ASSESSMENT OF LAMENESS SCORE AND MUSCLE ATROPHY AFTER EXTRACAPSULAR STABILIZATION OF CRANIAL CRUCIATE LIGAMENT RUPTURE IN TOY BREEDS

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Abstract

Ten dogs of different breeds, small size, were evaluated postoperatively, after cranial cruciate ligament rupture repair by the extracapsular method. The evolution of the lameness score and the degree of muscle atrophy were estimated at one month and three months postoperatively through discussions with the owners and/or physical evaluations. There were no pre- or postoperative complications in dogs that were involved in the study. At three months postoperatively, both the lameness score and the degree of atrophy underwent changes compared to the preoperative stage or one month postoperatively. Although the evolution of the patients was adequate, without intra and postoperative complications, the extracapsular method does not completely restore, at 3 months, the function of the affected limb.

Key words: cranial cruciate ligament, toy breeds, extracapsular stabilization, lameness.

INTRODUCTION

The anatomy of the knee joint in animals is complex. Over time, our understanding of the anatomy of the cranial and caudal cruciate ligament has developed, especially in the direction of microvascularization of the area. Recent work suggests the existence of a bloodligament barrier, analogous to the blood-brain barrier, a finding that helps explain the process that lead to the progressive rupture of the fibers of the ligament matrix of both cruciate ligaments. In addition to their biomechanical role in joint stabilization, cruciate ligaments probably have key roles in joint proprioception (Muir Peter, 2017).

Cranial cruciate ligament (CrCL) rupture is one of the most common orthopaedic conditions seen in veterinary medicine. The femoral-tibialpatellar joint, because of its strategic site between the hip and hock, plays a key role in the pelvic limb. In a standing posture, as a result of the position of the menisci interposed between the femoral and tibial condyles, the stifle joint supports the bodyweight, while the movement. it during allows the transmission of the propulsive thrust towards the coxo-femoral joint and the shortening of the

functional length of the pelvic limb (Kapandji, A.I., 2011; Neumann, D.A., 2017).

The role of the cranial cruciate ligament is to withstand the anterior translational and internal rotational movements of the tibia, this function having a role in preventing the anterior tibial subluxation of the knee joint (tibio-femoral and patello-femoral joint). Unlike in humans, CrCL rupture in dogs is rarely the result of a traumatic injury. The definitive etiopathogenesis of cruciate ligament rupture in dogs has not been completely clarified. It has been shown that this disorder appear during physiological daily load due to progressive degenerative changes in the stifle joint (Muir Peter, 2017).

The cranial cruciate ligament has been shown to have mechanoreceptors that detect changes in the position of the knee joint, in speed, and tension in performing movements. A key factor in limb instability after cranial cruciate ligament rupture is related to impaired neuromuscular function, secondary to reduced somatosensory information. Injuries to the cruciate ligament leads, over time, to joint degeneration (Smith et al., 2012). Most cases are not initially so easily recognized at the time of the partial rupture, and subsequently present with progressive instability. Many procedures have been put into practice over time, but none of them have proven to be most favorable in terms of technical simplicity, associated costs, prevention of secondary pathology, rate of complications, types of complications, medium or long term results. No technique for the treatment of cranial cruciate ligament deficiency (CrCL) has been shown to be superior to the other in terms of functional outcome (Bergh MS et al., 2014; Rey et al., 2014; Kim et al., 2012; Skinner et al., 2013). In the near future, advances in understanding the effects of homeostasis of the ligament matrix on the mechanical properties of the cruciate ligaments and finding specific biomarkers, should provide insight into the mechanism of fiber rupture in the early stages of the disease and early prevention of osteoarthritis (Muir Peter, 2017).

MATERIALS AND METHODS

This study involved small dogs of different breeds who were referred to the Faculty of Veterinary Medicine, department of Anesthetics and Surgical Propaedeutics, Cluj-Napoca for an orthopedic examination to establish the diagnosis of cranial cruciate ligament rupture. The extracapsular lateral suture stabilization

The extracapsular lateral suture stabilization technique was performed in 10 dogs.

