Cardiac Blood Tests in Cats

Another Tool for Detection of Heart Disease

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Detection of asymptomatic (occult) heart disease in cats is challenging.

Diagnosis is complicated by the fact that while heart murmurs are relatively common in adult cats, not every cat with a murmur has underlying heart disease. In a recent study of 100 cats presented to a teaching hospital, heart murmurs were detected in 44 cats but only 10 were diagnosed with disease.[1] In a similar study of 103 cats, murmurs were detected in 16 cats but only 5 were diagnosed with disease.[2]

DIAGNOSTIC CHALLENGES OF CARDIAC DISEASE

What should a clinician do in the case of an asymptomatic cat with a gallop heart rhythm, arrhythmia, or family history of cardiomyopathy?

The most prudent course of action would be to gather additional information about heart size, function, and electrical activity through chest radiographs, electrocardiography (ECG), and echocardiography (**Table**). Unfortunately, these tests represent an added commitment of time, equipment, and cost. If many heart murmurs in cats are indeed from benign causes,[1,3] are additional tests really needed? How strongly should pet owners be encouraged to pursue these additional diagnostics?

FIXING FELIX: TRICKY QUESTIONS

Felix, a 7-year-old castrated male domestic shorthair cat, has dental disease that requires anesthesia for cleaning and possible extractions. The owner reports that Felix has no abnormal signs or behavior.

On physical examination, you detect a 3/6 systolic heart murmur and a heart rate of 190 beats/min. Pulmonary auscultation, respiratory rate and effort, and femoral pulse quality are normal.

The following questions cross your mind:

- *Is it safe to anesthetize Felix?*
- *Does the heart murmur indicate the presence of underlying cardiomyopathy?*
- *Should I perform an ECG or chest radiographs?*
- *Should I recommend referral for an echocardiogram prior to the dental procedure?*

Electrocardiography

ECG is the gold standard for assessment of arrhythmias (and the least expensive of the diagnostics mentioned), but is relatively insensitive for detection of heart enlargement and dysfunction. Thus, many cats with underlying cardiomyopathy will have a normal ECG.

If arrhythmias are detected or ECG criteria for left ventricular enlargement are met (ie, increased R wave amplitude), the likelihood of underlying disease increases in the presence of these findings. However, a normal ECG still leaves much room for doubt.

Radiography

Chest radiographs are a useful modality for evaluation of heart size and shape, and the ventrodorsal or dorsoventral view is the most sensitive for detection of feline atrial enlargement. However, the classic "valentine"-shaped heart, which is highly specific for disease, is the exception rather than the rule in cats with mild or moderate asymptomatic disease.

In instances when congestive heart failure (CHF) is suspected, chest radiographs are the gold standard for diagnosis of pulmonary edema or pleural effusion, but in cats with asymptomatic disease, clinical signs are, by definition, absent and CHF would not be expected. Thus, while a better diagnostic choice compared with ECG, radiography still suffers from relatively low sensitivity.

Echocardiography

Echocardiography is the diagnostic test of choice for detection of occult heart disease in cats. 2D and M-mode echocardiography provides detailed examination of ventricular and atrial dimensions, morphology, and function.

Doppler echocardiography examines blood flow and detects abnormal mitral valve motion, mitral regurgitation, and high-velocity blood flow within the right ventricle, left ventricular outflow tract, and/or aorta, all of which are common causes of feline heart murmurs.

Therefore, a universal recommendation for any cat with a murmur is to pursue further investigation using echocardiography. For most general practitioners this recommendation will require examination by a local specialist, which involves additional travel, time, and expense on the part of the owner.

In my experience, compliance with this recommendation is exceedingly low, and is likely influenced by several factors, including the absence of alarming clinical signs as well as the uncertainty of the general practitioner as to whether or not significant heart disease is truly present.

THE DIAGNOSTIC GAP

Many pet owners decline further diagnostics and accept some additional risk (the magnitude of which is largely unknown) regarding anesthesia. However, owners would be more likely to pursue additional diagnostics if the veterinarian could:

- Ascertain that the likelihood of significant heart disease is high, which would influence subsequent anesthetic protocol
- Determine that cardiac medications may be needed to help mediate disease.

In my opinion, cardiac blood tests offer their greatest value in assessing risk of clinically significant underlying heart disease and, therefore, allow the veterinarian to present a much more persuasive case to the owner when advocating further diagnostics.

WHAT HEART HORMONES TELL US

In addition to its function as a muscular pump, the heart is a rich endocrine organ that produces and responds to a wide variety of neuroendocrine stimuli and substances. To help regulate fluid balance within the circulatory system, the heart produces diuretic and natriuretic hormones called natriuretic peptides.

