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Arterial Thromboembolism in Cats: Acute Crisis in 127 Cases (1992–2001) and Long-Term Management with Low-Dose Aspirin in 24 Cases

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Records of 127 cats with arterial thromboembolism (ATE) were reviewed. Abyssinian, Birman, Ragdoll, and male cats were overrepresented. Tachypnea (91%), hypothermia (66%), and absent limb motor function (66%) were common. Of 90 cats with diagnostics performed, underlying diseases were hyperthyroidism (12), cardiomyopathy (dilated [8], unclassified [33], hypertrophic obstructive [5], hypertrophic [19]), neoplasia (6), other (4), and none (3). Common abnormalities were left atrial enlargement (93%), congestive heart failure (CHF, 44%), and arrhythmias (44%). Of cats without CHF, 89% were tachypneic. Common biochemical abnormalities were hyperglycemia, azotemia, and abnormally high serum concentrations of muscle enzymes. Of 87 cats treated for acute limb ATE, 39 (45%) survived to be discharged. Significant differences were found between survivors and nonsurvivors for temperature ($P < .00001$), heart rate ($P = .038$), serum phosphorus concentration ($P = .024$), motor function ($P = .008$), and number of limbs affected ($P = .001$). No significant difference was found between survivors and nonsurvivors when compared by age, respiratory rate, other biochemical analytes, or concurrent CHF. A logistic regression model based on rectal temperature predicted a 50% probability of survival at 98.9°F (37.2°C). Median survival time (MST) for discharged cats was 117 days. Eleven cats had ATE recurrences, and 5 cats developed limb problems. Cats with CHF (MST: 77 days) had significantly shorter survival than cats without CHF (MST: 223 days; $P = .016$). No significant difference was found in survival or recurrence rate between cats receiving high-dose aspirin (≥40 mg/cat q72h) and cats receiving low-dose aspirin (5 mg/cat q72h). Adverse effects were less frequent and milder for the lower dosage.

Key words: Acute onset paralysis; Anticoagulation; Cardiomyopathy; Congestive heart failure; Hyperthyroidism; Left atrial enlargement; Rectal hypothermia.

Arterial thromboembolism (ATE) is a devastating complication of cardiac and other diseases in cats. ATE has been reported as a sequela of feline hypertrophic cardiomyopathy (HCM) in 13%[1] to 17%[2] of clinical cases and in 41% of cases in a postmortem examination survey.[3] ATE also occurs as a complication of dilated cardiomyopathy (DCM), unclassified cardiomyopathy (UCM), other forms of cardiac disease, hyperthyroidism, and neoplasia.[4] A cat with 1 episode of ATE is widely accepted to be at risk for an additional episode.[5] Other suggested risk factors include moderate to severe left atrial (LA) enlargement (>2.0 cm) and identification of spontaneous contrast (''smoke'') or thrombus within the left atrium on echocardiography.[4,6]

Arterial thromboembolism carries a poor to grave prognosis. The rate of survival to discharge in cats presenting with ATE is low, having been reported as 0%,[7] 33%,[8] 37%,[4] and 39%[9] of cases. The impact of concurrent or secondary problems (eg, congestive heart failure [CHF] or reperfusion injury) on prognosis is poorly understood. The ideal acute treatment for ATE has yet to be determined, but may include supportive care, anticoagulant therapy, and thrombolysis.

The long-term prognosis (ie, life expectancy in cats that survive the initial ATE episode) also is guarded because many cats die from additional manifestations of underlying disease or have recurrence of ATE. Cats with HCM and ATE had a median survival time (MST) of 61 days in 1 study, with no cats surviving for longer than 180 days after the initial ATE episode.[10] A larger retrospective of cats with HCM and ATE that survived the 1st 24 hours reported an MST of 184 days.[2] Other reviews of cats with ATE surviving to discharge indicate similar short MST of 51 days[8] and 184 days.[9] Reported ATE recurrence rates are variable at 24%,[8] 45%,[4] 47%,[8] and 75%[5] of cases. Because of the risk for additional thromboembolic episodes, prevention of recurrence has been a focus of long-term patient management. Recommendations for chronic anticoagulant therapy in cats at risk for thromboembolism have included aspirin,[11,12] low-molecular weight heparin,[8,13] and warfarin,[12,14] but the best drug for thromboprophylaxis in cats has not been determined.

Aspirin at standard anti-inflammatory doses, generally 81 mg per cat orally every 3 days, has been widely utilized for decades in an effort to prevent ATE in cats,[11,15] but continued reports of recurrence with this therapy have prompted clinicians to search for more effective approaches.[4,5,10] The rationale behind the use of aspirin to prevent ATE stems from its acetylation of platelet cyclooxygenase. The resultant reduction in production of thromboxane, a potent platelet agonist and vasoconstrictor, theoretically reduces platelet aggregation. However, in humans and experimental animals, high doses of aspirin not only acetylate platelet cyclooxygenase, but also affect endothelial cell cyclooxygenase. This effect results in decreased production of endothelial cell prostacyclin, an important platelet antagonist and vasodilator. To spare endothelial prostacyclin production, humans at risk for thrombosis and thromboembolism generally are treated with much lower doses of aspirin.[16]

We hypothesized that lack of success with anti-inflam-

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matory–dose aspirin therapy in cats may have been due to its impact on prostacyclin production at this dose. We extrapolated the dosage of aspirin used in humans on a milligram per kilogram basis, and adjusted the frequency of administration to that commonly used in cats because of their decreased salicylate metabolism, resulting in a low dose of 5 mg per cat q72h. Furthermore, platelet function as measured by aggregometry was diminished (as compared to normal cat platelets) in 2 cats receiving low-dose aspirin (LDA), thereby providing some in vitro confirmation of an inhibitory effect on feline platelets at this reduced dosage.

We undertook this study to supplement the currently available information on ATE in cats by presenting an overview of 127 ATE cases evaluated at the University of Minnesota Veterinary Teaching Hospital (UMVTH) over a 10-year period. The specific objectives of our study were to determine which aspects of the acute presentation of ATE provide useful prognostic information, to develop accurate survival curves for cats with acute limb ATE that survive the initial episode, and to compare the use of LDA versus standard anti-inflammatory–dose aspirin in cats that survive the initial ATE episode.

Materials and Methods

Data Collection

Medical records of cats diagnosed with ATE at the UMVTH from January 1992 to October 2001 were reviewed. Cats that were presented after experiencing an episode of acute onset limb paresis or plegia and clinical evidence of decreased perfusion (abnormal pulses, lack of identifiable blood flow with Doppler, limb cyanosis, and cold limb) were included. Cats with identification of ATE from postmortem examination also were included unless presented dead on arrival.

