INVITED REVIEW

Morphologic and Functional Features of the Canine Cruciate Ligaments

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Objective—To review the gross, microscopic, and functional anatomy of the cranial cruciate ligament (CCL) in dogs.

Study Design—Literature review.

Methods—Reports of the anatomy and function of the cruciate ligaments in dogs were retrieved by search of the 1975–2005 PubMed database.

Results—The CCL has an important biomechanical function resisting cranial drawer, hyperextension, and internal rotation and acts to fine tune and guide the stifle through its rolling and sliding motion. It has a complex architecture, and distinct geographic regions within the ligament have different functional roles depending on the angle and loading conditions. Collagen type I is the main component of the extracellular matrix; the fibrils have a crimped structure. The cruciate ligaments are almost completely covered by synovium, protecting them from synovial fluid. Cruciate blood supply is mainly of soft tissue origin. The intraligamentous network is relatively limited whereas the core of the middle third of the CCL is even less well vascularized. Neurohistologic studies are very limited in the dog. Various mechanoreceptors and proprioceptive receptors have been identified within the substance of the cruciate ligaments.

Conclusions—CCL structural characteristics play an important part in its complex behaviour with the crimped pattern of the collagen fibrils being an important determinant of its biomechanical properties. In contrast to reports of managing CCL rupture, there are few reports describing the microanatomy and neurovascular morphology of the cruciate ligaments.

Clinical Relevance—Cruciate disease is likely multi-factorial. Improved understanding of CCL degradation leading to CCL rupture is critical to development of new diagnostic tests for cruciate disease in dogs. Appropriate intervention during the early stages of disease process might preserve CCL structural properties by preventing further collagen degradation. Accurate knowledge of functional and fiber bundle anatomy is imperative for reconstruction and restoration of normal stifle joint physiology. Reconstructive goals should alleviate existing instability and mimic normal kinematics. Knowledge of the exact function of the CCL in the neuromuscular control around the stifle joint could possibly explain osteoarthritis progression after CCL damage.

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INTRODUCTION

ONE OF the most complex joints, the stifle joint, contains the cruciate ligaments that are required for craniocaudal joint stability. Morphologically and functionally complex, the cruciate ligaments are dynamic structures, strongly connecting the femur to the tibia. In early medical literature, the cruciate ligaments were called crucial ligaments because of their crossed arrangement.[1] Subsequently, the crucial role of the cruciate ligaments to stifle joint kinematics of the stifle joint has been appreciated.[2]

The distal femoral intercondylar notch is almost completely filled by the cruciate ligaments and some fat. The

cranial cruciate ligament (CCL) and the caudal cruciate ligament (CaCL) both attach to the intercondyloid area of the tibia.[3–6] Although the length of both canine cruciate ligaments is nearly equal, their distal attachment points on the tibia are separated by almost twice the distance of their femoral origins.[7] Because of their anatomy and spatial arrangement, the cruciate ligaments provide primary ligamentous support for craniocaudal and axial stability of the stifle joint throughout the functional range of motion.[5] The CCL controls cranial drawer motion, whereas the CaCL acts as a major stabilizer against caudal drawer motion. Furthermore, the CCL is considered to fine-tune normal stifle joint kinematics.

Published reports have primarily focused on the CCL, seemingly because it is the most vulnerable and important ligament of the stifle joint.[3,8] Its morphologic features and relationships with other joint structures have been studied extensively and comparative studies reinforce the importance of the CCL in various mammals. Although species differences in CCL anatomy, physiology, and biomechanics are minor,[9] there are nevertheless differences and information should clearly reference the species source. Unfortunately, this distinction has not always been clearly stated in veterinary reports, leading the less critical reader to believe that much more is known about canine cruciate ligaments than is actually so. Understanding the normal anatomy of the stifle joint, and in particular the normal cruciate anatomy, is essential for diagnosis and rational treatment of CCL rupture.

FIBER BUNDLE ANATOMY

The cruciate ligaments are not just a single-strand configuration of longitudinally orientated collagen fibers.[5] In humans and dogs, they contain twisted collagenous fascicles and fiber bundles that are subdivided into fascicles, subfascicular units, fibers, and fibrils.[10,11] The canine CCL and CaCL can each be divided into 2 functional components because they have individual attachment zones.[5]

The CCL originates on the axial aspect of the lateral femoral condyle, very close to the articular margin. It extends diagonally across the joint space and attaches to the cranial intercondyloid area of the tibial plateau.[3,5,12] The proximal attachment site is bordered cranially by the cranial meniscotibial ligament of the medial meniscus and caudally by the cranial meniscotibial ligament of the lateral meniscus.[4,13,14] The canine CCL is the narrowest in its mid region and fans out proximally and distally.[13] Its shape changes through the normal range of motion of the stifle joint,[5,13] and the decrease in cross-sectional area is also the greatest at the mid region when forces are acting.[15] CCL length is positively correlated with canine

body weight; taking the average length of its cranial and caudal borders, the mean length of the canine CCL has been reported as 13.5–18.7 mm.[16–18]

The canine CCL runs cranially, medially, and distally in an outward spiral as it passes from the femur to the tibia,[12,19] resulting in a gross appearance of distinct anatomic components. Two demonstrably separate bundles are apparent in the dog (Fig 1).[5,13] These components are termed craniomedial and caudolateral, based on their relative attachment sites onto the tibial plateau. The craniomedial subdivision is the most spiral and the longest, yet smaller component[13] and arises more proximally from the femur and inserts more cranially on the tibial attachment area, compared with the caudolateral subdivision.[5,13] The fibers of the caudolateral component originate from the most lateral and distal part of the attachment area of the lateral femoral condyle, have a straighter path, and insert on the most caudal region of the tibial attachment area.[5,13]

The geometry of the reciprocal attachment sites of the component parts of the CCL ligament is responsible for their slackening and tensioning caused by the relative rotations of their attachments through the normal functional range of motion of the stifle joint.[5] Different morphologic components of the CCL seemingly attach to different locations within the attachment area of each
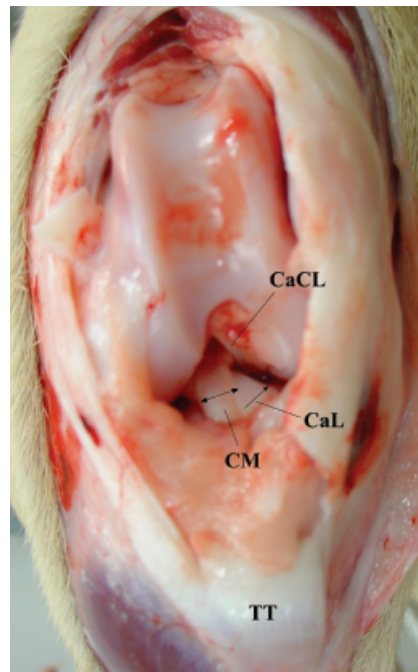

