Hypertrophic cardiomyopathy (HCM) is the most common cardiac disease in cats. In practice, it is currently necessary to use echocardiography to confirm the diagnosis and to assess disease severity. Early stages of the disease often show no or only subtle clinical symptoms and might therefore not be detected if echocardiography is not available. N-terminal proBNP (Nt-proBNP) has no physiological activity, but is more stable than BNP and therefore easier to measure. Measurement of NT-proBNP concentration is helpful to distinguish cardiac from non-cardiac causes of dyspnea in cats, dogs, and humans. Previous studies have shown elevated NT-proBNP concentrations even in the occult phase of cardiomyopathy.

The purpose of this prospective study was to evaluate the utility of Nt-proBNP to detect early disease stages of HCM in cats and to assess whether a differentiation between mild, moderate, and severe disease stages is possible using NT-proBNP measurements.

Nt-proBNP was measured in plasma samples from 159 cats using an ELISA (VETSIGN Feline CardioSCREEN Nt-proBNP, Guildhay Ltd, UK). The cats were classified according to echocardiography into one of the following groups: (1) clinical healthy (control) group (n = 33), (2) mild HCM with focal hypertrophy of the left ventricular (LV) free wall or septal hypertrophy between 5.5 and 5.9 mm (n = 13), (3) moderate HCM with focal or generalized LV free wall or septal wall between 6.0 and 7.0 mm and normal left atrial size (LA) (n=12), and (4) severe HCM with LV free wall or septal wall > 7.0 mm and enlarged LA (n = 43) and clinical symptoms.

Nt-proBNP was significantly higher in all HCM groups compared to healthy control cats. Mean NT-proBNP was 58 +/- 65 pmol/l in the control group (1), 333 +/- 244 pmol/l in the mild group (2), 433 +/- 299 pmol/l in the moderate group (3) and 835 +/- 314 pmol/l in the severe group (4). Values of the mild (2) and moderate (3) group cats were significantly lower than those of the severe (4) group cats, but there was no difference between the values of the mild (2) and moderate (3) group. It was shown that the recommended cut-off value of 49 pmol/l had a high specificity of 97.1% but only a specificity of 56% to differentiate healthy cats from cats with HCM. This low cut-off value revealed too many false positive results. Using a cut-off value of 100 pmol/l, Nt-proBNP had a sensitivity of 94.2% and a specificity of 81.3% for the differentiation of control and HCM cats and might therefore be preferable for use in practice. In conclusion, this feline ELISA Nt-proBNP assay is helpful in the diagnosis of even early cases of HCM in cats. Cats with elevated levels, therefore, should be further worked up with echocardiography.

Speaker Information
(click the speaker's name to view other papers and abstracts submitted by this speaker)
Intraday Variation in Feline N-Terminal Prohormone Brain Natriuretic Peptide Concentration
ACVIM 2009
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N-Terminal Prohormone Brain Natriuretic Peptide (NT-proBNP) is a neurohormone and like other hormones it is possible that its circulating concentration in the blood of the patient could be cyclical in nature. If this is the case, then it is important to understand the nature and shape of the cycle since it could have a profound effect on the timing and interpretation of blood sample values.

Five normal cats were recruited for the study. Physical exam, thoracic radiographs, echocardiogram, systolic blood pressure, BUN, creatinine, TT4, and urine specific gravity were evaluated to determine health status of the cat and confirm there was no significant disease. Plasma samples were obtained over 24 hours at 9am, noon, 3pm, 6pm, midnight, 6am, and 9am. NT-proBNP concentrations were determined for each time point.

Four of the five cats showed no change throughout the time-course study; one cat did show some variability. However a one-way analysis of variance (ANOVA) repeated-measures design revealed no significant difference between the times of the day that samples were taken from the cats with F(6,24)=1.42; p=0.25.

The major limitation with the study is that the low levels on NT-proBNP mean that the assay is operating at the very limit of sensitivity; any minor well-to-well differences could mask some subtle variations.

In conclusion, this study suggests that there is no significant, measurable, cyclic (diurnal) variation of NT-proBNP in normal cats.

Cardiac Biomarkers Measured in 500 Cats with Heart Disease, Heart Failure & Other Disease
ACVIM 2009
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The ability to measure cardiac biomarkers in dogs has been established. In the canine, the utility of cardiac biomarkers was convincingly reported by our group in 2008 (this paper has been submitted to a refereed journal for publication). The certainty of this utility in cats remains unresolved. In many smaller cardiac biomarker studies in cats, the markers that were chosen and the results varied, the conditions under which the studies were completed varied and the ability to utilize the results have not been clear. In this report, cats were studied under clinical conditions but the biomarkers themselves were taken with research level consistency. The blood samples were drawn and immediately
preserved with enzyme inhibitors; plasma samples were separated after refrigerated centrifugation. Samples were quickly separated, flash frozen and stored frozen, maintaining a constant temperature of -80°C. Samples were shipped to the laboratory for analysis under dry ice conditions, always arriving frozen. Measures were undertaken prior to the study to guarantee sample safety and consistency.

