Cardiac Biomarker Project by Professor Joanna Dukes-McEwan
BVMS, MVM, PhD, DVC, DipECVIM-CA(Cardiology), MRCVS (March 2017)

As the principal investigator in this project, I absolutely agree that no decisions should be made based on cardiac biomarker (blood test) results alone. The research aims to investigate whether they can be relied on to identify Dobermanns who are healthy and those requiring other investigations to see if they have dilated cardiomyopathy (DCM), or if they have another reason for increased biomarker results.

Until the results are analysed, we cannot say how sensitive or specific sole use of the cardiac biomarkers are (although work by Gerhard Wess suggested that dogs with low NT pro-BNP or Troponin I (much lower than the currently used reference ranges by the labs) were very unlikely to have DCM (so good specificity, but low sensitivity).

The gold standard for screening is still both echocardiography and 24 hour ECG monitoring (Holter), which identify dogs with both forms of cardiomyopathy. It is vital to appreciate that a Dobermann can show the arrhythmia from before any echo changes of structural heart disease, but this is still cardiomyopathy (the dog should not be claimed to be free from DCM). From the published literature, there are reliable criteria to define normal, and DCM affected Dobermanns. But there is a grey zone, where a dog may be labelled as "equivocal" where results are somewhere in between the values considered normal and those considered definitely abnormal.

Even if I, or another cardiologist, identifies a Dobermann with DCM, or an equivocal Dobermann, we would never give breeding advice – this is a decision for breeders and a decision to breed is not just based purely on heart testing results. We also need to remember that a young Dobermann with normal results may not remain normal, so serial testing is required. DCM can develop at any age, but it can never be considered normal; it is not an ageing change.

Watch this space! The cardiac biomarkers may be a useful "pre-screening" tool – but a breeder who is serious about reducing risk of DCM in progeny is urged to serially screen for DCM with both echo and Holter within 12 months of breeding. This is even more important in males, who are potentially responsible for many more progeny than a bitch if widely used. Even more important – if early DCM or arrhythmias are identified in your individual dog, we know medication can make a difference to outcome, and will slow down the progression of the disease or control the arrhythmia. So screening will benefit each individual dog and owner.

Dilated Cardiomyopathy (DCM)

Recent research and review of screening tests (June 2013) by Ruth Willis BVM&S DVC MRCVS

Prevalence of disease

Dilated cardiomyopathy (DCM) is a common disease in Dobermans. In a study surveying Dobermans >6years of age, 44% of dogs were affected. If Dobermans of all ages were assessed then 58% had signs of disease. It was reported that both male and female dogs were equally affected although males tended to show signs of disease at an earlier age.

Disease course

DCM is a disease which is likely to have a long pre-clinical phase where there are no clinical signs or symptoms but there may be evidence of heart enlargement, deterioration in heart function and/or abnormal heart rhythms. During the clinical phase of the disease there are signs such as fainting, weight loss, breathlessness, coughing and/or fluid retention resulting in distension of the abdomen. Sadly Dobermans with DCM can also experience sudden death which is likely to be due to abnormal rapid heart rhythms.

The diagnosis of this disease is made based on the combination of the history mentioned above, clinical signs suggesting poor heart output, echocardiography (ultrasound of the heart), an ECG to record heart rhythm in

the clinic and also a Holter monitor recording which involves use of a heart monitor that dogs can wear at home to record heart rate and rhythm over a longer period such as 24 hours.

The Holter monitor weighs about 150g and is attached to the dog using 3 adhesive pads called electrodes. The monitor is carried in a pouch inside a specially designed vest. By recording heart rate and rhythm over 24h and then analysing the recording we are able to detect abnormal beats which may occur singly or as multiple consecutive beats - this abnormal rhythm is known as ventricular tachycardia (VT) which may be life threatening. Some dogs with abnormal heart rhythms require treatment with medication and follow up Holter monitoring to assess the effectiveness of therapy.