Fig 1. Cranial view of the stifle joint. The cranial cruciate ligament (CCL) in the dog is composed of 2 separate bundles. CM Craniomedial bundle of the CCL, CaL Caudolateral bundle of the CCL, CaCL Caudal cruciate ligament, TT Tibial tubercle.

bone. Reciprocal tension and thus functional difference occur because their individual attachment sites rotate and translate relative to each other.[5] In stifle extension, the long axis of the CCL is aligned with the long axis of the femur. The femoral attachments of both craniomedial and caudolateral components are almost perpendicular to the joint surface and both are taut.[13] In flexion, the craniomedial component of the CCL curves and twists around the caudolateral component while the femoral attachment site moves distally and caudally.[5,13] This re-orientation of femoral attachment sites during stifle flexion results in an increased distance between the sites of femoral origin and tibial attachment of the craniomedial component, causing tension in this component during flexion. The relative relaxation of the fibers of the caudolateral component can be explained by the same principles, because the bone attachment sites move closer together as the stifle is flexed; thus, the caudolateral component is slack in flexion.[5,13]

The canine CaCL is slightly longer and broader than the CCL.[3–6,20] Even its collagen fibrils are thicker compared with the CCL.[21] The total midsection diameter of CaCL is the smallest as it fans out from the center, making the femoral and, to a lesser extent, the tibial attachments larger.[4] The CaCL also has 2 components although they are less distinct and often inseparable.[13,20] The cranial component is larger than the caudal component.[22] The restraining effect of both components of the CaCL also varies with stifle position, and they perform reciprocal functions at different angles of flexion because of the location of their attachment sites.[5,20] Similar to the CCL, the geometry of the femoral attachment is largely responsible for ligament tensioning[13]; the cranial component is taut in flexion and loose in extension, whereas these states are reversed for the caudal component.[5,20]

FUNCTIONAL ANATOMY

There is a ranked hierarchy of structures neutralizing specific forces acting on the stifle joint and resisting different kinds of joint laxity. Stifle function is complemented by static support from a complex (passive) restraining system consisting of bony and musculotendinous structures, menisci, and several ligaments. Furthermore, muscular forces and joint compression contribute to joint stability.[23,24] The cruciate ligaments have specific functions that are directly related to their anatomic locations and orientations within the stifle joint. Although the main functions of other intra-articular and peri-articular structures and ligaments differ from those of the cruciate ligaments, they act complementary as constraints of stifle joint motion in various planes.[14,25]

The CCL has to provide a stabilizing effect of the tibia on the femur throughout the whole range of motion, resisting forces that would cause the tibia to translate cranially relative to the femur and, to a lesser degree, resisting forces that would cause tibial rotation during flexion of the stifle joint.[5,22,26] In dogs, both cruciate ligaments have 2 components that behave independently and differently from each other throughout loading.[5] Every change in joint angle alters the tension in the separate bands as some fibers are stressed and others are not. This feature contributes to the CCL's ability to withstand the multi-axial stresses of normal function and range of motion. Most assessments of ligamentous function have been based on the changes in laxity observed after sequential cutting of selected ligaments in cadaveric human knees.[27–30] The actual proportion of their combined contributions to sustaining load varies with the angle of stifle flexion. With the stifle in extension, the entire CCL is taut and thus both components limit cranial translation of the tibia relative to the femur.[5,13] Because of combined interactions, an isolated lesion of a component part of the CCL does not necessarily provoke clinically detectable instability.[27,28] In the human knee, the CCL is the sole structure to limit cranial drawer motion near full extension of the joint, as tension in the hamstring muscles lacks to provide extra restraint.[31] It is probably much less so in the canine stifle joint where maximal extension is far less than 180°. The craniomedial component of the CCL is taut during the whole range of stifle motion and is the major contributor to craniocaudal stability in stifle flexion.[8,26] The relaxed caudolateral component only acts as a weak secondary restraint to this unidirectional cranial translating force and in fact, only contributes when the craniomedial band is damaged or severely stretched. Other joint structures seemingly contribute less to craniocaudal stability during flexion.[18]

In subtle balance with the capsular structures, the collateral ligaments, muscles, the condylar geometry, and joint surface contact, the cruciate ligaments control and produce rotation of the tibia relative to the femur.[3,8,20,22,29,32] An increased angle of stifle flexion is accompanied by increased internal rotation of the tibia if unrestricted.[8,14,32,33] Part of the valgus load is transformed into an axial rotatory force as the lateral collateral ligament begins to relax.[22,34] As the stifle flexes, the cruciate ligaments are not only wrapped upon each other but also spiral on themselves.[3,5,22] The higher strain in the ligaments also limits the amount of normal internal rotation of the tibia on the femur.[5,12,20,22] As the stifle extends, the lateral collateral ligament tightens and the lateral femoral condyle moves cranially, causing external rotation of the tibia. This motion has classically been described as the screw-home mechanism.[32] In extension, the medial and lateral collateral ligaments become the

primary restraints of rotation, and the cruciate ligaments provide only a secondary check from the tension in both ligaments.[3,12,17] No singular limiting effect on external rotation is provided by the cruciate ligaments in dogs, not even as secondary restraint structures.[5,20,32] By external rotation of the tibia, the cruciate ligaments start to untwist, and strain decreases.[8,12,32]

Axial tibial rotation of the canine stifle joint is coupled with varus–valgus rotation.[34] In a stable stifle joint, the collateral ligaments are considered the primary ligamentous structures providing sideways restraint when stifle joint motion is restricted. In fact, they share their function with other joint structures and ligaments.[32,34] Both cruciate ligaments together are important secondary restraints against varus and valgus angulation. Stresses on the cruciate ligaments during medial and lateral opening of the joint space generally increase slightly with the degree of flexion of the stifle joint, as the collateral ligaments begin to relax as the stifle joint is flexed.[32,34] In humans and dogs, the cruciate ligaments become primary restraints if there is loss of collateral ligament support.[28,32] In the fully hyperextended human knee, the cruciate ligaments can prevent joint opening by themselves.[28] When varus forces act, the CCL has to sustain larger strains than the CaCL although these forces are still much lower than those sustained by the lateral collateral ligament.[28] For medial restraint (valgus force), the relative contribution of the CaCL becomes greater with increases in flexion angle.[28,34]

Overextension is prevented by tension in the cruciate ligaments,[3] where the CCL acts as the primary restraint with both the craniomedial and the caudolateral components taut at full extension.[5,13] The caudolateral component of the CCL is under the greatest tension in extension,[13] and is thus the primary contributor to restraining hyperextension. The slightly longer caudal component of the CaCL can only be considered a secondary restraint.[3,5,22]

Hyperflexion of the stifle normally will not occur because of contact between the thigh muscles and the gastrocnemius muscle.[3] The cruciate ligaments spiral on themselves, and they are naturally twisted upon each other when the stifle is flexed.[3,5,22] During the stance phase, the angle of the stifle joint is ~140° in dogs. The twist of both cruciate ligaments upon each other prevents stifle collapse during stance.[5] Quadriceps contraction would cause cranial tibial subluxation at this flexion angle but by loading of an intact CCL this is prevented.[24]

