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Disease-related and overall survival in dogs with cranial cruciate ligament disease, a historical cohort study

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ABSTRACT

Objective: To analyse the effect of treatment method and other risk factors on survival in dogs with cranial cruciate ligament disease (CCLD).
Methods: A historical cohort study of 333 dogs presenting with CCLD at two University Hospitals (2011–2016) was performed. Signalment, history, treatment and follow-up details were retrieved from medical records, dog owners and referring veterinarians. Treatment groups were defined; conservative or surgical with either lateral fabellotibial suture (LFS) or osteotomy procedures. Multivariable Cox proportional hazards models were applied to evaluate risk factors for disease-related and overall survival.
Results: Sixty-five dogs were conservatively managed, 125 treated with LFS and 143 with osteotomy techniques. At follow-up (autumn 2018), 164 dogs (49.3 %) were alive and 169 (50.7 %) were dead. Both final Cox proportional hazards models included variables for treatment, age, weight and hospital. In addition, the final disease-related model included a variable for orthopaedic comorbidity, while non-orthopaedic comorbidities and a time-varying effect for age on a linear scale were included in the overall survival model. Treatment method was found to have an effect on both disease-related and overall survival and surgical treatment was associated with a lower hazard than conservative treatment.
Conclusion: Survival in dogs with CCLD is influenced by treatment strategy, comorbidities, age and weight.

1. Introduction

Cranial cruciate ligament disease (CCLD) is one of the most common orthopaedic conditions in dogs (Johnson et al., 1994). Many factors including anatomical configuration, genetic and environmental factors are thought to affect the development of CCLD, but the exact aetiopathogenesis is still unclear (Whitehair et al., 1993; Duval et al., 1999; Witsberger et al., 2008; Taylor-Brown et al., 2015). The disease can be treated either conservatively or surgically, and osteoarthritis progresses in the affected joint regardless of treatment method (Schulz, 2012). More than 60 variations of surgical procedures have been described (Bergh et al., 2014), including lateral fabellotibial suture stabilisation (LFS), tibial plateau levelling osteotomy (TPLO) and tibial tuberosity advancement techniques such as the tibial tuberosity advancement (TTA) and the modified Maquet procedure (MMP). The most studied procedures are TPLO and LFS, followed by TTA, and there are only a few studies comparing long-term outcomes for more than two surgical techniques (Moore and Read, 1995; Conzemius et al., 2005; Christopher et al., 2013; Bergh et al., 2014; Mölsä et al., 2014). Although no general agreement on which surgical method yields the best outcome exists, there is some evidence in favour of TPLO according to a systematic review by Bergh et al. (2014). Only a limited number of studies have evaluated the outcome after conservative treatment (Pond and Campbell, 1972; Vasseur, 1984; Wucherer et al., 2013).

Most studies assessing the outcome after surgical treatment of CCLD have a follow-up time of less than six months and/or focus on risk

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factors for postoperative complications (Pacchiana et al., 2003; Stauffer et al., 2006; Fitzpatrick and Solano, 2010; Bergh et al., 2014; Hans et al., 2017). Information obtained from dog owner interviews/questionnaires and visual gait observation is commonly used for assessment of long-term outcome, while objective measurements such as force plate gait analysis and thigh circumference are less often reported (Bergh et al., 2014). In addition, several outcome evaluation tools aiming to incorporate different aspects of the clinical picture have been developed in recent years (Hyytiainen et al., 2018; Pinna et al., 2019). Common to all outcome measurement tools is that they aim to evaluate the degree of lameness, chronic pain or loss of function in the affected hind limb. This could potentially result in euthanasia in severe cases, if the degree of pain and loss of function is deemed unacceptable. However, there are currently no studies evaluating the effect of treatment strategy on life expectancy in dogs with CCLD, hence the risk of euthanasia in dogs with the disease is unknown.

The main objective of the current study was to estimate the effect of treatment method, other risk factors and potential confounders on survival in dogs with CCLD. We hypothesised that surgically treated dogs would have a favourable outcome compared to dogs treated conservatively.

