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Contribution of Habitual Activity to Cruciate Ligament Rupture in Labrador Retrievers

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Abstract

Objective The aim of this study was to describe the contribution of signalment and habitual activity in the development of cruciate ligament rupture (CR) in Labrador Retrievers.

Study Design Four hundred and twelve client-owned purebred Labrador Retrievers were recruited. Dogs were assigned either as affected with CR or as controls based on signalment, physical examination and radiographic evidence of disease. Clients were asked to complete a questionnaire related to signalment, concurrent disease and a questionnaire pertaining to their dog's activity before development of CR or general activity during the dog's most active years.

Results Habitual activity was not significantly different between dogs affected with CR and controls. There was no significant difference in neuter status or body weight between CR affected dogs and controls. Labrador Retrievers with a yellow coat, and Labradors that did not maintain an optimal body weight in the opinion of their veterinarian were at increased risk of developing CR.

Conclusions Habitual activity level is not a risk factor for development of CR in Labrador Retrievers. Our study did not show neuter status, sex or body weight to be risk factors for CR. However, coat colour and not sustaining optimal body condition are significant risk factors for CR.

Keywords
- habitual activity
- dog
- cruciate ligament rupture
- questionnaire

Introduction

Cruciate ligament rupture (CR) is a spontaneous degenerative condition of the canine stifle that is responsible for ~20% of lameness in dogs.[1–3] The pathological basis of CR is not fully understood. Cruciate ligament rupture is a complex genetic disease with moderate heritability.[4–6] As a complex trait, CR has a multifactorial aetiopathogenesis with genetic and environmental risk factors. The environmental contribution to CR is not well characterized.[5,7] Breed is the only risk factor consistently associated with development of CR.[2,8] Body weight and neutering status may also contribute to disease risk.[2,8–10] Cruciate ligament rupture is common in Labrador Retrievers with an estimated prevalence between 3.81 and 5.79%.[2,8,11–13]

Contribution of habitual activity to development of CR has not been studied in detail. Clinical metrology instruments for use in client-owned dogs provide a standardized clinical assessment method of disease parameters, such as stiffness or exercise intensity.[14–16] For this study, we designed a custom questionnaire that had response elements chosen to specifically study activity associated with CR. Questions pertaining to patient information and background were also collected. A lifestyle section was created using a subset of questions from the Liverpool Osteoarthritis in Dogs (LOAD) questionnaire,[14] in combination with questions about additional orthopaedic disease and weight management. Patient information and background sections assessed pertinent information about the patient's signalment and medical

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history. The lifestyle section examined a patient's daily pattern of exercise, activity levels and ability to exercise, without reference to disease status.

The aim of this study was to assess whether differences in habitual activity, signalment and weight management exist between Labrador Retrievers affected by CR and control Labrador Retrievers without CR. We used a questionnaire to study a large population of pure-bred client-owned Labrador Retrievers. We hypothesized that habitual activity in Labrador Retrievers does not affect risk of CR.

Materials and Methods

Dogs

Owners of pure-bred Labrador Retrievers were recruited from the UW Veterinary Care Hospital at the University of Wisconsin-Madison between 2011 and 2018. A total of 412 dogs were enrolled, consisting of 166 CR affected dogs and 246 controls. All procedures were conducted with the approval of the Animal Care & Use Committee, School of Veterinary Medicine, University of Wisconsin-Madison (V1070). Dogs were recruited with informed written consent from each owner.

Case Selection Criteria

Dogs were diagnosed with non-contact CR through a combination of history, physical examination and orthopaedic examination including assessment of stifle instability, undertaken by a board-certified small animal surgeon. For cases, dogs were recruited throughout the United States. Dogs with a history of trauma or other types of stifle pathology were excluded. Control dogs were recruited through the UW Veterinary Care Hospital. All pure-bred Labrador Retrievers over the age of 8 years that were presented to the hospital were considered for participation. Interested owners in the catchment area of our hospital with qualifying unaffected pure-bred Labrador Retrievers were also invited to participate. All enrolled dogs had stifle radiographs that were examined by a board-certified small animal surgeon (SJS, PM) for signs of cranial tibial translation and CR-associated degenerative radiographic changes such as compression of the infrapatellar fat pad, synovial effusion and stifle osteophytosis.[17]