B-Type Natriuretic Peptide

One particularly important peptide is **B-type natriuretic peptide (BNP)** that is produced in the ventricular and atrial myocardium. BNP is produced in response to stretch, hypoxia, and activity of other neuroendocrine

OVERVIEW: NT-PROBNP TESTING IN CATS

- **Helps determine likelihood of heart disease** in cats with findings suspicious of underlying heart disease (eg, heart murmur, gallop, arrhythmias)
- **Helps determine etiology of disease** in cats with respiratory signs
- **Helps encourage owner compliance** with respect to additional and more definitive diagnostics, such as echocardiography
- **Helps achieve a diagnosis** when used in conjunction with findings from the history, physical examination, ECG, and radiographs
- **Not a test for breeding soundness**
- **Not for use in routine wellness examinations**

pathways, such as the renin-angiotensin-aldosterone axis and the sympathetic nervous system.

N-Terminal Pro—B-Type Natriuretic Peptide

Within the myocardial cell, BNP is produced as a precursor molecule that is subsequently and enzymatically cleaved into the active neurohormone, BNP, and a byproduct called **N-terminal pro—B-type natriuretic peptide (NT-proBNP)**. NT-proBNP can be detected in the circulation using standard laboratory techniques, such as enzyme-linked immunosorbent assay, and its concentration reflects the degree of cardiac activation secondary to the aforementioned stimuli.

Use in Humans

In humans, plasma concentrations of BNP and/or NT-proBNP are used in the hospital setting to:

- Diagnose CHF
- Differentiate etiology of respiratory signs (ie, CHF versus primary respiratory or airway disease)
- Provide prognostic information regarding morbidity and mortality.[4]

In human patients with respiratory distress, the combination of BNP or NT-proBNP assay and clinical assessment was superior to clinical assessment alone in identifying the cause of acute respiratory distress, shortening hospitalization time and reducing cost of treatment.[5]

Use in Veterinary Patients

Similar clinical utility has been demonstrated in canine and feline patients with respiratory signs.[6-8] These applications demonstrate the general utility of NT-proBNP in patients with clinical signs, but what about use of NT-proBNP to assess risk of occult disease in patients that are asymptomatic?

DIAGNOSTIC CARDIAC SCREENING

Diagnostic screening requires assays with high sensitivity and specificity so that false negatives and false positives are minimized, and standard guidelines typically recommend sensitivity and specificity values of 90% or greater.

With respect to both accuracy and cost effectiveness, the clinical utility of screening assays increases as the prevalence of disease increases.[9] For example, in a population where disease incidence is extremely low, a positive result in a test with very high specificity can still be a false positive. This relationship applies to many familar diagnostic tests: a positive heartworm antigen test from a dog living in Alaska would be viewed with much greater suspicion as a potential false positive result versus a positive test from a dog in Georgia.

Patient Selection

Screening is best performed in a subpopulation of individuals at high risk for disease, while arbitrary routine screening of large community populations is not particularly useful. For example, screening for cardiac disease in cats is best performed in those with:

- Heart murmur

- Gallop rhythm
- Arrhythmia
- Family history of cardiac disease.

Screening Results

Most[10-12] but not all[13] studies of NT-proBNP assay in cats indicate a high sensitivity and specificity for detection of occult disease.

The largest study to date involved 227 cats examined by board-certified cardiologists at 12 different specialty or teaching hospitals.

- NT-proBNP assay was 91.2% specific and 85.8% sensitive for detection of underlying heart disease based on findings from echocardiographic examination.[10]
- These results yielded a positive predictive value of 90.7% and negative predictive value of 86.7%.
- Therefore, in a cat that tested positive, the clinican could be 90.7% certain that underlying heart disease was present and, in a cat that tested negative, 86.7% certain that it was not present.

Given the limitations of the ECG and radiographs as previously discussed, NT-proBNP appears useful in helping clinicians assess the risk or likelihood of detecting disease in cats with suspected heart disease.

PRACTICAL APPLICATION OF NT-PROBNP ASSAYS

To help achieve an accurate diagnosis, whenever possible, the NT-proBNP assay should be used in combination with:

- Medical history
- Clinical signs
- Physical examination
- ECG
- Radiographs
- Echocardiography.

I recommend use of the NT-proBNP assay in 2 specific situations (**Table**):

Differentation: Cardiac versus Respiratory Disease

The test can be used in cats with respiratory signs to help differentiate cardiac disease versus primary respiratory etiologies (eg, asthma, pneumonia).