2. Materials and methods

2.1. Study design

A historical cohort study was performed utilising electronic medical records of dogs with CCLD examined at two referral Veterinary University Hospitals (VHs) in Uppsala, Sweden and Oslo, Norway between January 1st, 2011 and December 31st, 2016.

2.2. Data collection

The medical records were reviewed between January 1st and August 31st, 2018. Routine clinical data, including history, age, breed, sex, body weight and treatment method, was retrieved. Neuter status and orthopaedic examination findings were registered in all records and hence not included. Although inconsistently recorded in the medical records, standardised written postoperative care and rehabilitation recommendations were available at both VHs and routinely provided to owners.

Follow-up information regarding additional complications, contralateral CCLD and date and reason for death/euthanasia was obtained from the medical records and by standardised telephone interviews with the owners between August 1st and October 15th, 2018. Furthermore, if additional information was needed, referring veterinarians were contacted (i.e. owner could not remember date or cause of euthanasia). Dates were recorded as 1st of the month if the exact date was unknown.

Inclusion criteria was a diagnosis of CCLD confirmed by either a positive cranial drawer test, a positive tibial thrust or by visual inspection of a ruptured cranial cruciate ligament by arthroscopy or arthrotomy. Exclusion criteria were: missing information about duration of lameness before treatment initiation, euthanasia at time of diagnosis, less than 14 days follow-up time, concurrent collateral ligament rupture, joint inspection revealing less than 10 % CCL rupture, diagnosis at the VHs but surgical treatment at another clinic, and surgical treatment of contralateral CCLD at the VHs prior to the study period.

2.3. Outcome

Reasons for death/euthanasia were retrospectively classified. Euthanasia related to CCLD was defined as all deaths where owners stated lameness from the affected hindlimb(s) as contributing to the decision of euthanasia. It was classified by the authors into five different subcategories; persistent lameness, subsequent contralateral CCLD, postoperative complications, guarded prognosis for return to full function, and other reasons. Classification of death/euthanasia unrelated to CCLD was performed according to Fleming et al. (2011), with a few modifications: the original categories for organ system and pathophysiological process were used, but additional categories for “high age” and “behaviour-related” were added. If the reason for death/euthanasia could not be classified, it was recorded as “unclassified” rather than excluded.

Factors related to the dog, the owner and the examining veterinarian can influence the decision of euthanasia, and hence, classification of cause of death can be uncertain. Consequently, analysis of overall survival was included to confirm the validity of the disease-related survival analysis.

2.4. Risk factors

Treatment method was defined as the main exposure variable. All dogs without surgical correction of CCLD were defined as conservatively treated. Surgically treated dogs were categorised into two treatment groups; LFS and osteotomy (TPLO, TTA and MMP).

A tentative causal diagram was made to identify possible confounding and intervening variables for the association of treatment method with the outcome. In addition, a change of > 20 % in the coefficients in the statistical model with the potential confounder present was used to assess confounding. All post-surgical related variables (such as postoperative complications and subsequent contralateral CCLD) were considered as intervening variables, and thus not considered for inclusion in the statistical analyses. The variables hospital, age, sex, weight, orthopaedic and non-orthopaedic comorbidities (present at the time of treatment initiation), lameness more than eight weeks prior to treatment initiation, insurance status, overweight (body condition score > 5/9, > 3/5 or subjectively judged as overweight by the examining veterinarian), laterality of the affected stifle, and joint exploration were considered as potential determinants for survival. The variable for orthopaedic comorbidity included separate categories for common causes of hindlimb lameness; patellar luxation, stifle osteochondrosis, hip dysplasia, in addition to other orthopaedic conditions.

2.5. Statistical analysis

All statistical analyses were conducted in Stata 15 (StataCorp, 2017). Graphical assessment of the continuous variables showed deviance from normality, hence continuous variables are presented as median (range). Categorical variables are presented as number (percentage). The one-sample test of proportions was used to compare the number of female and male dogs. Dogs with concurrent or subsequent contralateral CCLD were included as a single case at the time of first CCLD treatment at the VHs. Kaplan-Meier survival curves were used to describe differences in time-to-event for the treatment groups and the median time-to-event and censoring was calculated. Follow-up time was defined as the time from treatment initiation to death/euthanasia, or owner-contact/latest follow-up in the medical records when the dog was alive. Maximum follow-up time was set to 6 years (72 months) for the analyses.

