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Tromboembolisi Olan Bir Kedide Doku Plazminojen
Aktivatörü Tedavisinin Tromboelastografi ile
Değerlendirilmesi****Thromboelastography Evaluation of Tissue Plasminogen Activator
Therapy in a Cat with Acute Aortic Thromboembolism due to
Hypertrophic Cardiomyopathy**Meriç KOCATÜRK¹, Pınar LEVENT¹, Zeki YILMAZ¹¹Bursa Uludağ Üniversitesi, Veteriner Fakültesi, İç Hastalıkları Anabilim Dalı, Bursa, Türkiye**ÖZ**

Akut arteriyel tromboembolizm (ATE), trombusun aortun trifürkasyonuna yerleştiği, hemen tedavi edilmezse ölüme veya organlarda ciddi hasara yol açan çok ağrılı ve ölümcül ciddiye bir durumdur. ATE tedavisinde ilk seçenek olarak doku plazminojen aktivatörü (tPA) gibi trombolitik ajanlar tercih edilmektedir; ancak insan ve hayvanlarda spontan kanama gibi olası yan etkileri nedeniyle dikkatli kullanılmaları gerekir. Bu nedenle pıhtılaşma durumunun izlenmesi, çözünen intravasküler pıhtıların yönetimi ve tedavisinde önemli bir rol oynar. Pıhtı oluşumu, gücü ve lizis dinamiklerini ölçen ve pıhtı tutarlılığı hakkında bilgi sağlayan tromboelastografi (TEG), pıhtılaşma durumunu ve trombolitik tedaviye yanıtı değerlendirmede yararlı bir araç olarak kabul edilmiştir. Kedilerde intravenöz tPA ile uygulanan trombolitik tedavinin tromboelastografik takibini gösteren bir çalışma bulunmamaktadır. Bu nedenle burada hipertrofik kardiyomiyopatiye (HCM) bağlı ATE'li bir kedide tPA kullanılarak başarılı bir tromboliz rapor edilmiş ve ilk kez TEG ile trombolitik tedavi izlenmiştir.

ABSTRACT

Acute arterial thromboembolism (ATE) is an extremely painful and fatal serious condition in which the thrombus lodges in the trifurcation of the aorta, resulting in death or severe damage to organs if not treated immediately. Thrombolytic agents such as tissue plasminogen activator (tPA) are preferred as a first choice of the treatment for ATE; however, they should be used carefully because of their possible side effects such as spontaneous bleeding in human and animals. Therefore, monitoring coagulation status plays an important role in the management and treatment of dissolving intravascular clots. Thromboelastography (TEG) that measures the dynamics of clot formation, strength, and lysis, and provides information of clot consistency has been accepted as a useful tool for assessing coagulation status and response to thrombolytic therapy. There is no study showing the thromboelastographic monitoring of the thrombolytic therapy with intravenous tPA in cats. Therefore, we reported here thrombolysis by using tPA successfully in a cat with ATE due to hypertrophic cardiomyopathy (HCM) and for the first time monitoring the lytic treatment by TEG.

INTRODUCTION

Aortic thromboembolism (ATE) is a condition in which a large blood clot (thrombus) has traveled and lodged itself in a location that cuts off the blood supply to parts of the body such as legs, kidneys, and brain.¹ Possible reasons for ATE include heart diseases, kidney diseases (renal failure and nephrotic syndrome), endocrine diseases (hypothyroidism and hyperadrenocorticism), neoplasia and pancreatitis.² ATE is one of the most common complications of hypertrophic cardiomyopathy (HCM) in humans^{3,4} and cats.⁵

In the case of HCM, enlarged left atrium (LA) that promotes smoke-like stagnant or turbulent blood flow activating the coagulation pathway and promote clot formation. The cats suffering from ATE (FATE) are presented in general with an acute and distressing presentation with hyperventilation and severe pain, and are suddenly unable to use their hind legs appropriately. Physical examination shows absence of pulse in the affected legs and cold paws with cyanotic (blue-tinged) pads and nail beds confirming loss of blood supply along the extremity.⁷