Signalment, History, Clinical Presentation, and Diagnostic Evaluation

Signalment data collected on all cats included age, gender, and breed. Historical information recorded included any history of previously identified cardiac abnormality or other disorders reported to predispose to ATE, and the time interval since onset of clinical signs of ATE. Clinical presentation was described in terms of body area affected, presence or absence of motor function, abnormalities on cardiac auscultation, and vital signs. Diagnostic evaluation results recorded included results of serum biochemistry, ECG, and echocardiography. All echocardiograms either were performed or reviewed by 1 of 2 of the authors (AHT, KAJ), both board-certified in cardiology by the American College of Veterinary Internal Medicine. CHF was defined as evidence from radiography or postmortem examination of pulmonary edema or pleural effusion in cats in which cardiac disease was present.

Treatment and Survival to Discharge

Medical records were reviewed to determine what treatments were administered. Treatments reported and comparisons of cats surviving to discharge versus those not surviving were performed only for those cats with acute limb ATE in which therapy was attempted. Those cats euthanized without any attempt at treatment were excluded from discussions of treatment for acute ATE and comparisons of survivors to discharge versus nonsurvivors because lack of survival was independent of attempts at clinical intervention. Similarly, cats without a clinical diagnosis of ATE (ie, diagnosed on postmortem examination only) were excluded because treatment was not initiated for this specific diagnosis. Cats presenting more than 2 days after the acute ATE episode also were excluded because their presentation did not reflect the acute phase of this disorder. Data were evaluated to ascertain any differences between survivors to discharge and nonsurvivors with regard to signalment, history, clinical presentation, and results of diagnostic evaluations.

Treatment, Recurrence, Complications, and Survival for Discharged Cats

Additional data collected on cats that survived to be discharged included type of anticoagulant used, other medications prescribed, development of complications of ATE, subsequent episodes of ATE, final patient outcome, and where available, cause of death or reason for euthanasia. Survival times were determined from the day of onset of clinical signs of ATE. The long-term anticoagulant used was either high-dose aspirin (HDA), defined as ≥40 mg aspirin per cat PO q24–72h, or LDA, defined as 5 mg aspirin per cat PO q72h. LDA was supplied as 5 mg aspirin powder reformulated into gelatin capsules. Decisions regarding long-term anticoagulant therapy to be administered were made by the client in conjunction with the attending clinician.

Statistical Analysis

Categorical data are presented either as percentages or ratios. Normally distributed continuous data are presented as mean ± standard deviation. Nonnormally distributed continuous data are presented as median (range). Fisher's exact test was used to compare categorical data. Continuous data were compared by Student's *t*-test where normally distributed and of equal variance. The Aspin-Welch test was used to compare normally distributed continuous data with unequal variance. Continuous data that were not normally distributed were compared by using a Mann-Whitney *U*-test. Multiple logistic regression was used to develop a predictive model for survival to discharge. Kaplan-Meier survival curves were used to analyze survival data and survival curves were compared using the log-rank test. Statistical analyses were performed using NCSS 2001.[a]

Results

Signalment, History, Clinical Presentation, and Diagnostic Evaluations

Signalment. During the period from January 1992 to October 2001, 127 cats were evaluated for a 1st episode of ATE. During this same time period, a total of 22,187 cats were evaluated at the UMVTH, giving an ATE prevalence rate of 0.57% (1 in 175 cats among our hospital population). Gender distribution was 67% males, which were overrepresented in the population with an odds ratio of 1.75 ($P = .003$). Ages ranged from 0.1 to 18.3 years (Table 1).

The majority of the cats (81%) were mixed breeds. Purebred cats that were overrepresented as compared to the hospital population were Abyssinian (5), Birman (4), and Ragdoll (3), with odds ratios of 6.03 ($P = .0019$), 10.52 ($P = .0001$), and 14.40 ($P = .0016$), respectively. Other purebred cats with expected prevalence included Siamese (4), Maine Coon (2), Persian (2), and 1 each of Rex, Tonkinese, Manx, and Havanah Brown.

History. Of the 127 cats presented for a 1st episode of ATE, 9 had been diagnosed previously with some form of cardiac disease (HCM [3], hypertrophic obstructive cardiomyopathy [HOCM, 1], UCM [4], supravalvular mitral stenosis [1]). Six of these cats were receiving aspirin to prevent ATE (LDA [3], HDA [3]). Two cats were diagnosed

Table 1. Data from 127 cats presenting with arterial thromboembolism.

	Reference Range	Data[a]	n[b]	%[c] Cases Increased	%[c] Cases Decreased
Signalment					
Gender (male : female)		85:42	127		
Age (years)		8.6 ± 4.2	127		
Clinical signs					
Limbs affected (1:2 or more)		31:94	125		
Motor function (present : absent)		39:77	116		
Rectal temperature (°F [°C])	100.0–102.5 (37.8–39.2)	98.7 (90.0–103.4) (37.1 [32.2–39.7])	110	4.5	65.5
Heart rate (beats per minute)	150–240	191 ± 45.8	112	10.7	16.1
Respiratory rate (breaths per minute)	12–38	60 (20–200)	109	90.8	0
Cardiac					
Left atrial dimension in systole (cm)	1.0–1.4	1.97 ± 0.42	78	91.0	0
Congestive heart failure (present : absent)		55:70	125		
Serum Biochemistry results					
Albumin (g/dL)	2.2–3.0	2.68 ± 0.39	71	14.1	7.0
Glucose (mg/dL)	64–145	179 (17–500)	86	72.2	2.5
Blood urea nitrogen (mg/dL)	13–35	34 (15–151)	87	41.3	0
Creatinine (mg/dL)	0.1–2.1	1.8 (0.6–6.6)	87	26.3	0
Na (mEq/L)	147–155	150 (133–170)	84	10.7	7.1
K (mEq/L)	3.7–5.3	4.4 (2.7–9.6)	84	11.9	14.3
P (mEq/L)	1.2–7.6	5.6 (1.8–20.9)	77	15.6	0
Ca (mg/dL)	8.7–11.1	9.5 (6.0–12.1)	81	6.2	19.8
Alanine aminotransferase (IU/L)	8–98	199 (15–7,650)	81	72.8	1.2
Aspartate aminotransferase (IU/L)	9–37	279 (29–7,560)	77	98.6	0
Creatine phosphokinase (IU/L)	5–400	287,434 ± 276,832	10	100.0	0

[a] A ratio is reported for categorical data; mean ± standard deviation is reported for normally distributed continuous data; median (range) is reported for nonnormally distributed continuous data.

[b] Number of cases for which data were reported.