Control Selection Criteria

The majority of CR affected Labrador Retrievers are diagnosed before the age of 8 years.[18] Therefore, we defined our control group as Labrador Retrievers 8 years of age and older with no clinical or radiographic evidence of CR. Orthopaedic examination and lateromedial weight-bearing radiographs of the stifle were used to screen the control population.[19]

Questionnaire

Clients were asked to complete a questionnaire consisting of three parts: patient information, background and lifestyle. The lifestyle section included questions as described in the original LOAD questionnaire, along with further questions asking about additional orthopaedic conditions other than CR and weight management plans. For CR-affected dogs, owners were instructed to answer questions regarding their dog's activity levels before development of CR. For control dogs that were healthy, owners were instructed to answer questions relative to their dog's current status; for control dogs with current co-morbidities that affected habitual activity, owners were instructed to answer questions regarding their dog's activity levels prior to relevant disease development. The patient information section included sex, coat colour, neuter status, age and weight. The background section collected pertinent information on other orthopaedic co-morbidities, additional non-orthopaedic disease and medications or supplements. The lifestyle section consisted of 13 questions which were divided categorically to assess various aspects of habitual activity.[20] Nine questions, each scored on a 4- or 5-point scale, were used to quantify each individual dog's overall habitual activity level. These questions were categorized into habitual activity and exercise (6 questions), stiffness from orthopaedic disease (2 questions) and effect of weather on stiffness (1 question). General activity level was calculated as the sum of responses to questions regarding the number of walks a dog undertook per day and owner's perspective on how active their dog was on a regular basis. Activity level during exercise was determined as the sum of responses regarding how far a dog was exercised each day, the type of exercise a dog undertook with respect to how often a dog was on leash, and how most exercises were performed (i.e. walking on or off leash, at a trot or a run).[20]

Questions relating to habitual activity and exercise were determined for all dogs, and also segregated into two groups, including (1) dogs whose owners reported that their dog had a second orthopaedic condition in addition to CR and (2) dogs whose owners did not consider their dog had any other orthopaedic conditions.

For owners who believed their dog had a second orthopaedic condition, stiffness was assessed using questions about how the non-CR condition affected their dog's ability to exercise and how stiff their dog was after exercise. To ascertain the effect of weather on stiffness, clients were asked to evaluate the effect of cold, damp weather on the ability to exercise.

The remaining four questions in the lifestyle section analysed habitual activity level in a categorical manner. These questions looked for trends in days of the week more frequently exercised, terrain dogs most frequently used during exercise and the perspectives on the dog's actual verses optimum body weight.

Statistical Analysis

A chi-squared test was used to evaluate coat colour, neuter status, activity levels during the week, terrain used during exercise and measures associated with body condition. When appropriate, data were analysed for normality using the D'Agostino & Pearson normality test. To compare owner scoring of questionnaire items between CR affected and control groups, the Student's *t* test or Mann–Whitney *U* test was used, as appropriate. Results were considered significant at $p < 0.05$. Groups of results considered together, including coat colour and questionnaire components relating to activity levels, were corrected for multiple comparisons using the false discovery rate under dependency method.[21] Data were

Table 1 Sex and neuter status distribution of cruciate ligament rupture case and control Labrador Retrievers

Sex	CR	Control	Odds ratio	*p*-Value
Male	7.8% (*n* = 13)	12.6% (*n* = 31)	0.59	0.12
Neutered male	45.8% (*n* = 76)	44.3% (*n* = 109)	1.06	0.77
Female	6.6% (*n* = 11)	6.5% (*n* = 16)	1.02	0.96
Spayed female	39.8% (*n* = 66)	36.6% (*n* = 90)	0.98	0.93
	100% (*n* = 166)	100% (*n* = 246)		

Abbreviation: CR, cruciate rupture.

reported as mean ± standard deviation for parametric data and median (range) for non-parametric data.

