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ORIGINAL RESEARCH

Plasma procalcitonin kinetics in healthy dogs and dogs undergoing tibial plateau leveling osteotomy

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Abstract

Background: Procalcitonin (PCT) is a well-established biomarker for bacterial infection in human patients.

Objectives: We aimed to analyze the kinetics of plasma PCT (pPCT) in healthy dogs and dogs with canine cranial cruciate ligament (CCL) rupture undergoing tibial plateau leveling osteotomy (TPLO).

Methods: This prospective, longitudinal study included 15 healthy dogs and 25 dogs undergoing TPLO. Hematology, pPCT, and C-reactive protein (CRP) were assessed on 3 consecutive days in healthy dogs and 1 day preoperatively and days 1, 2, 10, and 56 postoperatively. Inter- and intraindividual variability of pPCT were assessed in healthy dogs. Median pPCT concentrations of dogs with CCL rupture preoperatively were compared with healthy controls, and median pPCT concentrations, as well as percentage change post anesthesia, arthroscopy, and TPLO, were compared with baseline. For the correlation analysis, the Spearman rank correlation test was used.

Results: Inter- and intraindividual variabilities of pPCT in healthy dogs were 36% and 15%, respectively. Median baseline pPCT concentrations were not significantly different between healthy dogs (118.9 pg/mL; IQR: 75.3-157.3 pg/mL) and dogs undergoing TPLO (95.9 pg/mL; IQR: 63.8-117.0 pg/mL). Plasma PCT concentrations were significantly lower immediately post- than preoperatively ($P < 0.001$). CRP, WBC, and neutrophil concentrations increased significantly on post-OP day 2 and had normalized by day 10.

Conclusions: These results indicate that CCL rupture, as well as anesthesia, arthroscopy, and TPLO combined, are not associated with increased pPCT concentrations in dogs with uncomplicated recovery. Considering the high intraindividual variability, individual serial measurements rather than a population-based reference interval should be considered.

KEYWORDS
canine, interindividual variability, intraindividual variability, orthopedic surgery, surgical site infection

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1 | INTRODUCTION

Procalcitonin (PCT) was first characterized in 1975 and has since been established as a biomarker for bacterial infections in human medicine.[1,2] Procalcitonin is the precursor of the hormone calcitonin that is involved in calcium metabolism. Under physiologic conditions, PCT is produced in thyroid C-cells and, to a lesser extent, other neuroendocrine cells. In humans, it has been found that production is activated in all parenchymal tissues in response to bacterial infection, mediated by cytokines interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and IL-1β, leading to increased PCT plasma concentrations.[3–5]

In veterinary medicine, an experimental study in dogs demonstrated a significant increase in plasma PCT in response to the injection of bacterial lipopolysaccharide. Several clinical studies concluded that PCT might also be a useful biomarker for detecting bacterial infection in dogs.[6-8] However, PCT concentrations have been found to overlap between dogs with bacterial infection and healthy controls.[6,8] A more recent study found PCT to remain low in dogs with sepsis.[9]

In humans, PCT has been shown to be a useful biomarker to predict postoperative bacterial SSI in some studies.[10,11] However, in another study, PCT had similar or lower diagnostic accuracy than other biomarkers, such as C-reactive protein (CRP), with a sensitivity of <80%, for predicting bacterial surgical site infection after orthopedic surgery.[12]

One of the most common surgical procedures used to treat canine cranial cruciate ligament (CCL) rupture is the tibial plateau leveling osteotomy (TPLO).[13] The procedure is normally preceded by confirmation of CCL rupture via arthroscopy under the same anesthesia. The reported complication rate post-TPLO is relatively high, ranging from 11% to 34%.[14–16] Complications include soft tissue swelling, bruising, fracture of the tibial crest, and bacterial surgical site infection (SSI), which may lead to septic arthritis, osteomyelitis, delay in bone healing, and loosening of implants.[15,16] The treatment of SSI commonly involves systemic antimicrobials and potential implant replacement or removal.