[c] Percentage of cases for which data were reported.

previously with neoplasia. In an additional 6 cats, an abnormality had been auscultated at earlier veterinary visits (asymptomatic murmur [6], gallop [1], arrhythmia [1]). No further diagnostics had been performed in these cats. Four additional cats developed CHF 1–7 days before the ATE episode but had not yet had specific cardiac diagnoses made at the time of presentation for ATE. Seven cats had a previous diagnosis of hyperthyroidism and were currently euthyroid because of previous I^{131} therapy (2) or current methimazole therapy (5). In the remaining 97 cats (76.4%), the ATE episode was the 1st indication of any abnormality.

Cats vomited minutes to hours before onset of paralysis in 20 (15.7%) of the episodes. In 3 cats, the ATE episode occurred during hospitalization for CHF. Cats were presented for evaluation within 12 hours in 89 (80.1%) of 111 episodes where a precise time of onset of signs could be determined. Six cats initially were presented already showing signs of recovery, 5–15 days after their initial ATE episode.

Clinical Presentation. Cats primarily were presented with loss of limb function in the affected limb(s). In 91 of the 127 episodes, both rear limbs were affected; in 16 episodes, only 1 rear limb was affected (8 right, 8 left). Three additional cats had both rear limbs affected and also had an affected forelimb (1 right, 2 left). Fifteen cats were presented with only 1 forelimb affected (9 right, 6 left). One cat presented for an acute onset of circling, head tilt, and hemiparesis. Postmortem examination disclosed both cerebral and renal thrombosis. One cat was presented with abdominal pain and vomiting and was diagnosed with mesenteric thrombosis and intestinal necrosis on postmortem examination (Fig 1).

Among 116 episodes of limb ATE where motor function was described, some motor ability was present in 39 (33.6%) cats. Of cats with rear limbs affected, 28% of those with bilateral episodes had motor function and 66% of those with unilateral episodes had motor function on presentation. Cats that experienced unilateral rear limb episodes were more likely to be described as having motor function present ($P = .011$).

Recorded vital signs are presented in Table 1. Of the 110 episodes where rectal temperature was recorded on presentation, 72 cats were hypothermic (<100.0°F [<37.8°C]). Of the 12 cats with ATE affecting only a forelimb, 5 were hypothermic, 4 were normothermic, and rectal temperature was not recorded in 3. Among 112 episodes where heart rate (HR) was recorded, 12 cats were tachycardic (HR ≥ 240 beats per minute [bpm]) and 18 were bradycardic (HR ≤ 150 bpm). Of 109 episodes where respiratory rate (RR) was recorded, 99 were tachypneic (RR > 38 breaths per minute). An additional 8 cats had no RR recorded, but were described as panting or open-mouth breathing.

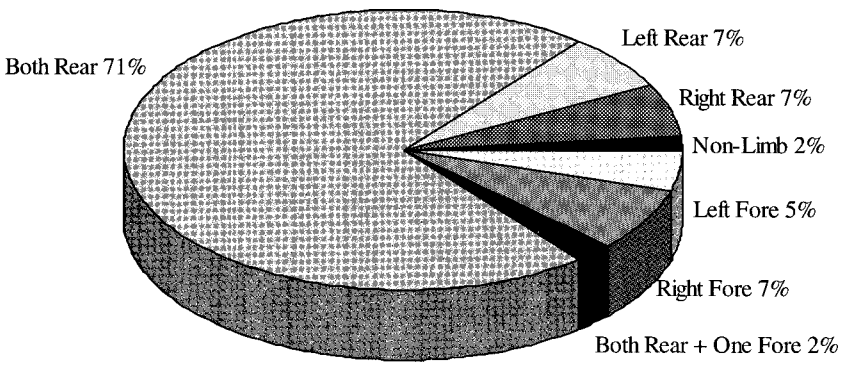

Fig 1. Body area affected by arterial thromboembolism in 127 cats as reflected by the most prominent clinical signs noted. All but 2 cats had limbs affected. The nonlimb sites were cerebral and renal in 1 cat and mesenteric in the other.

Aside from HR abnormalities, abnormal findings on cardiac auscultation that suggested the presence of underlying cardiac disease were reported in 72 cats. Abnormalities were a murmur in 25, a gallop in 18, an arrhythmia in 11, a murmur and a gallop in 9, a murmur and an arrhythmia in 5, and a gallop and an arrhythmia in 4 cats.

Diagnostic Evaluations. Ninety cats had antemortem diagnostic tests performed. Diseases diagnosed by echocardiography were DCM (8), UCM (33), HOCM (5), and HCM (19). Other diagnoses were idiopathic atrial fibrillation (1), renal failure with hypertension and left ventricular (LV) concentric hypertrophy (1), supravalvular mitral stenosis (1), and multiple congenital abnormalities in a single 4-week-old kitten. An additional 18 cats were found to have gross or histopathologic evidence or both of cardiac disease at postmortem examination. However, the type of cardiac disease was not clearly defined in these cats because of the lack of antemortem echocardiography. Postmortem diagnoses made by the evaluating pathologist were HCM in 14 cats and DCM in 4 cats. Gross criteria for the diagnosis of HCM were increased heart weight, increased LV posterior wall thickness, increased septal thickness, papillary muscle hypertrophy, and LA chamber enlargement. Histopathologic criteria for the diagnosis of HCM were myocyte hypertrophy, myocyte and myofibrillar disarray or disorganization, myocardial interstitial fibrosis, myocyte degeneration or necrosis, and increased myocardial arteriolar wall thickness. Criteria for the diagnosis of DCM were LV chamber enlargement with or without right ventricular chamber enlargement, and unremarkable myocardial histopathology.

Seven cats had a previous diagnosis of hyperthyroidism and were euthyroid at the time of the ATE episode. Of these 7 cats, 1 cat had evidence of gross cardiac hypertrophy on postmortem examination only, and 3 had echocardiography performed at the time of ATE. The heart was unremarkable on echocardiography in 1 cat. The other 2 cats had LA enlargement, with either asymmetric concentric LV hypertrophy (1) or symmetric concentric LV hypertrophy with dynamic LV outflow obstruction. An additional 5 cats were 1st diagnosed with hyperthyroidism during the evaluation for ATE. Of the 5 cats, 1 was diagnosed with bilateral thyroid follicular adenoma and HCM on postmortem examination. Serum thyroid hormone concentrations were measured and echocardiography was performed on the other 4 cats. The echocardiographic evaluation was unremarkable in 1 cat. The other 3 cats had LA enlargement with normal LV measurements (1), asymmetric LV hypertrophy (1), or symmetric LV hypertrophy (1).

Six cats were diagnosed with neoplasia (hepatocellular carcinoma, pulmonary carcinoma [2], anaplastic carcinoma, vaccine-associated fibrosarcoma, and squamous cell carcinoma) and 1 of these had neoplastic cells within the thrombus on histopathologic examination. No antemortem or postmortem evidence of cardiac disease was found in these cats.