Cox proportional hazards models were applied to estimate the effect of possible risk factors for disease-related and overall survival. Dogs alive at the end of the study period or lost to follow-up were censored. In addition, dogs that were dead/euthanised due to causes unrelated to CCLD were censored in the disease-related survival analysis. A single missing value was identified; a female Gordon setter without bodyweight recorded. In this case, the average bodyweight for female Gordon setters according to the breed standard[2] was used in the

[2] Fédération Cynologique Internationale breed standard Gordon setter,

Table 1
Descriptive features at time of diagnosis of 333 dogs with cranial cruciate ligament disease (2011-2016).

Variable	Surgery				Conservative		Total	
	LFS		Osteotomy					
Number of dogs (% of overall)	125	(37.5)	143	(43.0)	65	(19.5)	333	(100.0)
Dogs treated at Hospital 1	*25*	*(20.0)*	*77*	*(53.9)*	*19*	*(29.2)*	*121*	*(36.3)*
Dogs treated at Hospital 2	*100*	*(80.0)*	*66*	*(46.2)*	*46*	*(70.8)*	*212*	*(63.7)*
Age in years (min-max)	7.7	(0.9 – 12.8)	4.2	(0.9 – 10.7)	7.6	(0.2 – 13.3)	6.5	(0.2 – 13.3)
Weight in kg (min-max)†	11.3	(3.3 – 49.3)	35.0	(10.1 – 80.3)	17.9	(3.8 – 76.0)	23.6	(3.3 – 80.3)
Overweight (%)	41	(32.8)	35	(24.5)	19	(29.2)	95	(28.5)
Sex (%)								
Female	*74*	*(59.2)*	*71*	*(49.7)*	*40*	*(61.5)*	*185*	*(55.6)*
Male	*51*	*(40.8)*	*72*	*(51.3)*	*25*	*(38.5)*	*148*	*(44.4)*
Insured (%)	112	(89.6)	118	(82.5)	52	(80.0)	282	(84.3)
Stifle affected (%)								
Left	*60*	*(48.0)*	*82*	*(57.3)*	*28*	*(43.1)*	*170*	*(51.0)*
Right	*62*	*(49.6)*	*59*	*(41.3)*	*34*	*(52.3)*	*155*	*(46.6)*
Bilateral	*3*	*(2.4)*	*2*	*(1.4)*	*3*	*(4.6)*	*8*	*(2.4)*
Lameness > 8 w prior to treatment initiation (%)	47	(37.6)	74	(51.8)	33	(50.8)	154	(46.3)
Orthopaedic comorbidities (%)	34	(27.2)	30	(21.0)	18	(27.7)	82	(24.61)
Hip dysplasia	*7*	*(5.6)*	*9*	*(6.3)*	*2*	*(3.1)*	*18*	*(5.4)*
Patellar luxation	*19*	*(15.2)*	*2*	*(1.4)*	*5*	*(7.7)*	*26*	*(7.8)*
OC Stifle	*0*	*(0.0)*	*7*	*(4.9)*	*4*	*(6.2)*	*11*	*(3.3)*
Other	*8*	*(6.4)*	*12*	*(8.4)*	*7*	*(10.8)*	*27*	*(8.1)*
Non-orthopaedic comorbidities (%)	19	(15.2)	24	(16.8)	20	(30.8)	63	(18.9)

Categorical variables presented as number of dogs (% total number of dogs by treatment method if not specified). Continuous variables as median (min-max)..
LFS = Lateral Fabellotibial suture; OC = Osteochondrosis.
† Weight missing for one dog, N = 332.

analysis. Collinearity between variables was evaluated by Goodman and Kruskal's gamma for categorical or dichotomous variables and by Spearman rank-order correlation coefficient for continuous variables. A coefficient, hazard ratio (HR), its 95 % confidence interval and p-value, were calculated for each variable. All variables with $p < 0.15$ in univariable analyses were considered for inclusion in the multivariable models. A fixed effect for hospital was forced into the final models to account for differences between the two VHs.

