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CLINICAL RESEARCH

Arthroscopic synovitis severity scoring in canine stifles with cranial cruciate ligament disease

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Abstract

Objective: To investigate the occurrence, degree, and risk factors associated with arthroscopic stifle joint synovitis in dogs with cranial cruciate ligament (CCL) disease.

Study design: Retrospective, observational study.

Sample population: Canine CCL disease ($n = 163$) from 149 dogs and their arthroscopic video recordings.

Methods: Arthroscopic video recordings were reviewed. A synovitis severity (0–5) and a modified Outerbridge cartilage classification system score were assigned, along with recording the presence or absence of a medial meniscal bucket handle tear. Medical records were reviewed for age, sex, limb, and duration of clinical signs. Univariate analyses were performed via a Fisher's exact test for categorical independent variables, and ordered logistic regression was used for continuous variables. Multivariable ordered logistic regression considered independent variables with a p-value <.2 on univariate analyses. p-value <.05 was considered statistically significant.

Results: Synovitis was identified in 100% of the stifles examined. The most frequent synovitis severity score was 3/5. Univariate analysis showed a significant association between synovitis severity score and bodyweight

Abbreviation: CCL, Cranial crucaite Ligament; OA, Osteoarthritis.

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($p = .005$), median cartilage score ($p = .002$), and being female ($p = .032$). On multivariable analysis, the synovitis severity score was significantly associated with median cartilage score ($p = .042$) and duration of clinical signs ($p < .001$).

Conclusion: Synovitis was arthroscopically always identified in stifles with CCL disease. The severity of synovitis was associated with more progressive damage to the articular cartilage and a longer duration of clinical signs.

Clinical significance: Earlier intervention in dogs with CCL disease may be warranted to decrease synovitis and progression of osteoarthritis.

1 | INTRODUCTION

Cranial cruciate ligament (CCL) disease is a common cause of pelvic limb lameness in the dog and the leading cause of osteoarthritis (OA) in the canine stifle joint.[1–5] While altered joint mechanics in the CCL deficient stifle have received considerable attention as a trigger for the development and progression of stifle OA, the high frequency of synovitis in dogs with CCL tears suggests it is an important component of the disease.[6–8] In fact, the presence of synovitis prior to joint instability implies that it plays a significant role in the early stages of CCL disease.[9] Synovitis is regularly identified in clinically affected, stable and unstable canine stifle joints at the time of surgical intervention[8] (Figure 1) and, therefore, may be a contributing factor to the clinical manifestation of CCL disease. Additionally, although there are limited studies evaluating the presence and degree of synovitis following surgical stifle stabilization in the dog, OA progression is frequently recognized and residual lameness can be observed. These observations not only warrant further investigation into the role of synovitis during the initiation and progression phases of the disease, but also evaluation into its contribution to clinical symptoms.

At the time of CCL diagnosis, stifle synovitis is frequently observed, and its presence in the contralateral stifle correlates with an increased likelihood of a subsequent clinically relevant CCL tear.[9] Research also suggests that synovitis is present (at a histological level), prior to the onset of stifle instability, which potentially serves as an early marker of CCL damage (Figure 1).[9] However, the precise sequence of events regarding CCL damage and the initiation of synovitis remains undefined. It is unclear whether synovitis precedes and incites CCL fiber damage or if it occurs as a consequence of injury induced by factors such as age, sex, or genetic predisposition, among others.[3,10,11] Regardless of the exact sequence of events inciting synovitis, both