We will report on the normal levels of troponins (cTnl), NT-proANP and NT-proBNP in this study of approximately 500 cats from one hospital, evaluated between 2007 and 2009. We choose to measure biomarkers in a large number of cats in a manner that would permit us to determine the true normal levels for these animals and to do so under circumstances that allowed us to simultaneously evaluate the cats utilizing methods accepted by veterinary cardiologists.

When possible, multiple examinations (separated by weeks to months) were made on some of the cats so that repeatability and or changes in biomarker levels could be evaluated to test the reliability of the data or in cases of advancing medical disease, the effects of advancing disease and or medication on the data.

Perhaps the most difficult portion of this process turned out to be the ability to clearly and consistently evaluate the stage of heart disease, if present. Although multiple reports and recommendations are available in the veterinary literature on the scoring or classification of heart disease in dogs, we did not find any accepted grading system for cats with heart disease. The ISACH veterinary scoring system suggested for the canine did not clearly separate the various levels of disease short of overt heart failure. Our newly developed grading system for the dog was modified for the cat. This grading permitted us to repeatably define each patient's class of disease for the purpose of this trial. The system was subjected to blind evaluation by other board certified veterinary clinicians to validate that our system was robust. We do not know if the scoring system we use is better than others, but for the purpose of this trial it did allow us to separate cats sufficiently to determine if there was a difference in biomarker levels between grading class.

We will show what we believe to be the repeatable and reliable normal levels of cardiac biomarkers as well as the levels of these markers in the various states of disease as determined through clinical testing. We will show the variations of these biomarkers, where they exist, by age, breed, sex, and weight. We also looked at normal cats and those with cardiac and non cardiac disease. We will note the correlations made with other diseases, the relationship to specific cardiac and non cardiac conditions that also became apparent after the blinding period was ended. The repeatability of the studies in normal and cardiac states was determined. Other than the in house traditional cardiac information we had no access to the biomarker results until we were unblinded (March, 2009) when we began to identify individual cases to prepare this information.

We did not begin the project with the intent of defining pre-answered questions that we needed to validate but instead entered the project asking questions. We are still doing so and anticipate that the collection of such a large amount of data (and continuing) will provide us with many answers regarding the relevance of cardiac biomarkers as it relates to the knowledge of cardiac disease in the feline.

Classification of Feline Heart Disease
Caveat: This classification is intended to be universal, easily used by every veterinarian in a similar manner, leaving as little room for variation in the clinical determination of heart disease class as possible.

PHASE 0. No Heart Disease Present

There are no signs or findings of heart disease. This includes clinical signs, physical examination, or ancillary study findings (laboratory, electrocardiographic, radiographic, or ultrasonographic) that indicate or suggest a cardiac problem.

PHASE 1. No Clinical Signs

A murmur, arrhythmia, or mild cardiac changes are present. There are no clinical signs of congestive heart failure present. A heart murmur or extra heart sounds may be present but without clinical signs of disease. There may be an arrhythmia. There is no echocardiographic evidence of compensatory structural change.

- A: None to minimal cardiac structural changes; i.e., change in echogenicity or valvular abnormalities with no secondary changes in chamber size or function.
- B: Pathophysiology is present with no secondary compensatory changes. i.e., LVH with no atrial enlargement.

PHASE 2. No Clinical Signs But with Evidence of Cardiac Dysfunction and Compensation

- A: Pathophysiology is present. Echocardiogram reveals mild left or right atrial enlargement (LA: Ao of >1.5 and <=1.7) with one or more of the following present: abnormal FS, abnormal chamber size (LVH; LV dilation; segmental myocardial changes), abnormal structure or function of one or more of the four cardiac valves.
- B: Same as A with moderate or severe left or right atrial enlargement (LA: Ao > 1.7).

PHASE 3. Congestive Heart Failure Present that is Mild or Controlled

Clinical signs, physical exam and cardiac study abnormalities prove the presence of clinical heart failure requiring therapy. Signs are:

- A: Well-controlled with drug therapy such as: ACEI, digoxin, pimobendan, furosemide, spironolactone, beta-blockers, calcium channel blockers (CCB).
- B: Observed most days suggesting that sub-clinical or no congestive heart failure is present.

PHASE 4. Congestive Heart Failure is Present and Overt

Heart failure is observed by clinical signs, physical examination and anamnesis; supported by radiography and / or echocardiography. Signs observed can occur in association with other diseases and must be differentiated when making a diagnosis of congestive heart failure.
A: Left sided heart failure alone as indicated by pulmonary edema, dyspnea, tachypnea, or pleural effusion with or without pulmonary edema in the absence of right atrial enlargement.

B: Pleural effusion, pericardial effusion, or ascites with evidence of right atrial enlargement. Concurrent pulmonary edema and left sided heart failure may or may not be present.