In another 3 cats, the cardiac evaluation was normal and no disease processes were identified that would have predisposed to ATE despite multiple antemortem diagnostic tests. All 3 cats survived to discharge. In 19 cats, underlying diseases were not identified because no antemortem or postmortem diagnostics were performed (Fig 2).

Left atrial dimension in systole (LADs) measured by M-mode echocardiography was available for 78 cats. LA enlargement ($>$1.4 cm) was noted in 71 cats (Table 1). Only 6 cats had LA thrombi identified on echocardiography, but an additional 3 had intracardiac thrombi (LA [2], LV [1]) identified at postmortem examination.

Congestive heart failure was detected at presentation in 55 of 125 cats in which radiographs were obtained or postmortem examination was performed. Four cats without pleural effusion or pulmonary edema at presentation developed CHF during hospitalization. Eight cats were described as panting or open-mouth breathing with CHF (3), without CHF (4), or with unknown CHF (1). Median (range) RR for cats with CHF was 64 (24–200) breaths per minute and was 60 (20–160) breaths per minute for cats without CHF. Although the difference between the median RRs was statistically significant ($P = .025$), considerable overlap occurred between the CHF and non-CHF groups. Of cats without CHF, 89% were tachypneic. Consequently, distinguishing between cats with CHF and those without CHF based on RR or respiratory character was not possible.

Of 52 cats in which an ECG was evaluated, the following rhythms were noted: normal sinus rhythm (29), ventricular premature contractions (13 [2 with bigeminy]), atrial fibrillation (4), atrial premature contractions (2), sinus bradycardia (2), and sinus tachycardia (2).

Among 87 cats in which serum chemistry was performed at admission, common abnormalities included hyperglycemia, azotemia, and high serum concentrations of enzymes

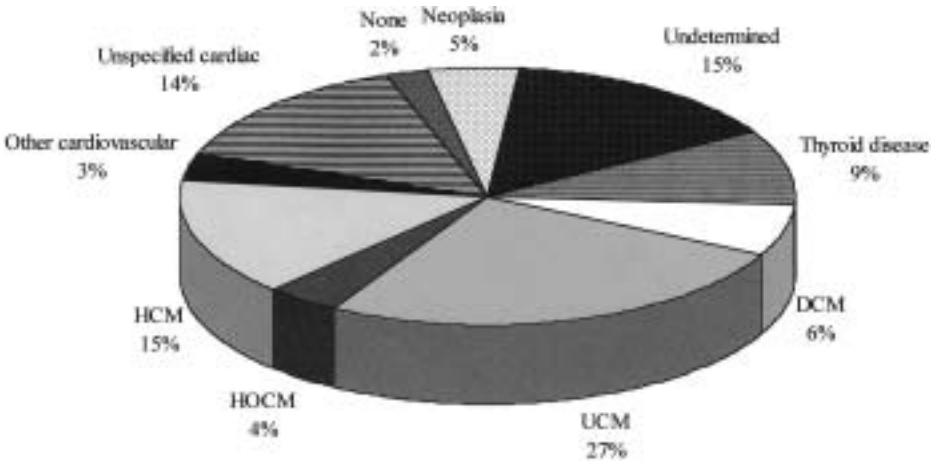

Fig 2. Disorders in 127 cats presenting with arterial thromboembolism (ATE). Postmortem examination indicated cardiac disease but no specific diagnosis was made because antemortem echocardiography was not performed in 18 cats (labeled ''unspecified cardiac''). No diagnostic tests were performed in 19 cats (labeled ''undetermined''). No disease was identified on echocardiography or other diagnostic tests in 3 cats (labeled ''none''). The category ''thyroid disease'' includes 5 cats 1st diagnosed with hyperthyroidism during evaluation for ATE and 7 cats previously diagnosed with hyperthyroidism. DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy; HOCM, hypertrophic obstructive cardiomyopathy; UCM, unclassified cardiomyopathy.

suggestive of muscle cell damage (Table 1). Serial serum electrolyte concentrations were measured in 28 cats. Eleven cats were hyperkalemic on admission, and hyperkalemia (up to 14.4 mEq/L) developed during hospitalization in 2 additional cats. Twelve cats were hyperphosphatemic initially, and 3 additional cats later developed hyperphosphatemia (up to 20.9 mg/dL). Fifteen cats were hypocalcemic on admission, and 2 cats developed hypocalcemia (down to 6.2 mg/dL) during hospitalization. Six cats were hyponatremic, and 9 were hypernatremic on admission, but no additional cats developed abnormalities of serum sodium concentration.

Treatment and Survival to Discharge

Treatment. Thirty-two cats were euthanized without any attempt at therapy. Cats presenting more than 2 days after the onset of clinical signs (6) were excluded from the following discussion of acute therapy, because they had already survived the initial crisis. The 2 cats without limb ATE also were excluded because both cats were not diagnosed antemortem, and could not reasonably be treated for ATE. Therapy for the remaining 87 episodes of acute limb ATE included supportive measures, thrombolysis, anticoagulation, and treatment for underlying cardiovascular disease and CHF. Therapy was provided according to the preferences of the supervising clinicians.

Supportive measures included fluid therapy (41), application of external heat sources (24), physical therapy (14), oxygen supplementation (34), and analgesic therapy (53). Some patients received multiple analgesic drugs. Analgesic drugs administered included butorphanol (32), oxymorphone (21), fentanyl dermal patch (10), and morphine (1).

Thrombolysis was attempted with streptokinase infusion in 4 cats. Anticoagulant therapies administered were unfractionated heparin (67) and aspirin (46). Unfractionated heparin was administered IV once in 25 cats at dosages ranging from 75 to 500 U/kg. All but 2 of these cats continued to receive heparin therapy via subcutaneous administration during hospitalization. Unfractionated heparin therapy was given SC only in 42 cats at dosages ranging from 10 to 300 U/kg q6–12h. The majority of cats received heparin at either 50–100 U/kg (29) or 200–250 U/kg (26) q6–8h. Aspirin was administered in conjunction with heparin in 33 cats (HDA [27], LDA [6]) and 13 cats received aspirin only (HDA [7], LDA [6]). Cats without motor function at presentation were more likely to be treated with heparin than cats with motor function in the affected limb (odds ratio 3.19, $P = .045$). Bleeding was not observed in any cat receiving heparin, but gastrointestinal bleeding was suspected in 1 cat in which a transfusion was needed, and a 2nd cat had evidence of hemorrhage at postmortem examination.

Acepromazine was administered to 18 cats. Other medications administered were furosemide (40), enalapril (18), diltiazem (15), nitroglycerin (4), digoxin (3), atenolol (2), amlodipine (2), and propranolol (1).