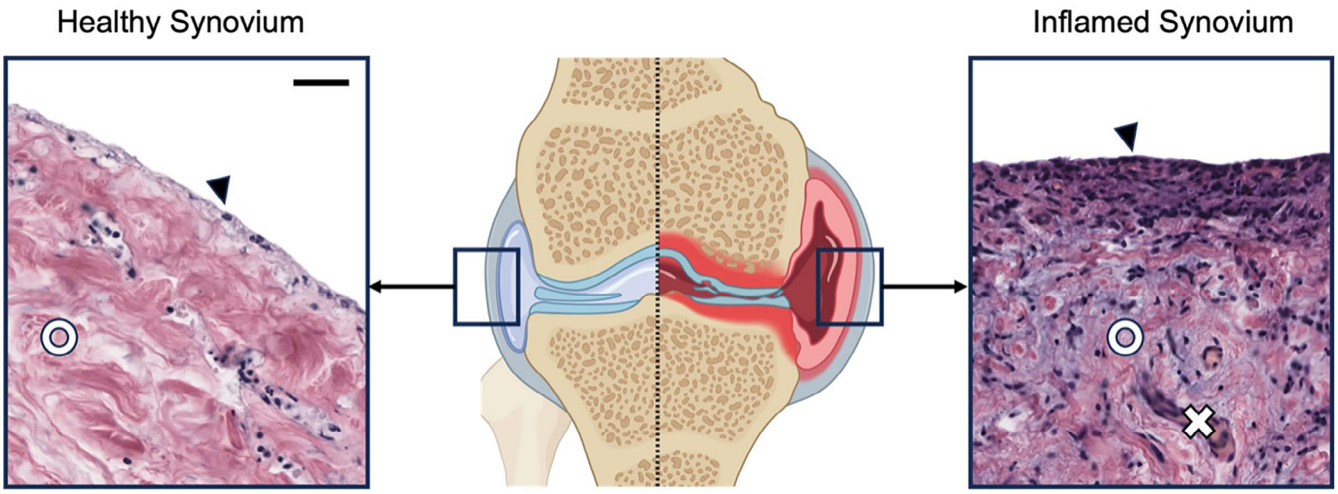

FIGURE 1 Schematic of healthy and diseased knee joint with corresponding representative 10X hematoxylin and eosin (H&E) synovial images from stifles of a healthy dog (healthy synovium) or a dog with a naturally occurring cranial cruciate ligament (CCL) tear (inflamed synovium). Black triangles represent the intima of the synovium, noticeably thickened in the inflamed synovium. Circles represent subintima region and X delineates subintimal vascularization in inflamed synovium. Scale bar = 25 mm.

experimental and naturally occurring models of CCL tears indicate that synovial inflammation predicts heightened levels of inflammatory, catabolic, and degradative biomarkers within the joint.[12–20] These increased catabolic inflammatory biomarkers (TNFα, IL-6, and IL-8) have been identified in the synovial fluid of human patients with anterior cruciate ligament tears as compared to healthy counterparts.[21] Additionally, in a recent study, mRNA analysis of synovial tissue from dogs showed a positive correlation between arthroscopic synovitis score and expression of inflammatory mediators, including *TNFα, IL-6, IL-1β, CXCL8, PTGER4*, and *PTGS2*, the gene encoding for cyclooxygenase-2.[22] If unresolved, this disruption to synovial homeostasis can lead to synovial fibrosis (Figure 1) and altered signaling in synovial cell populations, resulting in a loss of chondroprotective activity and subsequent acceleration of OA (Figure 1).[6]

The contribution of synovitis to the clinical manifestation of the CCL disease and OA in the dog is unknown. In people, evidence suggests that the degree of synovitis in human patients with OA is associated with worse clinical symptoms, such as pain and joint dysfunction, along with acceleration of cartilage degeneration.[23–26] Additionally, among individuals without radiographic OA who underwent meniscectomy surgery, 43% exhibited synovial inflammation upon synovial biopsy. Notably, these patients presented with worse pain and function parameters compared to their healthy counterparts.[27] Unfortunately, routine evaluation and synovial scoring are not frequently implemented clinical outcome measures in dogs with CCL disease and OA, so there is limited information on its role in clinical presentation. However, when utilized, arthroscopic grading of canine synovium is useful in characterizing the location and severity of synovial inflammation and may further our understanding of synovitis in relation to CCL tear pathology, clinical symptoms, and subsequent OA progression in CCL disease.[7,9,28]

The aim of this study was to describe the frequency and extent of arthroscopic joint capsular synovitis in dogs diagnosed with naturally occurring CCL disease. In addition, we investigated the association between synovitis severity scores and canine patient factors including the limb affected, presence of a bucket handle meniscus tear, sex, bodyweight, median cartilage score, body condition score (BCS), stifle stability, and owner-reported duration of clinical signs. We hypothesized that all dogs diagnosed with CCL disease would have some degree of joint capsular synovitis and that synovitis score would significantly associate with multiple patient factors, including duration of clinical signs and BCS.

