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Risk factors for severe postoperative complications in dogs with cranial cruciate ligament disease – A survival analysis

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ABSTRACT

Objective: To analyze the effect of surgical technique and other risk factors on severe postoperative complications in dogs with cranial cruciate ligament disease (CCLD).
Materials and Methods: A cohort study of 255 dogs (287 stifles) surgically treated for CCLD at two veterinary university hospitals (2011–2016) was performed. The electronic medical records were reviewed and dog owners and referring veterinarians contacted for additional information. The complications were classified as minor, major and catastrophic, where major and catastrophic were considered severe. A multivariable Cox proportional hazards model was applied to assess risk factors for severe postoperative complications.
Results: Three surgical techniques were used; lateral fabellotibial suture (LFS, 141 stifles), tibial plateau leveling osteotomy (TPLO, 77 stifles) and tibial tuberosity advancement (TTA, 69 stifles). The most common severe postoperative complications were surgical site infections or complications related to the surgical implant. Severe postoperative complications occurred in 31 % of the stifles treated with TPLO, 22 % of the stifles treated with LFS and 25 % of the stifles treated with TTA. The multivariable Cox proportional hazards model identified surgical technique ($p = 0.0258$) as a risk factor for severe postoperative complications; TPLO had a significantly lower hazard than LFS (hazard ratio (HR) = 0.37, $p = 0.007$) when controlling for body weight and age, which also were identified as risk factors (HR = 1.05, $p < 0.001$ and HR = 0.91, $p = 0.047$, respectively).
Conclusion and Clinical relevance: Although TPLO procedures had the highest occurrence of severe postoperative complications, the hazard was lower than for LFS after adjusting for body weight and age. This implies that it is important to consider potential effect-modifiers when comparing postoperative complications after CCLD surgery.

1. Introduction

Cranial cruciate ligament disease (CCLD) is one of the most common orthopedic conditions in dogs (Johnson et al., 1994). There are more than 60 variations of surgical procedures described for treatment of CCLD, including extracapsular stabilization techniques such as lateral fabellotibial suture (LFS) and osteotomy techniques such as tibial plateau leveling osteotomy (TPLO) and tibial tuberosity advancement (TTA) (Bergh et al., 2014). Both TPLO and TTA aim to neutralize the tibiofemoral shear force in the stifle joint with ruptured cranial cruciate ligament (CCL) by altering the geometry of the stifle, without replacing the ligament (Slocum and Slocum, 1993; Montavon et al., 2002). The LFS technique inhibits the cranial drawer motion, i.e. the cranial tibial subluxation that occurs when the cranial cruciate ligament is deficient, by placing a stabilizing, extracapsular suture (Schulz, 2012). Cranial cruciate ligament disease frequently results in chronic pain, and osteoarthritis progresses in the affected joint despite surgical treatment (Lazar et al., 2005; Au et al., 2010; Christopher et al., 2013; Mölsä et al., 2013).

The surgical techniques are associated with a variety of postoperative complications, ranging in severity from mild to catastrophic

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(Casale and McCarthy, 2009; Christopher et al., 2013). Complications can both delay the healing process, result in additional costs for the animal owner, increase patient morbidity, and cause greater post-operative pain (Nicoll et al., 2014). Some postoperative complications, such as surgical site infections (SSIs), may occur after any surgical procedure (Eugster et al., 2004). Others are procedure specific, such as tibial tuberosity fractures after TPLO and TTA, fibular fractures after TPLO, and complications associated with the suture material after LFS (Casale and McCarthy, 2009; Dymond et al., 2010; Bergh and Peirone, 2012). The reported complication frequency after CCLD surgery is typically between 11 and 36 % and several preventive or risk factors for complications have been evaluated, such as body weight, age, experience of the surgeon and the use of postoperative antibiotics (Pacchiana et al., 2003; Lafaver et al., 2007; Casale and McCarthy, 2009; Tuttle and Manley, 2009; Fitzpatrick and Solano, 2010; Steinberg et al., 2011; Taylor et al., 2011; Wolf et al., 2012; Christopher et al., 2013; Gordon-Evans et al., 2013; Coletti et al., 2014; Garnett and Daye, 2014; Yap et al., 2015; Hans et al., 2017; Lopez et al., 2018). However, comparing complication severity, occurrence and risk factors between studies can be challenging due to the heterogeneity in classification of the complications, study designs, study populations and differences in case follow-up. As a measure to facilitate comparison of complications between studies, a standardized definition with criteria for documentation of complications in clinical orthopedic studies in veterinary medicine was proposed by Cook et al. (2010), classifying complications as catastrophic, major or minor depending on their severity.