This study included (1) Pomeranian, (1) Mixed-Breed, (3) Westie, (1) Bichon, (2) Yorkshire, (1) Chihuahua, (1) Pinscher. Their age ranged from 3 to 10 years and they weighed between 3-12 kg. The study population consisted of 5 spayed females and 5 castrated males (Table 1).

Nr.	Breed	Age	Sex	Affected Limb	Lamness score Preoperative	Amiotrophy Degree Preoperative
1	Pomeranian	9	М	Left	2	2
2	Mixed-Breed	5	F	Left	3	2
3	Westie	10	F	Left	3	3
4	Bichon	6	М	Left	2	2
5	Westie	7	М	Bilateral	2/3	2
6	Yorkshire	5	F	Right	2	3
7	Chihuahua	4	F	Bilateral	4/1	3
8	Yorkshire	3	М	Left	4	3
9	Pinscher	3	F	Right	3	2
10	Westie	4	М	Left	4	3

Table 1. Presentasion of cases

The criteria by which they were chosen for the study were based on the acute or chronic duration of the disease; bilateral or unilateral rupture: joint instability; previous surgical history: the presence or absence of meniscal damage; severity and location of OA; weight and body condition; age. Patients data were recorded on the clinical examination records. Each owner gave their written consent for the animals to be subjected to the procedures. The ruptured ligaments were repaired with a lateral extracapsular suture using an artificial nylon ligament. The degree of lameness was assessed using Fitzpatrick's lameness score (no lameness - 0; mild lameness - 1; moderate intermittent lameness - 2; severe intermittent lameness - 3; persistent lameness, no weight bearing - 4) (Fitzpatrick et al., 2010). Ligament ruptures are also classified from grade I to grade III, depending on the severity of the matrix

damage. Ligaments rupture are defined biomechanically: grade I does not affect joint instability and is associated with mild damage to ligament tissue: grade II is associated with moderate fiber damage and a stretch to the point of detectable instability, and grade III ruptures are associated with severe ligament disruption and obvious joint laxity (Provenzano et al., 2002). Dogs with some joint stability have a partial cruciate ligament rupture, and those with instability present with a complete ligament rupture. Muscle atrophy was classified using a 3-point scale designed by us (normal muscles of the hip and thigh regions -0; mild atrophy of the muscles of the hip and thigh regions - 1; severe atrophy of the muscles of the hip and thigh regions - 2) applying the thigh girth measurement in a standing position. The diagnosis in complete rupture of CrCL is usually based on the anamnesis, physical,

neurological and orthopedic examination of the patient with the demonstration of the laxity of the stifle joint by specific tests (drawer test and tibial compression test). Other tests may be needed, including mid-lateral and caudo-cranial radiography of the joint or MRI. All owners were contacted by telephone to provide information on the clinical condition of patients at one and three months postoperatively and follow up videos in order to have data on the evolution of the animal in terms of lameness score and muscle atrophy degree. The owner used the Fitzpatrick's lameness score and the 3point scale for muscle atrophy.

RESULTS AND DISCUSSIONS

Owners have reported that their pet has experienced lameness after daily exercise, such as after jumping or playing time. All dogs that were diagnosed with a torn ligament were recorded as having a normal level of activity in daily life. The lameness that occurred due to the rupture of the cranial cruciate ligament was present for a variable period before the presentation at the clinic. CrCL rupture was complete in all dogs involved in this study, and two of them presented with bilateral rupture. The cranio-caudal instability assessed by the drawer test and the tibial compression test was present in all patients examined.

А re-examination at our hospital was recommended for owners at one month and then three months after surgery to assess the joint stability of the patients. Data collected included lameness score and degree of muscle atrophy. Four out of ten owners came with the patients for a check-up (the remaining ones were contacted by telephone with follow up videos because they never shown up for a reexamination). We reported an initial decrease in limb function, followed by a moderate increase, which usually occurs around six months after surgery, regardless of the surgical procedure used (Figure 1).

Establishing the owner's perspective on the success of the intervention remains important, as they spend most of their time with the pet. Studies documented that owners reported that their pet had a "good or excellent" result of 88.5-93% depending on the intervention (Innes John F. et al., 2000).