Several studies suggest the use of thrombolytic as a gold standard therapy for ATE since surgical removal of the clot have risks (anesthesia, spontaneous reperfusion, and sepsis, etc.) in patients with heart disease.^{1,5-7} However, there are limited clinical experience with thrombolytic agents such as streptokinase and recombinant tissue plasminogen activators (tPA) in dogs⁸ and cats.⁹⁻¹¹ It was reported that tPA achieved better lysis rate than streptokinase in humans¹³. Drugs of tPA (alteplase, reteplase and tenecteplase) are one of the key components of the dissolution of blood clots. Primary function of tPA includes catalyzing the conversion of plasminogen to plasmin, the primary enzyme involved in the dissolution of blood clots.⁹ The common points of the studies performed about thrombolytics are that close monitoring of coagulation during tPA therapy due to bleeding tendency and its intravenous administration as early as possible following diagnosis of ATE have been needed.⁹

Thromboelastography (TEG) is a viscoelastic hemostatic assay evaluating primary, secondary and tertiary hemostasis in whole blood. A major advantage of TEG compared to traditional methods evaluating hemostasis such as platelet count and global clotting times (prothrombin time – PT and activated partial thromboplastin time - aPTT) is the ability to assess clot formation from its initiation to fibrinolysis. TEG is also able to assess the interactions between platelets and clotting proteins, as well as other blood cells, a feature of coagulation that cannot be assessed by other currently clinically available methods.^{9,14,16-19} To the best of the authors' knowledge, there is no information yet on the use of TEG in monitoring coagulation status in cats receiving tPA therapy. In this report, therefore, the effect of tPA treatment was evaluated using TEG in a cat with ATE due to HCM, before and 24 hrs after administration.

Case Description

A 3-year-old intact female domestic shorthair cat was presented to the animal hospital with a history of acute onset of dyspnea / tachypnea (84 respiration per minute [rpm]), hypothermia (36.5 °C), lameness and severe pain in hind legs. First clinical examination

was performed at 6 hrs after initial of the symptoms and revealed the severe pain and loss of sensation in the hind legs, bruising on the extremity pads and ischemic purple color at the nail base. The cat was placed to oxygen cage after administering of furosemide (2 mg/kg, IV, bolus, and then two times at the same dose with 2 hrs. intervals; Lasix 20 mg/2 ml, Sanofi, İstanbul) and butorphanol (0.25 mg/kg, SC; Butomidor 10 mg/ml, Interhas, Turkey) for the treatment of respiratory distress (possibly due to pulmonary edema) and pain stabilization, respectively.

Just before furosemide administration, blood samples were collected to evaluate complete blood cell count (CBC; HM5, Abaxis, USA), serum biochemistry profile (VetScan VS2, Abaxis, USA) and coagulation status (TEG 5000, Haemoscope Hemostasis Analyser, USA). Results revealed a hemoconcentration and increases in serum total protein, albumin, alanine aminotransferase, and blood glucose levels. Serum NT-ProBNP level of 75 pmol/L (Vcheck, Bionote, USA) was compatible with the suspicious of a heart disease (Table 1). The immunochromatographic tests for FeCoV, FIV and FeLV were negative, as well.

Right after the patient stabilization (meaning that respiration rate was reduced from 84 rpm to 52 rpm with resolving in dyspnea), radiological examination was performed. Latero-lateral (A) and ventro-dorsal (B) x-ray of the thorax revealed pulmonary edema (just like in the first physical examination), mild pulmonary artery enlargement and elongation of the heart (cardiomegaly) with noticeable aerophagia due to dyspnea (Figure 1). Electrocardiographic (ECG) examination revealed sinus arrhythmia, QS complexes (absence of R waves and presence of deep S waves in lead II and III), right axis deviation, and a wide complex ventricular extra systole (VES), with a heart rate of 136 bpm (CareWell 1103L, China) (Figure 2).

Echocardiographic examination was performed as suggested.²⁰ Briefly, interventricular septum (IVSd) and left ventricular free wall thickness at diastole (LVFWd) and left atrial to aortic root diameter ratio (LA/Ao) were measured at right parasternal short axis view (RPSAx) of the LV at the papillary muscles and aortic levels, respectively (Caris Plus, Color Doppler, Esoate, Italy). Aortic flow was assessed by color Doppler at left apical 5 chamber view. Results showed asymmetrically thickened IVS (6.5 mm; reference ≤ 6 mm) and LVFW (7.1 mm; reference ≤ 6 mm), and increased LA/Ao (2.8, reference < 1.5), indicating a moderate asymmetric concentric LV hypertrophy and marked dilation of the LA, respectively. Severe spontaneous smoke echocardiographic contrast (SEC) in the enlarged LA was observed, as well.