Although many studies have evaluated postoperative complications after surgical treatment of CCLD, comparisons of complication frequency for more than two surgical techniques are sparse (Christopher et al., 2013; Mölsä et al., 2014). Typically, only dogs with complete data are included (per-protocol analysis) and logistic regression models, considering complications as either present or absent, are applied for data analysis. Survival analysis is an alternative to the classic regression techniques, and is superior in handling incomplete information, since the individuals that are lost to follow-up are included as long as they are observed. Survival analysis is rarely used in small animal orthopedics, although common in human orthopedic studies (Khan, 2017).

Identification of risk factors for the development of complications allows for interventions in order to decrease postoperative morbidity, and is important for veterinarians and dog owners facing a decision of CCLD treatment. Thus, the objective of the current study was to evaluate the effect of surgical technique and other risk factors on development of severe postoperative complications in dogs with CCLD, treated by either TPLO, TTA or LFS. The hypothesis was that surgical technique as well as other factors such as body weight and age of the dogs would influence the hazard of severe postoperative complications.

2. Materials and methods

2.1. Study design

A historical cohort study of dogs with CCLD surgically treated with either TPLO, TTA or LFS at two veterinary university hospitals (VHs, Hospital 1: University Animal Hospital, Norwegian University of Life Sciences and Hospital 2: University Animal Hospital, Swedish University of Agricultural Sciences) between 1st January 2011 and 31st December 2016 was performed.

2.2. Inclusion/exclusion criteria

Inclusion criteria was a diagnosis of CCLD confirmed by the cranial drawer test, a positive tibial thrust and/or inspection of the ruptured ligament by arthroscopy or arthrotomy. The medical records were reviewed between 1st January and 31st August 2018, and information including age, sex, breed, body weight, concurrent or subsequent contralateral CCLD, lameness duration prior to diagnosis, clinical examination findings, surgical technique, date of treatment and post-operative complications was recorded. If information was lacking in the medical records, telephone interviews were performed with dog owners or referring veterinarians between 1st August and 15th October, 2018. The dogs were followed until the date of the telephone interview with the dog owner, or to the last recorded visit in the medical record if the owner could not be reached. Neuter status was not consistently registered in the medical records and thus not recorded.

Exclusion criteria were missing information about lameness prior to treatment initiation, concurrent rupture of the collateral ligament, less than 14 days follow-up time, treatment of the contralateral CCL prior to the study period and dogs surgically treated with other techniques than LFS, TPLO and TTA. In addition, dogs with only mild fraying of the cranial cruciate ligament (assessed during visual inspection of the ligament) were excluded. These dogs had concurrent stifle joint disease (such as osteochondrosis), which was considered the main cause of the clinical signs by the responsible surgeon.

2.3. Classification of complications

The complications were classified as catastrophic, major or minor (Cook et al., 2010). According to the classification, a catastrophic complication resulted in unacceptable function/euthanasia/death, a major complication required further surgical or medical treatment and a minor complication resolved without further treatment. However, a few modifications were done; complications resolved by topical antibiotics or a few days of analgesic treatment were classified as minor instead of major. As the aim of the study was to explore severe postoperative complications, all major and catastrophic complications were combined into one category. Clinical signs from the gastrointestinal tract were not registered as complications.

Surgical site infections were not classified as deep/superficial according to the general definition (Horan et al., 2008), due to lack of information in the medical records (i.e. lack of bacterial samples from implants/bones when deep SSIs were suspected). A SSI was registered if the examining veterinarian suspected a SSI, regardless of the result of the bacterial samples (in case sampling was performed). Reoperations and joint lavage due to suspected postoperative septic arthritis were recorded. Surgical site infection or septic arthritis after reoperation were recorded as complications if the reoperation was <1 month after the index surgery.