Survival to Discharge. Of 127 cats, 44 survived the initial ATE episode, giving an overall survival rate of 35%. Among the 87 episodes of acute limb ATE where treatment was attempted, 39 (45%) survived. Survival gradually improved over the 10 years that were reviewed, with 8 of 11 (73%) cats treated for acute limb ATE from January to October 2001 surviving to discharge (Fig 3). Median duration of hospitalization among cats that survived to discharge was 2 (0–10) days.

Among cats in which treatment was attempted, no significant difference was found between survivors to discharge and nonsurvivors when compared by gender, age, RR, LADs, presence or absence of CHF, albumin, glucose, blood urea nitrogen (BUN), creatinine, sodium, potassium, calcium, alanine aminotransferase, or aspartate aminotransferase (AST) (Table 2). Significant differences between survivors and non-survivors were identified for rectal temperature and HR (Table 2), with both being higher among sur-

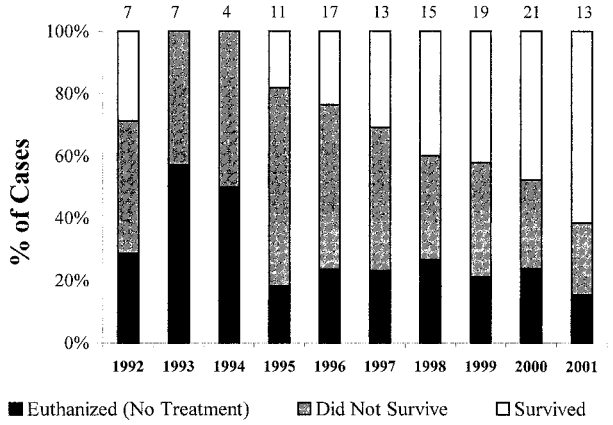

Fig 3. Short-term outcome (as percent of total cases presenting) for 127 cats by year of presentation. Euthanized (No Treatment), cats that were euthanized with no attempt at therapy; Did Not Survive, cats that were euthanized or died during the initial hospital stay despite attempted therapy; Survived, cats that survived to discharge from the hospital. Total numbers of cats presenting in each calendar year are included at the top of each bar.

vivors. Having only 1 limb affected and the presence of motor function were both significantly more frequent among survivors (Table 2; Fig 4). Serum phosphorus concentration was significantly higher among nonsurvivors (Table 2).

A logistic regression model for predicting survival to discharge was developed by using variables that were significantly different between survivors and nonsurvivors. Once rectal temperature was included in the model, no other variable improved the accuracy of prediction. This model predicts a 50% likelihood of survival at a rectal temperature on admission of 98.9°F (37.2°C) (Fig 5). The model correctly classified 25 (67%) of 37 survivors and 36 (79%) of 45 nonsurvivors.

Treatment, Recurrence, Complications, and Survival for Discharged Cats

Forty-four cats were discharged from the hospital after an ATE episode. This number included 39 of 87 cats initially presented with acute limb ATE for which treatment was attempted, and 5 of 6 cats initially presented more than 2 days after the ATE episode. Fifteen of the discharged cats were in CHF at the time of the initial ATE episode. Of 44 discharged cats, 18 were treated with HDA, 24 were treated with LDA, and 2 received no anticoagulant therapy. Two

Table 2. Data comparing cats that survived to discharge and cats that did not survive among 87 cases of acute limb arterial thromboembolism in which treatment was attempted.

	Survivor Data[a] (n = 39)	n[b]	Nonsurvivor Data[a] (n = 48)	n[b]	*P*-value
Signalment					
Gender (male : female)	30:9	39	28:20	48	0.074
Age (years)	8.9 ± 3.9	39	9.2 ± 4.2	48	0.350
Clinical signs					
Limbs affected (1:2 or more)[c]	17:22	39	8:40	48	0.008
Motor function (present : absent)[c]	20:13	33	11:35	46	0.001
Temperature (°F [°C])	99.9 ± 2.0 (37.7 ± 1.1)	37	96.5 ± 3.4 (35.8 ± 1.9)	45	<0.00001
Heart rate (beats per minute)	210 (100–300)	37	188 (80–350)	43	0.038
Respiratory rate (breaths per minute)	60 (20–160)	35	60 (30–150)	45	0.899
Cardiac					
Left atrial dimension in systole	1.90 (1.10–2.93)	37	1.96 (1.39–3.02)	27	0.749
Congestive heart failure (present : absent)	13:26	39	26:22	48	0.082
Serum biochemistry results					
Albumin (g/dL)	2.7 ± 0.3	31	2.7 ± 0.4	40	0.611
Glucose (mg/dL)	169 (89–334)	33	194 (17–500)	39	0.254
Blood urea nitrogen (mg/dL)	29 (15–79)	33	35 (15–93)	40	0.089
Creatinine (mg/dL)	1.6 (0.8–3.3)	33	1.8 (0.6–5.5)	40	0.179
Na (mEq/L)	149 (133–170)	34	151 (134–159)	38	0.061
K (mEq/L)	4.3 (2.8–7.1)	34	4.5 (2.7–96)	38	0.607
P (mEq/L)	5.4 (3.3–9.7)	29	6.4 (1.8–20.9)	37	0.024
Ca (mg/dL)	9.2 ± 0.67	29	9.6 ± 1.16	38	0.068
Alanine aminotransferase (IU/L)	259 (43–937)	30	141 (23–7,650)	37	0.160
Aspartate aminotransferase (IU/L)	548 (35–3,960)	28	180 (29–7,560)	38	0.095
Creatine phosphokinase (IU/L)	171,322 ± 226,097	6	461,604 ± 278,024	4	0.106

[a] A ratio is reported for categorical data; mean ± standard deviation is reported for normally distributed continuous data; median (range) is reported for nonnormally distributed continuous data.

[b] Number of survivors or nonsurvivors for which data were reported.

[c] Presented graphically in Figure 4.

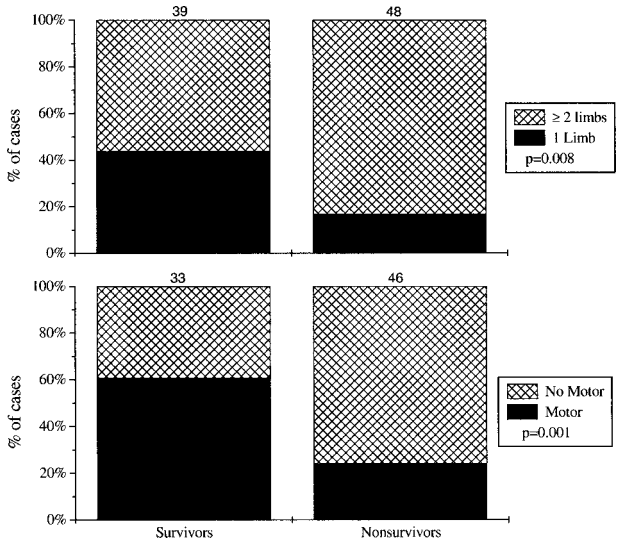

Fig 4. Histograms showing the ratios of motor function to no motor function, and 1 limb affected to 2 or more limbs affected among survivors and nonsurvivors. A significantly greater portion of survivors had only 1 limb affected and motor function present. Total numbers of survivors and nonsurvivors for which data are reported are presented above the bars.