2 | MATERIALS AND METHODS

2.1 | Study population

Canine patients with CCL disease managed via arthroscopic stifle exploration and surgical stabilization at the University of Pennsylvania between 2012 and 2022 were included in this study. All owners consented to the procedures and the use of data for study purposes. The dogs had no prior history of lameness or orthopedic procedures on the affected limb, weighed ≥15 kg, and had clinical signs associated with CCL disease, including lameness, stifle pain, and stifle effusion. Gross stifle instability was defined as the presence or absence of cranial drawer and tibial trust from physical examination. These tests were performed while the patient was awake and under general anesthesia at the time of arthroscopic evaluation. If stifle instability was appreciated the stifle was documented as unstable. Conversely, in the absence of cranial drawer and tibial thrust the stifle was recorded as stable. CCL pathology was confirmed on arthroscopic video recordings and documented as either complete or partial CCL disruption. Orthogonal radiographic views of the affected stifle were reviewed and excluded if additional abnormalities, besides degenerative changes, consistent with CCL disease, were identified. Medical records were reviewed to capture age, sex, limb, bodyweight, BCS, and owner-reported duration of clinical signs, such as changes in gait or lameness in the affected limb prior to surgery. Regarding BCS, each dog was scored using a nine-point scale further subgrouped into three classifications: lean to ideal (4, 5), overweight (6, 7), and obese (8, 9).[18,29] Records were excluded in terms of duration of clinical signs if a specific number of days, weeks, months, or years were not noted in the clinical history. To record clinical signs, 1 month was defined as 4 weeks.

2.2 | Stifle arthroscopy and scoring

A total of 163 complete video-recorded stifle arthroscopies (Stryker, San Jose, California), performed by a single experienced board-certified surgeon (KAA) were included. A stifle exploration was considered complete if it included videos of the patellofemoral joint, supratrochlear joint pouch, the medial and lateral trochlear joint spaces, the cranial and caudal cruciate ligaments, the medial and lateral femorotibial joints, and the medial and lateral menisci.[8] Videos were edited to include each of the above anatomic regions in separate videos, except for some cases in which the patellofemoral joint and the supratrochlear joint pouches or the medial and lateral

femorotibial joint and menisci were combined. Dogs were excluded if video recordings were incomplete or other pathology was identified (e.g., osteochondrosis lesion on the lateral femoral condyle). All patient identifying information was removed from the videos and the videos were randomized based on date of surgery. A single observer (KAA) utilized the video recordings to perform cartilage and synovial pathology scoring, along with the assessment for the presence or absence of a bucket handle medial meniscus tear. Other less significant medial meniscal pathology was not recorded in this study. All scoring occurred at least 1 year following arthroscopic surgery. The cartilage of the patella, trochlear groove, tibial plateau, and femoral condyles were graded using a modified Outerbridge classification system (Table 1).[28,30] Scoring was conducted at 10 sites within the stifle joint, which included the proximal, middle, and distal regions of the patella and trochlear groove[31] and the axial weight-bearing regions of the medial and lateral tibial plateau and femoral condyles.[8] A median cartilage score was then calculated for each stifle from these 10 locations. Synovial pathology was scored at the supratrochlear joint pouch in all stifles using a previously described classification system (Table 2) (Figure 2).[28] Synovitis scores were then subgrouped into three categories, specifically low (1, 2), middle (3), and high (4, 5).

TABLE 1 Modified Outerbridge arthroscopic scoring system for articular cartilage.[28,30]

Score	Arthroscopic characteristics
0	Smooth surface
1	Slightly fibrillated/roughened surface
2	Fibrillated surface with focal partial thickness lesions
3	Deep lesions with surrounding damage
4	Large areas of severe damage

TABLE 2 Arthroscopic synovial pathology scoring system.[28]

Score	Arthroscopic characteristics
0	Opal white, semitranslucent, smooth, with sparse well defined blood vessels (normal)
1	Focal involvement, slight discoloration, visible proliferation/fimbriation/thickening, notable increase in vascularity (slight)
2	Diffuse involvement, slight discoloration, visible proliferation/fimbriation/thickening, notable increase in vascularity (mild)
3	Diffuse involvement, severe discoloration, consistent notable proliferation/fimbriation/thickening, moderate vascularity (moderate)
4	Diffuse involvement, severe discoloration, consistent and marked proliferation/fimbriation/thickening, diffuse hypervascularity (marked)
5	Diffuse involvement, severe discoloration, consistent and severe proliferation/fimbriation/thickening, thickening to the point of fibrosis, and severe hypervascularity (severe)