2.4. Risk factors

Treatment was set as the main exposure variable and separated into three categories; LFS, TPLO and TTA. Dogs with concurrent or subsequent contralateral CCLD were included as two cases if both stifles were surgically treated at the VHs during the study period. A causal diagram for identification of risk factors, intervening and confounding variables for severe postoperative complications was created. In addition, a coefficient change of >20 %, with a potential confounder included in the statistical model was taken to indicate confounding (Dohoo et al., 2009). The following variables from the causal diagram were considered for inclusion in the statistical model: age, arthrotomy/arthroscopy, body weight, breed, concurrent medical and orthopedic comorbidities, duration of anesthesia, duration of lameness prior to treatment (<2 or ≥ 2 weeks), experience of the surgeon (experienced surgeon, resident, board-certified), hospital, insurance status, overweight (body condition score $>5/9$, $>3/5$ or judged as overweight by the examining veterinarian), sex, surgical technique and year of treatment (to control for unmeasured factors at the hospitals that may have changed during the study period, such as pre-operative routines). Breed was included as a categorical variable, with separate levels for breeds represented by >10 cases. The variable for orthopedic comorbidity included subcategories for common diseases causing hindlimb lameness; patellar luxation, stifle osteochondrosis and hip dysplasia as well as a category for other orthopedic conditions. The remaining variables in the causal diagram (postoperative antibiotic treatment, minor complications, postoperative physiotherapy and subsequent contralateral CCLD) were intervening variables and were therefore not included in the statistical model.

2.5. Statistical analysis

Analyses were performed with a commercially available software progam (StataCorp, 2019). Continuous variables are presented as median (min-max) and categorical variables as number (percentage of total number of stifles by treatment method). A non-parametric Kruskal--Wallis one-way ANOVA was used to compare the difference in medians between the treatment groups, since graphical assessment of the continuous variables body weight and age showed deviance from normality. A Bonferroni correction was applied to adjust for pairwise comparison between the treatment groups with an alpha level of 0.0167 (0.05/3). Follow-up time was defined as time from surgery to first severe postoperative complication or to censoring. Dogs were censored if they were lost to follow-up, euthanized/dead for reasons unrelated to severe postoperative complications or had minor/no postoperative complications. The number and percentage of severe postoperative complications was calculated, and the difference in time to first severe postoperative complication in each treatment group described with Kaplan-Meier survival curves. Maximum follow-up time was set to 1000 days in the analysis.

A Cox proportional hazards model was applied to evaluate possible risk factors for severe postoperative complications. Collinearity between variables was tested by Goodman and Kruskal's gamma for categorical or dichotomous variables and by Spearman correlation coefficient for continuous variables. A hazard ratio (HR), 95 % confidence interval (CI) and p-value was calculated for each variable. All variables with $p < 0.2$ in univariable analyses were included in the initial multivariable model. Manual stepwise backward elimination was used for variable selection and a p-value of <0.05 was considered statistically significant. Biologically plausible interactions were considered for inclusion, and fixed effects for surgical technique (since main exposure variable) and hospital (to account for differences between the two VHs) were forced into the final model. As some dogs were included twice in the analysis due to bilateral treatment of CCLD, a frailty term for individual was explored. The Wald test was used to evaluate the significance of the predictors. Schoenfeld residuals for each variable in the final model were used to evaluate the assumption of proportional hazards, and a sensitivity analysis was performed to evaluate the assumption of individual censoring. The functional form of the predictors was evaluated by plotting of martingale residuals. In order to detect outliers and influential observations, deviance and scaled score residuals were plotted against time at risk, and the model was refitted without the suspected outlying observations. Linear combinations of the coefficients from the model were used to check for differences between the treatment methods after the final model was fitted.

3. Results

3.1. Animals and treatment

A total of 287 stifles (Hospital 1: 101, Hospital 2: 186) in 255 dogs met the inclusion criteria. The most common breeds were mixed-breed (n = 50), Rottweiler (n = 19), Labrador Retriever (n = 14), Golden Retriever (n = 13) and Poodle (n = 11). Of the 287 stifles, 141 were treated with LFS, 77 with TPLO and 69 with TTA (using cage and a plate (Montavon et al., 2002)). Four single session bilateral procedures (three LFS, one TPLO) were performed. Both age and body weight differed between treatment groups (7.5 years, 5.6 years and 3.9 years/11.7 kg, 42.2 kg and 29.0 kg for LFS, TPLO and TTA, respectively, $p < 0.001$ for both comparisons). For additional descriptive features of the included dogs and the surgical procedures, see Tables 1 and 2. The procedures were performed by 14 surgeons, of which two were board-certified and four residents (Table 3).

3.2. Complications

Severe postoperative complications occurred in 24/77 (31 %) stifles treated with TPLO, 31/141 (22 %) stifles treated with LFS and 17/69 (25 %) stifles treated with TTA. Surgical site infections or complications related to the surgical implants were the most common severe postoperative complications (Table 4). The first severe postoperative complication occurred within 215 days after surgery in 90 % of the stifles with such complications. In total, 8 stifles (2.9 %) suffered catastrophic complications during the follow-up period, of these 4 were treated with LFS, 3 with TPLO and 1 with TTA. Eight dogs had mild

Table 1
Descriptive features at time of cranial cruciate ligament disease diagnosis in 287 stifles (255 dogs), in a historical cohort study of severe postoperative complications after surgical treatment.