Stifle joint stability in humans and dogs is dynamic as far as muscle control (active forces) is concerned.[4,23–25] On the cranial aspect of the stifle joint, the quadriceps muscle and the patellar tendon provide support. The popliteal muscle as well as the hamstring muscles and gastrocnemius provide additional support caudally.[35] In cats, through CCL-muscle reflexes, direct loading of the CCL causes quadriceps muscle inhibition and simultaneously increases hamstring muscle activity to reduce CCL loading.[36] Joint compression and muscle actions greatly contribute to joint stabilization.[24] Cranial tibial thrust is generated during weight bearing by the slope of the tibial plateau and by tibial compression because of musculotendinous attachments such as the tendon of the biceps femoris.[25,33] According to Slocum and Devine, the CCL is only a backup mechanism for control of cranial projection of the proximal aspect of the tibia as a dog walks, and experiences no stresses as long as the cranial tibial thrust is effectively opposed by the caudal pull of the biceps femoris and hamstring muscle group.[23,26] Only when these active muscle forces are insufficient to counteract cranial translation of the tibia will the CCL provide the first passive restraint. There is no perfect balance at all times and because of the functional cranial to caudal slope of the tibial plateau, the CCL must intermittently resist cranial tibial thrust.[26,33] A lesser tibial plateau slope is thought to account for less CCL strain because cranial translation is prevented by decreasing cranial tibial thrust.[23,26,37–39] However, a more recent study reported that the standing tibial plateau angle is not significantly different from a plane parallel to the ground in most dogs; furthermore, it failed to demonstrate differences in angles between dogs with and without risk of cruciate disease.[40]

In contrast to the individual functions of the CCL, selective transection of only one component of the CaCL does not result in caudal drawer in the canine stifle joint for any joint angle.[5,20] The importance of the CaCL in stability of the canine stifle joint is far less than that of the CCL although its exact contribution remains unresolved.[41] The CaCL is usually larger than the CCL; therefore, it seems unlikely that in the dog it does not have some important function. Prevention of caudal displacement of the tibia on the femur seems the only primary role of the CaCL.[5,8] In a flexed stifle joint, the cranial component of the CaCL is a primary restraint against caudal instability because of looseness of the collateral ligaments in this joint position.[20,22,32]

MICROANATOMY AND ULTRASTRUCTURE

Both cranial and caudal cruciate ligaments are covered by a fairly uniform fold of synovial membrane which incompletely divides the stifle joint in the sagittal plane.[6,42] This synovial tissue continues over the horns of the menisci.[43] These enveloping epiligamentous membranes consist mainly of dense connective tissue, small fibroblasts, and some adipocytes;[13,44] an intima and a thin sub-intimal layer can be distinguished. The intima is

a single layer of synoviocytes and the subintimal layer is areolar tissue containing small vascular structures.[17] Compared with the cruciate ligaments, the enveloping synovial membrane is relatively cellular.[13] Synovial lining does not occur on the surfaces in direct contact with the other cruciate ligament.[17] This synovial envelope makes the cruciate ligaments extrasynovial structures, protected from the degradative effects of the synovial environment, even though they are intra-articular.[5,6] The synovial envelope covering the CCL originates caudally at the intercondylar notch and extends to the cranial aspect of the tibial attachment.[45] At that point, the epiligamentous tissue communicates with a fold of the distal joint capsule.[45] The CaCL is ensheathed by 2 folds of synovial membrane. The cranial envelope originates proximally from the cranial aspect of the joint capsule, while distally the caudal fold originates from the caudal aspect of the joint capsule.[45]

Grossly, the canine cruciate ligaments each have 2 components.[5,13] This uncomplicated and distinct subdivision does not carry through to their intricate microarchitecture.[13] Each ligament component is a multifascicular structure, and contains many wavy fascicular subunits. The fascicles located at the periphery of the CCL appear to follow a spiral path of waviness around the fascicle axis.[11,30,46] In the canine CCL, there is a great variability in the elliptical-shaped fascicle size, as fascicles may be composed of 1–10 subfascicles, subdivided by loose endoligamentous tissue.[11,13] The subfascicles contain bundles of collagen fibers. Each fiber bundle is not oriented such that it is isometric during stifle joint motion.[30] Every subtle 3-dimensional change in stifle joint position recruits fibers differently.[47] Individual fibers change length by straightening their crimp as they are recruited into tension. This change is not visible at a gross anatomic level, but is confirmed by histologic assessment.[11,30] At the osseous attachment sites of the CCL, the collagen fibers are not arranged entirely parallel to the longitudinal axis of the ligament and, especially in younger specimens, columns of chondroid cells do penetrate into the CCL (Fig 2B).[12,45] Where the CCL and CaCL are in contact, the collagen fibers are more dense and oriented tangential to the surface instead of parallel to the long axis.[17] Those fibers maintain an orientation tangential to the surface of contact, even when the cruciate ligaments start to twist about each other.[17] Fibers are formed by fibrils, which are composed of organization of repeated collagen subunits.[13,17,44,45] Collagen fibril morphology and architecture is also characterized by uniform crimp parallel to the long axis of the fascicle (Fig 2A).[48,49] The internal collagen fibrils are nearly straight, whereas the fibrils undergo a maximum crimp at the fascicular periphery.[12,45] The collagen fibrils are the smallest visible structures on electron microscopy.[10,11,50]
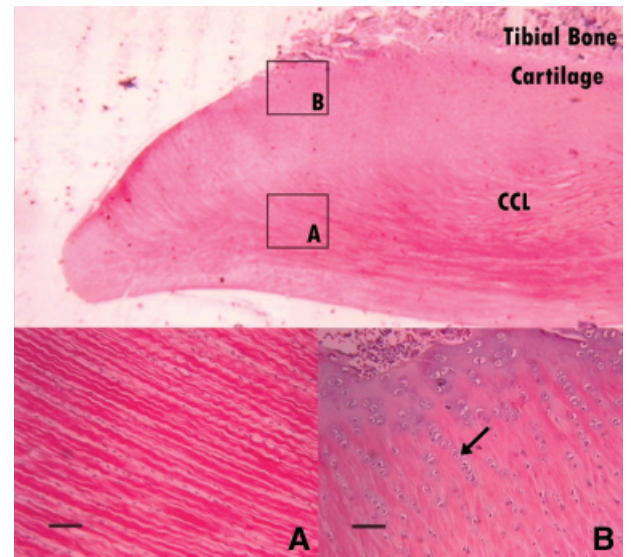

Fig 2.   Normal cranial cruciate ligament (CCL) of a 4-month-old Riezenschnauzer, harvested at its tibial attachment site (H&E stain). (A) Along the CCL, dense collagen is aligned parallel to the longitudinal axis of the ligament (bar = 100 µm). The collagen fibers have a recurrent crimped pattern. (B) At the osseous attachment site of the CCL, the collagen fibers are not arranged entirely parallel to the long axis of the ligament. Columns of chondroid cells (arrow) do penetrate into the CCL (bar = 100 µm).