Results

Four hundred and twelve pure-bred Labrador Retrievers were enrolled in this study. The study population included 185 castrated males, 75 ovariohysterectomized females, 44 intact males and 27 intact females (►**Table 1**). There was no significant difference in neuter status between CR affected and control dogs. No significant difference in body weight was seen between CR affected (37.2 ± 0.56 kg) and control dogs (33.8 ± 0.42 kg). Coat colour was identified as a potential risk factor for CR. Black dogs had decreased risk of CR (odds ratio, OR = 0.77, $p = 0.02$), whereas dogs with a yellow coat were at increased risk of CR (OR = 1.91, $p = 0.01$). Chocolate coat colour did not significantly influence CR risk (►**Table 2**).

An orthopaedic disease other than CR was reported by 142 owners, including 56 CR-affected and 86 control dogs. Other diseases reported by owners included osteoarthritis (OA) ($n = 53$), hip dysplasia ($n = 14$), elbow dysplasia ($n = 13$), shoulder disease ($n = 7$), disc disease ($n = 4$), unspecified soft tissue injury ($n = 4$), luxating patella ($n = 2$), osteosarcoma ($n = 2$), metatarsal fracture ($n = 1$) and unspecified ($n = 53$).

Table 2 Distribution of coat colours amongst cruciate ligament rupture case and control Labrador Retrievers

Coat colour	CR	Control	Odds ratio	*p*-Value
Black	28.4% (*n* = 46)	41.4% (*n* = 101)	0.77	0.02
Chocolate	32.0% (*n* = 32)	22.5% (*n* = 55)	0.85	0.92
Yellow	51.9% (*n* = 84)	36.1% (*n* = 88)	1.91	0.01
	100% (*n* = 162)	100% (*n* = 244)		

Abbreviation: CR, cruciate rupture.
p-Values were adjusted for multiple comparisons using false discovery rate correction.[21]

Table 3 Habitual activity in Labrador Retrievers

	CR affected	Controls	*p*-Value
General activity level			
Total score	5 (2–10)	5 (2–10)	1
Q2: No. of walks per day	1 (1–5)	2 (1–5)	0.017
Q7: Activity level on a regular basis	3 (1–5)	3 (1–5)	0.32
Activity level at exercise			
Total score	8 (3–13)	8 (3–13)	1
Q1: Miles walked per day	2 (1–5)	2 (1–5)	1
Q3: Exercise on or off leash	3 (1–5)	3 (1–5)	1
Q6: Type of exercise	3.5 (1–4)	3 (1–4)	1
Ability to exercise			
Q10: Total score	4 (1–5)	4 (2–5)	1

Abbreviation: CR, cruciate rupture.
$n = 152–166$ for CR cases and 225–245 for control. *p*-Values were adjusted for multiple comparisons using false discovery rate correction.[21]

Habitual Activity and Exercise

Habitual activity was measured in three ways: general activity level, activity level at exercise and ability to exercise. General activity level was determined by combining question responses relating to the number of walks per day and the owner's overall impression of how active their dog was on a regular basis.[20] With regard to general activity level, there were no significant differences between CR and control dogs (►**Table 3**), regardless of whether dogs did or did not have other orthopaedic disease (►**Table 4**). Activity level at exercise was determined by combining question responses that related to the miles walked per day and the type of exercise most often performed.[20] No differences in activity levels at exercise were seen between CR and control dogs, regardless of concurrent orthopaedic disease (►**Tables 3** and **4**). The ability to exercise was also not found to be a risk factor for development of CR, regardless of concurrent orthopaedic disease (►**Tables 3** and **4**).

Stiffness from Other Orthopaedic Disease

For dogs whose owners reported orthopaedic diseases other than CR, responses to questions relating to a dog's ability to exercise and stiffness after exercise were not significantly different in CR and control dogs (►**Fig. 1**).

Effect of Weather on Exercise

The effect of weather on stiffness was not significantly different between CR and control dogs, regardless of the presence or absence of other orthopaedic disease (►**Fig. 2**).