In cats with respiratory signs, a low NT-proBNP concentration is highly specific as a rule-out test for congestive heart failure.[7] A high NT-proBNP concentration is more consistent with congestive heart failure; however, in cats with both respiratory disease and concurrent mild or moderate heart disease, false positive results can occur.

A recent study involving assessment of case data by veterinarians blinded to the final diagnosis found that the accuracy and

Table. Cardiac Diagnostics: Indications, Advantages, & Disadvantages

Diagnostic Modality	Indications	Advantages	Disadvantages
Echo-cardiography	Cats with: • Heart murmurs	• Provides detailed evaluation of ventricular/atrial dimensions, morphology, & function • Detects abnormal mitral valve motion, mitral regurgitation, & high-velocity blood flow	• Requires local specialist plus travel and expense for owner • Compliance is low due to absence of clinical signs and uncertainty about presence of heart disease
Electro-cardiography (ECG)	Cats with: • Arrhythmias • Heart murmurs	• Gold standard for assessment of arrhythmias • Detects left ventricular enlargement (ie, increased R wave amplitude)	• Relatively insensitive for detection of heart enlargement & dysfunction • Many cats with underlying cardiomyopathy have normal ECG
NT-proBNP assay	Cats with: • Arrhythmias • Family history of cardiac disease • Gallop rhythm • Heart murmurs	• High sensitivity and specificity for detection of occult disease in high-risk populations • Provides guidance with regard to pursuing additional diagnostics • Helps achieve diagnosis when used with additional diagnostics	• Not the gold standard for diagnosis of heart disease • Does not diagnose heart disease • Negative test does not ensure future health • Not a test for breeding soundness or routine wellness examinations
	Cats with: • Respiratory signs	• Differentiates cardiac disease from respiratory etiologies • Accuracy improved when NT-proBNP used with other diagnostics	• In cats with both respiratory disease & concurrent mild/moderate heart disease, false positive results can occur
Radiography	Cats with: • Suspected congestive heart failure (CHF)	• Gold standard for diagnosis of pulmonary edema or pleural effusion • Evaluates heart size & shape	• Low specificity for atrial enlargement in subclinical disease • No indication in subclinical CHF

confidence of diganosis was improved when NT-proBNP assay was combined with traditional diagnostics.[14]

Detection of Occult Disease

As previously described, NT-proBNP assays are indicated for the detection of occult disease in high-risk populations. This population includes cats with an arrhythmia, murmur, gallop, family history of disease, or mild clinical signs that may be due to heart disease.

Wellness Screening

Routine inclusion of NT-proBNP assay as part of general wellness examinations in cats with no risk factors for heart disease is not currently recommended.

ADDITIONAL CONSIDERATIONS

Several important points merit consideration:

- **Not a Gold Standard**: NT-proBNP assay is not the gold standard for diagnosis of heart disease; echocardigraphy remains the standard by which all other diagnostics are measured.
- **Provides Guidance, Not Diagnosis**: NT-proBNP assay does not necessarily diagnose heart disease; it provides guidance regarding the importance of further diagnostics, especially when asking the owner to pursue additional testing.
- **Encourages Additional Diagnostics**: Further diagnostics, such as echocardiography, may discover heart disease, which will affect anesthetic protocols for procedures or, alternatively, whether medical treatment is needed to prevent future clinical signs.
- **Cardiac Disease Can Still Develop**: It is imporatant to remember that BNP is produced in the presence of active heart disease; a negative test does not ensure future health.
- **Not for Breeding Suitability**: The use of the assay to determine fitness for breeding in young healthy intact animals is not appropriate. In these cases, screening for the presence of known heritable genetic mutations is the recommended option.

WHAT THE FUTURE HOLDS

Cardiac blood testing in veterinary medicine is a relatively new science, and there is still much to be learned.

Advances in assay technology as well as in our understanding of the heart as an endocrine organ will increase accuracy of detection in very early disease. In addition, future studies will help determine if NT-proBNP concentrations can:

- Help practitioners manage CHF
- Predict risk of morbidity or mortality.

Novel neuroendocrine substances await discovery, and along with NT-proBNP, could provide additive information about presence and progression of heart disease. Thus, combinations of several assays to form a "cardiac blood panel" could be available one day just as renal or hepatic panels evaluate the various functions of those organ systems.

The future of cardiac blood tests is an exciting prospect, and in the present time, proper use and interpretation of results can assist veterinarians in providing the highest standard of care for their patients. ■

BNP = B-type natriuretic peptide
CHF = congestive heart failure
ECG = electrocardiography
NT-proBNP = N-terminal pro—B-type natriuretic peptide

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