Usually, the presence of an SSI in dogs having undergone TPLO is suspected if signs of inflammation, such as pain, swelling, heat, dysfunction (lameness), or wound secretion, develop.[15,17] Confirmation of an SSI requires the detection of organisms via cytology and/or culture and susceptibility testing. In the early stages of SSI, affected dogs may show lameness without other obvious clinical or radiographic signs of infection. In these cases, it is difficult to confirm infection, and dogs are often treated for a suspected SSI with empirically chosen antimicrobials.[18]

In previous studies, CRP and serum amyloid A (SAA) have been shown to significantly increase 24 hours post-TPLO surgery and return to baseline by day 6 postsurgery in dogs with uncomplicated recovery. CRP and SAA concentrations were significantly higher on day 6 in dogs developing SSI compared with uncomplicated cases. As SSI typically develops around this time, these findings suggest that CRP and SAA could be useful biomarkers to monitor for infectious complications post-TPLO.[19]

Veterinary studies evaluating the usefulness of PCT in the context of orthopedic surgery are lacking; however, there are studies proving that PCT might be a useful biomarker to provide information on the course of other diseases, such as pyometra or acute diarrhea.[20,21]

The aims of this study were to evaluate the day-to-day variability of plasma procalcitonin (pPCT) concentrations in healthy dogs, to assess baseline pPCT concentrations in dogs with CCL rupture, and to determine the effect of general anesthesia, arthroscopy, and TPLO combined with pPCT concentrations in dogs with uneventful surgical recovery.

2 | MATERIALS AND METHODS

2.1 | Study design, inclusion, and exclusion criteria

The study was designed as a prospective longitudinal study involving privately owned healthy dogs and dogs with CCL rupture undergoing arthroscopy and TPLO at the Small Animal Clinic of the Vetsuisse Faculty Bern. Dogs were recruited into the study between June 2020 and March 2021. Informed consent was obtained prior to enrollment of dogs into the study.

Dogs were included if their body weight was above 5 kg and their character allowed for repeated blood sampling with minimal restraint. Dogs were excluded if they showed signs of illness other than CCL rupture or had received antimicrobial treatments for any reason within 2 months prior to the intervention. To assess the combined effect of anesthesia, arthroscopy, and TPLO on pPCT, only dogs with uneventful recovery over a period of 8 weeks were included in the overall analysis.

Complete blood counts (CBCs) and CRP and pPCT concentrations were assessed in healthy dogs on 3 consecutive days (D1, 2, and 3). In dogs with CCL rupture, sampling time points were chosen to reflect those most commonly used in clinical medicine for pPCT. Procalcitonin and CRP were assessed on the day of admission (D1), the day of surgery directly postoperatively (D2), the day after surgery (D3), at suture removal (D10), and recheck 8 weeks post-TPLO (D56). Blood for CBCs was collected at D1, D2, D3, and D56. Sampling time points for healthy and TPLO dogs are shown in Figure 1.

2.2 | Animals

2.2.1 | Healthy dogs

Healthy dogs were either staff or student owned or belonged to a cohort of military dogs. Dogs were deemed clinically healthy based on an uneventful history, unremarkable clinical examination, and unremarkable hematology and biochemistry panels including CRP measurements.

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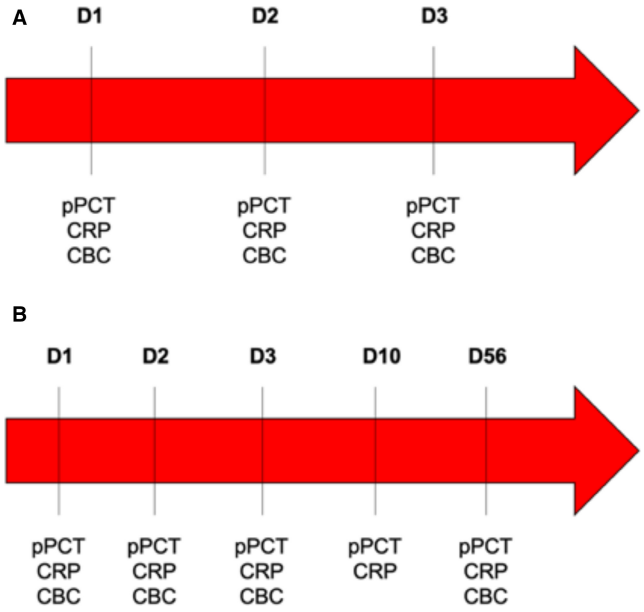

FIGURE 1 Sampling time points in (A) healthy dogs and (B) dogs undergoing tibial plateau leveling osteotomy (TPLO). CBC, complete blood count; CRP, C-reactive protein; pPCT, plasma procalcitonin.