In addition to these findings, that LV outflow tract diameter (LVOT: 7.0 mm) and Ao maximal pressure gradient (Ao-maxPG: 6.7 mmHg) were found within reference ranges showed the presence of non-

obstructive HCM.²¹ Doppler ultrasonography revealed the absence of pulse and flow in the femoral arteries bilaterally. The findings were clinically indicative of ATE due to HCM.²²

Table 1. Hematologic and serum biochemistry panel of the patient presented with feline references.

Hemogram	Patient	Reference	Serum Biochemistry	Patient	Reference
WBC (K/ μ L)	6.16	5-12	ALB (G/dL)	4.9	2.2-4.4
Nötrofil (K/ μ L)	4.01	2.50-12.50	ALP (U/L)	42	10-90
Lenfosit (K/ μ L)	2.09	0.4-6.8	ALT (U/L)	733	20-100
Monosit (K/ μ L)	0.04	0.15-1.70	AMY (U/L)	1191	300-1100
Eozinofil(K/ μ L)	0.01	0.1-0.79	TBIL (mg/dL)	0.3	0.1-0.6
Bazofil (K/ μ L)	0.00	0.00-0.10	BUN (mg/dL)	29	10-30
RBC (M/ μ L)	12.50	5.5-8.5	Ca (mg/dL)	10.3	8.0-11.8
HCT (%)	60.9	30-45	Phos (mg/dL)	3.7	3.4-8.5
HGB (G/dL)	18.9	9-15	Crea (mg/dL)	2.2	0.3-2.1
MCV (fL)	49	41-58	Glu (mg/dL)	284	70-150
MCH (pg)	15.2	12-20	Na ⁺ (mmol/L)	153	142-164
MCHC (G/dL)	31.1	29-37.5	K ⁺ (mmol/L)	4.2	3.7-5.8
RDW (%)	19.2	17.3-22	TP (G/dL)	9.7	5.4-8.2
PLT (K/ μ L)	269	200-500	GLOB (G/dL)	4.8	1.5-5.7
MPV (fL)	14.4		NT-ProBNP	75	<100 pmol/L
PDW (%)	37.3				
PCT (%)	0.39				

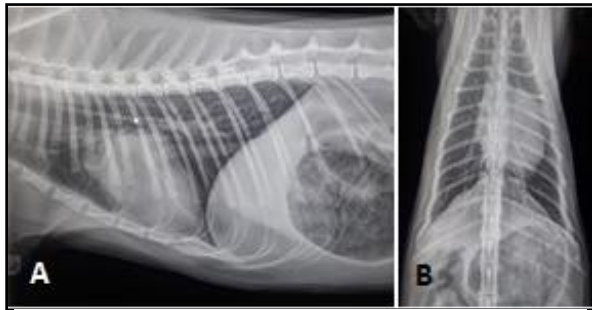


Figure 1: Laterolateral (A) and ventrodorsal (B) x-ray of the thorax revealed broncho-alveolar pattern and elongation of the heart with noticeable aerophagia due to dyspnea.

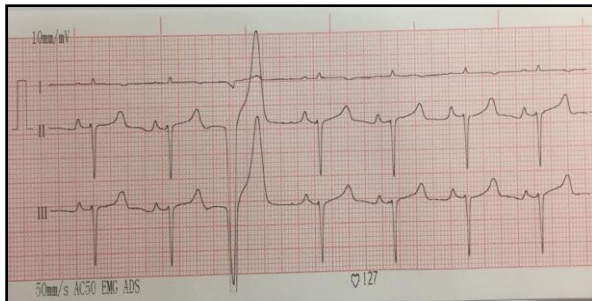


Figure 2: Electrocardiographic examination of the cat revealed sinus arrhythmia, QS pattern, and a wide complex ventricular extra systole (50 mm/sec., 10 mm/1 mV).

A magnetic resonance angiography (MRA) was performed to confirm the presence of ATE, as reported in a previous study.²³ MRA images showed that the contrast medium (Iohexol, 10 ml, iv.;

Omnipaque, Opakim, Türkiye) did not progress caudally at the level of femoral arteries (data not shown).²³ Based on the results of clinical and laboratory examinations, another risk factor for the development of ATE was not found.

