between CK-MB and LVd (P<0.01), cTnI and LA/AO (P<0.05), LA and CK_MB (P<0.01), LA and NT-proBNP (P<0.05), cTnI and CK-MB (P<0.05) and a negative correlation was found between LVOT and NT-proBNP (P<0.05) in all animals. Depending on the statistical analysis of group II by Pearson correlation test, positive correlation was detected between IVSs and IVSd (P<0.05), LVs and LVd (P<0.01), LVWd (P<0.01), FS and LVWs (P<0.05), LVOT and FS (P<0.05, CK_MB and IVSd (P<0.05), CK-MB and FS (P<0.05), NT-proBNP and IVSs (P<0.05), and negative correlation was found between LVWs and LVd (P<0.01), LVWs and LVs (P<0.05), LA and LVOT (P<0.01).

Discussion

Feline arterial thromboembolism is a considerable complication of feline cardiomyopathy which is having a poor prognosis [2,16-18]. Thromboembolism was seen in 20-50% of cats with cardiomyopathy [17,19]. It is known that the blood serum levels of cardiac biomarkers such as CK-MB, TnI, TnT and NT-proBNP are being elevated in cats with cardiomyopathies [2,4-6,8]. One of the cats (no: 4 in group II) involved in the current study was brought 6 h before the acute onset of FATE, and the obviously elevated laboratory results in this study depended on the prior examination. This case also inspired the creation of the current study to investigate the role of cardiac biomarkers in FATE by comparing the data of cats with HCM that didn't develop FATE.

The gender of the animals was predominantly male (24/33). Compatible with our results, most of the cats with FATE and HCM were found to be male in many studies and it indicates that males are at increased risk for FATE [8,16,18,20-22].

The echocardiographic examinations are important in feline medicine. As no auscultable abnormalities suggesting of an underlying cardiac disease could be detected in more than 40% of the cats diagnosed with FATE [18]. Severe left atrial enlargement and identification of smoke contrast or thrombus inside the left atrium are known to be considerable risk factors of FATE [18]. In one study conducted on cats with FATE, LA/AO was measured as 2.06±0.52 in 30 cats. However, no difference was found in survival based on LA/AO (P=0.780) [17]. It was reported that most of the cats with FATE were having LA enlargement while 45% had a LADs greater than 2.0 [23]. In our study, the mean result of LA/AO of group II was measured as 2.158 (1.47-2.50) cm and significance was found between the groups (P<0.05). It was considered that a correlation between left atrial dilation and thrombus formation was existent. Compatibly, Fuentes [16] reported that the blood stasis in left atrium results in local platelet activation and thrombus formation.

The survival rate was known to be between 20% and 50% independently from the type of the treatment used. The treatment protocol depends on supportive care and antithrombotic, surgical thrombolectomy or administration of thrombolytic agents [19]. Streptokinase, which is an expensive prescription and not easily available in our country, is one of the preferred choices in the treatment [17]. However, 100% mortality rate was reported in 8 streptokinase treated cats [24]. Short term survival rate of 33% was found in the cats treated with streptokinase in another study [17]. In recent years, low molecular weight heparin is suggested for treatment. However; in brief, survival rates differ through 35%-39% in conservative therapy or 33% in thrombolytic therapy; whereas natural death rates show similarity to euthanasia with the rates of 28-40%, 25-35%, respectively [25]. Also, tissue plasminogen activator is a new drug used in human medicine, whereas high rate of side effects occurred in administration to cats [19]. It is observed that complications related to TPA are fever (33%), minor hemorrhage (50%) and reperfusion injury (33%) [26]. The survival rate is not much different from these studies; however only antithrombotic agents were used. Also, it is reported that there is no statistically different results in terms of treatment outcomes and complications between the cases that treated with and without TPA [27]. Recently, some researchers recommended the antithrombotic drugs as a first-treatment choice, as the thrombolytic therapy could lead to adverse effects and high mortality rates [16]. Additionally, in one study, cats with FATE and HCM had a mean survival time of 61 days [28]. Cats with single limb episodes had a better prognosis than bilateral involvement [18]. In our study; bilateral involvement was observed in 16 of 24 cats. Also in one study, cats that died between 24 h and 7 days had a median age of 11 years (2-19) and 73.6% of them had two or more limbs affected whereas 33.3% of them had one limb effected. In our study; the median age of cats that died between 24 h and 7 days was 5.66 years (3-10) and it was similar to median age of cats that survived for 7 days and more (5.93 years, 2-13). However, there were fewer cats that had one limb affected in the group of animals that died between

24 h and 7 days (11% versus 40%) [29]. According to those information, it is deliberated that the high mortality rate in our study also could be depended on the number of the affected limbs.