A p-value of < 0.05 was considered statistically significant and manual stepwise backward elimination was applied for selection of variables. The Wald test was used to evaluate the significance of the predictors. Biologically plausible interactions were considered for inclusion. Schoenfeld residuals for each variable in the final models were used to evaluate the assumption of proportional hazards. If a violation of the proportional hazards assumption was identified and graphical assessment indicated a time-varying effect (TVE) of a variable, an interaction term between the variable and time on the appropriate scale was included in the model. Sensitivity analysis was performed to evaluate the assumption of individual censoring. Plots of martingale residuals were used to test the functional form of the predictors. Deviance and scaled score residuals were plotted against time at risk for detection of outliers and influential observations, respectively. The models were fit with and without the suspected outlying observations. Linear combinations of the coefficients from the models were used to check for differences between the treatment methods after the final models were fitted.

3. Results

3.1. Animals and treatment

Of the initial 436 dogs with CCLD identified within the study period, 333 (Hospital 1: 121, Hospital 2: 212) met the inclusion criteria and were enrolled in the study (see Table 1 for descriptive features). The most common breeds were mixed-breed (n = 66), Rottweiler (n = 24), Labrador Retriever (n = 15), Golden Retriever (n = 15) and Jack Russel Terrier (n = 13). There were more female than male dogs (p = 0.03). Of the 333 dogs, 65 (19.5 %) were conservatively treated, 125 (37.6 %) treated with LFS and 143 (42.9 %) treated with an osteotomy technique (71 TPLOs, 54 TTAs, 18 MMPs).

In total, 134/333 dogs (40.2 %) had a comorbidity recorded at the time of treatment initiation. The most common orthopaedic and non-orthopaedic comorbidities were patellar luxation and dermatological disease, respectively. Of the conservatively treated dogs, 18/65 (27.7 %) had concurrent orthopaedic conditions while 20/65 (30.8 %) had other non-orthopaedic diseases. The corresponding numbers for the LFS group were 34/125 (27.2 %) and 19/125 (15.2 %), and for the osteotomy group 30/143 (21.0 %) and 24/143 (16.8 %), respectively.

3.2. Outcome

At follow-up, 164/333 dogs (49.3 %) were still alive, while 169/333 (50.7 %) were dead or euthanised; 61/333 (18.3 %) of disease-related causes. Nineteen of the 65 (29.2 %) dogs in the conservatively treated group were dead due to disease-related causes, with corresponding numbers 19/125 (15.2 %) in the LFS group and 23/143 (16.1 %) in the osteotomy group (Table 2). Concurrent comorbidities contributed to the decision in 9/19 (47.4 %) conservatively treated dogs, 6/19 (31.6 %) dogs treated by LFS and 7/23 (30.4 %) dogs treated with osteotomy. None of the dogs excluded due to < 14 days follow-up time were recorded as dead/euthanised. The most common disease-related reason for euthanasia was persistent lameness (see Table 3 for further details). The most common non-disease-related reasons were high age or related to the urogenital organs, gastrointestinal system or the musculoskeletal system (lameness of the affected hindlimb excluded).

3.3. Survival analysis

Kaplan-Meier survival curves for disease-related and overall survival in the different treatment groups are presented in Fig. 1. Collinearity between variables was not detected.

The final multivariable disease-related survival model included

(*footnote continued*)
accessed 13.02.2019: http://www.fci.be/Nomenclature/Standards/006g07-en.pdf

Table 2
Treatment and follow-up details of 333 dogs with cranial cruciate ligament disease (2011-2016).