Coagulation status was evaluated by TEG (TEG 5000, Haemoscope Hemostasis Analyser, USA), using anticoagulated blood samples (Vacuette[®], sodium citrate 3.2% Greiner Bio-One, Germany). TEG analyses were performed before (baseline) and 6 and 24 hrs after the treatment, within 30 minutes following the blood collection²⁴. TEG analysis included reaction time (R time) and kinetic time (K time) of clot kinetic, alpha angle (α -angle) of clot strengthening, maximum amplitude (MA) of platelet function, and lysis rate (LY30, the percentage of lysis 30 min after MA) of clot stability.¹⁶

For thrombolytic treatment, tPA was preferred because of achieving better lysis rate as compared with other well-known agents such streptokinase.^{9,10} Central venous catheter (CVC) was placed and then tPA therapy was started as suggested in a previous study.²⁵ Briefly, alteplase (Actilyse[®], Boehringer Ingelheim, Germany), a recombinant tPA, was administered at 1 mg/kg IV via cephalic veins over 1 hr with the first 10% of the infusion administered as an IV bolus over 10 min.⁹ Right after the drug administration, the cat was evaluated by physical examination and abdominal and thoracic ultrasonography for any evidence of external or cavitory hemorrhage, respectively.

TEG analysis showed that R time, MA and LY30 values were found to be normal, but K time and α -angle were out of the reference ranges at admission (Table 2 and Figure 3A). R time increased dramatically from 6.2 min of pre-treatment value to 112.7 min at 6 hrs after tPA treatment (Figure 3B), with value returning to normal at post-treatment 24 hrs. K time, α -angle, MA and LY30 could not be measurable at 6 hrs following the tPA administration, and then while K and LY30 values were normalized, α -angle and MA values increased at 24 hrs compared to those of their initial values (Figure 3c). In this period, clinically a significant decrease in pain perception, along with the patient's starting to step on his hind legs, and an increased perception of deep pain were observed in the neurological examination. Bruised extremity pads and ischemic nail bases returned almost to their healthy colors and respiration rate returned below 30 rpm.

The cat was discharged home with a medical protocol of thromboprophylaxis; clopidogrel (18.75 mg, PO, SID; Plavix 75 mg tb., Sanofi, Türkiye) and aspirin (5 mg/kg, PO, once every 72 hr, Coraspin 100 mg tb., Bayer Türk Kimya, Türkiye), and cardiomyopathy (HCM); furosemide (1 mg/kg, PO, BID, Lasix 40 mg tb., Sanofi, Turkey) and benazepril (0.25 mg/kg, PO, SID, Cibacen 5 mg tb., MEDA, Türkiye)²¹. An echocardiographic follow up was applied seven days later to re-evaluate the health status. At the time of writing, the cat was still living with drugs with reducing dosage of furosemide (1 mg/kg, once a day) and close contact with the owner was established to control the drug regimen and patient wellness. Also, the periodical controls including ECG, thoracic x-ray, CBC and renal panel (serum BUN and Cr) as well as serum electrolytes such as Na and K were carried out to observe possible side effects of medicals in every 3 months during the patient monitorization. The cat received thromboprophylaxis but did not need thrombolytic treatment after the first admission.

Table 2. Thromboelastographic evaluation of the cat.

Time / TEG parameters	R minutes	K minutes	α angle degrees	MA mm	LY30 %
Pre-treatment	6.2	11.4	21.8	58.3	0.0
6 hrs after the treatment	112.7	-	-	-	-
24 hrs after the treatment	7.2	3.8	41.4	77.6	0.0
References*	2.4-9.5	1.2-3.9	45.5-73.5	46.8-66.1	0.0-9.0

R: reaction time; K: clotting time; α angle: alpha angle; MA: maximum amplitude; LY30: clot lysis 30 min after MA is reached.

* Marschner C.B., Bjørnvad C.R., Kristensen A.T., Wiinberg B.: Thromboelastography results on citrated whole blood from clinically healthy cats depend on modes of activation. Acta Vet Scand. 2010, 52(1):38.



Figure 3: Thromboelastographic evaluation of the cat before (A), 6 hrs (B) and 24 hrs (C) after the tPA treatment.

