Small Animal *Review*

Summary: Plasma atrial natriuretic peptide and troponin concentrations interpreted together are useful in assessing the severity of mitral valve disease in the dog and are useful measures to augment echocardiographic findings.

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Canine mitral valve disease diagnosis

Mitral valve disease (MVD) due to mitral valve degeneration, a common disorder in dogs, results in left ventricular hypertrophy and left atrial dilatation, and often congestive heart failure. The diagnosis can be suspected from clinical examination and a diagnosis can be made using echocardiography, but neither can reliably assess the extent of myocardial damage or function. Measurements of blood atrial natriuretic peptide (ANP) and B-type natriuretic peptide (BNP) concentrations are used to assess cardiac function, since plasma concentrations of these hormones increase with atrial or ventricular overload respectively, while myocardial damage can be assessed by assaying cardiac troponin.

The value of measuring ANP and troponin in dogs with naturally occurring MVD has been assessed by Hori et al (Evaluation of atrial natriuretic peptide and cardiac troponin I concentrations for assessment of disease severity in dogs with naturally occurring mitral valve disease. J Am Vet Med Assoc. 2020;256(3):340–348. https://doi.org/10.2460/javma.256.3.340). They carried out a prospective multicentre study involving 316 privately-owned dogs with mitral valve disease and 40 healthy control dogs. Within the diseased group, 142 were in stage B1, 102 in stage B2 and 72 in stage C, with 63 dogs receiving a variety of drugs. Stage B1 and B2 dogs were those not showing clinical signs, with stage B1 dogs having left atrium-to-aortic root ratio on echocardiography of <1.7 or a left ventricular internal diameter in diastole normalised to body weight of <1.7 cm/kg$^{0.294}$, while stage B2 dogs had values of ≥1.7 and ≥1.7 cm/kg$^{0.294}$ for the two measured parameters respectively. The stage C group contained those dogs with a history of clinical signs of congestive heart failure. As expected, the median vertebral heart score and left ventricular internal diameter at end diastole were greater in dogs with disease compared to the control group, and within the disease population this parameter along with median heart rate and fractional shortening were also higher in dogs with stage B2 and C than for those in stage B1.

The authors used assays marketed for human use, but as human and canine ANP and cardiac troponin show high homology the tests were considered to be appropriate, and this was confirmed using appropriate standards. Median plasma ANP concentration was 436.7 pg/mL for stage C dogs, 274.2 pg/mL for stage B2, and 105.3 pg/mL for stage B1, all higher than the control group (61.9 pg/mL); The values for stage B2 and C groups were also greater than that for stage B1 group. For troponin the median plasma concentrations of 0.249 ng/ml reported for stage C dogs was significantly greater than that for each of the other groups, whilst the result for the stage B2 dogs (0.098 ng/mL) was greater than that for the B1 dogs (0.068 ng/mL and control animals (0.058 ng/mL).

Based on their results, the authors suggest plasma ANP concentrations of 112.9, 184.2, and 277.8 pg/mL for identifying dogs in stage B1 or worse, stage B2 or worse, and stage C, respectively. For troponin they suggest concentrations of 0.089, 0.139, and 0.163 ng/mL for detection of dogs in stage B1 or worse, stage B2 or worse, and stage C, respectively. Their results indicate that assaying plasma ANP allows dogs in the earlier stages (B1 and B2) of mitral valve disease to be detected, whereas troponin does not. For those with advanced (stage C) disease, both parameters were equally useful.

The median plasma ANP and troponin concentrations for the healthy dogs varied considerably from previous studies. For ANP the authors speculate this was because a different assay method was used; however, for troponin no explanation was evident. They suggest it is necessary to establish reference intervals for ANP and troponin concentrations in dogs if these assays are to be reliable. The study confirms that monitoring ANP is useful for assessing atrial overload, which is expected to develop with mitral valve disease, and that as the severity of disease increases so the plasma ANP concentration also increases. The observation in this study of raised ANP concentrations in a variety of dog breeds with stage B1 and B2 disease conflicts with a study in Cavalier King Charles Spaniels (CKCS's), where the mean ANP concentration for dogs at similar stages did not differ significantly from control dogs. The authors suggest this is due to differences in the populations studied and most likely reflects the different breeds in the groups and differing interpretations of the criteria used to classify the severity of MVD. For example, left ventricular and left atrial dimensions did not differ between the affected CKCSs and control dogs, whereas those same measurements in dogs with subclinical MVD in the Hori et al paper were significantly greater than those for the control dogs. In conclusion, the authors suggest that assaying plasma ANP is useful in the detection of dogs with mitral valve disease and that as left atrial congestion is an important regulator of ANP concentration, and atrial overload will develop prior to clinical signs developing, an increase in plasma ANP concentration in preclinical stages is expected. Also, as the concentration correlates well with the disease stage it can provide an indication of the severity of disease. In contrast, for troponin, although its concentration increased with severity of disease, it was unable to differentiate dogs in the earlier stages of disease. This too is expected; as troponin is released from damaged cardiac myocytes and in the earliest stages of disease such damage is minimal, plasma concentrations may not rise to significant levels. Thus, troponin is of most use in identifying late stage disease, but be aware that many conditions can result in myocardial damage and hence an increase in plasma troponin. Newer assays in development may allow myocardial damage to be identified at an earlier stage. CA