Ultrastructurally, the CCL is a heterogenic composite structure formed by an extracellular matrix composed of macromolecules with highly specific arrangements and interactions.[44,51] Collagen is the chief macromolecule prevalent in the framework of the CCL. Type I collagen comprises >90% of the collagen content of the CCL, with the remainder being type III collagen.[52,53] The molecules are produced by the fibroblasts in the loose supporting connective tissue. The cells are present in long parallel columns between the collagen fibers, their axes parallel to the surrounding collagen fibers. Neurovascular components follow the same longitudinal orientation.[13,42,45,46] Besides fibroblasts, the cell population also consists of various stages of chondrocyte-like cells.[17,49,54]

MICROVASCULAR SUPPLY

The major vascular contribution to the center of the stifle joint occurs from branches of the middle genicular artery,[55–57] which arises from the popliteal artery, penetrates the caudal joint capsule, and passes craniodistally to the fossa intercondylaris, running cranially between the cruciate ligaments (Fig 3).[58] The vascular structures to the proximal part of the CCL are more numerous and

the middle genicular artery and from some branches of the other genicular arteries.[55,57] The cruciate ligaments are also nourished by passive permeation from the synovial fluid.[61,62]

The blood supply to both cruciate ligaments is predominantly of soft tissue origin; the contribution from the osseous attachments is negligible.[42,56,57,63,64] The infrapatellar fat pad and the well-vascularized synovial membranes that form an envelope around the cruciate ligaments are the most important sources of vessels and the major pathway for delivery of nutrients.[42,45,59,61,63,64] The synovial vessels arborize into a finely meshed network of epiligamentous vessels that ensheath the cruciate ligaments throughout their entire length (Figs 4 and 5).[42,64] In general, the vascular arrangement and structural characteristics of the vasculature inside the CaCL and the CCL are similar.[42,45,64] In the inner part of the cruciate ligaments, around and along the bundles of collagen fibers, an endoligamentous vascular network courses in the supporting connective tissue.[42,45] The larger vessels, usually one artery accompanied by two veins, mainly course in a longitudinal direction both proximally and distally and lie parallel to the collagen fascicles.[45] Some of them have a tortuous path in the interfascicular areolar tissue.[57] Only small capillaries branching from the longitudinal endoligamentous vessels, running in a transverse direction, encircle the collagen bundles.[45] The core of the midportion of the CCL is less well vascularized compared with the remainder of the ligament.[12,17,42,45,59,63]

Anastomoses exist between extra- and intraligamentous blood networks.[42,45,64] Epiligamentous vessels penetrate transversely into the cruciate ligaments (Fig 5 A).[64] Their branches ramify and anastomose with the endo-
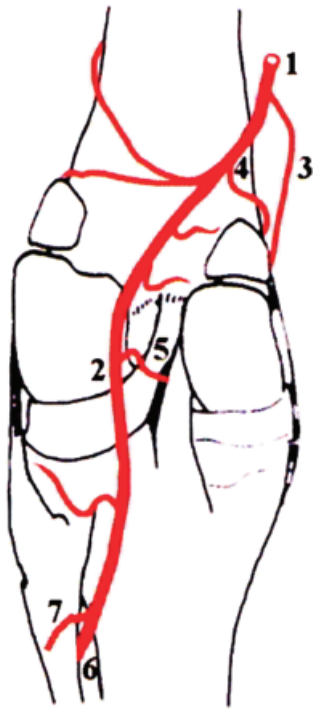

Fig 3. Caudal view of the major blood supply to the stifle joint in the dog. (1) Femoral artery, (2) popliteal artery, (3) descending genicular artery, (4) proximal medial genicular artery, (5) middle genicular artery, (6) cranial tibial artery, (7) caudal tibial artery.

have a larger diameter compared with those on the tibial side.[12,45] Most of these vascular structures originate from a branch of the middle genicular artery and from some branches of the distal genicular arteries.[55–57,59,60] Also for the CaCL most of the vessels originate from branches of
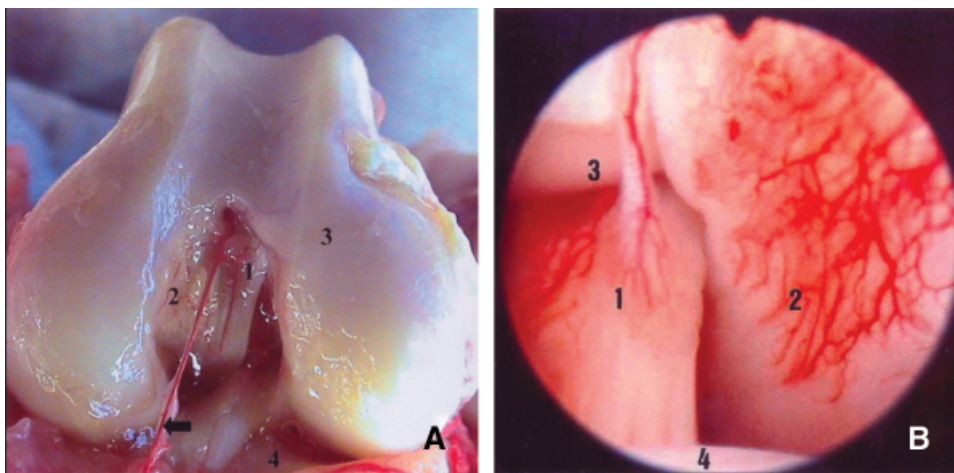

Fig 4. Superficial vascularization of normal cruciate ligaments in the dog. (A) Macroscopic view after injection of latex in a canine cadaver specimen. (B) Arthroscopic view of a stifle joint in a normal dog. (1) Cranial cruciate ligament (2) caudal cruciate ligament (3) lateral femoral condyle, (4) tibial plateau. Arrow, artery originating from infrapatellar fat pad.
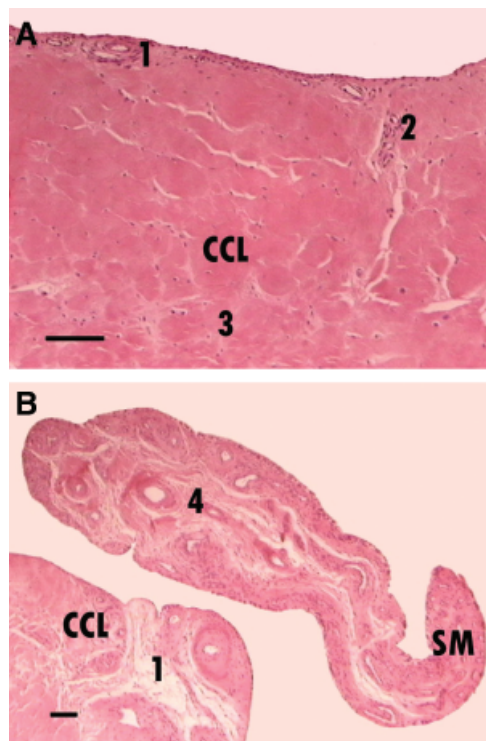
Fig 5. Normal cranial cruciate ligament (CCL) of an adult dog (H&E stain). (A) The CCL is ensheathed by epiligamentous vessels (bar = 100 μm). (B) The well-vascularized synovial membrane (SM) forms an envelope over the CCL (bar = 100 μm). (1) Epiligamentous vessels, (2) Anastomosis between epiligamentous and endoligamentous vessels, (3) hypovascular zone, (4) synovial vessels.