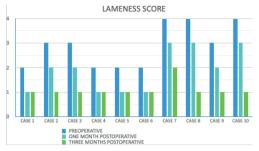


Figure 1. Evolution of the lameness score at one month and three months postoperative

However, these findings need to be interpreted with great caution due to differences in the questions asked, the method of delivering the answer and other factors that significantly influence owners reporting of the outcome such as the fact that the animal should not gain weight, because weight gaining is often cited as an explanation for the incidence of ligament rupture. This is a subjective issue and the animals in this study should have been observed and seen for a longer period of time. Consistent use of a questionnaire validated by the owner should be considered. Several questions have been created which addresses pain, limb function, quality of life, and/or patient activity. Following the physical reexamination of the four patients which presented at the clinic and telephone conversations with the other owners, we found out that at one month after the intervention, in four of the patients a slight lameness score was observed (1 out of 4) in 3 patients a lameness score of 2 out of 4 was seen and 3 of the patients showed a 3 out of 4 lameness score. At three months, nine patients presented with mild persistent lameness, and in one patient the owners reported that their pet had moderate persistent lameness. Moderate muscle atrophy of the hip and thigh regions was observed in five dogs, and in the five a severe muscle atrophy (Figure 2). After one month of the postoperative period, there was improvement in muscle atrophy in five of the patients (being between 1-1.5), and in the others a moderate muscle atrophy due to the fact that the dog's activity during that period should be limited to the maximum. At three months, a reduced muscle atrophy of the hip and thigh regions was observed in all ten dogs involved in this study, based on the 3-point

scale for muscle atrophy. The owners noticed an improvement in the gait of their pets, with subjective observations on the lameness score and the degree of muscle atrophy. Strength deficiencies have been reported in the limb muscles up to 30% compared to the other hind limb, due to the fact that muscle atrophy contributes to weakening of the quadriceps (weakening of the quadriceps is almost ubiquitous due to injury and reconstruction of the cranial cruciate ligament) (Abbey C. Thomas et al., 2015). Early return to function is desirable to reduce muscle atrophy and maintain range of motion at the level of the stifle joint after surgery. Muscle atrophy can alter the forces, acting on the stifle joint and influence the progression of the thus degenerative processes at the joint level. Pain, edema, restriction of activity and bandaging contribute to the postoperative loss of normal movement of the affected limb, requiring a strict range of exercises as part of a rehabilitation program. The exercises are performed under controlled conditions with therapeutic aims. The aims of exercises include properly limb use, strengthening, improving joint and soft tissue mobility, promoting proprioception and eliminating weight shifts. Exercises are adapted to the stage of recovery. During the early postoperative period, exercises may include static exercises, slow walking and exercise in water where loads placed on joints are reduced (Muir Peter, 2017).

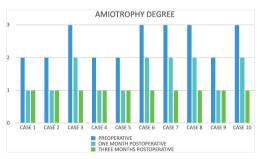


Figure 2. Evolution of muscle amyotrophy degree at one month and three months postoperative

Obesity, defined as exceeding the ideal body weight by 15-20%, puts excessive forces on the joints and articular cartilage, being exacerbated by inactivity, spreading a vicious circle of muscle atrophy and decreased desire to perform physical exercises (Impellizeri et al., 2000;

Kealy et al., 2000). Although there is no clear relationship between the effect of obesity and OA, fat is considered a metabolically active tissue that promotes inflammation (Greenberg and Obin, 2006). There is growing evidence that mediators released from adipose tissue, including interleukin 6 (IL-6), tumor necrosis factor alpha $(TNF-\alpha)$, leptin. visfatin. adiponectin, adipsin, and resistin, may play important roles in the pathogenesis of OA (Frye et al., 2016). Elevated adipsin and leptin levels are associated with OA progression in humans (Martel-Pelletier et al., 2016). It has also been suggested that leptin may play a role in the development of cruciate ligament rupture in dogs by altering the fiber ligament and collagenase activity (Comerford et al., 2005).