2.2.2 | Dogs undergoing tibial plateau leveling osteotomy (TPLO group)

Dogs in this group were diagnosed with CCL rupture based on consistent historical, clinical, and radiographic criteria. After initial clinical assessment, dogs underwent routine general anesthesia, stifle arthroscopy, and TPLO. All dogs received perioperative antibiotics (ampicillin-sulbactam 30 mg/kg or cefazolin 22 mg/kg intravenously, starting 30-60 minutes prior to the surgical procedure and continuing every 90 minutes until skin closure). Anesthesia time ranged from 195 to 280 minutes, and the time of the surgical intervention was between 80 and 165 minutes.

For the TPLO, commercially available implants were used (Arthrex TPLO system, Synthes TPLO system). Either nonabsorbable skin sutures or absorbable intradermal sutures were placed to oppose skin. All incisions were covered with a protective primary bandage layer, and an Elizabethan collar was placed on all dogs. All dogs were discharged 1 day after surgery.

Owners were instructed to restrict the activity of their dog for 8 to 10 weeks postoperatively and to monitor the wound for evidence of redness, swelling, or discharge. Dogs had to wear an e-collar to prevent them from licking or chewing at the area of the incision for 10-14 days.

Postoperatively, nonsteroidal anti-inflammatory drugs were prescribed for 7 days: carprofen (4 mg/kg once a day [SID]), meloxicam (0.2 mg/kg once, followed by 0.1 mg/kg SID), or robenacoxib (1 mg/kg SID). No antibiotics were dispensed postoperatively.

Removal of skin sutures (if present) was performed 10-14 days postoperatively, and a clinical and radiographic recheck was performed on average 8 weeks postoperatively.

2.3 | Sample collection and handling

Blood was withdrawn by puncture of the cephalic or saphenous veins using 21-gauge needles or by withdrawal from a peripheral intravenous catheter. In that case, a purge sample of 0.3 mL of blood was discarded before taking the actual sample. Blood was collected into EDTA and lithium heparin tubes (Monovette, Sarstedt AG Nümbrecht, Germany). Lithium heparin samples for measurement of pPCT and CRP were centrifuged within 1 hour of sampling for 10 minutes at 20°C with a relative centrifugal force (RCF) of 3000.

Directly following centrifugation, plasma was separated and aliquoted into five 0.5 mL microtubes (SARSTEDT AG & Co. KG) and frozen at −80°C until analysis. Frozen storage time ranged between 1 and 9 months.

In human plasma samples, pPCT concentrations have been demonstrated to remain stable for several hours at room temperature with a decline of 2% per hour. Plasma PCT was stable for up to 4 days at 4°C and during frozen storage at −80°C with a decline of around 10% after 3-5 years.[22–24]

Blood for hematology was directly analyzed using an automated analyzer (ADVIA 2120i, Siemens Healthcare, Zürich, Switzerland; Cobas c501, Roche diagnostics, Basel, Switzerland).

2.4 | Procalcitonin measurement

Plasma from lithium heparin anticoagulated blood was used for the PCT measurements. PCT was measured batch wise using a previously extensively validated canine PCT ELISA (Biovendor, Nashville, USA), validated for the measurement of PCT concentrations in citrated plasma samples.[6] An in-house preliminary study showed that measurement of pPCT concentrations in serum, citrate, and lithium-heparin plasma samples gave comparable results (Figure S1).