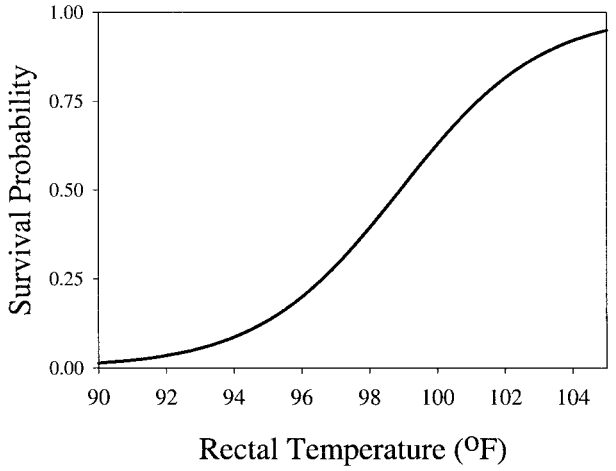

Fig 5. Logistic regression model predicting survival to discharge based on rectal temperature (T) at admission. The equation for the predictive model is $P = 1/(1 + e^{-47.58593+0.4811605T})$.

cats treated with aspirin also received heparin in the 1st few weeks after the ATE episode. Additional medications prescribed for cardiovascular disorders were furosemide (15), enalapril (15), diltiazem (7), atenolol (4), digoxin (3), methimazole (2), amlodipine (2), nitroglycerin (1), taurine (1), and propranolol (1).

Eleven of the 44 cats experienced 16 additional thromboembolic events, 9 of which were fatal (died [3], euthanized [6]). Time to 1st recurrence was 191 ± 152 days. Of 2 cats with LA thrombi that survived to discharge, both had long-term survival without any embolic episodes (275 and 590 days). Two cats had limb necrosis requiring limb amputation. Two other cats had minor tissue necrosis requiring wound management, and 1 cat developed limb contracture.

Nine of the 44 cats were alive at the end of the study. The MST was 117 days. Cats with CHF during the initial ATE episode had significantly shorter survival than cats without CHF (MST: 77 and 223 days, respectively; $P = .016$; Fig 6). One of the 2 cats receiving no anticoagulant survived 5 days. The other was alive at 83 days and then lost to follow-up.

Median survival of cats on HDA was 149 days. Five of the 18 cats had a recurrence of ATE (single episode [4], 2 episodes [1]). Two episodes were fatal, and 3 episodes prompted euthanasia. One cat developed hematemesis, and 3 cats developed anorexia, vomiting, or both while receiving HDA, which resolved when the drug was discontinued.

Median survival of cats on LDA was 105 days. Six of the 24 cats had a recurrence of ATE (single episode [4], 2 episodes [1], 4 episodes [1]). Four of these 10 episodes prompted euthanasia. Four episodes were mild enough that out-patient management was possible. One cat vomited while receiving LDA, but vomiting resolved when the drug was discontinued.

No significant difference was detected in survival curves between cats receiving HDA and cats receiving LDA ($P = .882$).

Discussion

Feline ATE was diagnosed in 1 in 175 cats evaluated at the UMVTH over the last decade. The prevalence of this disorder does not seem to have changed appreciably in the last 40 years, as prevalence of ATE at the University of Pennsylvania was reported to be 1 in 142 cats in 1966.[17]

Males have been reported to be at increased risk for ATE.[4,8,9] This increased risk also was apparent in our population. However, of the cats with ATE diagnosed with HCM or HOCM, 83% were male. When cats with this underlying disease were excluded from consideration, no difference was found between the gender distribution of cats presenting for ATE secondary to other diseases and the general hospital population. This finding suggests that males

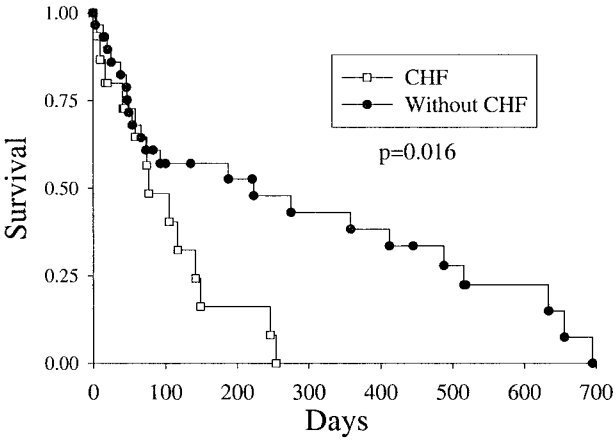

Fig 6. Kaplan-Meier survival curves for cats that survived the initial episode plotted by presence (15) or absence (29) of congestive heart failure (CHF) during the initial ATE episode. Median survival time for cats with CHF was 77 days. Median survival time for cats without CHF was 223 days.

probably are at increased risk for HCM or HOCM rather than specifically for ATE.

Ragdolls and Birmans were overrepresented in the ATE population as compared to the general hospital population, but were similarly overrepresented in a population of cats presented over the same time period to the UMVTH for CHF (Smith et al, unpublished data), suggesting that the risk of ATE in these breeds is associated with the risk of serious cardiac disease. Of the 5 Abyssinians presented with ATE, 4 were diagnosed with a disease known to predispose to ATE (DCM [3], neoplasia [1], undetermined [1]). Abyssinians were overrepresented in the ATE population as compared to the general hospital population, but underrepresented in the comparison CHF population (Smith et al, unpublished data), suggesting that this breed may have an additional risk factor for ATE that is independent of the presence of cardiac disease.

In this study, development of clinical manifestations of cardiac disease before the thromboembolic event was rare in the ATE population with underlying cardiac disease. The occult nature of the predisposing disease limits the veterinary clinician's ability to prevent this devastating disorder.

We suspected that lack of successful treatment may have been in part associated with a delay in presentation, but in the population we studied, most cats were presented to the UMVTH within hours of onset of signs, and those presenting later were referred from primary care hospitals where they also had presented within hours. Delay in seeking veterinary care generally was associated with lack of observation when a client was not at home. The rapid presentation of these cats likely is a manifestation of the degree of distress apparent to the owners of affected cats.