Since surgery is a relatively invasive procedure that presents its own risks for each patient, it is very reasonable to consider the advantages and disadvantages when discussing the choice of surgical technique. No current stabilization technique will result in a return to normal limb function, but each technique has been shown to improve lameness and patient comfort over a long period of time and result in high customer satisfaction. No current technique completely interrupts the evolution of osteoarthritis (Voss K et al., 2008; Ballagas AJ et al., 2004; Gordon-Evans WJ et al., 2013). In our study, no complications were reported after the surgery, none of the patients required another surgery.

The current recommendation for the prevention of postoperative meniscal disease is to improve the detection of pre-existing lesions at the time of the onset of ligament rupture. This is best achieved by arthroscopy (Plesman et al., 2013; Ritzo et al., 2014).

Reports on the improvement of clinical signs in surgical remediation of cruciate ligament rupture vary between 85 and 95% regardless of the surgical technique used (Moore and Read, 1995). The use of an artificial nylon ligament is the most commonly used method in small animals, and it was used in restoring the stability of the knee joint of the 10 dogs involved in this study. This can't be done completely after using the extracapsular technique, the purpose of the surgery being to reduce the clinical signs. Despite many studies showing that conservative management

remains a viable option for some patients, as long as proper care is taken in selecting cases (patients that are not limping, patiens with a partial CrCL rupture), we considered that surgery provided the best results for most patients included in this study. There will be owners who, for different reasons, will choose conservative treatment over surgical intervention. We exposed all the the pro an cons for surgery/conservative treatment and all the owners decided that surgery treatment is the best option for their animals. However, not all surgical procedures offer an equivalent level of recovery. Currently, the best available evidence provides strong support for Tibial Plateau Leveling Osteotomy (TPLO), which allows dogs to regain normal clinical limb function (Au KK et al., 2010; MacDonald et al., 2013; Berger et al., 2015). It is necessary to compare the technique chosen by us (extracapsular method - ECR) with other methods, such as TPLO, to assess the speed of recovery, which is important for both owners and animals, the two methods being the most used in toy breeds. ECR stabilizes the joint by a circumfabelartibial suture that mimics the function of the cranial cruciate ligament (CrCL) and tries to prevent cranial thrust of the tibia, and TPLO ensures the functional (dynamic) stability of the knee joint by eliminating cranial thrust of the tibia rather than restoring the function of the cranial cruciate ligament (Slcoum B et al., 1993). Many studies suggest a faster return to normal function of the affected hind limb after stabilization by TPLO than other surgery procedures of stabilizing the knee joint after ligament rupture. A short period of time after strictly surgery, without following an established rehabilitation program, dogs that have undergone stabilization by TPLO get a faster return to normal joint function within a vear than those that have undergone stabilization by ECR. Previous studies that normally used gait to assess the long-term outcome of TPLO and ECR did not find a significant difference between them, therefore differences in the functioning of the affected limb and mild lameness can be omitted (Au KK et al., 2010; Conzemius MG et al., 2005). Since mild to moderate lameness during more alert gait cannot be a quality factor in the life of sedentary dogs, there is a substantial impact on

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active and athletic dogs (Samantha Nelson et al., 2016). Usually animals that are subjected to the TPLO technique are younger than those with extracapsular stabilization. The reason for this difference may be that young dog owners may choose TPLO for financial reasons, older dog owners may be less inclined to invest in TPLO which is more expensive and time consuming in the operating room, so TPLO may be an appropriate recommendation to return to normal function as soon as possible. None of these procedures repair or reconstruct ligament rupture, and each procedure is associated with a relatively high risk of subsequent meniscal injury and OA (Slocum and Slocum, 1993; Rayward et al. 2004; Lazar et al., 2005; Morgan et al., 2010). A successfully restored function of the ligament could provide dynamic and passive stability while maintaining proprioception and avoid some of these long-term complications. However, any attempt to stimulate CrCL healing begins with the question of why the ligament fails to heal in the first place. This inability to heal is even more surprising, given that collateral ligaments heal spontaneously with minimal treatment (Frank et al., 1983a; Frank et al., 1983b; Hannafin et al., 1999). Cruciate and collateral ligament cells have similar capabilities in terms of proliferation, migration, and biosynthesis (Murray et al., 1999; Murray et al., 2000a; Murray et al., 2000b; Murray et al., 2002; Murray et al., 2007a). However, it has been found that injuries to the cruciate ligaments, unlike injuries to the collateral ligaments, do not form clots between the torn ends of the tissue: consequently, there is no reason for cell migration and tissue repair (Murray et al., 2000a). This inability to form a clot can be attributed to high intra-articular levels of plasminogen after joint injury (Brommer et al., 1992; Rosc et al., 2002). Despite the high incidence of infection and antimicrobial resistance, joint infections generally have a favorable prognosis if treated properly. The resolution of the infection was obtained in 95% of cases, and the average resolution of the lameness can be observed on day 38 (interval 15-45 days) after the initiation of treatment (Fitzpatrick et al., 2010; Savicky et al., 2013). In many cases, treatment requires prolonged