In our hands, the assay showed excellent dilutional linearity for pPCT based on serial dilutions of samples of four different dogs (Figure S2). Intraassay variability was calculated based on measurements of three samples (V1, V2, and V3) as duplicates on one ELISA plate. Interassay variability was calculated based on measurements of three samples (V1, V2, and V3) on all 12 ELISA plates, yielding excellent intra-assay variability (4%) and an interassay variability of 14%. Usually, coefficients of variation <10% to 15% are set as an acceptable standard.[25,26]

All samples and standards were measured in duplicates. The assay was performed manually according to the manufacturer's recommendations, except that a 1:2 dilution (twofold dilution) of the sample with the dilution buffer provided by the manufacturer was used instead of a 1:5 dilution (fivefold dilution), as suggested by the manufacturer. This decision was based on a previous study demonstrating that a fivefold dilution commonly results in concentrations that were below the lowest standard.[6] Absorbance was measured at $\lambda = 450$ nm using a microplate spectrophotometer (Biotek, Model EL800). A series of standards were prepared from the master standard provided in the kit, resulting in the following concentrations:

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800, 400, 200, 100, 50, 25, and 12.5 pg/mL. Samples were reanalyzed if the coefficient of variation (CV) between duplicates was above 15%. The upper limit of the assay was defined as the absorbance of the highest standard after having observed that linearity requirements were met. If the absorbance of a sample exceeded the absorbance of the highest standard, it was measured again at a higher dilution.

Samples from different days of the same dog were measured on the same plate.

2.5 | CRP measurement

Plasma CRP was measured batch wise using an automated analyzer Cobas c501 (Roche Diagnostics, Basel, Switzerland) with a previously validated CRP assay (Gentian Canine CRP; Scil Animal Care company, Viernheim, Germany).[27] The lower limit of quantification was set at 6.4 mg/L by the manufacturer.

2.6 | Hematology

WBC concentrations, as well as hematocrits, were obtained using an automated analyzer (ADVIA 2120i, Siemens Healthcare, Zürich, Switzerland) using veterinary software: ADVIA multispecies software, version 6.3.2. Manual 200-cell differential blood counts were performed by experienced laboratory technicians at the Clinical Diagnostic Laboratory of the University of Bern.

2.7 | Statistical analysis

Statistical analysis was performed using NCSS 2020 (NCSS, LLC. Kaysville, Utah, USA).

The normality of the data was examined using normality plots and the Shapiro-Wilk test. Day-to-day variability and interindividual variability of pPCT were assessed in the group of healthy dogs by calculation of CVs (%) via the following formula: Standard deviation / Mean × 100%.

Patient characteristics, including sex, neuter status, age, and body weight, as well as baseline pPCT concentrations, were compared between healthy dogs and dogs with CCL rupture using Chi-square test for discrete and Kruskal-Wallis ANOVA test for continuous variables. As CRP and CBC within normal limits were inclusion criteria for healthy dogs, those parameters were not compared between groups.

Median pPCT, CRP, WBC, and neutrophil concentrations were compared between sampling days by Friedman's rank test. To adjust the significance level for multiple comparisons, the Bonferroni correction was used. To account for the lack of concurrent controls on days 10 and 56, the percentage change per individual vs baseline was calculated for pPCT using the following formula: pPCT(D1) − pPCT(D2) / pPCT (D1).

To correct pPCT concentrations postoperatively for the effect of hemodilution, the equation of Dill & Costill was used with the following formula:

$$\Delta PV = \frac{Hb\ pre \times (1 - Hct\ post)}{Hb\ post \times (1 - Hct\ pre)} - 1$$

$$PM\ post,c = PM\ post,u \times (1 + \Delta PV).$$ [28]

(Abbreviations: ΔPV: change in plasma volume; Hb: hemoglobin concentration; Hct: hematocrit; pre: before; post: after; PM post,c: corrected plasma biomarker after TPLO; PM post,u: uncorrected plasma biomarker after TPLO).

Correlations among pPCT, CRP, WBC, and neutrophil concentration were examined using the Spearman rank correlation test. The statistical significance level for all calculations was set at $P < 0.05$.

3 | RESULTS

3.1 | Study population

3.1.1 | Healthy dogs

A total of 21 healthy dogs were initially assessed for inclusion in the study. Of these, 15 dogs fulfilled inclusion criteria; six dogs were excluded due to the presence of clinically relevant changes in history, physical examination (n = 3), and/or baseline laboratory findings (n = 3) or diagnosis of neoplasia (mast cell tumor) within 11 months following sampling (n = 1). Three dogs were only sampled on D1. Three dogs were crossbreds and 12 were purebreds belonging to seven different breeds, with the most common breeds being Malinois (n = 3), German Shepherd (n = 2), Tervueren (n = 2), and Dutch Shepherd (n = 2).