Variable	LFS (N = 141)		TPLO (N = 77)		TTA (N = 69)		Total	
Age (years)	7.53	(0.94–12.8)	5.63	(0.94–10.5)	3.89	(0.93–10.8)	6.1	(0.93–12.8)
Body weight (kg)	11.7	(3.3–49.3)	42.2	(19.0–80.3)	29.0	(9.8–66.0)	24.5	(3.3–80.3)
Overweight	47	(33.3)	25	(32.5)	12	(17.4)	84	(29.3)
Sex								
Female	*83*	*(58.9)*	*36*	*(46.8)*	*41*	*(59.4)*	*160*	*(55.8)*
Male	*58*	*(41.1)*	*41*	*(53.3)*	*28*	*(40.6)*	*127*	*(44.3)*
Insured	128	(90.8)	71	(92.2)	50	(72.5)	249	(86.8)
Lameness*								
<2 w	*41*	*(29.1)*	*11*	*(14.3)*	*18*	*(26.1)*	*70*	*(24.4)*
≥2 w	*100*	*(70.9)*	*66*	*(85.7)*	*51*	*(73.9)*	*217*	*(75.6)*
Comorbidities								
Orthopedic	34	(27.2)	30	(21.0)	18	(27.7)	82	(24.6)
Hip dysplasia	*9*	*(6.4)*	*2*	*(2.6)*	*5*	*(7.3)*	*16*	*(5.6)*
Patellar luxation	*22*	*(15.6)*	*0*	*(0.0)*	*3*	*(4.4)*	*25*	*(8.7)*
Osteochondrosis stifle	*0*	*(0.0)*	*6*	*(7.8)*	*1*	*(1.5)*	*7*	*(2.4)*
Other	*8*	*(5.7)*	*8*	*(10.4)*	*4*	*(5.8)*	*20*	*(7.0)*
Non-orthopedic	24	(15.2)	24	(16.8)	20	(30.8)	63	(18.9)

Continuous variables as median (min-max). Categorical variables presented as number of stifles (% total number of stifles by treatment method). LFS; lateral fabellotibial suture, TPLO; tibial plateau leveling osteotomy, TTA; tibial tuberosity advancement.
* before diagnosis.

Table 2
Details on the surgical treatment, severe postoperative complications and reoperations in a cohort of 287 stifles (255 dogs) with cranial cruciate ligament disease.

	LFS		TPLO		TTA		Total	
Number of surgeries	141	(49.1)	77	(26.8)	69	(24.0)	287	(100)
Surgeries at Hospital 1	*27*	*(19.2)*	*5*	*(6.5)*	*69*	*(100)*	*101*	*(35.2)*
Surgeries at Hospital 2	*114*	*(80.8)*	*72*	*(93.5)*	*0*	*(0.0)*	*186*	*(64.8)*
Joint inspection (%)	130	(92.2)	77	(100)	36	(52.2)	243	(84.7)
Arthrotomy	113	(80.1)	16	(20.8)	32	(46.4)	161	(56.1)
Arthroscopy	25	(17.7)	75	(97.4)	4	(5.8)	104	(36.2)
Meniscal injury	32	(22.7)	14	(18.2)	18	(26.1)	64	(22.3)
Antimicrobial use	97	(68.8)	75	(97.4)	69	(100)	241	(84.0)
Only peri-operative	*85*	*(87.6)*	*71*	*(94.7)*	*24*	*(34.8)*	*180*	*(74.7)*
Peri- and postoperative	*12*	*(12.4)*	*4*	*(5.3)*	*45*	*(65.2)*	*61*	*(25.3)*
Duration of anesthesia* (minutes)	145	(45–263)	280	(125–380)	198	(110–320)	185	(45–380)
Severe postoperative complication	31	(22.0)	24	(31.2)	17	(24.6)	72	(25.1)
Reoperation/joint lavage	22	(15.6)	15	(19.5)	11	(15.9)	48	(16.7)
Follow-up time (years)	2.1	(0–7.6)	1.9	(0–7.1)	3	(0–7.4)	2.3	(0–7.6)
Time to complication (days)	26	(4–768)	23	(2–444)	16	(1–525)	22	(1–768)

Time reported in median (range). Categorical variables as number of stifles (% total number of stifles by treatment method). LFS; lateral fabellotibial suture, TPLO; tibial plateau leveling osteotomy, TTA; tibial tuberosity advancement.
* n = 239.