medication and leads to additional client visits, additional days of hospitalization, or other surgeries, but not all clients are willing to return with the animal (in this study six owners did not return for physical re-examination with the patients), probably not following diet or exercise restrictions and strict administration of the drugs, therefore this study is an indicative and limited one from this point of view. The frequency of injury to the knee joint requires efforts to increase our knowledge of the stifle joint. With the advent of advanced investigative methods, such as ultrasound, computed tomography, and nuclear magnetic resonance imaging, knowledge of the normal anatomy of the knee joint is essential for the correct assessment and definition of the lesion (Reed et al., 1995; Baird et al., 1998; Kramer et al., 1999). As we understand the structural and functional components of the joint, the potential of the equipment increases and procedures that will provide advanced and longlasting treatments for complicated joint injuries. Beyond the loss of function caused by a torn cranial cruciate ligament, a major concern is the accelerated onset of osteoarthritis. An understanding of this complex issue is to define the events that take place after the initial trauma. It has been observed that immediate injection of triamcinolone after CrCL rupture reduces the amount of synovial fluid and secondary degradation of collagen (Sieker et al. 2016). Given the emerging role of joint inflammation in the pathogenesis of cruciate ligament rupture, a combination of medical and surgical treatment will likely be necessary for a result as quickly and effectively as possible. Genetic research suggests that rupture of the cruciate ligament is a complex polygenic trait (Innes JF, 2007). Dogs with such pathology are 50% more likely to have the other ligament ruptured at 12 months after the initial diagnosis (Doverspike et al., 1993; Moore and Read, 1995; de Bruin et al., 2007 a,b; Cabrera et al., 2008; Buote et al., 2009).

CONCLUSIONS

Although the lameness score decreased postoperative at both intervals studied, a slight degree of lameness persisted in the last interview with the owners.

At one month and three months postoperative, the thigh muscles developed significantly.

Although the evolution of the patients was adequate, without intra- and postoperative complications, the extracapsular method does not completely restore, at 3 months, the function of the limb.

The limits of the study are represented by the small population being observed.

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REFERENCES

- Abbey C. Thomas, Edward M Wojtys, Catherine Brandon, Riann M Palmieri-Smith (2015). *Muscle atrophy contributes to quadriceps weakness after anterior cruciate ligament reconstruction.* J Sci Med Sport 19(1):7-11.
- Au KK, Gordon-Evans WJ, Dunning D, J O'Dell-Anderson, Kim E Knap, Dominique Griffon, Ann L Johnson (2010). Comparison of short and long-term function and radiographic osteoarthrosis in dogs after postoperative physical rehabilitation and tibial plateau leveling osteotomy or lateral fabellar suture stabilization. Vet Surg., 39: p. 173-180.
- Baird, D. K., J. T. Hathcock, P. F. Rumph, S. A. Kincaid, D. M. Visco (1998). Low-field magnetic resonance of the canine stifle joint: normal anatomy. Vet. Radiol. Ultrasound 39, 87-97.
- Ballagas AJ, Montgomery RD, Henderson RA, Gilette R (2004). Pre- and postoperative force plate analysis of dogs with experimentally transected cranial cruciate ligaments treated using tibial plateau leveling osteotomy. Vet Surg.; 33:187-190.
- Berger B, Knebel J, Steigmeier-Raith S, S Reese, A Meyer-Lindenberg (2015). Long-term outcome after surgical treatment of cranial cruciate ligament rupture in small breed dogs. Comparison of tibial plateau leveling osteotomy and extra-articular stifle stabilization. Tierarztl Prax Ausg K Kleintiere Heimtiere, 43: p. 373-380.
- Bergh MS, Tan CJ, Schembri MA, Mark A Schembri, Kenneth A Johnson (2014). Accuracy of tibial osteotomy placement using 2 different tibial plateau leveling osteotomy jigs. Vet Surg., 43, 525-533.
- Brommer EJ, Dooijewaard G, Dijkmans BA, F C Breedveld (1992). Depression of tissue-type plasminogen activator and enhancement of urokinase-type plasminogen activator as an expression of local inflammation. Thromb Haemost 68: p. 180-184.