DISCUSSION

This case report represents the therapeutic effectiveness of administration of intravenous tPA for thrombolysis, and how the coagulation status could be monitored using TEG in a cat with ATE due to HCM in practice. Considering the operative and anesthetic risks of thrombectomy, we have shared this case report stating that using tPA in the elimination of thrombus at the dose described here can lead to success with a much cheaper and risk-free method, and for the first time, TEG may be a useful and practical tool in monitoring the safe management of the thrombolysis in the first 24 hrs. of the treatment. ATE, a very painful and fatal serious condition, affects approximately 25-30 percent of cats with heart disease such as HCM.²⁶ In this case, HCM as a causative factor for ATE was diagnosed based on the clinical, radiographic, and echocardiographic examinations, and the presence of ATE was confirmed using the MRI as reported previously.^{22,23} Based on the imaging techniques and the comprehensive clinical and laboratory examinations, there were no other underlying disease for the development of ATE was found.

In cats with HCM, SEC and/or thrombus formation occurred especially in enlarged LA are associated with the blood stasis leading to increase in platelet activity (hypercoagulation) and endothelial damage.^{1,5-7} Formatted thromboses may remain mobile or adhered to a wall of the LA, become enlarged and block the exit to the LV, or may break apart as an emboly and pass from the Ao to femoral arteries.^{1,5-7} Arterial occlusion and impaired collateral circulation may explain the presence of the bruising on the

extremity pads and ischemic purple color at the nail base in the presented cat.

If the thrombus can be surgically removed or medically resolved within a short time, survival time may be longer and life quality may be increased.²⁷ However, the surgical treatment (embolectomy) is not recommended because of the high risk of death during and potential re-embolization after the procedure.⁶ In human medicine, after an acute ischemic stroke, intervention with intravenous tPA for up to 6 hrs can provide complete cure.^{3,4,28,29} Thus, thrombolytic therapy is suggested as a standard practice for acute thromboembolism in humans, as well as dogs and cats.^{9-11,25} On the other hand, there are limited clinical experience with thrombolytic agents such as streptokinase and tPA in dogs⁸ and cats.⁹⁻¹¹ In this case, we decided to use the tPA to resolve the thrombus and improve the tissue perfusion since the timing of starting thrombolytic therapy seemed appropriate, and it achieves better lysis rate than streptokinase.¹²

tPA, a 69 kD glycoprotein and an enzyme of serine protease family, shows thrombolytic activity by catalyzing the conversion of plasminogen to plasmin, the primary enzyme involved in the dissolution of blood clots.³⁰ Thus, while thrombolytics are used, close monitorization of coagulation is needed due to spontaneous bleeding tendency.⁶ In this cat, TEG, a whole blood coagulation analyzer, was used to evaluate coagulation status because it is accepted as a sensitive and useful method to evaluate coagulation abnormalities such as hypercoagulopathy, hypocoagulopathy and disseminated intravascular coagulation in dogs^{14,19,31} cats^{15,17,18,24}, and humans.³² Additionally, that TEG is used to characterize the whole clotting cascade from initiation of clot formation to fibrinolysis provides it a great advantage as compared with the traditional coagulation tests such as PT and aPTT.³¹

In veterinary medicine, TEG analysis has been used to evaluate coagulation status in health and disease in dogs and cats. Yilmaz et al.¹⁹ evaluated the hemostatic function by TEG in dogs with dilated cardiomyopathy (DCM) in which majority of the dogs showed a hypercoagulation rather than hypocoagulation state. In another study, Bae et al.³² used TEG to therapeutically monitor the use of rivaroxaban (anticoagulant) in dogs, and the usefulness of TEG in determining the individual dose regimen and monitoring the treatment was noted. TEG analysis was performed in healthy^{15,34,35} or diseased cats such as obesity³⁶, acute trauma³⁷, hyperthyroidism³⁸, infection³⁹, liver disease¹⁸, and was used to monitor feline anticoagulant therapy.³⁴ In a study conducted in healthy cats, significant changes in the TEG parameters after an anticoagulant (factor Xa inhibitor) administration was found compatible

with hypocoagulable state.⁴⁰ However, there is no study yet showing the thromboelastographic monitoring of the thrombolytic therapy with intravenous tPA in cats with heart disease.

In this cat, TEG values before the treatment showed an abnormal clot kinetic and strengthening based on the prolonged R time and decreased α -angle compared to the references reported for healthy cats¹⁵, although we expected to see a hypercoagulation state. Six hours after the tPA administration, prolonged coagulation time was revealed by a straight line, and TEG analysis was thus truncated at 112 min., which was most probably due to thrombolytic activity of tPA relating with catalyzing the conversion of plasminogen to plasmin. Following the tPA treatment, at 24 hrs, all TEG parameters measured in this cat were within reference ranges, indicating that coagulation cascade was returned to normal coagulation status from hypocoagulation due to thrombolytic.