Table 3
Number of procedures performed by each surgeon in a historical cohort study of 287 stifles (255 dogs) surgically created for cranial cruciate ligament disease.

	Hosital 1				Hospital 2			
Surgeon	LFS	TPLO	TTA	Total	LFS	TPLO	TTA	Total
B1	0	0	0	0	15	19	0	34
B2	0	0	0	0	23	16	0	39
E1	11	0	36	47	0	0	0	0
E2	0	0	0	0	6	10	0	16
E3	0	0	0	0	16	1	0	17
E4	0	0	0	0	22	8	0	30
E5	4	0	0	4	0	0	0	0
E6	0	0	0	0	19	7	0	26
E7	3	5	4	12	0	0	0	0
E8	3	0	21	24	0	0	0	0
R1	0	0	0	0	4	0	0	4
R2	1	0	0	1	1	1	0	2
R3	5	0	8	13	0	0	0	0
R4	0	0	0	0	8	10	0	18

B; board-certified; E; experienced surgeon, R; resident, LFS; lateral fabellotibial suture, TPLO; tibial plateau leveling osteotomy, TTA; tibial tuberosity advancement.

lameness that resolved with analgesic treatment and two dogs had a skin irritation close to the surgical wound that was treated with local antibiotics. These complications were classified as minor instead of severe.

3.3. Survival analysis

A Kaplan-Meier survival plot for the different treatment groups is presented in Fig. 1. Collinearity between variables was not detected. The results from the univariable Cox proportional hazards models are presented in Table 5. The final multivariable model included variables for treatment, hospital, age, and body weight (Table 6). Age and body weight were confounders for treatment method. There was a significant effect of surgical technique ($p = 0.0258$). The hazard of severe postoperative complications was significantly lower for dogs treated with TPLO compared with dogs treated with LFS (HR = 0.37, $p < 0.01$). No difference was found between TTA and LFS (HR = 0.56, $p = 0.361$) or between TPLO and TTA ($p = 0.495$, Wald test). In addition, the hazard increased with body weight (HR = 1.05, $p < 0.001$) and decreased with age (HR = 0.91, $p < 0.05$). The frailty term for individual did not reach statistical significance. The model validation did reveal some influential observations, but no violations of the model assumptions.

Table 4
Overview of severe postoperative complications in a historical cohort study of 287 stifles (255 dogs) surgically treated for cranial cruciate ligament disease.

Complication type	LFS (N = 141)		TPLO (N = 77)		TTA (N = 69)		Total (N = 287)	
Delayed wound healing	2	(1.4)	1	(1.3)	0	(0.0)	3	(1.0)
Implant-related	16	(11.3)	8	(10.4)	7	(10.1)	31	(10.8)
Meniscal injury	4	(2.8)	2	(2.6)	2	(2.9)	8	(2.8)
Osteomyelitis	0	(0.0)	0	(0.0)	2	(2.9)	2	(0.70)
Other	1	(0.7)	1	(1.3)	0	(0.0)	2	(0.70)
Patellar luxation	0	(0.0)	0	(0.0)	1	(1.4)	1	(0.35)
Septic arthritis	4	(2.8)	3	(3.9)	0	(0.0)	7	(2.4)
Seroma	0	(0.0)	1	(1.3)	1	(1.4)	2	(0.70)
Surgical site infection	7	(5.0)	14	(18.2)	6	(8.7)	27	(9.4)
Tuberositas tibia fracture	0	(0.0)	0	(0.0)	2	(2.9)	2	(0.70)

Reported as number of stifles (% total number of stifles by treatment method). LFS; lateral fabellotibial suture, TPLO; tibial plateau leveling osteotomy, TTA; tibial tuberosity advancement. Each complication type is registered only once for each stifle, regardless of how many times it occurred. Other complications: the dog treated with TPLO had an acute postoperative lameness on the treated limb and was euthanized without further diagnostics, and the dog treated with LFS had suspected immune-mediated arthritis, even though septic arthritis could not be ruled out despite negative bacterial culture.

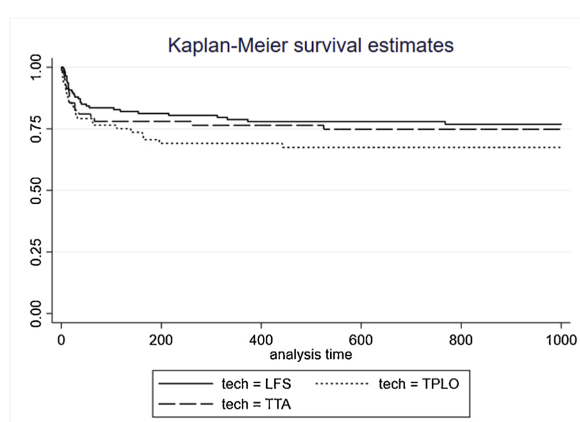

Fig. 1. Kaplan-Meier curves by treatment method describing time to severe postoperative complications (in days) after surgical treatment of CCLD in 287 stifles (255 dogs).