2.3 | Statistical analysis

All statistical analyses were performed using STATA BE (College Station, Texas) and GraphPad Prism (San Diego, California). Categorical variables (Figure 3A–F) are reported as frequencies. Continuous variables are reported as median values with ranges as Shapiro–Wilk test suggested non-normal distribution (Figure 3G–J). Univariate analyses were performed to evaluate the statistical association of each independent variables with the dependent variable of interest (synovitis score). Specifically, Fisher's exact or X^2 contingency test was used for the categorical independent variables, and ordered logistic regression was used for the continuous variables. The analysis initially included sex as four groups (male castrated, male intact, female spayed, and female intact), but no differences were found between the male intact and male castrated, nor the female intact and female spayed. Therefore, the intact male and female cohorts were combined with either the male castrated or female spayed subgroups for subsequent analyses. Independent variables with a p-value <.2 in univariate analyses were considered in the subsequent multivariable ordered logistic regression, which was used to estimate the association of these variables, while controlling for confounding variables. For all tests, a two-sided p-value <.05 was considered for statistical significance.

3 | RESULTS

This study included 163 stifles (83 right, 80 left) from 149 dogs with naturally occurring CCL disease (Figure 3A). The breeds represented in this study included mixed breed ($n = 55$), Labrador Retriever ($n = 26$), Golden Retriever ($n = 12$), Newfoundland ($n = 9$), Rottweiler ($n = 7$), American Pitbull Terrier (n = 5), German Shepherd Dog ($n = 6$), Boxer ($n = 4$), Mastiff ($n = 4$), English Bulldog ($n = 3$), Bernese Mountain Dog ($n = 3$), Doberman ($n = 2$), Belgian Malinois ($n = 2$), Alapaha Blue Blood Bulldog ($n = 1$), Bouvier Des Flanders ($n = 1$), Cane Corso ($n = 1$), Great Dane ($n = 1$), Great Pyrenees ($n = 1$), Husky ($n = 1$), Norwegian Elkhound ($n = 1$), English Pointer ($n = 1$), Portuguese Water Dog ($n = 1$), Spanish Water Dog ($n = 1$), Weimaraner ($n = 1$). A total of 14 dogs

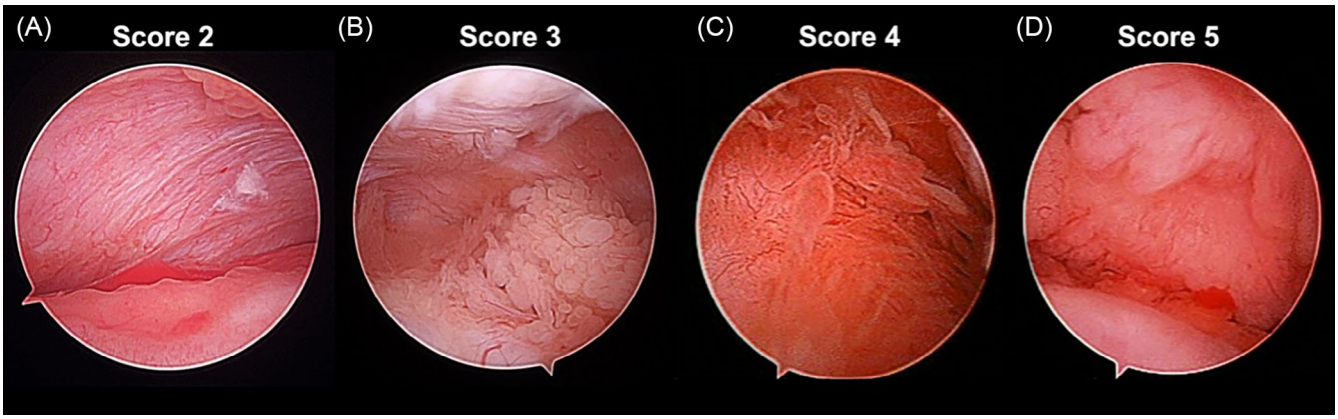

FIGURE 2 Representative arthroscopic images of the stifle joint capsule synovium. (A) Score 2 shows diffuse involvement of the synovium with a mild increase in vascularity and some proliferation/fimbriation. (B) Score 3 represents diffuse involvement and with a moderate increase in vascularity and more proliferation/fimbriation. (C) Score 4 shows diffuse involvement with marked vascularity and more consistent, diffuse proliferation/fimbriation. (D) Score 5 shows diffuse involvement, severe hypervascularity, with consistent and severe proliferation/fimbriation along with thickening and fibrosis of the joint capsule. No scores of 0 or 1 were present in the current study.

had bilateral disease: Labrador Retriever ($n = 3$), mixed Breed ($n = 3$), Newfoundland ($n = 2$), Alapaha Blue Blood Bulldog ($n = 1$), English Bulldog ($n = 1$), Bernese Mountain Dog ($n = 1$), Boxer ($n = 1$), American Pit Bull Terrier ($n = 1$), and Rottweiler ($n = 1$).