ligamentous vessels. There are numerous endosteal vessels at the ligamentous–osseous junctions; however, communications with intrinsic endoligamentous vessels are quite poor, especially at the tibial attachment of the CCL where most of the endosteal vessels seem to terminate in subchondral loops instead of crossing the ligamentous–osseous junction.[42,45,61,64,65] A number of endosteal vessels communicate with the epiligamentous vascular network overlying the CCL.[45] Vessels from the menisci anastomose with the epiligamentous vascular plexus.[45]

The web-like network of epiligamentous and synovial vessels surrounding the CaCL appear to be slightly more extensive than the vascular plexus around the CCL;[42,59,63] however, the CaCL does not have a more abundant intrinsic vascular supply than the CCL.[10,56,57,60] Endosteal vascular communications are present proximally and distally, although they are rare.[45,65]

INNERVATION

Three major articular nerves arise from the saphenous nerve, tibial nerve, and common peroneal nerve to in-

nervate the periarticular tissues of the canine stifle joint (Fig 6).[66] In each of the studied species, the main trunk of the nerve bundles is found at the femoral end of the cruciate ligaments, an area that becomes strained only at high loads.[10,66–68] Other nerves may contribute afferent fibers to a variable extent to the cruciate ligaments.[66,69]

In dogs, the medial articular nerve, which branches from the saphenous nerve in the mid thigh region, is the largest supply to the stifle joint. Some of its branches course through the infra-patellar fat pad to terminate within the proximal or distal attachments of the cruciate ligaments or within the meniscal horns.[66] Other branches of the medial articular nerve pass cranially through the joint capsule to supply an extensive innervation of the femoral attachment of the CaCL.[66] The caudal articular nerve is variably present in dogs. Its branches arise either directly from the tibial nerve or from a muscular branch of the tibial nerve.[66] The caudal articular nerve runs to the caudal aspect of the joint capsule, where it may communicate with branches of the medial articular nerve.[66] The lateral articular nerve branches from the common peroneal nerve at the level of the fibular head, deep to the biceps femoris muscle, and supplies the lateral aspect of the stifle joint.[66]

Nerves of differing sizes are located in the richly vascularized synovial tissue covering the cruciate ligaments.[46,70] From this peripheral synovium, axons radiate toward the center of the ligaments.[70] Within the cruciate ligaments, most nerves course along the epiligamentous and endoligamentous blood vessels in the interfascicular areolar spaces. It is believed that their function is primarily associated with autonomic nervous regulation of blood flow[10,46] and pain perception.[71]

In 1992, the first neurohistologic studies of the canine cruciate ligaments were published.[70,72] Various types of sensory nerve endings (receptors and free nerve endings) were identified in the middle of the ligaments, well beneath the synovial sheath.[70] In the dog, the highest number of mechanoreceptors was found in the proximal third of the CCL, and the lowest in the distal third.[71] This finding is in contrast to human and feline CCLs where the middle third of the cruciate ligaments has less sensory endings.[69,73–75]

The sensory network of the cruciate ligaments has an important role in the neurosensory system around the stifle joint, providing information about joint movement and position as well as noxious events.[73,76] Mechanoreceptors located near the surface of the cruciate ligaments respond to longitudinal extension and deformation of the ligament.[72,77,78] Mechanoreceptors within the substance of the cruciate ligament activate local reflex patterns to protect the ligament from tearing and warn against possible joint damage.[69,75] A CCL-muscle reflex has been reported in cats, dogs, and humans.[46,68,73,75,76,79] By
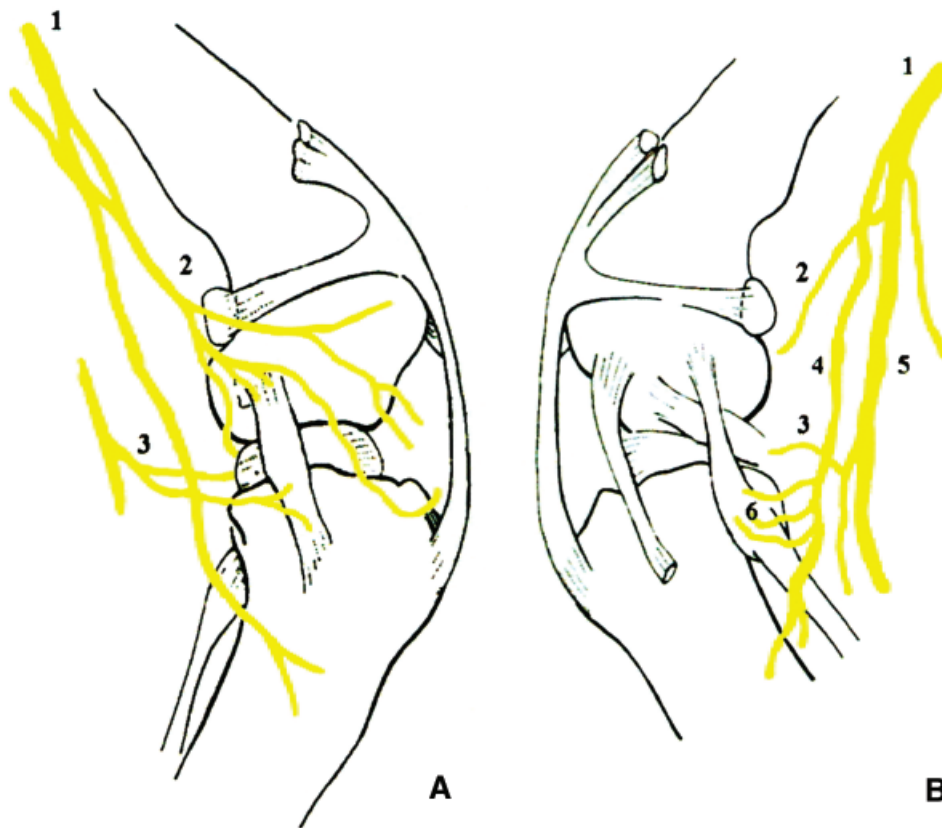
Fig 6.   Major nerve supply to the stifle joint in the dog. (A) Medial view, (B) lateral view, (1) saphenous nerve, (2) medial articular nerve, (3) posterior articular nerve (4) common peroneal nerve, (5) tibial nerve, (6) lateral articular nerve.

reflex arches, periarticular muscle groups are triggered to contract to avoid ligamentous injury by extremes of motion.[46,68,73,75,76] It is not a matter of conscious perception, but rather a reaction to mechanically evoked electrical signals. By this potent reflex, the sensory system of the cruciate ligaments is able to contribute to the functional stability of the joint by modifying the stiffness of the surrounding muscles.

