Current thoughts on cruciate ligament failure

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Disease of the cranial cruciate ligament (CCL) is the most common condition to affect the canine stifle joint. Despite this it is still a poorly understood disease. The postulated factors involved in the pathogenesis of CCL rupture are many. These include: genetics, breed, age, gender, neutering, ischaemia, obesity, immune mechanisms, tibial plateau angle, intercondylar notch, and local biomechanics. Some of these factors have been investigated, and some are currently under investigation.

Risk factors for CCL disease – age, breed, gender

CCL rupture occurs in all sizes of dogs but affects larger breed dogs more than smaller dogs, and at a younger age. Obesity is also likely to be a risk factor although further work is required in this area. Epidemiological studies have indicated an increased prevalence of CCL disease in breeds such as the Newfoundland, Rottweiler and Labrador Retriever, with infrequent occurrence in the Greyhound, Bassett Hound and Old English Sheepdog.

CCL rupture occurs more commonly in neutered animals, particularly females. It is unknown if this is secondary to abnormal weight gain as certain authors have reported that 45.4% of spayed bitches are obese.

Metabolism of the CCL

With the increased risk of CCL disease in certain breeds and neutered animals, one can ask many questions relating to the nature of the tissue in these animals. Is the CCL “normal” in these animals? For example, is the structure and turnover of the CCL normal? Is the biochemistry of the CCL normal? Does hormonal status influence CCL metabolism and function?

We recently published studies wherein we examined CCL biochemistry, ultrastructure and biomechanics of CCLs from two at-risk breeds (Labrador and Golden Retriever) and compared these to a low-risk breed (Greyhound). In these studies, the CCLs were harvested from dogs euthanatized for reasons unrelated to stifle disease and all dogs had grossly normal stifle joints and CCLs.

We examined the ultrastructure of the CCLs in these breeds using transmission electron microscopy. We have assessed collagen fibril diameter and found that the mean fibril diameter in the Labrador is significantly smaller than that of the Greyhound. This is interesting in that previous experimental work has demonstrated that following CCL transection, the collagen fibril diameter of the caudal cruciate ligament decreases. This suggests that collagen fibril diameter is a marker for altered loading.

We have also examined markers of collagen turnover in CCLs from these breeds of dog. We have used gelatin gel zymography to demonstrate that tissue concentrations of gelatinase (matrix metalloproteinase [MMP]-2) are upregulated in the at-risk breeds compared to controls. Furthermore, using reverse zymography we have demonstrated that concentrations of tissue inhibitor of MMPs (TIMP-2) are lower in the at-risk breeds compared to control. In addition, we have studied cross-linking profiles of collagen within these tissues using HPLC. Breeds at risk for CCL disease show more intermediate collagen cross-links compared to controls. Taken together, these data suggest that collagen turnover in CCLs from at-risk breeds is increased. This could be constitutive, or induced. The intercondylar notch has previously been investigated as an etiological factor and we found some further evidence that this may be an influence on CCL biochemistry. Whilst the studies described above were of grossly normal ligaments, it is also important to study end-stage disease so that markers of disease can be determined. We and others have investigated ruptured CCLs retrieved at surgery and undertaken a variety of biochemical and morphological studies.

One problem with these studies is that delay between rupture and sampling may complicate the picture as inflammatory repair mechanisms are initiated.

CCL disease – endocrinological perspectives

Connective tissue metabolism has been shown to be influenced by the endocrine system. Female human athletes are more prone to anterior cruciate ligament rupture compared to male athletes. In rabbits, estrogen has been shown to downregulate metabolism of CCL cells in vitro. Furthermore, estrogen has been reported to decrease collagen synthesis in the human anterior cruciate ligament and an increased incidence of rupture has been recognised at certain stages in the female menstrual cycle. Estrogen receptors have been demonstrated on the surface of ACL cells. Neutering in dogs has been shown to increase in risk of CCL...

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disease and this may relate to change in hormonal status. However, it is also possible that this increased risk relates to increased bodyweight caused by obesity induced by neutering. Conversely, one should also consider the hormonal output of white adipose tissue and the possibility that these hormones (e.g. leptin) may affect connective tissue metabolism. We have recently identified the long form of the leptin receptor on canine CCL cells but its physiological role in these cells is yet to be elucidated.

CCL disease – biomechanical perspectives

Tibial plateau angle: In recent years, the tibial plateau has been a subject of much debate. Does an excessive slope to the tibial plateau contribute to the incidence of CCL disease? One study suggests that dogs with CCL rupture do have an excessive slope to the tibial plateau. However, other studies have failed to substantiate these data. Wilke and colleagues measured traditional and standing TPAs in affected and unaffected Labradors and unaffected Greyhounds. The authors concluded that although TPA may be associated with damage to the cruciate ligaments, many dogs with a steep TPA do not develop cruciate ligament disease.

Stifle biomechanics: We have recently published studies on the in vivo biomechanics of the normal Greyhound and normal Labrador. We have used a combination of kinetic, kinematic and morphometric measures to estimate the moments, work and power acting through the canine stifle joint. Our findings indicate consistent differences between these two breeds of dog. Interestingly, the Labrador has a peak cranial caudal force of 1N/Kg acting through the stifle joint at the trot but a similar estimate for the Greyhound is only 0.5 N/Kg. This is the force that the CCL must resist. Our future studies will investigate the alterations in these parameters in dogs with CCL rupture and also the effect on these parameters of various surgical techniques.

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References


