Journal of Veterinary Cardiology (2015) 17, S306—S317

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Journal of Veterinary Cardiology
ESVC

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Secondary prevention of cardiogenic arterial thromboembolism in the cat: The double-blind, randomized, positive-controlled feline arterial thromboembolism; clopidogrel vs. aspirin trial (FAT CAT)

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Received 17 November 2014; received in revised form 9 September 2015; accepted 7 October 2015

These data were presented at the American College of Veterinary Internal Medicine Scientific Forum, 2013.

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http://dx.doi.org/10.1016/j.jvc.2015.10.004

KEYWORDS
Thromboprophylaxis;
Thrombosis;
Antithrombotics;
Infarction;
Cardioembolic

Abstract *Objectives:* To determine if clopidogrel administration is associated with a reduced likelihood of recurrent cardiogenic arterial thromboembolism (CATE) in cats compared to aspirin administration. Secondary aims were to determine if clopidogrel administration had an effect on the composite endpoint of recurrent CATE and cardiac death and to identify adverse effects of chronic clopidogrel or aspirin therapy.
Animals: Seventy-five cats that survived a CATE event.
Methods: Multicenter, double-blind, randomized, positive-controlled study. Cats were assigned to clopidogrel (18.75 mg/cat PO q 24 h) or aspirin (81 mg/cat PO q 72 h). Kaplan–Meier survival curves were created for each endpoint and the log rank test performed to compare treatment groups with respect to time to event and the likelihood of the event occurring.
Results: The mean age of all cats was 8.0 ± 3.5 yr and 57/75 (76%) were male ($p < 0.001$); 62/75 (83%) were mixed breed with the remainder including Persian, Abyssinian, American Shorthair, Bengal, Birman, Himalayan, Maine Coon, Ragdoll, Snowshoe, and Sphynx breeds. Only 15% (11/75) of cats had a history of heart disease recorded prior to the CATE event. Clopidogrel administration was associated with significantly reduced likelihood of recurrent CATE compared to aspirin ($p = 0.024$) and had a longer median time to recurrence [443 (95% CI 185–990) days vs. 192 (95% CI 62–364) days, respectively]. Clopidogrel was also associated with a significantly reduced likelihood of the composite endpoint of recurrent CATE or cardiac death ($p = 0.033$) with a longer median time to event [346 (95% CI 146–495) days vs. 128 (95% CI 58–243) days].
Conclusions: Clopidogrel administration significantly reduces the likelihood of recurrent CATE compared with aspirin in cats; both drugs were well tolerated.

Abbreviations

ADP	adenosine diphosphate
ALP	alkaline phosphatase
ALT	alanine aminotransferase
CATE	cardiogenic arterial thromboembolism
CHF	congestive heart failure
DCM	dilated cardiomyopathy
GGT	gamma-glutamyl transpeptidase
HCM	hypertrophic cardiomyopathy
HOCM	hypertrophic obstructive cardiomyopathy
RCM	restrictive cardiomyopathy
SAM	systolic anterior motion of the mitral valve
UCM	unclassified cardiomyopathy

Introduction

Cardiogenic arterial thromboembolism (CATE) is a well-recognized and devastating clinical morbidity with feline cardiomyopathy. When fragments of an intracavitary thrombus gain access to the systemic circulation, they may obstruct distant arterial segments which can result in tissue injury or organ infarction. Distal aortic occlusion or "saddle thrombus" occurs in approximately 90% of cases[1] while right brachial, renal, splanchnic, and cerebral infarction occur less commonly.[1,2] The underlying mechanisms of CATE are distinctly different from arterial thrombosis with the most appropriate human corollary being cardioembolic disease secondary to atrial fibrillation.[3,4] Previous retrospective studies have reported that 6%–17%[5–7] of cats with underlying cardiac disease go on to develop CATE with mortality rates of 61%–67%.[1,8–10] Euthanasia, similar in frequency to natural death, is often selected in part because of lack of evidence for management strategies that might prevent recurrent CATE.

Antithrombotic drugs are the standard of care for cardioembolic prevention in humans[11,12] and this has been incorporated into clinical protocols for cats. However, there have been no prospective clinical trials in cats evaluating antithrombotic therapy for primary (initial CATE) or secondary (recurrent CATE) prevention. A number of retrospective studies have reported recurrent CATE rates of 17%–75%[1,8–10,13] in cats receiving antithrombotic therapy with one year recurrence rates of 25%–61%.[9,10] Aspirin, the most commonly used antithrombotic in cats, is an antiplatelet drug