3.1.2 | Dogs undergoing TPLO

A total of 25 dogs with CCL rupture undergoing TPLO and having an uneventful recovery were included in the overall analysis. Five dogs were crossbred and 20 were purebred, belonging to 16 different breeds, with the most common breeds being Rottweiler (n = 2), Bernese Mountain Dog (n = 2), American Staffordshire Bullterrier (n = 2), and Labrador Retriever (n = 2).

On D1 and D2, all 25 dogs were sampled; on D3, 17 dogs were sampled; on D10, three dogs were sampled; and on D56, five dogs were sampled.

3.2 | Demographic information

There were no significant differences in age, weight, body condition scores, sex, and neuter status between the healthy and TPLO group (Table 1).

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TABLE 1 Patient characteristics of healthy dogs and dogs with cranial cruciate ligament rupture undergoing tibial plateau leveling osteotomy.

	Healthy	TPLO	
Variable	Median (IQR)	Median (IQR)	*P*-value
Age (y)	4 (2-7)	6 (4-7)	0.2
Body weight (kg)	26.4 (23.1-29.7)	25.4 (19.7-32.9)	0.9
Sex			
Male/Female	6/9	13/12	0.5
Intact/neutered	3/12	1/24	0.02

Abbreviations: IQR, interquartile range; TPLO, tibial plateau leveling osteotomy.

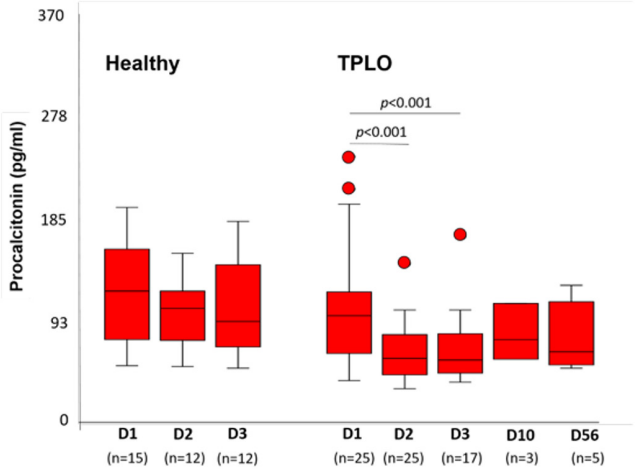

FIGURE 2 Median plasma procalcitonin concentrations in healthy dogs and dogs undergoing tibial plateau leveling osteotomy (TPLO). Plasma procalcitonin concentrations were assessed on 3 consecutive days (D1, D2, and D3) in healthy dogs and 1 day preoperatively (D1) and days 1 (D2), 2 (D3), 10 (D10), and week 8 (D56) postoperatively. The central lines in the boxes represent the median values, and the top and bottom of the boxes represent the 75th and 25th percentiles, respectively. TPLO, tibial plateau leveling osteotomy.

3.3 | Plasma PCT

In healthy dogs, pPCT concentrations of all 39 samples were normally distributed and showed a wide range between 48.8 and 193.6 pg/mL with a median of 110.3 pg/mL (IQR 74.7-138).

There was no significant difference in median pPCT between sampling days (D1: 118.6 pg/mL; D2: 102.8 pg/mL; and D3: 91.1 pg/mL; $P = 0.2$; Figure 2). Interindividual variability (36%) for pPCT in healthy dogs was higher than the intraindividual variability (15%).

There was no significant difference in pPCT concentrations between the healthy and TPLO group on D1 ($P = 0.09$).

In the TPLO group, pPCT concentrations were significantly reduced on D2 (57.6 pg/mL; IQR 43.5-77.8) and D3 postoperatively (56 pg/mL: IQR 48.5-77.2) compared with D1 (96 pg/mL; IQR 63.8-117). There was no significant difference between the other time points (Figure 2). Median percentage changes from baseline (D1) were 38.4% (IQR −45.8 to -20.9; $P < 0.001$) for D2; −31.8% (−45.9 to −16.3; $P < 0.01$) for D3; 0% (IQR −17.4 to 7.5; $P = 0.5$) for D10; and 27.4% (IQR 18.8 to 58.8; $P = 0.3$) for D56.