Frequency of Exercise and Terrain

Analysis of exercise showed no significant differences between CR and control groups with regard to the frequency of exercise or terrain on which dogs were most commonly

Table 4 Habitual activity in Labrador Retrievers with and without other orthopaedic disease

	CR dogs without other OD	Controls without other OD	*p*-Value	CR dogs with other OD	Controls with other OD	*p*-Value
Habitual activity level and exercise						
Total score	5 (2–10)	5 (2–10)	1	4 (2–9)	5 (2–10)	0.98
Q2: No. of walks per day	1 (1–5)	2 (1–5)	0.76	1 (1–4)	2 (1–5)	0.98
Q7: Activity on a regular basis	3 (1–5)	3 (1–5)	0.12	3 (1–5)	3 (1–5)	1
Activity level at exercise						
Total score	8 (3–13)	8 (3–13)	1	8 (3–12)	8 (3–12)	1
Q1: Miles walked per day	2 (1–5)	2 (1–5)	1	2 (1–5)	2 (1–5)	1
Q3: Exercise on or off leash	3 (1–5)	3 (1–5)	1	3 (1–5)	3 (1–5)	1
Q6: Type of exercise	4 (1–4)	3 (1–4)	1	3 (1–4)	3 (1–4)	1
Ability to exercise						
Q10 score	5 (1–5)	5 (2–5)	1	4 (1–5)	4 (2–5)	1

Abbreviations: CR, cruciate rupture; OD, orthopaedic disease.
$n = 152$–166 for CR cases and 217–245 for controls. *p*-Values were adjusted for multiple comparisons using false discovery rate correction.[21]

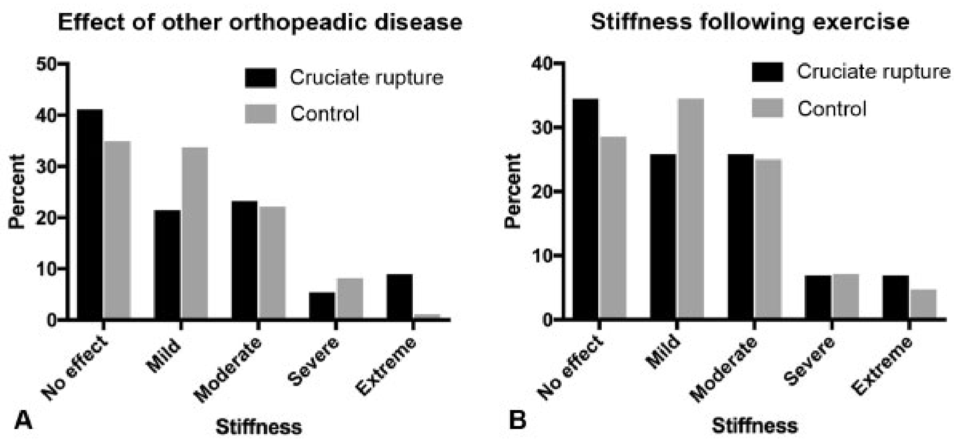

Fig. 1 Owner responses to questions pertaining to the effect of orthopaedic conditions other than cruciate rupture (CR) on activity levels in CR case and control Labrador Retrievers. (**A**) When owners were asked to what degree stiffness affected their dog's ability to exercise, no significant difference between CR and control dogs was seen ($p = 0.99$). (**B**) When owners were asked to what degree their dog showed stiffness after exercise, no significant difference between CR and control dogs was seen ($p = 0.76$). $n = 163$ CR cases, $n = 244$ controls.