Hertzsch et al.[30] have reported that cTnI is a sensitive and specific indicator for asymptomatic cats and a cutoff of >0,06 ng/ml for cTnI can be used as a screening test to detect the cats that have asymptomatic HCM. Langhorn et al.[5] have found that cTnI and especially cTnT are remarkably sensitive and specific indicators for detecting myocardial damage in cats with HCM, however their sensitivity and specificity can be changed between individual cases. However, non-survival cats (17 of 36) that suffering from HCM has shown remarkably higher concentrations of cTnI and cTnT, the cTnI and cTnT concentrations have not been elevated in survival cats as much as non-survivals but difference between healthy cats and cats with HCM was greater for cTnT. Two of the non-survival cats were euthanized from development of FATE. Similarly, in our study, serum levels of cTnI and cTnT were remarkably high in non-survival cats. Also, in our study; although cTnI levels were under 3.0 ng/mL in all survival cats (n=9), that kind of identity couldn't be observed on serum cTnT levels. Serum cTnT levels were higher than 0.1ng/mL in some of the survival cats (4 of 9) which was below in the rest of the cats. This information may indicate that serum cTnI and cTnT levels can be minimally variable on cats with FATE that has better prognosis and serum levels of cTnI and cTnT may help to determine the severity of the disease beside complete cardiac examination. Since the mentioned study was performed on cats with HCM (only 2 of them was developed ATE during the study) more studies with more cats with FATE must be performed to support this study.

In one study conducted on the cats with HCM, no correlation was found between cTnI and echocardiographic parameters. But only weak correlation was detected between cTnI and LVWd [2]. Ironside et al.[31] have reported that cats having a LA:Ao ≥1.5 are approximately four times more at risk of a cardiac-related event such as congestive heart failure and FATE. Also, the risk level is the same for the cats with ≥700 pmol/l NT-proBNP concentrations. A week correlation was found on cTnI with LA/AO ($P<0.05$) in the current study. However, positive correlation was found between CK-MB and LVD and LA ($P<0.01$). Similar but weaker correlation was also valid between NT-proBNP and LA. These correlations of CK-MB and NT-proBNP with LA might indicate the possible damage that occurred by dilation in the left atrial wall due to HCM. Also, negative correlation was found between NT-proBNP and LVOT and positive correlation between NT-proBNP and LA ($P<0.05$). As NT-proBNP is substantially known to be produced in atrial myocardiocytes [32], our findings are consistent and significant.

Herndon et al.[2] found an extreme increase in cTnI in two cats with HCM and FATE (10.93 ng/ml and 2.98 ng/mL). No macroscopic evidence of myocardial infarction was detected in postmortem examination of one of these cats. The researchers offered two explanations for these apparent increases. One was the possible cross-reaction. Although cTnI was a highly specific indicator for myocardial damage, it was not clear in animals. The second opinion depended on the formation of an additional small thrombi that embolized to the coronary vessels [2]. The other hypothesis might be depended on left ventricular damage due to increased pressure in left ventricle occurred by the thrombus in distal aorta. In the present study, however, lowest value of cTnI was detected in three cats which had survived. Also, an extreme result of cTnI was detected in the cat no: 4 of group II, 6 h before the acute onset in this study. These findings may lead to possible diagnostic and prognostic value of cTnI. In our study, positive correlation was also found between CK-MB and cTnI ($P<0.05$). Significant increases were detected in NT-proBNP and cTnI in human patients with pulmonary thromboembolism [33-35]. As a prognostic value, it was found that the patients with elevated cTnI levels had more serious vital parameters [34].

In conclusion; our data demonstrate that remarkably elevated serum levels of cardiac biomarkers (CK-MB, cTnI, cTnT and NT-proBNP) are associated with the cats diagnosed as having acute onset of FATE with HCM. Especially, detection of extremely high results of cTnI and cTnT in one case 6 hours before acute onset of FATE indicates the diagnostic utility of cardiac biomarkers for FATE. cTnI and cTnT may also play a role for the risk assessment of cats with FATE. Although serum cTnI and cTnT levels can be variable on cats with FATE that has better prognosis, remarkably high levels of both cTnI and cTnT can indicate poor diagnosis. It is considered that the cats with remarkably high levels of cTnI (>3.0 ng/mL) and cTnT (>0.1 ng/mL) may have poor prognosis with survival days shorter than 10 days despite antithrombotic treatment.

Limitations

Since it is known that interspecies homology is much greater for proANP than pro BNP [14,15], assessing the samples with human reagents for NT-proBNP must be considered as a limitation for this study. Although only the difference between the groups have been evaluated for NT-proBNP, it must be compared with the data that acquired by assessing the same samples on animal and/or cat reagents. In future studies, comparison of NT-proBNP levels that assessed with human and animal reagents between similar groups may also be considered.

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Conflict of Interest

The authors declared that there is no conflict of interest.

Author Contributions

Design of the study: BAKIREL U. and ULGEN SAKA S. Preparation of the study, management of the patients and data collection: BAKIREL U., ULGEN SAKA S. and YILDIZ K. Article writing, data analysis and editing: BAKIREL U., ULGEN SAKA S. and YILDIZ K.

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