Dill & Costill equation resulted in a corrected median postoperative pPCT concentration of 94.9 pg/mL.

3.4 | Plasma C-reactive protein

Plasma CRP concentrations in dogs undergoing TPLO surgery are shown in Figure 3A. Median CRP concentrations increased progressively postoperatively, with significant increases between D1 and D2 (<6.4 mg/L vs 8.3 mg/L; IQR 6.4-19.3; $P < 0.001$) and D2 and D3 (28.4 mg/L; IQR: 21.5-45.2; $P < 0.001$). Concentrations on D10 were lower than on D3 but were still increased, however, not significantly, compared with D1 (8.2 mg/L: IQR 7.05-10.7). On D56 concentrations had returned to baseline. When comparing concentrations of D56 to those of D3, they were significantly lower ($P < 0.001$).

3.5 | Hematology

White blood cell and neutrophil concentrations in dogs undergoing tibial plateau leveling osteotomy are shown in Figure 3B,C. The median hematocrit was significantly lower on D2 (41%; IQR: 36-47) compared with D1 (50%; IQR: 45-53; $P < 0.001$). White blood cell and neutrophil concentrations increased postoperatively and were significantly higher on D3 compared with D1 preoperatively (WBC: 6.8×10^9/L vs 10.5×10^9/L; IQR: 5.8-8.3 vs 9.2-13.9; segmented neutrophils: 4.67×10^9/L vs 8.1×10^9L/; IQR: 4.3-6 vs 6.9-10.4; $P < 0.001$).

3.6 | Correlation analysis

Spearman rank correlation test showed no correlation between median pPCT and CRP concentrations ($r = 0.04$, $P = 0.9$), WBC ($r = 0.3$, $P = 0.09$), or neutrophil counts ($r = 0.2$, $P = 0.5$). C-reactive protein concentrations were moderately and positively correlated with WBC ($r = 0.4$, $P < 0.05$).

4 | DISCUSSION

Tibial plateau leveling osteotomy is a standard therapy for dogs with CCL rupture, a common condition in large-breed dogs.[29] Compared with other orthopedic surgeries, the reported complication rate is relatively high, ranging from 11 to 34%.[10–12] Prediction or early