- Buote N, Fusco J, Radasch R. Age (2009). *Tibial plateau* angle, sex, and weight as risk factors for contralateral rupture of the cranial cruciate ligament in Labradors. Vet Surg., 38: p.481-489.
- Cabrera SY, Owen TJ, Mueller, MG. (2008). Comparison of tibial plateau angles in dogs with unilateral versus bilateral cranial cruciate ligament rupture: 150 cases (2000–2006). J. Am Vet. Med. Assoc., 232: p. 889-892.
- Comerford Eithne J., Tarlton John F., Innes John F., Kenneth A. Johnson, Andrew A. Amis, Allen J. Bailey (2005). Metabolism and composition of the canine anterior cruciate ligament relate to difference in knee joint mechanics and predisposition to ligament rupture. J Orthop Res., 23: p. 61-66.
- Conzemius MG, Evans RB, Besancon MF, Wanda J Gordon, Christopher L Horstman, William D Hoefle, Mary Ann Nieves, Stanley D Wagner (2005). Effect of surgical technique on limb function after surgery for rupture of the cranial cruciate ligament in dogs. J Am Vet Med Assoc., 226: p. 232-236.
- de Bruin T., de Rooster H., van Bree H., Eric Cox (2007a). Evaluation of anticollagen type I antibody titers in synovial fluid of both stifle joints and the left shoulder joint of dogs with unilateral cranial cruciate disease. Am. J.Vet. Res. 68, p. 83-289.
- de Bruin T., de Rooster H., van Bree H., T. Waelbers, Eric Cox (2007b). *Lymphocyte proliferation to* collagen type I in dogs. J. Vet. Med. A Physiol. Pathol. Clin. Med. 54: p. 292-296.
- Doverspike M, Vasseur PB, Harb MF, Walls, C.M. (1993). Contralateral cranial cruciate ligament rupture: Incidence in 114 dogs. J Am Anim. Hosp. Assoc., 29, p. 167-170.
- Fitzpatrick N, Johnson J, Hayashi K, Sarah Girling, Russell Yeadon (2010). *Tibial plateau leveling and medial opening crescentic osteotomy for treatment of cranial cruciate ligament rupture in dogs with tibia vara.* Vet Surg., 39, 444-453.
- Frank C, Amiel D, Akeson W. (1983a). Healing of the medial collateral ligament of the knee. A morphological and biochemical assessment in rabbits. Acta Orthop Scand 54: p. 917-923.
- Frank C, Woo SL, Amiel D, F Harwood, M Gomez, W Akeson, (1983b). Medial collateral ligament healing. A multidisciplinary assessment in rabbits. Am J Sports Med 11: 379-389.
- Frye CW, Shmalberg JW, Wakshlag JJ. (2016). Obesity, exercise and orthopedic disease. Vet Clin North Am Small Anim Pract., 46, 831-841.
- Gordon-Evans WJ, Griffon DJ, Bubb Carrie, Kim M. Knap, Meghan Sullivan, Richard B. Evans (2013). Comparison of lateral fabellar suture and tibial plateau leveling osteotomy techniques for treatment of dogs with cranial cruciate ligament disease. JAVMA; 243:675-680.
- Greenberg AS, Obin MS. (2006). Obesity and the role of adipose tissue in inflammation and metabolism. Am J Clin Nutr., 83: S461-S465.
- Hannafin JA, Attia ET, Warren RF, MM Bhargava (1999). Characterization of chemotactic migration and growth kinetics of canine knee ligament fibroblasts. J Orthop Res 17: p. 398-404.