Table 5
Univariable Cox proportional hazards model for selection of variables in a historical cohort study assessing severe post-operative complications in 287 stifles (255 dogs) surgically treated for cranial cruciate ligament disease.

Variable	P-value
Age (years)*	0.01
Acute lameness*	0.02
Arthrotomy/arthroscopy	0.50
Body weight (kg)*	<0.01
Breed	0.84†
Hospital	0.22
Insurance*	0.50
Non-orthopaedic comorbidity*	0.94
Orthopaedic comorbidity*	0.10†
Overweight*	0.93
Sex	0.34
Surgeon experience	0.99†
Technique	0.29†
Year of treatment	0.42†

* at time of diagnosis.
† p-values from Wald test presented for multilevel categorical variables.

Table 6
Results from a multivariable Cox proportional hazards model assessing severe postoperative complications in a historical cohort study of 287 stifles (255 dogs) surgically created for cranial cruciate ligament disease.

Variable and level	Coefficient	HR	95 % CI	P
Treatment				0.026*
LFS		1	–	–
TPLO	−0.99	0.37	(0.18–0.76)	0.007
TTA	−0.57	0.56	(0.16–1.93)	0.361
Hospital				
Hospital 1		1	–	–
Hospital 2	0.5	1.65	(0.58–4.70)	0.345
Age (years)	−0.09	0.91	(0.83–1.00)	0.047
Body weight (kg)	0.05	1.05	(1.03–1.07)	<0.001

LFS; lateral fabellotibial suture, TPLO; tibial plateau leveling osteotomy, TTA; tibial tuberosity advancement.
Age and body weight at time of diagnosis.
* Wald-test.

4. Discussion

To the authors' knowledge, this cohort study is the first study comparing the occurrence of severe postoperative complications after TPLO, TTA and LFS. The overall frequency of severe postoperative complications was 25 %, but varied with surgical technique; for TTA it was 25 % which is higher than the 6.5–19.8 % reported in most other studies (Lafaver et al., 2007; Dymond et al., 2010; Hirshenson et al., 2012; Wolf et al., 2012; Costa et al., 2017; Hans et al., 2017), but below the 38.9 % reported by Christopher et al. (2013). The corresponding number for LFS was 22 %, but no comparisons could be made since previous studies evaluating complications after LFS lack classification of complication severity (Casale and McCarthy, 2009; Gordon-Evans et al., 2013). The frequency of severe postoperative complications after TPLO (31 %) was higher than the 3.1–27.8 % reported previously (Fitzpatrick and Solano, 2010; Christopher et al., 2013; Coletti et al., 2014; Garnett and Daye, 2014; Brown et al., 2016; Hans et al., 2017). Due to the different complication classification systems, caution is warranted at direct comparison of complications between studies. Even though the frequency of severe postoperative complications in the current study appears quite high, a wider definition of severe complications was used compared to several other studies, where a major complication was defined as a complication requiring surgical revision (Lafaver et al., 2007; Coletti et al., 2014; Garnett and Daye, 2014). However, the frequency of revision surgery in the current study (16.7 %) was also higher than the 3.1–12.3 % in other studies (Pacchiana et al., 2003; Lafaver et al., 2007; Casale and McCarthy, 2009; Coletti et al., 2014; Garnett and Daye, 2014). This may be due to different routines for when a revision surgery is recommended at different hospitals, but an inferior outcome with higher need for revision surgery in the current study cannot be excluded.