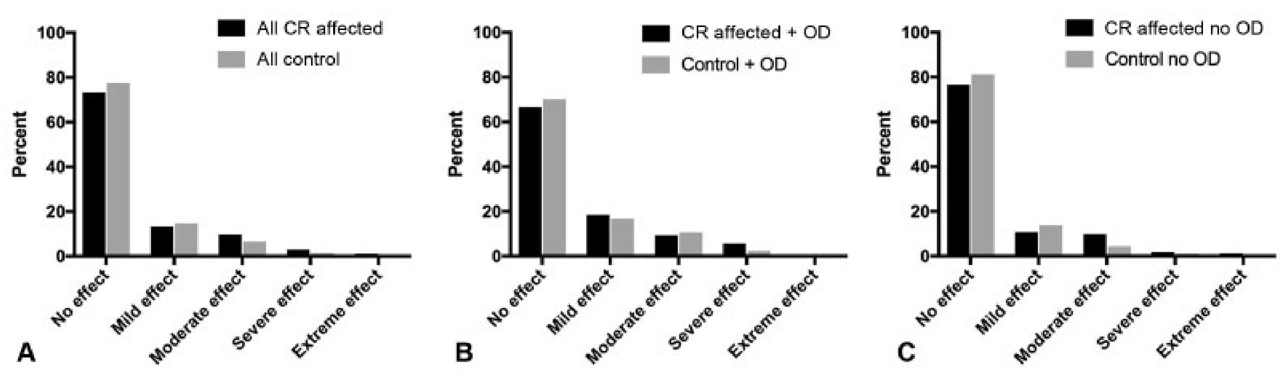

Fig. 2 Owner responses to questions pertaining to the effect of weather on lameness in cruciate rupture (CR) case and control Labrador Retrievers. (**A**) Responses of all owners showed no significant difference between dogs that were affected with CR and controls ($p = 0.24$). $n = 165$ CR cases, 244 controls. (**B**) When responses were analysed only from owners who reported their dog to have another orthopaedic condition, no significant difference between dogs affected with CR and controls was seen ($p = 0.24$). $n = 54$ CR cases, 84 controls. (**C**) When responses were analysed only from owners who reported their dog to not have any other orthopaedic conditions, no significant difference between dogs affected with CR and controls was seen ($p = 0.64$). $n = 111$ CR cases, 160 controls. OD, other orthopaedic disease.

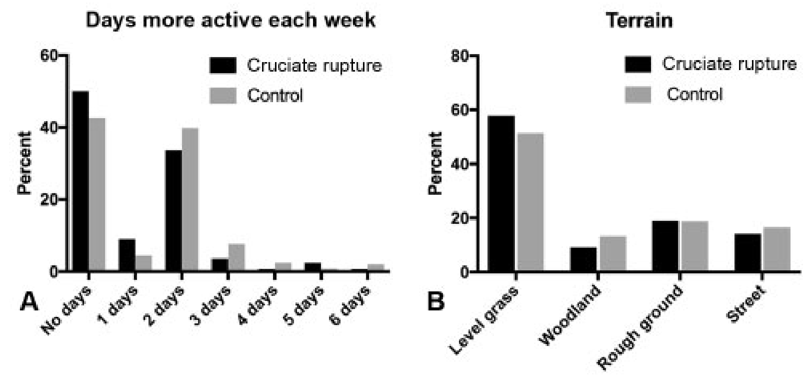

Fig. 3 Owner responses to questions pertaining to changes in activity level over a given week and terrain upon which dogs were most commonly exercised in cruciate rupture (CR) case and control Labrador Retrievers. (**A**) Responses from owners regarding the number of days over the course of a week dogs had higher activity than the rest of the week showed no significant difference between CR case and control dogs. $n = 166$ CR cases, 246 controls. (**B**) Responses from owners regarding the type of terrain that their dog most frequently exercised on showed no significant difference between CR case and control groups. $n = 142$ CR cases, 218 controls.

exercised. No differences were seen between groups with regard to whether dogs were more active on a given number of days over the course of the week than the rest of the week (►**Fig. 3A**). There was also no difference between CR dogs and control dogs with regard to the type of terrain they most commonly exercised on (►**Fig. 3B**).

Weight Management

Cruciate rupture dogs were significantly more likely to have been on a weight management plan than control dogs ($p = 0.005$). When only castrated or ovariohysterectomized dogs were considered, CR dogs were significantly more likely to have been on a weight management plan than control dogs (OR = 1.90, $p = 0.01$). When only intact dogs were considered, there was no significant difference between CR and control dogs (►**Table 5**).

Based on feedback from their veterinarian, CR dogs were significantly less likely to be an optimum weight overtime than control dogs ($p = 0.0001$). When only neutered dogs or only intact dogs were considered, in both instances CR dogs were less likely than control dogs to have sustained an optimum weight over time based on veterinarian feedback (OR = 2.30, $p = 0.002$; OR = 7.5, $p = 0.009$ respectively) (►**Table 5**).

