Journal of Veterinary Cardiology (2014) **16**, 245—255

Journal of Veterinary Cardiology
ESVC

www.elsevier.com/locate/jvc

Multi-centered investigation of a point-of-care NT-proBNP ELISA assay to detect moderate to severe occult (pre-clinical) feline heart disease in cats referred for cardiac evaluation

Maggie C. Machen, DVM [a], Mark A. Oyama, DVM [a,*], Sonya G. Gordon, DVM, DVSc [b], John E. Rush, DVM, MS [c], Sarah E. Achen, DVM [d], Rebecca L. Stepien, DVM [e], Philip R. Fox, DVM [f], Ashley B. Saunders, DVM [b], Suzanne M. Cunningham, DVM [c], Pamela M. Lee, DVM [f], Heidi B. Kellihan, DVM [e]

[a] *Department of Clinical Studies — Philadelphia, School of Veterinary Medicine, University of Pennsylvania, 3900 Delancey St, Philadelphia, PA 19104, USA*
[b] *Department of Small Animal Clinical Sciences, College of Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station, TX 77843, USA*
[c] *Department of Clinical Sciences, Cummings School of Veterinary Medicine at Tufts University, 200 Westboro Rd, North Grafton, MA 01536, USA*
[d] *Michigan Veterinary Specialists, 29080 Inkster Rd, Southfield, MI 48034, USA*
[e] *Department of Medical Sciences, University of Wisconsin, 2015 Linden Dr, Madison, WI 53706, USA*
[f] *The Animal Medical Center, 510 East 62nd St, New York, NY 10065, USA*

Received 10 February 2014; received in revised form 2 September 2014; accepted 9 September 2014

(1) Work was performed at the University of Pennsylvania, Texas A&M University, Tufts University, Michigan Veterinary Specialists, University of Wisconsin, and the Animal Medical Center. (2) Study was supported by a grant from IDEXX Laboratories Inc., Westbrook, ME. (3) Preliminary results presented at the 2013 ACVIM Forum, Seattle, Washington USA.
* Corresponding author.
E-mail address: maoyama@vet.upenn.edu (M.A. Oyama).

http://dx.doi.org/10.1016/j.jvc.2014.09.002

KEYWORDS
Blood tests;
BNP;
Natriuretic peptides;
Cardiomyopathy

Abstract *Objective:* To prospectively evaluate the diagnostic accuracy of a point-of-care (POC) N-terminal pro-B-type natriuretic peptide (NT-proBNP) ELISA to assess the likelihood of moderate to severe occult heart disease (OcHD) in a clinical population of cats suspected to have heart disease.
Animals: One hundred and forty-six asymptomatic client-owned cats with a heart murmur, gallop rhythm, arrhythmia, or cardiomegaly.
Methods: Physical examination, blood pressure measurement and echocardiography were performed prospectively. Point-of-care ELISA was visually assessed as either positive or negative by a reader blinded to the echocardiographic results.
Results: Forty-three healthy cats, 50 mild OcHD, 31 moderate OcHD, 6 severe OcHD, and 16 cats equivocal for OcHD were examined. Cats with OcHD included 65 with hypertrophic cardiomyopathy, 6 with restrictive or unclassified cardiomyopathy, 1 with arrhythmogenic right ventricular cardiomyopathy, and 15 with non-cardiomyopathic forms of heart disease. Point-of-care ELISA differentiated cats with moderate or severe OcHD with sensitivity/specificity of 83.8%/82.6% and overall accuracy of 82.9%. Positive POC ELISA increased likelihood of moderate or severe OcHD by a factor of 4.8 vs. those that tested negative. Point-of-care ELISA differentiated cats with moderate or severe cardiomyopathic OcHD with sensitivity/specificity of 88.6%/81.3% and overall accuracy of 83.2%.
Conclusion: In a select sample of cats referred for cardiac evaluation, positive POC NT-proBNP ELISA increases likelihood of moderate to severe OcHD while negative POC NT-proBNP ELISA result excludes moderate to severe OcHD.

Abbreviations

ARVC	arrhythmogenic right ventricular cardiomyopathy
AV	atrioventricular
HCM	hypertrophic cardiomyopathy
IQR	interquartile range
IVSd	interventricular septum thickness in diastole
LA:Ao	left atrium to aorta ratio
LVIDd	left ventricular internal diameter in diastole
LVIDs	left ventricular internal diameter in systole
LVPWd	left ventricular free wall thickness in diastole
NT-proBNP	N-terminal pro-B-type natriuretic peptide
NPV	negative predictive value
OcHD	occult heart disease
POC	point-of-care
PPV	positive predictive value
R/UCM	restrictive/unclassified cardiomyopathy

Introduction

Diagnosis of occult (preclinical) feline heart disease (OcHD) is challenging. Echocardiography is useful for non-invasive evaluation of cardiac structure and function, but is costly, technically challenging and might not be readily available. The sensitivity of the medical history, physical examination, thoracic radiography, and serum biochemistries for detection of OcHD is relatively low. Moreover, many heart murmurs in cats are benign in origin.[1] One study found that only 53% of cats with heart murmurs had echocardiographic evidence of heart disease.[2] Thus, a simple, widely-available, and cost-effective means to predict the presence of OcHD is attractive.

The physiology of B-type natriuretic peptide and its N-terminal pro-BNP precursor (NT-proBNP) in cats has been reviewed.[3] Previous studies revealed that quantitative NT-proBNP concentration discriminates occult cardiomyopathy from healthy cats with relatively high sensitivity and specificity and is best at detecting cats with more advanced severity of disease vs. those with only mild structural changes.[4–9] Collectively, these studies indicated that NT-proBNP assay detected occult cardiomyopathy with a sensitivity between 86 and 100% and specificity between 89 and 100%. Samples from these studies were submitted to a central reference laboratory where a plate ELISA assay was performed. Return of assay results can take up to 72 h.

Point-of-care (POC) assays enable testing and return of results at the time of patient