Based on limited information acquired from humans, the synovia seem to serve as primary pain receptors.[75] The cruciate ligaments themselves are considered relatively insensitive to pain, although some sensation of pain might also be transmitted by a small population of free nerve endings that ramify in the cruciate ligaments.[46,78] Comparable information for cats or dogs was not identified.

PATHOGENESIS OF CCL DISEASE

The CCL is a critical stabilizer of the stifle joint, and CCL rupture is the most common cause of stifle joint lameness in dogs. CCL rupture can occur after trauma;

however, in most dogs, mid-substance rupture occurs under conditions of normal loading because of pre-existing progressive fatigue and is often bilateral. Because dogs in the early phase of cruciate disease might have a stable stifle joint on palpation, the condition is not readily diagnosed.

With extensive knowledge of the normal microanatomy, subtle changes might be detectable in the early phase of cruciate disease in dogs, facilitating selection of appropriate medical (or surgical) treatments. An accurate understanding of the fiber bundle and functional anatomy is imperative if reconstructions are to restore normal stifle joint physiology. The goal of reconstructive methods should not only be to alleviate the existing instability of the unstable stifle joint but also to mimic normal kinematics as closely as possible. In addition to its biomechanical function as a primary restraint to cranial translation, the proprioceptive functions of the normal CCL are undoubtedly important for prevention of joint damage as well as for postoperative rehabilitation. Only the first step toward understanding the role of mechanoreceptors in proprioception is made by identifying their distribution in the canine CCL, and further research is

certainly needed. Knowledge of the exact function of the CCL in neuromuscular control around the stifle joint could possibly explain the progression of OA after CCL damage.

In the search for the mechanisms for pathologic CCL rupture, most studies have focused on the affected stifle joint after CCL rupture. This is a major limitation when examining degenerative and immunologic phenomena involved in CCL degeneration because these joints have reached the end stage of the disease. Prospective long-term studies in the contralateral joint of unilaterally affected dogs may bypass this flaw.

Cruciate disease is likely to be multi-factorial with no single factor accounting for all aspects of its progression. Furthermore, pathogenesis may differ for different sub-groups of cruciate patients. The classic picture of old, sedentary patients is more and more complemented with that of young, active large-breed dogs.

The loads experienced by the CCL may be influenced by several factors. It has been suggested that steep tibial plateau angles predispose to CCL rupture. Nevertheless, many dogs with a steep angle do not seem to develop cruciate disease.[40] It is known that structural properties of the CCL are affected by age, more commonly in heavier dogs where onset of the degenerative changes occurs earlier.[12,17]

Dogs with CCL rupture typically have inflammatory changes in the synovial membrane and the CCL epiligament, as well as in the synovial fluid.[48] Although further studies are needed to evaluate whether this inflammation precedes actual CCL rupture, Muir et al[49] recently hypothesized that the inflammation develops in the early phase of cruciate disease and before the development of stifle instability. It has also been shown recently that the epiligamentous synovial membrane reveals many small holes that would allow infiltration of the CCL by synovial fluid.[64]

Joint inflammation, mechanical loading, ligament microinjury, and ischemia may influence cellular metabolism, resulting in matrix changes. Progressive mechanical overload diminishes the typical crimped structure of the collagen fibrils seen in intact CCLs, and further tensile loading causes disruption of the ligament fascicles.[48,80] Increased collagen remodeling predisposes the CCL to increased laxity leading to progressive OA.

It has been postulated that vascular mechanisms are important in the pathophysiology of cruciate disease. The blood supply to the core region of the CCL is already marginal and tissue hypoxia because of microinjury further weakens the midsubstance of the ligament. Extensive tissue repair processes in response to hypoxia occur in the epiligamentous tissue, which fails to bridge the site of injury.[48] A microvascular study in canine CCLs provided evidence that the blood flow in the CCL is affected by disturbance of joint fluid and that the blood–CCL barrier of the endothelium is not very effective.[64]

Immune-mediated phenomena may play a role in CCL degradation. Several studies support the hypothesis that the inflammation within the synovium found in dogs with CCL rupture is, at least in part, immune mediated.[49,81,82] Because intact cruciate ligaments are in fact extra-synovial because of a protective layer of synovium, collagen type I is normally obscured from immunologic surveillance and therefore has the potential to act as a self-antigen when it is exposed after microinjury. Antibodies to collagen type I have been found in the synovial fluid of dogs with CCL rupture, but it remains to be elucidated whether they are not just a secondary phenomenon.[81] The search for collagen reactive T-cells as a proof of cellular immune reaction is ongoing.[83]

There is clinical evidence for major underlying biochemical processes. Collagen might be weakened by biochemical factors such as collagenases and gelatinases. Expression of the matrix metalloproteinases (MMPs) that are able to degrade collagen has been studied in dogs with cruciate disease.[82] MMP targeting may offer a new therapeutic approach to canine cruciate disease. Anti-inflammatory medical therapy may possibly slow down further degeneration of the CCL, ameliorate joint degradation, and eventually prevent rupture in the contralateral stifle joint.

REFERENCES

1. Palmer I: On injuries of the ligaments of the knee joint. A clinical study. Acta Chir Scand 53(Suppl) 1938
2. Arnoczky SP, Brinker WO: The functional anatomy of the knee: a comparative analysis between the dog and man, in *Proceedings Comparative aspects on hip and knee joint lesions in dog and man*, Uppsala Sweden, 16–19 September 1992, pp 25–29
3. Singleton WB: The diagnosis and surgical treatment of some abnormal stifle conditions in the dog. Vet Rec 69:1387–1394, 1957
4. Rudy RL: Stifle joint, in Archibald J (ed): Canine Surgery. Santa Barbara, CA, American Veterinary Publications Inc, 1974, pp 1104–1115
5. Arnoczky SP, Marshall JL: The cruciate ligaments of the canine stifle: an anatomical and functional analysis. Am J Vet Res 38:1807–1814, 1977
6. Evans HE, Christensen GC: Ligaments and joints of the pelvic limb, in Evans HE, Christensen GC (eds): Miller's Anatomy of the Dog (ed 2). Philadephia, PA, Saunders, 1979, pp 225–268
7. Badoux DM: The geometry of the cruciate ligaments in the canine and equine knee joint, a Tchebychev mechanism. Acta Anat 119:60–64, 1984
8. Arnoczky SP, Marshall JL: Pathomechanics of cruciate and meniscal injuries, in Bojrab MJ (ed): Pathophysiology of

Small Animal Surgery. Philadelphia, PA, Lea & Febiger, 1981, pp 590–603

9. Radford WJP, Amis AA, Stead AC: The ovine stifle as a model for human cruciate ligament surgery. Vet Comp Orthop Traumatol 9:134–139, 1996