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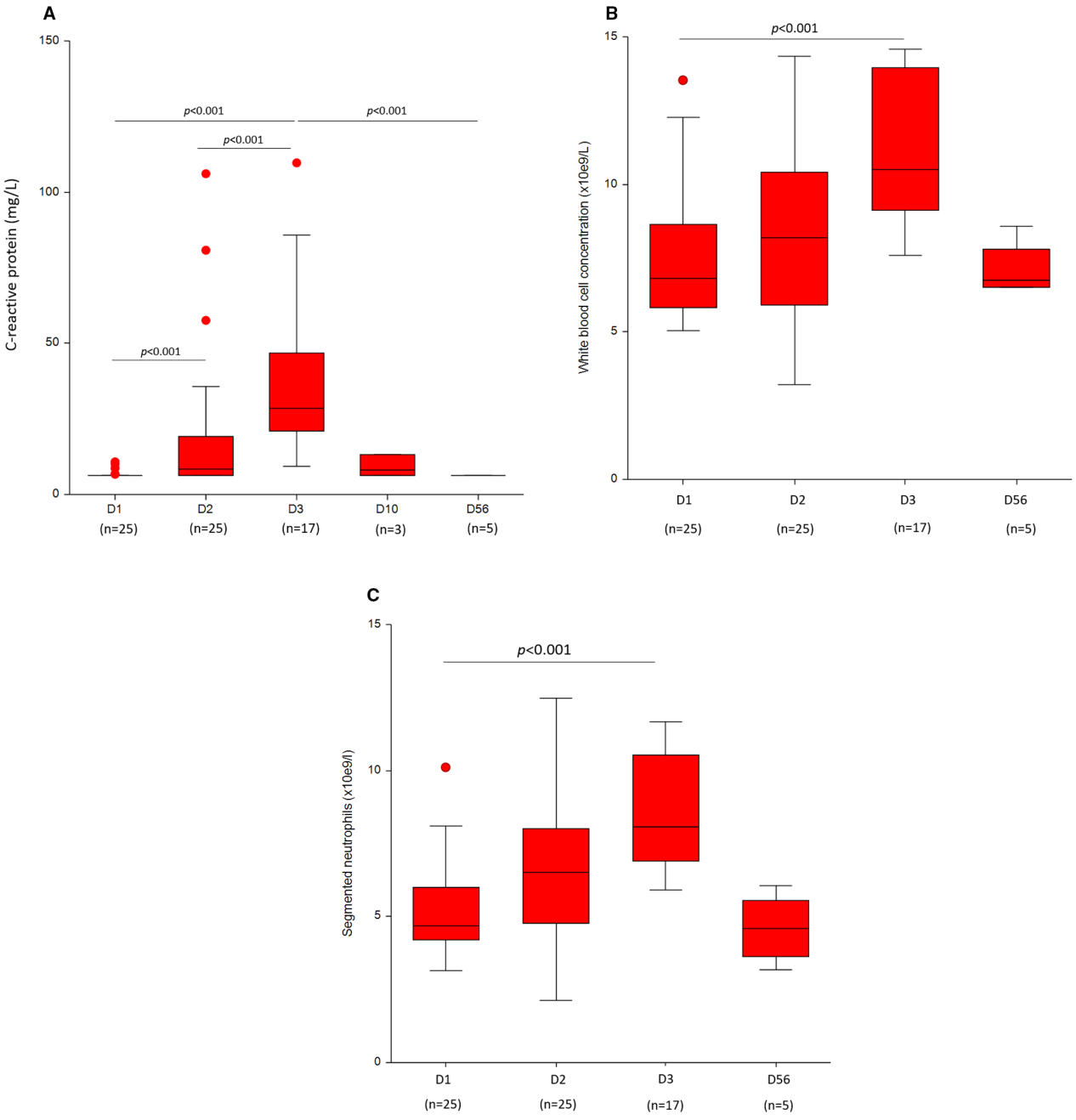

FIGURE 3 C-reactive protein, white blood cell, and neutrophil concentrations in dogs undergoing tibial plateau leveling osteotomy on day 1 (D1) presurgery and days 1 (D2), 2 (D3), 10 (D10), and week 8 (D56) postsurgery. The central lines in the boxes represent the median values, and the top and bottom of the boxes represent the 75th and 25th percentiles, respectively.

detection of SSI via a biomarker would be of immense value and support prudent antimicrobial use. The aim of this study was to evaluate pPCT kinetics in healthy dogs and dogs with CCL rupture undergoing TPLO. The impact of CCL rupture and the combined effect of anesthesia and arthroscopy/TPLO on pPCT in dogs was assessed.

Plasma PCT in healthy dogs showed a wide range (48.8-193.6 pg/mL) and a mean value (108.7 pg/mL), which is well above the concentrations reported in a previous study, including 52 healthy dogs (mean 49.8 pg/mL). In that same study, a reference interval for pPCT of between 5.9 and 91.1 pg/mL was proposed.[6] If this reference value had been applied to the present population, 80% of healthy dogs would have had values above the reference interval. Furthermore, in a recently published experimental study in dogs with induced endotoxemia, some control dogs also had PCT concentrations exceeding this proposed reference interval.[8]

Although the same assay has been used across these three studies, differences in methodology causing the differences in pPCT concentrations in healthy dogs cannot be excluded. The reference interval proposed by Goggs et al is based on citrate plasma samples while lithium heparin plasma was used in the present study.[6]

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However, prior to the study, we observed that pPCT measured in citrated or lithium heparin plasma samples showed similar results. Given the high interindividual variability of pPCT in healthy dogs, differences across different cohorts of dogs are to be expected, and the upper limit of the proposed reference interval could be questioned.[23] In any case, the high intraindividuality for pPCT would suggest using serial individual measurements rather than comparison to a population-based reference range. While a reference interval for human pPCT exists, one study assessing pPCT concentrations daily in 16 individuals over a 17-day period suggested equally high interindividual variability.[31]