Of these dogs, 79 were spayed females, 64 castrated males, five males, and one female (Figure 3B). The median age of the population was 5 years (range 1–12 years) and the median bodyweight was 35.2 kg (range 15.1–81.8 kg) (Figure 3H). In this study, this cohort of dogs had 20 stable and 143 unstable stifles (Figure 3C). All 20 stable stifles had partial disruption of the CCL. A total of 67 (41%) of the stifles had a bucket handle medial meniscus tear and 96 of the stifles did not have a bucket handle meniscus tear (Figure 3D).

Of the 163 stifles dogs included in this study, 131 had a specific duration of signs and 136 a BCS recorded in the medical records appropriate for inclusion in analyses (see Section 2). The median duration of signs for these dogs prior to surgical intervention was 3 months (range 0.2–14 months) (Figure 3I). In terms of BCS, 46/136 dogs (33.8%) had a BCS of lean to ideal (4–5/9), 67/136 (49.3%) were classified as overweight (6, 7), and 23/136 (16.9%) were evaluated as obese (8, 9) at the time of surgery (Figure 3E). Of the 163 stifles evaluated, the median cartilage score was 1 (range 0–4) (Figure 3J).

Joint capsular synovitis was identified in all 163 of the stifles examined (100%). The most frequent synovitis severity score in 90 of the 163 stifles (55.2%) was a score of 3/5. The next most common synovitis severity score was 4/5, seen in 40/163 stifles (24.5%), followed by a synovitis severity score of 2/5 in 32/163 (19.6%), and 1/163 stifles (.61%) had a score of 5/5. No stifles had a score of 0/5 or 1/5. When subgrouped into three categories, low (1, 2), middle (3), and high (4, 5) synovitis (see Section 2), 32/163 (19.6%) had low, 90/163 (55.2%) had middle, and 41/163 (25.2%) had high scores (Figure 3F).

In univariate analyses, the severity of synovitis scores was not associated with stifle laterality (p-value = .88), age (p-value = .42), BCS (p-value = .34), presence or absence of a meniscus tear (p-value .87), or stifle stability (p-value = .45). The extent of synovitis scores showed a statistically significant association with bodyweight (p-value = .005). For every kilogram increase in bodyweight, the likelihood of a stifle having a high synovitis score versus a middle or low score combined was 1.04 greater. The severity of synovitis score was also associated with median cartilage score ($p = .002$), where for one unit increase in median cartilage score the odds of a high synovitis score versus a middle or low score combined was 2.36 greater. Additionally, sex was statistically associated with severity of synovitis score (p-value = .032) with females having a .51 greater odds of a high synovitis score versus the combined middle and low categories. Lastly, duration of clinical signs reported for each stifle was also statistically associated with increasing synovitis scores (p-value <.001), where for each month increase in reported duration of clinical signs, the odds of a high synovitis score versus the combined middle and low categories was 1.27 times greater.

The multivariable ordered logistic regression analysis included the bodyweight, median cartilage score, sex, and duration of clinical signs as their p-value was less than .2 in the univariate analyses. In the multivariable analysis, median cartilage score was statistically associated with severity of synovitis score when controlling for sex, duration of clinical signs, and