Although intravenous alteplase (tPA) is cleared primarily by the liver with an initial half-life of fewer than 5 min. and a terminal half-life of 72 min.⁴¹, in our case thrombolytic activity/hypocoagulation state in response to tPA was stable till 6 hrs. This may be due to species differences, and/or long-lasting elimination of tPA clearance in cats. In addition to the normalization of TEG parameters, cat improved clinically and started to step on his hind limbs. In this period, bruised extremity pads and ischemic nail bases returned almost to their healthy colors and respiration rate returned into the reference range at rest. The cat was discharged home with a medical protocol of thromboprophylaxis (clopidogrel and aspirin) and cardiomyopathy (furosemide and benazepril). Cats receiving tPA therapy could be monitored on the possible tPA-related side effects such as reperfusion injury and acute kidney injury.^{25,42} We couldn't observe any side effects and/or replaces of ATE during 3 months, based on the comprehensive diagnostic approaches.

As a result, the case report presents the advantages of clinical therapeutic monitoring of tPA treatment with TEG include the following: (i) prevention of possible over-dose drug administration; (ii) gives chance to safely monitor the thrombolytic process created during the treatment; (iii) assesses the effectivity of anticoagulant drug regimen immediately during the monitorization of tPA treatment in cats with ATE. Clinicians should be kept in mind that coagulation should be closely monitored in both HCM and thrombolytic treatments in cats with ATE, and TEG may be considered as a useful and practical tool to evaluate coagulation status and to monitor tPA treatments in cat practice.