10. Arnoczky SP: Anatomy of the anterior cruciate ligament. Clin Orthop 172:19–25, 1983

11. Yahia L-H, Drouin G: Microscopical investigation of canine anterior cruciate ligament and patellar tendon: collagen fascicle morphology and architecture. J Orthop Res 7:243–251, 1989

12. Zahm H: Die Ligamenta decussata in gesunden und arthrotischen Kniegelenk des Hundes. Kleintierprax 10:38–47, 1965

13. Heffron LE, Campbell JR: Morphology, histology and functional anatomy of the canine cranial cruciate ligament. Vet Rec 102:280–283, 1978

14. Robins GM: The canine stifle. Anatomy, function and kinesiology, in Whittick WG (ed): Canine Orthopaedics. Philadelpia, PA, Lea & Febiger, 1990, pp 693–702

15. Alm A, Ekström H, Strömberg B: Tensile strength of the anterior cruciate ligament in the dog. Acta Chir Scand 445(Suppl): 15–23, 1974

16. Dorlot J-M, Ait Ba Sidi M, Tremblay GM, et al: Load elongation behavior of the canine anterior cruciate ligament. Trans ASME 120:190–193, 1980

17. Vasseur PB, Pool RR, Arnoczky SP, et al: Correlative biomechanical and histologic study of the cranial cruciate ligament in dogs. Am J Vet Res 46:1842–1854, 1985

18. Wingfield C, Amis AA, Stead AC, et al: Cranial cruciate stability in the Rottweiler and racing Greyhound: an in vitro study. J Small Anim Pract 41:193–197, 2000

19. Haut RC, Little RW: Rheological properties of canine anterior cruciate ligaments. J Biomech 2:289–298, 1969

20. Harari J: Caudal cruciate ligament injury. Vet Clin North Am: Sm Anim Pract 23:821–829, 1993

21. Brunnberg L: Klinische Untersuchungen zu Ätiologie und Pathogenese der Ruptur des Ligamentum cruciatum craniale beim Hund. 2. Mitteilung: Zur Ätiologie und Diagnose der Ruptur des Ligamentum cruciatum craniale beim Hund. Kleintierprax 34:445–449, 1989

22. Hulse DA, Shires PK: The stifle joint, in Slatter DH (ed): Textbook of Small Animal Surgery. Philadelphia, PA, Saunders, 1985, pp 2193–2235

23. Slocum B, Devine T: Tibial plateau leveling osteotomy for repair of cranial cruciate ligament rupture in the canine. Vet Clin North Am: Sm Anim Pract 23:777–795, 1993

24. Korvick DL, Pijanowski GJ, Schaeffer DJ: Three-dimensional kinematics of the intact and cranial cruciate ligament-deficient stifle of dogs. J Biomech 27:77–87, 1994

25. Markolf KL, Bargar WL, Shoemaker SC, et al: The role of joint load in knee stability. J Bone Joint Surg (Am) 63A:570–585, 1981

26. Slocum B, Devine T: Algorithm for diagnosis and treatment of the stifle for cranial cruciate ligament rupture, in Bojrab MJ (ed): Current Techniques in Small Animal Surgery. Baltimore, MD, Williams & Wilkins, 1998, pp 1187–1193

27. Furman W, Marshall JL, Girgis FG: The anterior cruciate ligament. A functional analysis based on postmortem studies. J Bone J Surg (Am) 58-A:179–185, 1976

28. Grood ES, Noyes FR, Butler DL, et al: Ligamentous and capsular restraints preventing straight medial and lateral laxity in intact human cadaver knees. J Bone J Surg (Am) 63-A:1257–1269, 1981

29. Fukubayashi T, Torzilli PA, Sherman MF, et al: An in vitro biomechanical evaluation of anterior–posterior motion of the knee. Tibial displacement, rotation, and torque. J Bone J Surg (Am) 64-A:258–264, 1982

30. Amis AA, Dawkins GPC: Functional anatomy of the anterior cruciate ligament. Fiber bundle actions related to ligament replacements and injuries. J Bone J Surg (Br) 73-B:260–267, 1991

31. More RC, Markolf KL: Measurement of stability of the knee and ligament force after implantation of a synthetic anterior cruciate ligament. In vitro measurement. J Bone J Surg (Am) 70A:1020–1031, 1988

32. Vasseur PB, Arnoczky SP: Collateral ligaments of the canine stifle joint: anatomic and functional analysis. Am J Vet Res 42:1133–1137, 1981

33. Slocum B, Devine T: Cranial tibial thrust: a primary force in the canine stifle. J Am Vet Med Assoc 183:456–459, 1983

34. Monahan JJ, Grigg P, Pappas AM, et al: In vivo strain patterns in the four major canine knee ligaments. J Orthop Res 2:408–418, 1984

35. Aron DN: Traumatic dislocation of the stifle joint: treatment of 12 dogs and one cat. J Am Anim Hosp Assoc 24:333–340, 1988

36. Solomonow M, Baratta R, Zhou BH, et al: The synergistic action of the anterior cruciate ligament and thigh muscles in maintaining joint stability. Am J Sports Med 15:207–213, 1987

37. Morris E, Lipowitz AJ: Comparison of tibial plateau angles in dogs with and without cranial cruciate ligament injuries. J Am Vet Med Assoc 218:363–366, 2001

38. Warzee CC, Dejardin LM, Arnoczky SP, et al: Effect of tibial plateau leveling on cranial and caudal tibial thrust in canine cranial cruciate deficient stifles: an in vitro experimental study. Vet Surg 30:278–286, 2001

39. Reif U, Hulse DA, Hauptman JG: Effect of tibial plateau leveling on stability of the canine cranial cruciate-deficient stifle joint: an in vitro study. Vet Surg 31:147–154, 2002

40. Wilke VL, Conzemius MG, Besancon MF, et al: Comparison of tibial plateau angle between clinically normal Greyhounds and Labrador Retrievers with and without rupture of the cranial cruciate ligament. J Am Vet Med Assoc 211:1426–1429, 2002

41. Arnoczky SP: Surgery of the stifle—the cruciate ligaments (Part I). Compend Contin Educ Pract Vet 2:106–116, 1980

42. Arnoczky SP, Rubin RM, Marshall JL: Microvasculature of the cruciate ligaments and its response to injury. An experimental study in dogs. J Bone J Surg 61A:1221–1229, 1979

43. Arnoczky SP, Warren RF: The microvasculature of the meniscus and its response to injury. An experimental study in the dog. Am J Sports Med 11:131–141, 1983

44. Jackson DW, Heinrich JT, Simon TM: Biologic and synthetic implants to replace the anterior cruciate ligament. Arthroscopy 10:442–452, 1994

45. Alm A, Strömberg B: Vascular anatomy of the patellar and cruciate ligaments. A microangiographic and histologic investigation in the dog. Acta Chir Scand 445(Suppl): 25–35, 1974