Loss of limb function, primarily of the rear limbs, is the most widely recognized manifestation of ATE in cats, but clearly other arterial sites can be affected. Because of the anatomy of the arterial supply for the left forelimb, the suggestion has been made that this site is affected less commonly than the right forelimb.[18] In the population in this study, the frequency of ATE in the left forelimb was similar to that of ATE in the right forelimb. Among cats with the distal aortic trifurcation site, motor function more frequently was present in cats in which only 1 limb was affected. This difference likely occurs because larger thrombi are more likely to lodge in a more proximal location, obstruct perfusion to both limbs, and affect function of more nerves and muscles. Smaller thrombi that progress into a more distal location in the femoral artery are more likely to allow for collateral circulation.

Rectal hypothermia was common in cats presenting with acute ATE, affecting 66% of cats in which a rectal temperature was obtained. The suggestion previously has been made that the rectal hypothermia associated with distal aortic ATE may be due to obstruction of flow to the rectum.[8,17] The fact that 56% of cats with forelimb thrombosis only also presented with rectal hypothermia indicates that obstruction of rectal perfusion is unlikely to be the cause of the hypothermia. Rectal hypothermia may instead be an indicator of poor systemic perfusion due to shock.

Most cats were tachypneic or had markedly abnormal respiratory character. Although RR was statistically higher in cats with CHF, the difference between medians of 4 breaths per minute is not clinically relevant. The occurrence of abnormal respiration was not indicative of CHF, because 89% of cats without CHF were tachypneic or showed open-mouth breathing. The tachypnea or respiratory distress instead may be a manifestation of pain. This interpretation is supported by clinicians' observations that panting or tachypnea often improve or resolve with analgesic therapy. Alternatively, tachypnea could be due to pulmonary venous distension causing a sensation of dyspnea secondary to stimulation of alveolar J receptors.[19] The lack of association between tachypnea and the presence of CHF presents a therapeutic challenge because many veterinary clinicians would prefer to manage the apparently dyspneic cat with presumptive therapy until respiratory status has improved enough to make radiography less risky. Unfortunately, the ATE cat that is tachypneic should not be treated for possible CHF without additional supportive evidence because the dehydration or vasodilatation resulting from medications used for CHF may worsen the perfusion of cats not in CHF. Thoracic radiography, when feasible, is indicated before administration of furosemide for any cat with ATE, regardless of respiratory status.

Hyperthyroidism previously has been observed in association with ATE,[4] but we assumed that hyperthyroidism predisposed cats to ATE by causing cardiac disease. Several cats in this study with hyperthyroidism had echocardiographically normal hearts, and 7 cats previously treated for hyperthyroidism were euthyroid at the time of ATE. Therefore, thyroid disease may pose a risk factor for ATE that is independent of the cardiac effects of hyperthyroidism.

Neoplasia was identified as an underlying disease in 5% of the cats with ATE. Pulmonary tumors were reported previously in several cats with ATE.[4,8] Two of the cats described here had histopathologically confirmed pulmonary carcinoma. Although pulmonary neoplasia appears to be a risk factor for ATE, examination of our data indicates that the presence of other types of neoplasia also may be associated with ATE.

More than 40% of cats presented with ATE did not have auscultable abnormalities suggestive of underlying cardiac disease, despite the fact that nearly 70% of the ATE population had confirmed cardiovascular disease. In a retrospective study of cats with various manifestations of HCM that included ATE, 22% had no auscultable murmur or gallop.[2] Occult cardiac disease may be common in cats presented with ATE. Consequently, a complete cardiac evaluation is appropriate for any cat presented with ATE.

Left atrial dimension in systole of greater than 2.0 cm may be associated with development of ATE in cats with cardiac disease.[20] Most of the cats with ATE described here had LA enlargement, but only 45% had a LADs greater than 2.0 cm. This frequency is similar to that observed in cats presented with CHF without ATE (Smith et al, unpublished data), where 44% had a LADs of greater than 2.0 cm. Had echocardiography been performed immediately before the ATE episode, the value of 2.0 cm likely would have been of little value in predicting ATE in these cats. Although cats with cardiac disease certainly are at risk for ATE, the degree of LA enlargement may not in itself be a clinically relevant risk factor. Our findings are in contrast

to a recent report that indicated that cats with HCM that presented with ATE had significantly larger LADs than those with HCM that presented with CHF. [2]

Common serum biochemical abnormalities included electrolyte disturbances, azotemia, and high serum concentrations of enzymes associated with muscle damage. Electrolyte disturbances likely are associated with reperfusion injury and the effects of decreased perfusion on renal function. The frequency of hyperkalemia and hyponatremia in this study was similar to that reported elsewhere.[8] Hypocalcemia has been reported to occur with ATE in 23%[8] to 38%[4] of affected cats, and occurred in 20% of the cats in our study. Total serum calcium concentration cannot consistently be corrected for hypoalbuminemia in cats[21]; therefore, the clinical relevance of this hypocalcemia cannot be assessed. Many of the affected cats may have had blood ionized calcium concentration within the reference range had it been measured. However, in 3 cats in which hypocalcemia was severe, physiologic hypocalcemia was confirmed with ionized calcium measurements. In these 3 cats, hypocalcemia was associated with marked hyperphosphatemia and hyperkalemia. Serious reperfusion effects were suspected in these cats. Hypocalcemia may occur secondary to hyperphosphatemia as intracellular phosphorus is released and complexes with calcium. The azotemia probably is an additional indicator of decreased systemic perfusion, because increases in BUN were generally more severe than those of creatinine, but renal artery obstruction preventing renal perfusion also is possible. Interestingly, almost all cats with ATE had high AST, possibly originating from ischemic muscle.

Examination of our results suggests that ATE in cats is associated with a poor prognosis, with only 35% of the cats in this study surviving the initial episode. This survival rate is similar to the 33% reported by Moore et al,[8] 37% reported by Laste and Harpster,[4] and 39% reported by Schoeman.[9] However, when cats that were euthanized without treatment were eliminated from the group, survival was 45%. All of the cats reported by Moore et al[8] received treatment, but other reports did not distinguish between euthanasia without attempting treatment and euthanasia due to deterioration or lack of response to treatment.

Consistent treatments were not applied, so comparison of the efficacy of specific therapies is not possible. The dosages and interval for heparin varied greatly among patients, but most patients received what is commonly referred to as low-dose (50–100 U/kg) or high-dose (200–250 U/kg) heparin.[12] A prospective, outcome-based study would be required to determine an effective dosage of heparin for cats with ATE.