REFERENCES

1. Payne J., Borgeat K., Brodbelt D.C., Connolly D.J., Luis Fuentes V.: Risk factors associated with sudden death vs. congestive heart failure or arterial thromboembolism in cats with hypertrophic cardiomyopathy. *J. Vet. Cardiol.* 2015, (17): 318-328.
2. Whelan M., O'Toole T.: The use of thrombolytic agents. *Compendium.* 2007; 29: 28.
3. Niedermeyer J., Meissner E., Fabel H.: Thrombolytic therapy in pulmonary embolism. Indications and therapeutic strategies. *Z. Gesamte Inn. Med.* 1993, 48(6-7): 332-43.
4. Heiferman D.M., Li D.D., Pecoraro N.C., Smolenski A.M., Tsimpas A., Ashley W.W.: Intra-Arterial Alteplase Thrombolysis during Mechanical Thrombectomy for Acute Ischemic Stroke. *J. Stroke Cerebrovasc. Dis.* 2017, 26(12): 3004-3008.
5. Borgeat K., Wright J., Garrod O., Payne J.R., Fuentes V.L.: Arterial Thromboembolism in 250 Cats in General Practice: 2004–2012. *J. Vet. Intern. Med.* 2014; 28(1): 102-108.
6. Fuentes V.L.: Arterial Thromboembolism: Risks, realities and a rational first-line approach. *J. Feline Med. Surg.* 2012, 14 (7): 459-470.
7. Fuentes V.L., Abbott J., Chetboul V., Côté E., Fox P.R., Häggström J., Kittleson M.D., Schober K., Stern J.A.: ACVIM consensus statement guidelines for the classification, diagnosis, and management of cardiomyopathies in cats. *J. Vet. Intern. Med.* 2020, 1-16.
8. Martin U., Sponer G., Strein K.: Evaluation of thrombolytic and systemic effects of the novel recombinant plasminogen activator BM 06.022 compared with alteplase, anistreplase, streptokinase and urokinase in a canine model of coronary artery thrombosis. *J. Am. Coll. Cardiol.* 1992, 19(2): 433-40.
9. Diaz D.M., Scansen B.A., Lake Z., Shropshire S., Orton E.C., Guillaumin J.: Clinical use of tissue plasminogen activator for systemic thrombolysis in dogs and cats. *J. Vet. Cardiol.* 2022, 41: 154-164.
10. Sutton B., Long Mays E., McLaughlin C.: Case Report: Successful Reperfusion of Pulmonary Thromboembolism Using tPA in a Cat. *Front. Vet. Sci.* 2022, 20(9): 851106.
11. Moore K., Morris N., Dhupa N., Murtaugh R., Rush J.: Retrospective Study of Streptokinase Administration in 46 Cats with Arterial Thromboembolism. *J. Vet. Emerg. Crit. Care.* 2000, 10: 245-257.
12. White H.D.: Comparison of tissue plasminogen activator and streptokinase in the management of acute myocardial infarction. *Chest.* 1989, 95(5 Suppl): 265S-269S.
13. Gravanis I., Tsirka S.E.: Tissue-type plasminogen activator as a therapeutic target in stroke. *Expert Opin. Ther. Targets.* 2008, 12(2): 159-70.
14. Bauer N., Eralp O., Moritz A.: Establishment of reference intervals for kaolin-activated thromboelastography in dogs including an assessment of the effects of sex and anticoagulant use. *J. Vet. Diagn. Invest.* 2009, 21: 641-648.
15. Marschner C.B., Bjørnqvad C.R., Kristensen A.T., Wiinberg B.: Thromboelastography results on citrated whole blood from clinically healthy cats depend on modes of activation. *Acta Vet. Scand.* 2010, 52(1): 38.
16. Eralp O., Yılmaz Z., Failing K., Moritz A., Bauer N.: Effect of experimental endotoxemia on thromboelastography parameters, secondary and tertiary hemostasis in dogs. *J. Vet. Intern. Med.* 2011, 25: 524-531.
17. Lubas G., Caldin M., Wiinber B., Kristensen A.T.: Laboratory Testing of Coagulation Disorders. In: Weiss DJ, Wardrop KJ, editors. *Schalm's Veterinary Hematology.* 6th ed. Ames, IA, USA: Wiley-Blackwell, 2010, sayfa: 1082-1100.
18. Elliott A., Wetzel J., Roper T., Pivalizza E., McCarthy J., Wallace C., Hess M.J., Peng H., Rahbar M.H., Sangha N., Grotta J.C.: Thromboelastography in patients with acute ischemic stroke. *Int. J. Stroke.* 2015, 10(2): 194-201.
19. Bae J., Kim H., Kim W., Kim S., Park J., Jung D.I., Yu D.: Therapeutic monitoring of rivaroxaban in dogs using thromboelastography and prothrombin time. *J. Vet. Intern. Med.* 2019, 33(3): 1322-1330.
20. Alwood A.J., Downend A.B., Brooks M.B., Slensky K.A., Fox J.A., Simpson S.A., Waddell L.S., Baumgardner J.E., Otto C.M.: Anticoagulant effects of low-molecular-weight heparins in healthy cats. *J. Vet. Intern. Med.* 2007, 21(3): 378-87.
21. Col R., Montgomery A., Maria C.I., Defelice A., Saavedra P.V., Couto G.: Whole-blood thromboelastography using calcium chloride activation in healthy cats. *Turkish J. Vet. Anim. Sci.* 2013, 37: 68-75.
22. Bjornvad C.R., Wiinberg B., Kristensen A.T.: Obesity increases initial rate of fibrin formation during blood coagulation in domestic shorthaired cats. *J. Anim. Physiol. Anim. Nutr. (Berl).* 2012, 96: 834-841.
23. Muri B.M., Jud Schefer R., Sigrist N.E.: Serial evaluation of haemostasis following acute trauma using rotational thromboelastometry in cats. *Vet. Comp. Orthop. Traumatol.* 2019, 32: 289-296.
24. Cui Y., Heuser K., Bauer N., Neiger R.: Coagulation parameters in hyperthyroid cats before and after radioiodine treatment compared with healthy controls. *J. Feline. Med. Surg.* 2019, 21(12): 1134-1140.
25. Conner B.J., Hanel R.M., Brooks M.B., Cohn L.A., Birkenheuer A.J.: Coagulation abnormalities in 5 cats with naturally occurring cytauxzoonosis. *J. Vet. Emerg. Crit. Care (San Antonio).* 2015, 25(4): 538-45.
26. Fiakpui N.N., Hogan D.F., Whittem T., Green H.W. 3rd, Shipley E.A., Sederquist K.A.: Dose determination of fondaparinux in healthy cats. *Am. J. Vet. Res.* 2012, 73(4): 556-61.
27. Reed M., Kerndt C.C., Nicolas D.: Alteplase. [Updated 2022 Jul 12]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-Available from: <https://www.ncbi.nlm.nih.gov/books/NBK499977/>
28. Guillaumin J., DeFrancesco T.C., Scansen B.A., Quinn R., Whelan M., Hanel R., Goy-Thollot I., Bublot I., Robertson J.B., Bonagura J.D.: Bilateral lysis of aortic saddle thrombus with early tissue plasminogen activator (BLASTT): a prospective, randomized, placebo-controlled study in feline acute aortic thromboembolism. *J. Feline Med. Surg.* 2022, 24(12): e535-e545.
29. Hall D.J., Rush J.E., deLaforcade A.M., Shaw S.P.: Kaolin-activated thromboelastography in echocardiographically normal cats. *Am. J. Vet. Res.* 2012, 73(6): 775-778.
30. Kakar N., Daniel G., Fellman C., de Laforcade A., Webster C.R.: Thromboelastography in cats with cholestatic liver disease. *J. Feline Med. Surg.* 2021, 23(2):160-167.
31. Yılmaz Z., Kocatürk M., İnan O.E., Levent P.: Thromboelastographic Evaluation of Hemostatic Function in Dogs with Dilated Cardiomyopathy. *Turkish J. Vet. Anim. Sci.* 2017, 41(3): 372-379.
32. Boon J.A.: *Veterinary Echocardiography.* 2nd ed., USA, Wiley-Blackwell; 2010.
33. Ware W.A.: *Cardiovascular Disease in Small Animal Medicine.* UK, Manson Publishing; 2011.
34. Pouzot-Nevoret C., Barthélemy A., Goy-Thollot I., Boselli E., Cambournac M., Guillaumin J., Bonnet-Garin J.M., Allaouchiche B.: Infrared thermography: a rapid and accurate technique to detect feline aortic thromboembolism. *J. Feline Med. Surg.* 2018, 20(8): 780-785.
35. Salcı H., Kocatürk M., İpek V., Çetin M., Kahraman M.M., Yılmaz Z.: Echocardiographic, Magnetic Resonance Angiography and Pathologic Results of an Iliac Arterial Thromboembolism (Saddle Thrombus) in a Cat. *Kafkas Univ. Vet. Fak. Derg.* 2016, 22 (6): 977-978.
36. Engelen C., Moritz A., Barthel F., Bauer N.: Preliminary reference intervals and the impact of citrate storage time for thromboelastography in cats including delta and the velocity curve. *BMC Vet. Res.* 2017, 29; 13(1): 366.
37. Guillaumin J., Gibson R.M., Goy-Thollot I., Bonagura J.D.: Thrombolysis with tissue plasminogen activator (TPA) in