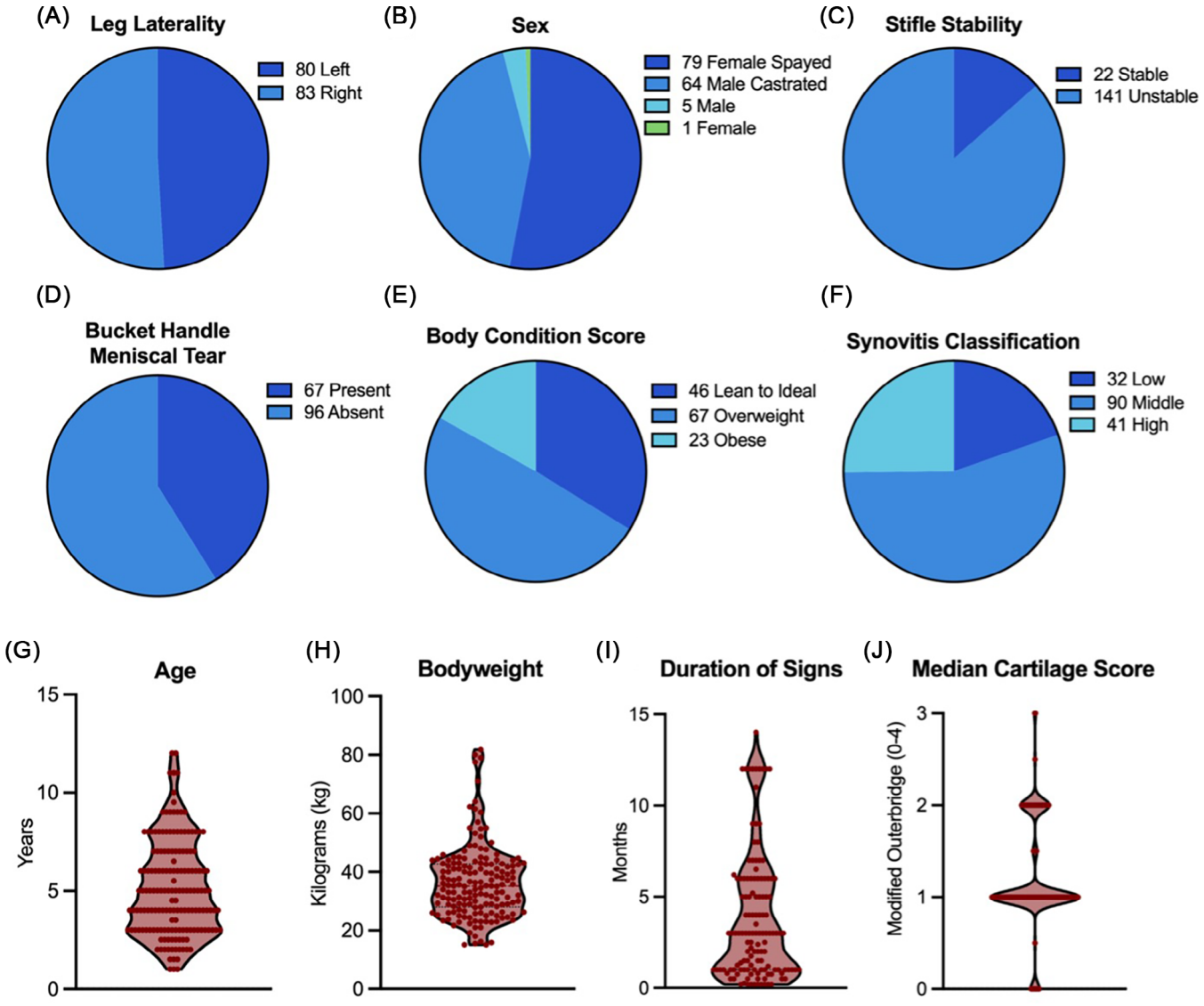

FIGURE 3 Demographic and distribution data of dogs with naturally occurring cranial cruciate ligament (CCL) tears included in this study. Parts-of-whole graphs for variables (A) leg laterality, (B) sex, (C), stifle stability, (D) bucket handle medial meniscus tear presence or absence, (E) body condition score (BCS), and (F) synovitis classification. Violin plots for continuous data variables (G) age, (H) bodyweight, (I) duration of signs, and (J) median cartilage score.

bodyweight (p-value = .042). In this model, for each unit increase in median cartilage score, the odds of high synovitis score versus the combined middle and low categories were 2.1 times greater. Furthermore, the duration of clinical signs was also statistically associated with synovitis score severity, where with each month increase in reported duration of clinical signs the odds of a high synovitis score versus the combined middle and low categories were 1.27 times greater ($p < .001$). However, when controlling for other covariates in the model, bodyweight was only marginally (p-value = .083), and sex was not (p-value = .17) statistically associated with severity of synovitis score.