Thrombolysis with streptokinase (SK) may improve survival in cats with ATE. In 1 prospective evaluation of SK use in 6 cats with ATE, mortality was 100%.[7] A retrospective study of 46 cats that received SK reported 33% survival.[8] Only 4 of 87 cats described here with limb ATE were treated with SK. Of the 83 treated cats in our study that did not receive SK, 42% survived. When we compared the published 46 SK-treated cats to the 83 cats not treated with SK in the present study, no significant difference was found in survival ($P = .349$). Also, no difference was found in survival rates when the cases were divided into bilateral and unilateral episodes ($P = .514$ and .632, respectively). Use of SK was associated with hemorrhage in 24% of the reported cases, with 6% requiring transfusion.[8] Bleeding was not observed in any of the 83 patients in the present study that were treated with heparin, aspirin, or both, but 2 cats (2%) had other evidence of hemorrhage. This comparison is retrospective and does not necessarily involve identical populations, but the use of SK does not seem to improve outcome. Given the cost of SK, the risk of hemorrhage associated with SK, and the lack of evidence for improved outcome, we find the use of thrombolytic therapy with SK impossible to justify in cats with ATE.

Support for cats presented with ATE has included treatment with acepromazine to improve collateral blood flow and decrease anxiety.[22,23] However, acepromazine may cause hypotension because of its effect as an α_1-receptor antagonist. Because many aspects of the clinical presentation of cats with ATE suggest the presence of shock, acepromazine should be avoided.

Cats with single limb episodes had a better survival rate than those with bilateral involvement. This observation also was made in previous studies.[4,8,9] Better survival in cats with a single affected limb is likely associated with the smaller volume of the vascular bed lost to the systemic circulation, less muscle mass affected by loss of perfusion, less reperfusion injury, and less release of vasoactive substances that may cause shock.

Cats presented with motor function had better survival and cats with unilateral ATE were more likely to have motor function present. Presence of motor function likely indicated partial perfusion due to a smaller thrombus or more distal location of the thrombus allowing for collateral circulation. Diminished reperfusion injury would be expected when perfusion is better at the time of embolism.

The most useful prognostic indicator noted in the cats of this study was rectal temperature. This finding was consistent with that of a previous report in which hypothermia was associated with poor outcome.[8] Rectal temperature accurately predicted survival or mortality in approximately 75% of patients. As a diagnostic tool, rectal temperature assessment is easily performed, is quick and inexpensive, and provides valuable information on prognosis. Hypothermia and azotemia in these cats are probably interdependent as manifestations of inadequate systemic perfusion. Bradycardia may occur as a consequence of hypothermia. Consequently, because rectal temperature by itself is a reasonable indicator of overall systemic perfusion, these other factors failed to contribute significant additional prognostic information to the model.

The proportion (25%) of surviving cats affected by recurrence of ATE in the population in the present study was much lower than that described in several other reports, but similar to that (24%) reported by Schoeman[9] for cats that received either aspirin or no treatment to prevent thrombosis. Some cats with long survival times reported by Schoeman[9] did not experience recurrent thrombosis even without anticoagulant therapy. Two other reports in which cats received primarily warfarin to prevent thrombosis described recurrence rates of 45%[4] and 47%.[8] Recurrent thromboembolism was the ultimate cause of death or euthanasia in only 20% of the cats in the present study.

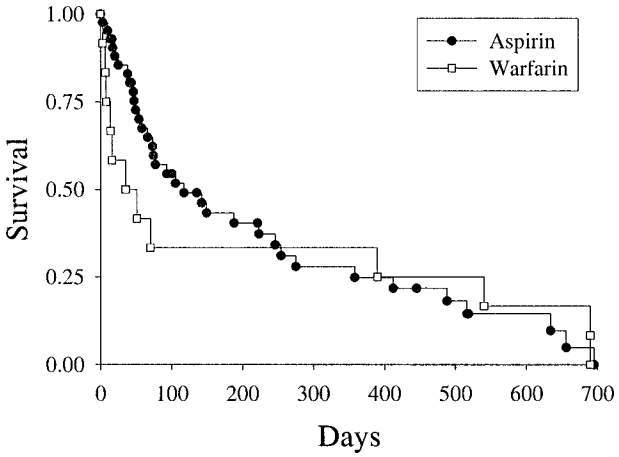

Fig 7. Kaplan-Meier survival curves for cats that survived the initial episode and were given aspirin for thromboprophylaxis (current study) compared to reported[8] cats that survived initial treatment with streptokinase and then were given warfarin. Median survival time for cats from the UMVTH that received aspirin was 117 days. Median survival time for reported cats[8] that received warfarin was 51 days. The curves were not statistically different ($P = .214$).

Although concurrent CHF at the time of the ATE episode did not affect short-term survival, it had a significant impact on long-term survival. Cats with CHF were more likely to die soon after discharge, and none survived longer than 254 days. In previous reports of long-term outcome in cats with ATE, a group of cats with fairly short-term survival usually has been observed, and a 2nd group with prolonged survival also has been described.[8,9] The divergence of the CHF Kaplan-Meier curve from the non-CHF curve (Fig 6) may explain the bimodal appearance of survival curves reported elsewhere. The most common known cause for death or euthanasia in the cats of this study was inadequate control of CHF. These findings suggest that cats with ATE have a poor long-term prognosis primarily because of difficulty in managing their cardiac disease, rather than difficulty in preventing recurrence of thrombosis.

When we compared survival data on the cats in the present study that were treated with aspirin (both doses combined) to published data for cats that received warfarin for prevention of recurrence,[8] the MST for warfarin-treated cats was 51 days, versus 117 days for the aspirin-treated cats in the present study. No difference was detectable in the Kaplan-Meier curves (Fig 7), but adverse effects of aspirin were rare and mild, whereas 17% of cats that received warfarin experienced fatal hemorrhage (Table 3).[8] Another report described fatal hemorrhage in 11% of cats that received warfarin.[4] Although this comparison is retrospective and does not necessarily involve comparable groups, given the lack of demonstrable improvement in long-term survival, the need for repeated recheck visits, the cost of anticoagulation monitoring, and the risk of fatal hemorrhage, we find the use of warfarin in cats at risk for thromboembolism difficult to justify.

No difference was detectable in recurrence rate or survival curves between cats that received LDA versus cats that received HDA. Fewer recurrent episodes were fatal for cats on LDA than HDA, but the numbers were small, precluding meaningful statistical comparison. LDA was associated with fewer gastrointestinal adverse effects (Table 3). LDA is an inexpensive and safe option for thromboprophylaxis that appears to be at least as effective as standard aspirin therapy or warfarin. The use of LDA for thromboprophylaxis in cats deserves further investigation.

Table 3 Comparisons of outcome between cats receiving high-dose aspirin (HDA), low-dose aspirin (LDA), and previously reported[8] cats receiving warfarin.

	HDA	LDA	Warfarin[8]
Number of cats	18	24	12
Median survival time (days)	149	105	51
% Cats with ATE recurrence	28	25	45
If recurrent ATE, % fatal	83	40	Unknown
% Cats with gastrointestinal signs	22	4	0
% Fatal hemorrhage	0	0	17

Footnotes

[a] NCSS 2001, Number Cruncher Statistical Systems, Kaysville, UT

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