- feline acute aortic thromboembolism: a retrospective study of 16 cases. *J. Feline Med. Surg.* 2019, 21(4): 340-346.
38. Silva D.M., Caramalac S.M., Caramalac S.M., Gimelli A., Palumbo M.I.P.: Feline Aortic Thromboembolism Diagnosed by Thermography. *Acta Sci. Vet.* 2022, 50(Suppl 1): 752.
39. Vezzosi T., Buralli C., Briganti A., Vannozzi I., Giacomelli E., Talamanca G.F., Sansoni A., Domenech O., Tognetti R.: Surgical embolectomy in a cat with cardiogenic aortic thromboembolism. *J. Vet. Cardiol.* 2020, 28: 48-54.
40. Sharifi M., Bay C., Nowroozi S., Bentz S., Valeros G., Memari S.: Catheter-directed thrombolysis with argatroban and tPA for massive iliac and femoropopliteal vein thrombosis. *Cardiovasc. Intervent. Radiol.* 2013, 36(6): 1586-1590.
41. Demaerschalk B.M., Kleindorfer D.O., Adeoye O.M., Demchuk A.M., Fugate J.E., Grotta J.C., Khalessi A.A., Levy E.I., Palesch Y.Y., Prabhakaran S., Saposnik G., Saver J.L., Smith E.E.: American Heart Association Stroke Council and Council on Epidemiology and Prevention. Scientific Rationale for the Inclusion and Exclusion Criteria for Intravenous Alteplase in Acute Ischemic Stroke: A Statement for Healthcare Professionals from the American Heart Association/American Stroke Association. *Stroke.* 2016, 47(2): 581-641.
42. Hossain S., Sar- kar B., Prottoy N.I., Araf Y., Taniya M.A., Ullah A.: Thrombolytic Activity, Drug Likeness Property and ADME/T Analysis of Isolated Phytochemicals from Ginger (*Zingiber officinale*) Using in Silico Approaches. *Modern Res. Inflamm.* 2019, 8: 29-43.