4 | DISCUSSION

In this cohort of dogs examined, all stifles exhibited joint capsular synovitis, with varying degrees of severity. Notably, the most prevalent synovitis score was 3/5, followed by 4/5, while scores of 0/5 or 1/5 were absent. These findings are consistent with other reported outcomes in dogs with naturally occurring CCL tears with respect to synovitis on arthroscopic scoring.[7,9] Univariate analyses identified associations between synovitis severity and bodyweight, median cartilage score, sex, and duration of clinical signs. Interestingly, synovitis severity was not significantly correlated with the stifle side affected, age,

BCS, presence of a meniscus tear, or stifle stability. Both bodyweight, median cartilage score, and duration of clinical signs exhibited positive correlations with synovitis severity. Multivariable analysis confirmed the independent associations of median cartilage score and duration of clinical signs with synovitis severity, even after adjusting for other covariates. Specifically, each unit increase in median cartilage score was associated with a 2.1 times greater odds of high synovitis score, while each month increase in reported duration of clinical signs was associated with a 1.27 times greater odds of high synovitis score. Notably, bodyweight and sex showed weaker associations with synovitis severity in the multivariable model.

Although the etiology of CCL disease and the subsequent occurrence of tears in dogs is multifaceted, the precise role of synovitis in disease progression remains ambiguous. It is uncertain whether synovitis serves as an initiator of the disease process or if it ensues subsequent to disease onset. However, it is widely recognized that synovitis constitutes a pivotal characteristic of stifle joints with CCL disease and tears.[7–9] In this study, the median arthroscopic cartilage score of the affected stifle had the highest significance in relation to severity of synovitis scores, when controlling for other covariates. This finding is consistent with the understanding that joint-wide synovitis worsens with progressive OA and is perpetuated by a cycle of cartilage degradation contributing to increasing levels of inflammatory cytokines, synovial angiogenesis, and ultimately synovial fibrosis.[32–35]

The second statistically significant variable contributing to increased synovitis score was owner reported duration of clinical signs. Recent research has advocated for earlier surgical intervention in dogs with CCL disease to slow the progression of OA, as it was found that the severity of CCL tearing was correlated with the degree of radiographic OA.[37,38] To the best of our knowledge, the association between the duration of clinical signs and the degree of CCL tearing has not been previously investigated, but our findings also align with these guidelines to intervene early in an attempt to lessen the degree of synovitis and cartilage damage. Unfortunately, the reduction of synovitis following surgical intervention has also not been investigated, but potentially any treatment to mitigate joint-wide synovitis could be beneficial to decrease the progression of OA. Additionally, it is not clear if severe synovial pathology, such as synovial fibrosis, can be reversed once it is established, and therefore, potentially, if the intervention is performed too late, the synovial changes may be permanent.

While not significant in the multivariate analysis, it is important to discuss bodyweight and sex, two variables that had statistical significance with increasing severity of synovitis scores in the univariate analyses. In other studies reporting the frequency of synovitis in dogs with naturally occurring CCL tears, increased bodyweight was significantly correlated with severity of synovitis.[7,9,36] Furthermore, in one study, dogs with a higher bodyweight had increased levels of S100A8/S100A9 (calprotectin) positive macrophages in their synovium.[36] This marker is linked to the activation of proinflammatory macrophage types recently drawn to a location of injury, suggesting ongoing inflammation rather stabilization within the synovium of these dogs.[37,38] Particularly, this increase in macrophages was appreciated in dogs >15 kg,[36] which was the weight inclusion criteria for this current study. Our finding that higher bodyweight independently correlates with elevated synovitis scores aligns with these prior conclusions. However, within our study population, consisting of dogs weighing 15 kg and greater, increasing bodyweight was not the primary factor contributing to heightened synovitis severity in the multivariate analysis. In addition to bodyweight, sex was statistically significant in univariate analysis. Specifically, being female ($n = 79$ spayed, $n = 1$ intact) showed an increased association with synovitis score severity compared to being a male ($n = 64$ neutered, $n = 5$ intact). Current research shows that neutering, particularly at a younger age, may lead to an increased risk of CCL disease.[39,40] In this study, due to the small sample size of intact animals, a difference between these two populations could not be appropriately evaluated. Nonetheless, both of the above findings suggest that, among this cohort of larger dogs, there are additional factors (median cartilage score and duration of clinical signs) that are more important contributors to the increase in synovitis scores beyond bodyweight and sex.