Variable	Surgery				Conservative		Total	
	LFS (N = 125)		Osteotomy (N = 143)		(N = 65)		(N = 333)	
Follow-up time in months (min-max)	34.0	(0.8 – 91.3)	36	(0.5 – 89.3)	23.5	(0.6 – 90.4)	34	(0.5 – 91.3)
Bilateral rupture (% of dogs with unilateral CCLD)*	47	(38.5)	49	(34.8)	10	(16.1)	106	(32.6)
Joint inspection (%)	115	(92.0)	104	(72.7)	5	(7.7)	224	(67.3)
Hospital 1	*16*	*(64.0)*	*38*	*(49.4)*	*4*	*(21.1)*	*58*	*(47.9)*
Hospital 2	*99*	*(99.0)*	*66*	*(100.0)*	*1*	*(2.2)*	*166*	*(78.3)*
Arthrotomy (%)	101	(80.1)	42	(29.4)	2	(3.1)	145	(43.5)
Arthroscopy (%)	21	(16.8)	73	(51.1)	3	(4.6)	97	(29.1)
Meniscal injuries (%)	29	(23.2)	29	(20.3)	1	(1.5)	59	(17.7)
Post-operative complications (%)	32	(25.6)	52	(36.4)	NA		NA	
Dogs alive (%)	69	(55.2)	76	(53.2)	19	(29.3)	164	(49.3)
Dogs dead/euthanised (%)	56	(44.8)	67	(46.8)	46	(70.7)	169	(50.7)
CCLD-related	*19*	*(15.2)*	*23*	*(16.1)*	*19*	*(29.2)*	*61*	*(18.3)*
Other causes	*37*	*(29.6)*	*44*	*(30.7)*	*27*	*(41.5)*	*108*	*(32.4)*
Months to CCLD-related euthanasia (min-max)	19.9	(2.3 – 45.1)	21.9	(0.5 – 68.1)	2.4	(0.6 – 74.0)	15.6	(0.5 – 74.0)
Months to censoring (min-max)	37.4	(0.8 – 91.3)	38.7	(0.8 – 89.2)	25.4	(0.6 – 90.3)	36.2	(0.6 – 91.3)

Continuous variables reported as median (range), categorical variables as number of dogs (percentage).
CCLD = Cranial Cruciate Ligament Disease; LFS = Lateral Fabellotibial suture; NA = Not applicable; OC = Osteochondrosis.

Table 3
Classification of cause of cranial cruciate ligament disease-related euthanasia in 61 dogs from a cohort study of 333 dogs (2011-2016).

Reason for euthanasia	CCLD only	Comorbidity	Combined
	N (%)	N (%)	N (%)
Persistent lameness	13 (52.0)	12 (48.0)	25 (41.0)
Contralateral CCLD	16 (94.1)	1 (5.9)	17 (28.9)
Other	2 (22.2)	7 (77.8)	9 (14.8)
Post-operative complications	7 (87.5)	1 (12.5)	8 (13.1)
Guarded prognosis	2 (100.0)	0 (0.0)	2 (3.3)
Total	40 (65.6)	21 (34.4)	61 (100)

CCLD = Cranial cruciate ligament disease.
Comorbidity = additional non – CCLD related factors contributing to the decision of euthanasia.
Guarded prognosis = prognosis perceived as guarded for return to full function by either examining veterinarian or owner.

Table 4
Results from a multivariable Cox proportional hazards model of disease-related survival in a cohort of 333 dogs with cranial cruciate ligament disease.

Variable and level	Coeff.	HR	95 % CI	P
Treatment				0.035†
Conservative		*1.00*	–	–
LFS	*−0.58*	*0.56*	*(0.28 – 1.14)*	*0.109*
Osteotomy	*−0.91*	*0.40*	*(0.19 – 0.81)*	*0.012*
Hospital				
Hospital 1		*1.00*	–	–
Hospital 2	*0.20*	*1.21*	*(0.65 – 2.25)*	*0.547*
Orthopaedic comorbidity				< 0.001†
None		*1.00*	–	–
Patellar luxation	*0.45*	*1.57*	*(0.52 – 4.73)*	*0.420*
Hip dysplasia	*0.09*	*1.10*	*(0.34 – 3.59)*	*0.873*
OC Stifle	*−0.24*	*0.78*	*(0.22 – 2.80)*	*0.706*
Other	*1.12*	*3.09*	*(1.59 – 6.00)*	*0.001*
Age (years)	0.11	1.12	(1.01 – 1.25)	0.040
Weight (kg)	0.03	1.03	(1.01 – 1.05)	0.001