Median pPCT concentrations were not significantly different in the group of dogs with CCL rupture prior to surgery compared with healthy dogs, suggesting that the potential sterile articular or periarticular inflammation associated with CCL rupture does not increase pPCT concentrations. Similarly, surgical trauma and wound healing were not associated with increases in pPCT concentrations in dogs with uncomplicated recovery post-TPLO. In fact, the only significant change was a decrease in median pPCT concentrations on D2 and D3 postoperatively compared with D1 preoperatively. Correction of pPCT concentrations for the effect of hemodilution using the equation of Dill & Costill suggests that decreases in pPCT concentrations are likely due to a dilutional effect of peri- and intraoperative fluid adminstration.[28]

We, therefore, conclude that neither CCL rupture nor the combined effect of anesthesia, arthroscopy, and TPLO surgery is associated with a significant increase in pPCT concentrations. This finding is in accordance with human studies evaluating the usefulness of PCT in predicting bacterial SSI in orthopedic surgery.[31] It also offers the opportunity to assess pPCT concentrations in dogs with TPLO that develop SSI in future studies.

In contrast to pPCT, WBC and CRP concentrations increased significantly during the days postoperatively, which is in accordance with other studies and reflects a physiologic response to an inflammatory insult.[32] CRP is a major acute phase protein, characterized by an increase in blood levels more than 10-fold (up to 1000-fold) following infection or other inflammatory stimuli and a short half-life (hours), causing plasma concentrations to decrease soon after inflammation has subsided.[32] Our results corroborate the results of Löfqvist et al, where CRP and SAA increased in all dogs during the first 24 hours post-TPLO. In dogs developing SSI, levels continued to be elevated 6 days postoperatively, whereas, in dogs with uneventful recovery, CRP and SAA had returned to baseline.[19] In contrast to CRP, pPCT did not increase in our cohort postoperatively, which may indicate higher specificity for the detection of SSI than CRP and SAA.[33,34] Further studies are needed to compare pPCT concentrations in dogs with SSI and uneventful recovery to assess the diagnostic utility of pPCT as a marker of SSI in dogs undergoing TPLO and to study its superiority to CRP.

Our study has several limitations, most importantly the small population size, which results in low statistical power.

Another limitation might be the limited sampling time points. To obtain complete data on kinetics, values would ideally be measured daily during the study period. By only obtaining samples at the given time points, we cannot comment on the evolution of PCT concentrations between our sampling time points. We chose these time points for practical reasons, as dogs often only stay for 1 or maximum 2 days in hospital before/after TPLO surgery. When recovery is uneventful, dogs only return for a control radiograph 8 weeks later. Whenever possible, we obtained samples on day 10 (recheck time for wound healing and suture removal), a time around which SSI—should it occur—often becomes clinically apparent.

In our study, pPCT concentrations of dogs with CCL rupture were compared with healthy controls, and median pPCT concentrations, as well as percentage change postanesthesia, arthroscopy, and TPLO, were compared with baseline. Ideally, the effect of anesthesia, arthroscopy, and TPLO would have been compared individually to a respective control group including dogs not undergoing any procedures and dogs undergoing sham procedures. However, such a study design would have been unacceptable for most owners of healthy control dogs and would have required the use of experimental dogs. Furthermore, only small numbers of dogs were available for assessments at 10 and 56 days postadmission. As SSI typically becomes apparent at approximately 14 days post-surgery, asymptomatic patients with abnormal pPCT concentrations could have been missed.[34]

In healthy dogs, we included a cohort of five military dogs, which limits variability in our group of healthy dogs, as dogs from military service are often of similar breeds and have a different lifestyle from regular pet dogs.

In conclusion, concentrations of pPCT in healthy dogs were higher than previously reported. In dogs with uneventful surgical recovery, CCL rupture and the combined effect of anesthesia and arthroscopy/TPLO were not associated with an increase in pPCT. The results of this study can be used as a basis for future research into the usefulness of pPCT as an early marker of bacterial SSI in dogs after TPLO surgery.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATIONS

The study design was approved by the local animal welfare committee (BE127/19).

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