Interestingly, another variable that was not associated with synovitis severity score was the presence of a bucket handle tear of the caudal horn of the medial meniscus. Bucket handle meniscal tears in conjunction with CCL disease are frequently associated with increased severity of clinical signs when compared to CCL tears alone.[41] The precise cause of why the meniscus leads to considerable clinical symptoms has not been fully elucidated, however, similar to another study, bucket handle meniscal tears were not associated with synovitis severity.[42] Additionally, it has been reported that bucket handle meniscal tears in dogs with CCL disease were also not associated with increased cartilage lesions at the time of surgical intervention.[43]

Several limitations exist in this study. One limitation is the potential variability in scoring the gross synovial appearance and articular cartilage. We attempted to decrease the variability of the synovial scoring by using a previously reported scoring system with reported good

interobserver agreement[33] and using a single, experienced observer to score all synovial tissue. Similarly, we chose the modified Outerbridge classification system for cartilage scoring, which has substantial intraobserver agreement when scoring canine stifle joints.[44] Another limitation is that the observer scoring the videos was the surgeon who performed the arthroscopies. In an attempt to decrease bias of knowing the clinical presentation while scoring the arthroscopic videos, all patient identifying information was removed from the videos and the scoring was performed at least 1 year following the date of the surgery. Additionally, there could be bias when the observer was scoring one anatomic structure as another structure could be in the same video. For instance, if there was a high synovitis severity score one might be biased to say there was also higher cartilage scores. We attempted to minimize this potential source of bias by placing each anatomic region of the arthroscopy in separate videos; however, in some of the videos it was impossible to remove other portions of the joint that were not the exact structure being graded, so the observer saw both anatomic regions in a single video. Similarly, even though the videos were separated by the anatomic regions, the observer was aware that all of the individual videos were from the same stifle joint.

As mentioned above, another limitation of this study was the inability to appropriately evaluate factors influencing synovitis score in intact versus neutered dogs due to the small sample population included in this study. Additionally, since this study only included dogs weighing 15 kg and greater these results cannot be applied to smaller breed dogs. Finally, this was a single-center study, and future research comparing factors contributing to the severity of synovitis across institutions is necessary to increase the generalizability of these findings across centers and populations. Ultimately, although we aimed to include as many pertinent variables as possible, this study might not have addressed all confounding factors impacting the correlation between the covariates and synovitis score. This could potentially affect the precision of the conclusions drawn.

Additionally, we only evaluated the synovium at the time of surgical intervention. The progression of OA following surgical stabilization techniques is well documented, albeit at a slower rate than dogs with untreated instability.[2,45,46] Unfortunately, there are limited second-look studies in canine patients evaluating the presence and degree of synovitis following stabilization techniques.[47] It is unknown if the progression of OA is due to a lack of restoration of mechanical forces and stability of the stifle, the influence of proinflammatory or catabolic factors in the joint that allow for persistent synovitis, or if it is multifactorial. Further second-look studies are warranted to evaluate the presence and severity of synovitis and its role in long-term progression of disease along with clinical symptoms.

In conclusion, joint-wide synovitis is common in dogs with naturally occurring CCL tears and all dogs in this study population had abnormal synovium on arthroscopic scoring. When accounting for confounding variables, our results show that median cartilage score and duration of clinical signs are associated with greater synovitis severity scores. These findings suggest that early interventions aimed at reducing inflammation in the stifle joint in dogs with CCL disease should be considered. However, the persistence and severity of synovitis in the joint following the current, widely used surgical stabilization techniques in dogs is still unknown. Additionally, the contribution of synovitis to clinical presentation remains unclear, even though it is thought to contribute to pain and joint dysfunction, as described in people with OA.[23–26] Further research is necessary to understand not only the specific role of synovitis in CCL disease and clinical presentation, but also as a potential future target for treatment intervention.

AUTHOR CONTRIBUTIONS

Lemmon EA, VMD, PhD: Contributed to study design; data acquisition, analysis, and interpretation, along with manuscript preparation and revision. Xiao R, PhD: Contributed statistical data analysis and interpretation; and manuscript preparation and revision. Mauck RL, PhD: Contributed to data analysis and interpretation; and manuscript preparation and revision. Agnello KA, DVM, MS, DACVS (Small Animal), DACVSMR (Canine): Contributed to study conception and design; data acquisition, analysis, and interpretation; and manuscript preparation and revision. All authors provided critical review and final approval of the submitted manuscript. All authors are aware of their respective contributions and have confidence in the integrity of all contributions.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

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