During the follow-up period a total of 61/333 dogs suffered disease-related euthanasia. Age, weight and orthopaedic comorbidities at time of diagnosis.
HR = Hazard ratio, LFS = Lateral fabellotibial suture technique, OC = Osteochondrosis.
† Wald-test.

variables for treatment method, orthopaedic comorbidities, age, weight and hospital (Table 4). The hazard for dogs treated by osteotomy was lower than for the conservatively treated dogs (HR 0.40, p = 0.012). It was also lower for the dogs treated by LFS (HR 0.56, p = 0.109). No statistical difference was found between LFS and osteotomies (p = 0.370). The hazard increased with other orthopaedic comorbidities (HR 3.09, p = 0.001), increasing age (HR 1.12, p = 0.039) and increasing body weight (HR 1.03, p = 0.001). The model validation for the disease-related survival model did not reveal violations of the model assumptions.

In the final multivariable overall survival model, the assumption of proportional hazards was violated for age. The graphical assessment indicated that the effect of age increased on a linear time scale. Thus, a TVE interaction between age and time was included in the overall survival model. The variables for treatment method, non-orthopaedic

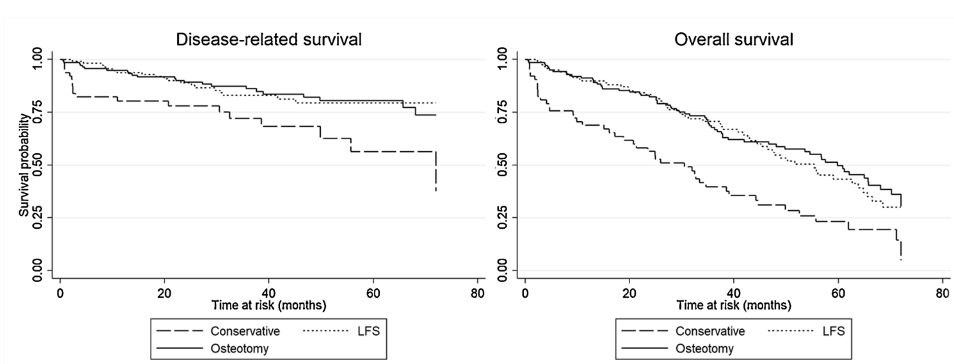

Fig. 1. Kaplan-Meier curves by treatment method describing survival in a cohort of 333 dogs with cranial cruciate ligament disease.

Table 5
Results from a multivariable Cox proportional hazards model of overall survival in a cohort of 333 dogs with cranial cruciate ligament disease.

Variable and level	Coeff.	HR	95 % CI	P
Treatment				0.002[†]
Conservative		*1.00*	–	–
LFS	*−0.63*	*0.53*	*(0.35 − 0.80)*	*0.003*
Osteotomy	*−0.63*	*0.53*	*(0.35 − 0.81)*	*0.003*
Hospital				
Hospital 1		*1.00*	–	–
Hospital 2	*0.20*	*1.22*	*(0.85 − 1.77)*	*0.278*
Non-orthopaedic comorbidity	0.42	1.53	(1.05 − 2.22)	0.028
Age (years)	0.11	1.12	(1.01 − 1.24)	0.028
Weight (kg)	0.03	1.03	(1.02 − 1.04)	< 0.001
TVC (age)	0.00	1.00	(1.00 − 1.01)	0.006

During the follow-up period a total of 169/333 dogs where dead/euthanised. Age, weight and non-orthopaedic comorbidities recorded at time of diagnosis. HR = Hazard ratio, LFS = Lateral fabellotibial suture technique, TVC = Time-varying covariate.
[†] Wald-test.

comorbidities, age and weight had a significant effect on survival. The final multivariable overall survival model is presented in Table 5.

None of the tested interactions were significant in either model. In both the disease-related and overall survival model, weight and age were confounded with treatment method.