- Impellizeri JA, Tetrick MA, Muir P. (2000). Effect of weight reduction on clinical signs of lameness in dogs with hip osteoarthritis. J Am Vet Med Assoc., 216, 1089-1091.
- Innes John F. (2007). Outcomes-based medicine in veterinary surgery: Levels of evidence. Vet Surg 36: p. 610-612
- Innes John F., Bacon D, Lynch C, Pollard A. (2000). Long-term outcome of surgery for dogs with cranial cruciate ligament deficiency. Vet Record, 147, 325-328.
- Kapandji, A.I. The Knee (2011). The Physiology of the Joints, the Lower Limb, 6th ed.; Kapandji, A.I., Ed.; Elsevier: London, UK, 2, 66–154.
- Kealy RD, Lawler DF, Ballam JM, G Lust, D N Biery, G K Smith, S L Mantz, (2000). Evaluation of the effect of limited food consumption on radiographic evidence of osteoarthritis in dogs. J Am Vet Med Assoc., 217, 1678-1680.
- Kim SE, Lewis DD, Pozzi A., 2012. Effect of tibial plateau leveling osteotomy on femorotibial subluxation: in vivo analysis during standing. Vet Surg., 41, 465-470.
- Kramer, M., H. Stengel, M. Gerwing, E. Schimke, C. Sheppard (1999). Sonography of the canine stifle. Vet. Radiol. Ultrasound 40, p. 282-293.
- Lazar TP, Berry CR, deHaan JJ, Jeffrey N Peck, Maria Correa (2005). Long-term radiographic comparison of tibial plateau leveling osteotomy versus extracapsular stabilization for cranial cruciate ligament rupture in the dog. Vet Surg., 34:133-141.
- MacDonald TL, Allen DA, Monteith GJ., (2013). Clinical assessment following tibial tuberosity advancement in 28 stifles at 6 months and 1 year after surgery. Can Vet J, 54: p. 249-254.
- Martel-Pelletier J, Raynauld JP, Dorais M, François Abram, Jean-Pierre Pelletier (2016). The levels of the adipokines adipsin and lep- tin are associated with knee osteoarthritis progression as assessed by MRI and incidence of total knee replacement in symptomatic osteoarthritis patients: a post hoc analysis. Rheumatology (Oxford), 55, 680-688.
- Moore KW, Read RA, (1995). Cranial cruciate ligament rupture in the dog – A retrospective study comparing surgical techniques. Aust. Vet. J. 72: p. 281-285.
- Morgan JP, Voss K, Damur DM, Tomás Guerrero, Michael Haessig, Pierre M Montavon (2010). Correlation of radiographic changes after tibial tuberosity advancement in dogs with cranial cruciate- deficient stifles with functional outcome. Vet Surg 39, 425-432.
- Muir Peter, Lauren Baker (2017). Epidemiology of Cruciate Ligament Rupture *in Advances in the Canine Cranial Cruciate Ligament*, Second Edition, Ed.; Wiley-Blackwell: Hoboken, NJ, USA, 109-117, 347-351.
- Murray MM, Bennett R, Zhang X, Spector M (2002). Cell outgrowth from the human ACL in vitro: regional variation and response to TGF-beta1. J Orthop Res 20: p. 875-880.
- Murray MM, Martin SD, Martin TL, M Spector (2000a). Histological changes in the human anterior cruciate

ligament after rupture. J Bone Joint Surg Am 82: p. 1387-1397.