46. Kennedy JC, Weinberg HW, Wilson AS: The anatomy and function of the anterior cruciate ligament. As determined by clinical and morphological studies. J Bone J Surg (Am) 56-A:223–235, 1974

47. Butler DL, Guan Y, Kay MD, et al: Location-dependent variations in the material properties of the anterior cruciate ligament. J Biomech 25:511–518, 1992

48. Hayashi K, Frank JD, Dubinsky C, et al: Histologic changes in ruptured canine cranial cruciate ligament. Vet Surg 32:269–277, 2003

49. Muir P, Schamberger GM, Manley PA, et al: Localization of Cathepsin K and Tartrate-resistant acid phosphatase in synovium and cranial cruciate ligament in dogs with cruciate disease. Vet Surg 34:239–246, 2005

50. Danylchuk KD, Finlay JB, Krcek JP: Microstructural organisation of human and bovine cruciate ligaments. Clin Orthop Rel Res 131:294–298, 1978

51. Figgie HE, Bahniuk EH, Heiple KG, et al: The effects of tibial–femoral angle on the failure mechanics of the canine anterior cruciate ligament. J Biomech 19:89–91, 1985

52. Amiel D, Frank C, Harwood F, et al: Tendons and ligaments: a morphological and biochemical comparison. J Orthop Res 1:257–265, 1984

53. Wildey GM, McDevitt CA: Matrix protein mRNA levels in canine meniscus cells in vitro. Arch Biochem Biophys 353:10–15, 1998

54. Riitano MC, Pfister H, Engelhardt P, et al: Effects of stimulus with proinflammatory mediators on nitric oxide production and matrix metalloproteinase activity in explants of cranial cruciate ligaments obtained from dogs. Am J Vet Res 63:1423–1428, 2002

55. Müller A: Topographisch-anatomische Grundlagen zu den Kniegelenkoperationen des Hundes. Inaugural-Dissertation, Universität Zürich, 1968.

56. Marshall JL, Arnoczky SP, Rubin RM, et al: Microvasculature of the cruciate ligaments. Phys Sports Med 7:87–91, 1979

57. Scapinelli R: Studies on the vasculature of the human knee joint. Acta Anat 70:305–331, 1968

58. de Vos NR, Simoens PJ: Angiologia, in Schaller O (ed): Illustrated Veterinary Anatomical Nomenclature. Stuttgart, Germany, Ferdinand Enke Verslag, 1992, pp 322–325

59. Tirgari M: The surgical significance of the blood supply of the canine stifle joint. J Small Anim Pract 19:451–462, 1978

60. Arnoczky SP: Blood supply to the anterior cruciate ligament and supporting structures. Orthop Clin North Am 16:15–28, 1985

61. Whiteside LA, Sweeney RE: Nutrient pathways of the cruciate ligaments. An experimental study using the hydrogen wash-out technique. J Bone Joint Surg (Am) 62-A:1176–1180, 1980

62. Skyhar MJ, Danzig LA, Hargens AR, et al: Nutrition of the anterior cruciate ligament. Effects of continuous passive motion. Am J Sports Med 13:415–418, 1985

63. Rubin RM, Marshall JL: Vascular anatomy of the cruciate ligaments in the dog—normal and injured states. Trans 22nd Annual Meeting of Orthop Res Soc 1:148, 1976

64. Kobayashi S, Baba H, Uchida K, et al: Microvascular system of anterior cruciate ligament in dogs. J Orthop 24:1509–1520, 2006.

65. Clancy WG, Narechania RG, Rosenberg TD, et al: Anterior and posterior cruciate ligament reconstruction in rhesus monkeys. J Bone Joint Surg (Am) 63-A:1270–1284, 1981

66. O'Connor BL, Woodbury P: The primary articular nerves to the dogs knee. J Anat 134:563–572, 1982

67. Kennedy JC, Alexander IJ, Hayes KC: Nerve supply of the human knee and its functional importance. Am J Sports Med 10:329–335, 1982

68. Schultz RA, Miller DC, Kerr CS, et al: Mechanoreceptors in human cruciate ligaments. A histological study. J Bone J Surg (Am) 66-A:1072–1076, 1984

69. Krauspe R, Schmidt M, Schaible H-G: Sensory innervation of the anterior cruciate ligament. J Bone J Surg (Am) 74-A:390–397, 1992

70. Yahia LH, Newman NM, St Georges M: Innervation of the canine cruciate ligaments. A neurohistological study. Anat Histol Embryol 21:1–8, 1992

71. Arcand MA, Rhalmi S, Rivard C-H: Quantification of mechanoreceptors in the canine anterior cruciate ligament. Int Orthop 24:272–275, 2000

72. Goertzen M, Gruber J, Dellmann A, et al: Neurohistological findings after experimental anterior cruciate ligament allograft transplantation. Arch Orthop Trauma Surg 111:126–129, 1992

73. Johansson H, Sjölander P, Sojka P: A sensory role for the cruciate ligaments. Clin Orthop Rel Res 268:161–178, 1991

74. Freeman MAR, Wyke B: The innervation of the knee joint. An anatomical and histological study in the cat. J Anat 101:505–532, 1967

75. Biedert RM, Stauffer E, Friederich NF: Occurrence of free nerve endings in the soft tissue of the knee joint. A histologic investigation. Am J Sports Med 20:430–433, 1992

76. Miyatsu M, Atsuta Y, Watakabe M: The physiology of mechanoreceptors in the anterior cruciate ligament. An experimental study in decerebrate-spinalised animals. J Bone J Surg (Br) 75-B:653–657, 1993

77. Boyd IA, Roberts TDM: Proprioceptive discharges from stretch-receptors in the knee-joint of the cat. J Physiol 122:38–58, 1953

78. Schutte MJ, Dabezies EJ, Zimmy ML, et al: Neural anatomy of the human anterior cruciate ligament. J Bone J Surg (Am) 69-A:243–247, 1987

79. Gómez-Barrena E, Nuñes A, Martinez-Moreno E, et al: Neural and muscular electric activity in the cat's knee. Acta Orthop Scand 68:149–155, 1997

80. Hayashi K, Frank JD, Hao Z, et al: Evaluation of ligament fibroblast viability in ruptured cranial cruciate ligament of dogs. Am J Vet Res 64:1010–1016, 2003

81. De Rooster H, Cox E, van Bree H: Prevalence and relevance of antibodies to type-I and -II collagen in synovial fluid of dogs with cranial cruciate ligament damage. Am J Vet Res 61:1456–1461, 2000
82. Muir P, Danova NA, Argyle DJ, et al: Collagenolytic protease expression in cranial cruciate ligament and stifle synovial fluid in dogs with cranial cruciate ligament rupture. Vet Surg 34:482–490, 2005
83. de Bruin T, de Rooster H, van Bree H, Cox E: Lymphocyte proliferation to collagen type I occurs in dogs with cranial cruciate disease. Submitted for publication.