4. Discussion

Chronic clinical dysfunction due to persistent lameness resulting in euthanasia is the most serious outcome of CCLD. This study is the first to evaluate survival in dogs with CCLD. In total, 18.3 % of the dogs were dead/euthanised of disease-related causes within the follow-up time, which is substantially higher than the 2% reported by Mölsä et al. (2013). Due to differences in study design and study samples, a direct comparison of results is inappropriate and should be avoided. For example, the study by Mölsä et al. (2013) was based on a questionnaire completed by owners of 253 surgically treated dogs (followed for a mean of 2.7 years), and it could be that owners of euthanised dogs were less likely to return such a questionnaire. At one-year follow-up, 43/333 (12.9 %) dogs in the current study had died or been euthanised. This finding supports the fact that exclusion of euthanised dogs has the potential to bias the results in long-term studies evaluating clinical function of dogs with CCLD.

Results from both the disease-related and the overall survival model showed a favourable outcome for surgically treated dogs, with the lowest hazard for dogs treated with osteotomy procedures. These findings seem to be in line with the current evidence regarding long-term outcome of dogs with surgically treated CCLD. The systematic review by Bergh et al. (2014) concluded that, although the evidence is too sparse to compare the effect of different treatment interventions, there is some evidence in favour of TPLO as the preferred surgical technique. One of the few randomised blinded controlled clinical trials included in the systematic review was a study by Gordon-Evans et al. (2013), which reported 1-year outcome after LFS and TPLO surgery in 80 dogs. The results indicated that both groups improved after surgery and 93 % of owners were very satisfied after TPLO and 75 % after LFS. Moreover, the superiority of osteotomy techniques in regard to functional outcomes is also supported by the views of veterinary practitioners and surgeons; a 2016 survey of American veterinary orthopaedic surgeons found that TPLO was the preferred surgical technique for dogs > 15 kg (von Pfeil et al., 2018).

Further, in the current study there was a risk of treatment failure resulting in euthanasia following conservative treatment. This finding is supported by a study by Wucherer et al. (2013) including overweight dogs > 20 kg followed for one year, where conservative treatment resulted in a less favourable outcome than TPLO. It should, however, be noted that the outcome was reported as successful in two-thirds of the conservatively treated dogs. Since body weight was identified as a risk factor in both survival models in the current study, with a lower hazard for smaller dogs, it seems reasonable that conservative management could still be a viable alternative in smaller dogs. These arguments can explain why conservative treatment is commonly chosen for small dogs, as reported in a recent UK surgeon survey by Comerford et al. (2013). However, bodyweight is a widely known risk factor for survival in dogs (irrespective of CCLD); large and giant breed dogs generally have a shorter life span than smaller dogs (O'Neill et al., 2013). In the context of CCLD, the lower hazard for smaller dogs observed in the current study could potentially be confounded by the generally longer life expectancy in smaller dogs.

Orthopaedic comorbidity increased the risk of failure in the disease-related survival model. A possible explanation is that the outcome might be influenced by the co-existing condition. In addition, owners of dogs with concurrent orthopaedic conditions could have perceived the prognosis as more guarded than owners of dogs with an isolated CCLD. Thus, they could be less motivated to pursue further treatment. In the overall survival model, non-orthopaedic comorbidity increased the risk of failure. This would be expected, since other diseases such as idiopathic epilepsy and heart failures are common reasons for euthanasia/death in dogs, thereby influencing the overall survival (Bonnett et al., 2005). As with the orthopaedic comorbidities, owners of dogs with non-orthopaedic diseases might be more reluctant to proceed with treatment of CCLD. A similar reasoning is likely to explain why the hazard of death/euthanasia increased with age in both survival models. For the overall survival, the effect of age on the hazard of death/euthanasia increased over time, implying that death/the decision of euthanasia was more influenced by age in older dogs compared with younger.

In our study, surgeons with different levels of experience performed the procedures. The literature provides conflicting results regarding the impact of the surgeon's experience on the outcome. While a few studies have reported a positive correlation between surgeon experience and outcome (Christopher et al., 2013), no association has been found in several others (Pacchiana et al., 2003; Conzemius et al., 2005; Casale and McCarthy, 2009; Gordon-Evans et al., 2013; Wilson et al., 2018). It was not possible to determine the level of experience of the surgeons in the present study; thus, the effect on survival could not be evaluated and this should be acknowledged as a limitation. However, including surgeons with different levels of experience could increase the external validity of this study, since the outcome after procedures performed by surgeons with variable levels of experience may more accurately reflect common practice.