Discussion

This study was designed to compare habitual activity levels of Labrador Retrievers before development of CR to control dogs that did not develop CR by 8 years of age. We also evaluated signalment and weight management for associations with development of CR. Based on the results of this study, we accepted our hypothesis that habitual activity level in Labrador Retrievers is not a major risk factor for the development of CR.

We chose to create a customized questionnaire designed to evaluate habitual activity in dogs with and without CR. We used a subset of questions for this work from the LOAD questionnaire,[14] which was developed to assess dogs with OA[14] including response to therapeutic treatment.[22] The questionnaire used for this study was designed to advance knowledge regarding differences in habitual activity between dogs affected with CR and a control population. The original LOAD questionnaire was designed to determine habitual activity in patients with OA through three measures, including general activity levels, activity level at exercise and ability to exercise. The questionnaire used for this study also assessed these measures as they relate to CR.

Table 5 Responses from owners regarding weight management

	All dogs			Neutered dogs			Intact dogs		
Q12: Has your dog been on a weight management plan?									
	CR, *n* (%)	Control, *n* (%)	*p*-Value (OR)	CR, *n* (%)	Control, *n* (%)	*p*-value (OR)	CR, *n* (%)	Control, *n* (%)	*p*-Value (OR)
Yes	51 (30.7)	46 (18.7)	0.005 (0.52)	46 (32.4)	40 (20.1)	0.002 (2.30)	5 (20.8)	6 (12.8)	0.37 (1.80)
No	115 (69.3)	200 (81.3)		96 (67.6)	159 (79.9)		19 (79.2)	41 (87.2)	
Q13: Based on feedback from your veterinarian, do you think you dog has sustained his/her optimum weight over time?									
	CR, *n* (%)	Control, *n* (%)	*p*-Value (OR)	CR, *n* (%)	Control, *n* (%)	*p*-Value (OR)	CR, *n* (%)	Control, *n* (%)	*p*-Value (OR)
Yes	119 (72.1)	215 (87.4)	0.0001 (2.68)	102 (71.8)	170 (85.4)	0.002 (2.30)	18 (75.0)	45 (95.7)	0.009 (7.50)
No	46 (27.9)	31 (12.6)		40 (28.2)	29 (14.6)		6 (25.0)	2 (4.3)	

Abbreviations: CR, cruciate rupture; OR, odds ratio.

We found general activity levels were not significantly different between CR dogs and control dogs, regardless of whether animals had other orthopaedic disease. General activity level was determined by combining question responses relating to the number of walks per day and activity on a regular basis.[20] We did not find activity level at exercise to be different between CR dogs and control dogs. Activity level has previously been hypothesized to associate with CR development,[1,13,23] while other work investigating differences between protected and high-risk breeds failed to show activity level to be a substantial risk factor for CR development.[19] Time spent on and off leash has also been shown to be similar in CR case and control dogs.[24]

We did not find significant differences between CR dogs and controls with respect to changes in exercise levels during the week. Similarly, there were no differences between CR dogs and controls with respect to the type of terrain on which dogs most frequently exercised. Collectively, these findings are consistent with previous work that showed long-term exercise does not alter properties of articular cartilage that could lead to degenerative changes in the joints,[25] and based on the current study, probably does not contribute to the development of CR.

Other orthopaedic disease besides CR was reported by owners in 142 dogs, with OA being most common. By analysing our data collectively and then looking at subsets of dogs with and without other orthopaedic disease, we were able to minimize confounding changes in activity level that could be attributed to other conditions affecting dog mobility.

Interestingly, we found that Labrador Retrievers with a yellow coat colour had an increased the risk of CR, while a black coat colour was protective. The inheritance of coat colour in Labrador Retrievers is a result of gene interactions between two loci. Black coat colour is a dominant trait and chocolate is the result of a recessive allele. Yellow coat colour is also recessive and suppresses both the black and chocolate alleles.[26] It is possible that breeding two dogs with recessive alleles to obtain a yellow or chocolate coat colour may be a form of positive selection pressure on the CR trait. The chocolate coat colour is associated with a significantly shorter life-span.[27] Further work investigating the genetic relationships between coat colour and CR in the Labrador Retriever is needed.