Tibial plateau leveling osteotomy had the highest frequency of severe postoperative complications. However, when adjusting for the confounding effects of age and body weight in the multivariable Cox proportional hazards model, TPLO was associated with a significantly decreased hazard of severe postoperative complications compared to LFS. This supports our hypothesis that both surgical technique, age and body weight are important risk factors for severe postoperative complications. The median body weight for dogs treated with TPLO was 42.2 kg, which is higher than in previous studies (Pacchiana et al., 2003; Fitzpatrick and Solano, 2010; Christopher et al., 2013; Coletti et al., 2014; Garnett and Daye, 2014; Brown et al., 2016). This could potentially explain the higher complication frequency in dogs treated by TPLO, since higher body weight has been reported as a risk factor for postoperative complications after CCLD surgery (Casale and McCarthy, 2009; Tuttle and Manley, 2009; Fitzpatrick and Solano, 2010; Steinberg et al., 2011; Taylor et al., 2011; Wolf et al., 2012; Coletti et al., 2014). A likely explanation is the higher mechanical stress on the implants in heavier dogs, and locking plates have been reported to reduce the risk for implant-related complications in heavy dogs (Solano et al., 2015; Chiu et al., 2019). In addition, activity restriction during the postoperative period could possibly be more difficult in large dogs, which could increase the risk of severe postoperative complications. It should be noted that, as smaller dogs were generally treated by LFS while larger dogs were treated by TPLO or TTA, the body weight of the dogs differed accordingly. Thus, the effect of each procedure on the hazard of severe postoperative complications is only applicable in the body weight range of each procedure. This should be acknowledged as a limitation to the generalizability of the results, and further studies of TPLO and TTA in small dogs are warranted.

In concordance with the results of a study by Casale and McCarthy (2009) evaluating complications after LFS, younger age was associated with an increased hazard of severe postoperative complications. Although injured tissue in general heals faster in young individuals compared to older (Wolf, 2010), younger dogs are also generally more active. Therefore, controlling the activity level during the postoperative period in young, active dogs is a well-known problem, and the results of our study implies this as an important challenge. Overall, these findings show that factors besides surgical technique should be considered when assessing risk of severe postoperative complications development in dogs after CCLD surgery.

The most common severe postoperative complications in the current study were implant-related, SSIs and subsequent meniscal injuries, which is in concordance with the most common severe complications reported for TTA, TPLO and LFS in other studies (Lafaver et al., 2007; Casale and McCarthy, 2009; Dymond et al., 2010; Fitzpatrick and Solano, 2010; Wolf et al., 2012; Christopher et al., 2013; Coletti et al., 2014; Hans et al., 2017). The frequency of SSI was 9.4 %, which is higher than the 3.9–8.4 % in previous reports (Casale and McCarthy, 2009; Fitzpatrick and Solano, 2010; Frey et al., 2010; Yap et al., 2015; Brown et al., 2016; Costa et al., 2017; Lopez et al., 2018). Administration of postoperative antibiotics has been identified as a protective factor for postoperative infection/inflammation and complications in some studies (Fitzpatrick and Solano, 2010; Frey et al., 2010; Hans et al., 2017), but not in others (Aiken et al., 2015; Yap et al., 2015). A lower occurrence of SSIs was seen after TTA (8.7 %) compared to TPLO (18.2 %) in the current study, which could be attributable to less administration of postoperative antibiotics in the TPLO group. However, due to the retrospective nature of the study, no causal conclusions could be drawn. A more stringent protocol for handling TPLO cases including modifications such as usage of triclosan-coated sutures, changes in distribution of intra- and postoperative antibiotics and mandatory usage of Elizabethan collars has been associated with a dramatic decrease in SSIs (Stine et al., 2018). Triclosan-coated sutures were not routinely used in the current study (data not shown).

The experience of the surgeon did not have a significant impact on the hazard of severe postoperative complications. The effect of surgeon experience is conflicting in the literature; some studies report no association between surgeon experience and complications (Pacchiana et al., 2003; Casale and McCarthy, 2009; Gordon-Evans et al., 2013), while others found higher risk of complications in surgeries performed by less experienced surgeons (Christopher et al., 2013; Lopez et al., 2018). The experience of the surgeon has also been associated with other factors, such as longer duration of surgery and anesthesia in less experienced surgeons (Freeman et al., 2017; Shaver et al., 2019), which are well known risk factors for SSI in dogs (Brown et al., 1997; Eugster et al., 2004). Information regarding duration of surgery was not available in the current study, and, as duration of anesthesia only was registered in 239 of the procedures (Table 2), it could not be included in the multivariable analysis without a substantial loss of observations and thus power. The duration of anesthesia was generally shorter for LFS procedures compared to TPLO and TTA, which could be due to the fact that the surgical procedures in TPLO and TTA are more time-consuming than LFS. In addition, postoperative radiographs were routinely taken before recovery from anesthesia in TPLO and TTA, but not LFS, which further increases anesthesia time.