Other treatments for dogs with clinical disease include diuretics to reduce fluid retention, pimobendan ("Vetmedin") to increase the force of heart muscle contraction, ACE inhibitors to improve blood flow and also ameliorate the harmful side effects of diuretics.

Recent research - PROTECT Study

In this study a large number of Dobermans were screened using echocardiography and also 24 hour Holter to detect dogs with pre-clinical DCM. These dogs were then treated with pimobendan or a placebo drug and monitored regularly. We recorded the time until these dogs either died suddenly or developed signs of congestive heart failure. This study demonstrated that pimobendan prolongs survival and extends the time to onset of clinical signs by about 9 months (718 days in the pimobendan groups versus 441 days in the placebo group).

Therefore screening dogs is of benefit to the individual as well as to the breed.

Screening

The ideal screening test is:

 accurate and therefore detects all cases of disease with no false positives or negatives

 capable of detecting disease at a very early stage

 non-invasive – not painful and risk-free for the individual being screened

 widely available

 reasonably priced.

Accuracy

Test accuracy is often expressed in terms of sensitivity and specificity.

Sensitivity = the proportion of correctly identified positives. For example if 100 patients known to have disease were tested and 95 test positive then the test has a sensitivity of 95%. High sensitivity is important in tests used for screening.

Specificity = the proportion of correctly identified negatives. For example if 100 patients with no disease are tested and a negative result is obtained for 96 then the test has a specificity of 96%.

Suggested screening tests

1. Echo and Holter

These tests would be the current gold standard for screening Dobemans for DCM.

2. NTproBNP

BNP is a substance released into the blood in response to stretching of the heart muscle. New sample tubes are available so sample no longer needs to be transported frozen however this test can be affected by concurrent disease.

One study reported a sensitivity of 81% and a specificity of 75% to detect all stages of DCM in Dobermans.

3. Troponin

This is a substance released into the blood in response to heart muscle damage.

One study reported sensitivity of 79% and specificity of 74%.

4. 5 minute ECG

This test involves recording an ECG for 5 minutes and has been reported to have lower sensitivity (64%) and higher specificity (97%). The lower sensitivity suggests that it is less suitable as a screening test.

As DCM is generally a disease of middle aged and older dogs, screening should be repeated annually.

Some dogs may have equivocal results which is an understandable source of frustration for both owners and vets. In these cases tests may have to be repeated at a later date.

A genetic test for this disease would be a fantastic development allowing us to detect cases at an earlier age. There are several tests marketed at present but the results are conflicting and further research is required.

Summary of performance of tests available for screening

Certificate, echo and Holter - Sensitivity (%) GOLD Specificity (%) GOLD

BNP and Holter - Sensitivity (%) 94 Specificity (%) 87

BNP - Sensitivity (%) 81 Specificity (%) 75

Troponin - Sensitivity (%) 79 Specificity (%) 74

5min ECG - Sensitivity (%) 64 Specificity (%) 97

References are available on request.

Summary

 DCM is common in Dobermans.

 Screening to detect early disease is possible and beneficial both to the individual dog and also to the larger breeding population.

 Many screening tests are available with varying accuracy and cost.

 Screening needs to be done annually.

Contact details

Vets Now Referrals, North Street, Glasgow. Email:

Holter Monitoring Service, Dollar. Email:

About The Author

I graduated from Edinburgh Vet School in 1996 and spent two years in general practice before starting a three year post-graduate training program in cardiology at Glasgow Vet School where I obtained the Royal College of vet Surgeons Certificate and Diploma in Veterinary Cardiology and was also awarded Royal College Specialist Status in 2003. Since then I have worked in private referral practice in Stirling from 2002 – 2009 and at Vets Now Glasgow from September 2011. I founded Holter Monitoring Service in 2005 and since then have gained a lot of experience in the diagnosis and management of abnormal heart rhythm in dogs.

I live in Dollar with my husband, two children, a Labrador and a crazy 3-legged cat.