Our study showed that neuter status and sex are not risk factors for CR in this population of Labrador Retrievers. While this finding of neuter status has been reported previously,[1] current evidence suggests that across breeds, neutering increases risk of CR when compared with intact dogs.[2,8–10,12,13,24,28] The reason our results differ from previous findings is unclear, although it may be a consequence of the relatively low number of intact CR dogs in the study, or a reflection of only including pure-bred Labrador Retrievers. Intact dogs accounted for 17% of our population, whereas studies that showed increased risk for CR in gonadectomized dogs had 32 to 70% intact dogs.[2,8,9,12,28] We did not find a relationship between sex and CR. Earlier work has shown mixed results with respect to an influence of sex on CR development.[8,9,11,28,29] Based on our results, sex does not appear to be a risk factor for the development of CR in the Labrador Retriever.

We did not find body weight to be an environmental risk factor for CR. However, we did find that CR dogs were more likely to have been on a weight management plan than control dogs, and based on veterinarian feedback, CR dogs were more likely to have been overweight than control dogs. Body weight is not the best indicator of body condition due to body size variation, which can be substantial in the Labrador Retriever. This suggests that in Labrador Retrievers, body condition, rather than body weight, may be an important environmental risk factor for the development of CR. Additionally, Labrador Retrievers are at increased risk of being overweight or obese when compared with other breeds.[27] Taken together, these findings support earlier work showing obesity is an environmental risk factor for the development of CR.[13]

This study was based on owner questionnaires, and therefore has limitations inherent to this method of data collection. Other approaches to data analysis, such as modelling, could have been be considered. Notably, the questionnaire used in this study has not been validated. The LOAD questionnaire, from which some questions in our survey instrument were derived, was validated for OA,[14,20] a condition distinct from CR. Importantly, bias associated with recall must also be considered, as owners of CR affected dogs and a subset of owners of control dogs were asked to retrospectively evaluate features of their pet's habitual activity. It is possible that owners were not able to accurately recall features of their pet's past habitual activity levels. Furthermore, there is a difference between the age of CR affected dogs and control dogs, which may have influenced results, although differences in activity that might be expected with increasing age were not seen. We found that owners who reported their dogs to have an additional orthopaedic disease had a variable understanding of what other orthopaedic disease processes their dogs had, and future work would benefit from more diagnostics to confirm or diagnose the presence of other diseases that could affect a dog's mobility.

In conclusion, our study indicates that habitual activity level, as assessed by owner questionnaire, is not a significant risk factor for the development of CR in Labrador Retrievers, suggesting that activity does not have a substantial role in disease development. However, this work supports earlier findings that body condition is a relevant environmental risk factor for disease development. Our study did not show neuter status, sex or body weight to be risk factors for CR. Interestingly, we found that coat colour is a significant risk factor for CR, a finding that warrants further investigation. More research is needed to fully understand other environmental risk factors, such as body mass index and nutrition, that may play a role in the development of CR.

Authors' Contributions

Hannah M. Terhaar assisted in data analysis & interpretation, drafting of the manuscript, approval of the manuscript and is publicly accountable for relevant content. Peter Muir assisted in conception of the study, study design, acquisition of data, data analysis & interpretation, drafting of the manuscript, approval of the manuscript and is publicly accountable for relevant content. Lauren A. Baker assisted in acquisition of data, data analysis & interpretation approval of the manuscript and is publicly accountable for relevant content. Emily E. Binversie assisted in acquisition of data, approval of the manuscript and is publicly accountable for relevant content. Jacqueline Chi assisted in acquisition of data, approval of the manuscript and is publicly accountable for relevant content. Susannah J. Sample assisted in conception of the study, study design, acquisition of data, data analysis & interpretation, drafting of the manuscript, approval of the manuscript and is publicly accountable for relevant content.

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Conflict of Interest

None declared.

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