- Murray MM, Martin SD, Spector M (2000b). Migration of cells from human anterior cruciate ligament explants into collagen-glycosaminoglycan scaffolds. J Orthop Res 18: p. 557-564.
- Murray MM, Spector M., (1999). Fibroblast distribution in the anteromedial bundle of the human anterior cruciate ligament: the presence of alpha-smooth muscle actin-positive cells. J Orthop Res 17: p. 18-27.
- Murray MM, Spindler KP, Ballard P, Tyler P Welch, David Zurakowski, Lillian B Nanney (2007a.) Enhanced histologic repair in a central wound in the anterior cruciate ligament with a collagen-plateletrich plasma scaffold. J Orthop Res 25: p. 1007-1017.
- Neumann, D.A. (2017). Kinesiology of the Musculoskeletal System, Foundations for Rehabilitation, Neumann, D.A., Ed.; Elsevier: St. Louis, MO, USA, 3, 538–594.
- Paolo P. Provenzano, Daniel A. Martinez, Richard E. Grindeland, Kelley W. Dwyer, Joanne Turner, Arthur C. Vailas, Ray Vanderby Jr. (2002). *Hindlimb* unloading alters ligament healing, 94(1):314-24.
- Plesman, R., Gilbert, P., Campbell, J. (2013). Detection of meniscal tears by arthroscopy and arthrotomy in dogs with cranial cruciate ligament rupture: a retrospective, cohort study. Veterinary and Comparative Orthopaedics and Traumatology 26 (1), 42-46.
- Rayward RM, Thomson DG, Davies JV, JF Innes, RG Whitelock (2004). Progression of osteoarthritis following TPLO surgery: a prospective radiographic study of 40 dogs. J Small Anim Pract., 45: p. 92-97.
- Reed, A. L., J. T. Payne, and G. M. Constantinescu (1995). Ultrasonographic anatomy of the normal canine stifle. Vet. Radiol. Ultrasound 36, 315-321.
- Rey J, Fischer MS, Böttcher P., (2014). Sagittal joint instability in the cranial cruciate ligament insufficient canine stifle. Caudal slippage of the femur and not cranial tibial subluxation. Tierarztl Prax, 42, 151-156.

- Ritzo ME, Ritzo BA, Siddens AD, Stephanie Summerlott, James L Cook (2014). Incidence and type of meniscal injury and associated long-term clinical outcomes in dogs treated surgically for cranial cruciate ligament disease. Vet Surg., 43: p. 952-958.
- Rosc D, Powierza W, Zastawna E, Wanda Drewniak, Aleksander Michalski, Maria Kotschy (2002). Posttraumatic plasminogenesis in intraarticular exudate in the knee joint. Med Sci Monit 8:CR371–CR378.
- Samantha Nelson, Ursula Krotscheck, Jeremy Rawlinson, Rory J. Todhunter, Zhiwu Zhang, Hussni Mohammed (2016). Long-Term Functional Outcome of Tibial Plateau Leveling Osteotomy Versus Extracapsular Repair in a Heterogeneous Population of Dogs. Vet Surg, 45(2): p. 38; p. 48.
- Savicky R, Beale B, Murtaugh R, J Swiderski-Hazlett, M Unis (2013). Outcome following removal of TPLO implants with surgical site infection. Vet Comp Orthop Traumatol 26: p. 260-265.
- Sieker JT, Ayturk UM, Proffen BL, Manuela H Weissenberger, Ata M Kiapour, Martha M Murray (2016). Immediate administration of intraarticular triamcinolone acetonide after joint injury modulates molecular outcomes associated with early synovitis. Arthritis Rheumatol 68: p. 1637-1647.
- Skinner O, Kim SE, Lewis DD, A Pozzi (2013). In vivo femorotibial subluxation during weight-bearing after tibial tuberosity advancement. Vet J., 196, 86-91.
- Slocum B, Slocum TD. (1993). Tibial plateau leveling osteotomy for repair of cranial cruciate ligament rupture in the canine. Vet Clin North Am Small Anim Pract., 23: p. 777-795.
- Smith KD, Vaughan-Thomas A, Spiller DG, PD Clegg, JF Innes, E J Comerford (2012). Variations in cell morphology in the canine cruciate ligament complex. Vet J., 193, 561-566.
- Voss K, Damur DM, Guerrero T, Haessig M, Montovan P N, (2008). Force plate gait analysis to assess limb function after tibial tuberosity advancement in dogs with cranial cruciate ligament disease. Vet Comp Orthop Trauma, 21:243-249.

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