Joint exploration with meniscal inspection is generally recommended and has been performed in most studies of surgically treated CCLD in dogs (Conzemius et al., 2005; Stauffer et al., 2006; Fitzpatrick and Solano, 2010). It should be noted that joint exploration was rarely performed in the conservatively treated dogs in the current study. As such, undetected meniscal injury is a potential confounding bias in the conservatively treated group.

There are some additional limitations in the current study that should be mentioned. Importantly, survival only represents one aspect of treatment outcome. The quality of life (QoL) for dogs with CCLD should also be taken into consideration. Several standardised clinical metrology instruments measuring chronic pain (HCPI and CBPI) or function (COI) have been evaluated for assessment of musculoskeletal disorders in dogs (e.g. Brown et al. (2007); Brown (2014); Hielm-Bjorkman et al. (2009)). However, due to the long follow-up time in our study, a high percentage of the dogs were dead at the time of follow-up. Consequently, such assessments would only have provided results for a selected group of dogs.

Moreover, the categorisation of the reasons for death/euthanasia relied on the authors' judgement, without further investigation or post-mortem examinations. A decision of euthanasia is often complex and disease-related survival is not a completely objective endpoint. However, the results concerning disease-related survival were supported by the overall survival model. Any misclassification bias is consequently likely to be non-differential and only reduce the likelihood to observe associations between exposures and the outcome.

The animal welfare legislation in Norway and Sweden supersedes the EU regulations with more stringent requirements and a generally higher standard for animal welfare than many other European countries (Veissier et al., 2008). Thus, in both countries, it is common to regard lameness as a welfare concern, and euthanasia is likely to be recommended when limb function is considered unacceptable. We believe this is important for the generalizability of the results in the current study.

As this study was not conducted on a randomised group of patients, the decision on which treatment to take for CCLD was not random. Thus, both the initial treatment choice and the final decision of euthanasia was likely influenced by inherent bias, including financial considerations, and perceived risk and prognosis associated with the treatment. It is likely that older dogs, and dogs with co-morbidities were managed with cheaper methods (conservative, LFS) rather than the more expensive osteotomy techniques. Likewise, owners investing less in their pet may be more likely to choose euthanasia, rather than treatment, for co-morbidities which are treatable, but comprehensive and/or expensive to treat at the end of life. Since the present study was conducted at referral hospitals, a selection bias towards complicated cases cannot be excluded. Thus, it is possible that the success of conservative treatment in the target population may be better than in the current study. As shown in Table 1, relatively more osteotomy procedures were performed at hospital 1 compared to hospital 2. Thus, choice of surgical technique was to some degree dependent on where the procedure was performed, which is most likely due to differences in routines and technique familiarity at the hospitals, in addition to the preference of individual surgeons. This is in line with the survey by von Pfeil et al. (2018) and illustrates that not only the signalment of the dog, but also the surgeon's preference are important determinants for treatment choice. Although factors which could have directed the treatment decision, such as hospital, insurance status, concurrent disease, weight and age of the dog were included in the analysis, unmeasured factors such as owners' financial considerations and perceived prognosis of both owners and clinicians likely influenced our results.

5. Conclusion

Disease-related euthanasia due to CCLD was not uncommon in this population of dogs, which shows that CCLD can affect life expectancy. Both treatment strategy and variables related to signalment and history of the dog were identified as risk factors for death/euthanasia. Surgically treated dogs had a lower hazard compared to conservatively treated dogs, which is in concordance with our hypothesis. In addition, comorbidity and increasing age and weight increased the hazard. Information regarding life expectancy in relation to risk factors is valuable facing a decision about treatment of CCLD.

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Author contributions

All authors contributed to the study design. KE and GSB registered the data under supervision from OH, AB and ERM. KE and GSB also carried out the data analysis and interpretation under supervision from RK with contribution from UE, ES and JH. KE and GSB was major contributors to the manuscript, with substantial input from the other authors. All authors participated in the discussions and revisions of the entire text. All authors read and approved the final manuscript.

Declaration of Competing Interest

None.

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Appendix A. Supplementary data

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