Longer duration of anesthesia can also be expected if joint inspection is performed. In the current study all TPLO procedures included a joint inspection, most LFSs but only 52 % of the TTAs. Thus, evaluation of the menisci was not equally distributed between the procedures. Further, joint inspections were performed more often at VH1 than VH2. Bureau (2017) reported a low frequency of postoperative complications after TPLO without joint inspection, and an increasing number of surgeons have questioned the need for a routine meniscal examination (Jandi and Schulman, 2007; McCready and Ness, 2016). Others recommend joint inspection to confirm the diagnosis of CCLD and to evaluate meniscal injuries as well as other joint comorbidities (Ritzo et al., 2014). In the current study, joint inspection was included as a risk factor in the univariable analysis, but did not reach statistical significance.

Several additional study limitations should be mentioned. Due to the retrospective nature of the study, dogs were not randomly assigned to undergo a specific surgical technique. Thus, the treatment choice was influenced by inherent bias, including factors such as 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 the cheaper and technically less challenging LFS method rather than the more expensive and complicated osteotomy techniques. Although measured factors which could have directed the treatment decision, such as insurance status, concurrent disease, body weight, and age of the dog were included in the analyses, unmeasured factors such as owners' financial considerations likely influenced our results. Even though dog owners and, in some cases, referring veterinarians were contacted for supplementary information, there is a risk that not all complications were identified, for example due to recall bias. It has been shown that dog owners report lower complication rates compared to those documented by veterinarians in medical records (except for catastrophic complications) (Christopher et al., 2013). In addition, financial considerations could have influenced the probability of owners bringing their dogs back for rechecks and complication treatment. However, as the outcome of this study was severe postoperative complications, we find it likely that most owners would have contacted the hospitals or recalled if their dog had been treated elsewhere. There is also a risk that complications such as postoperative meniscal damage remained undiagnosed, if no revision surgery was performed. Moreover, there is a risk that some of the implant-related complications were in fact deep SSIs, since samples for culture and sensitivity from the implants were not routinely taken in dogs with implant-related complications. The current study only evaluated severe postoperative complications, and therefore risk factors for minor postoperative or intra-operative complications were not assessed.

Postoperative antibiotics, as all other postoperative factors (such as physiotherapy), were intervening variables. Intervening variables occur after the main exposure but before the outcome in the causal sequence, and are regarded as an integrated part of the main exposure, which was the surgical intervention in the current study. Since the aim of this study was to assess the total effect of the surgical techniques on the hazard of postoperative complications, all intervening variables were excluded from the analysis. To assess the causality of postoperative antibiotic administration, a more strictly designed study aimed at this purpose with a prospective, randomized design would be necessary. A variable for hospital was forced into the final multivariable Cox proportional hazards model to account for unmeasured differences between the hospitals, such as differences in preoperative routines. We do, however, acknowledge that although adding a fixed effect for hospital ensures internal validity of the analysis, the retrospective nature of this study, together with the lack of standardized procedures for antimicrobial administration, could reduce the generalizability of the results to other hospitals.

It was not possible to evaluate the effect of duration of surgery or anesthesia or the pre- and perioperative antiseptic protocol on the hazard of postoperative complications, due to missing data. Since this was a retrospective study without predefined, standardized protocols, the level of details in the records varied. Although the information in the records was sufficient for a broader classification of the complications, a more detailed classification (i.e. type of implant-related complication) would introduce a high risk of misclassification bias. It is important to consider that retrospective studies are not suitable for assessing causality, but should rather be used to identify associations and generate hypothesis for future randomized, prospective studies.

The modification in the complication classification in the current study may limit the possibility of result comparison between studies. However, we believe that the modification is justified, since the reclassified complications had the characteristics of minor complications (i.e. skin irritation treated with local antibiotics or mild lameness that resolved with analgesic medication). These mild complications should have been classified as severe according to the classification scheme, but that would have biased the results towards a false high rate of severe postoperative complications. The surgical techniques for CCLD treatment at the hospitals during the study period included TPLO, TTA and LFS. In addition, a few dogs were treated with modified Maquet technique, but these dogs were excluded as there would have been low statistical power in any comparisons. Intra-articular stabilization procedures were not performed at the hospitals during the study period, and thus the included techniques could not be compared to intra-articular stabilization procedures or the modified Maquet technique.

In conclusion, osteotomy procedures had a lower hazard of severe postoperative complications compared to the extracapsular stabilization technique LFS, with the lowest hazard for TPLO. Moreover, age and body weight were identified as risk factors for severe postoperative complications and confounders for surgical technique. These findings highlight the importance of considering not only the surgical technique, but also other potential effect-modifying factors such as age and body weight of the dog when assessing risk for severe postoperative complications after CCLD surgery in observational orthopedic studies.

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 were 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

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Transparency document

The Transparency document associated with this article can be found in the online version.

Declaration of Competing Interest

None

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