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Photobiomodulation therapy in dogs undergoing TPLO after cranial cruciate ligament rupture shows promise but no statistically significant difference in a randomized trial

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OBJECTIVE
Effect of photobiomodulation therapy (PBMT) in patients with CCLR after TPLO surgery by measuring C-reactive protein (CRP), percentage weight bearing, lameness using a short form of a composite measure pain scale, evaluated by the clinician and owners, and surgical site infection.

SAMPLE
54 client-owned dogs with CCLR undergoing unilateral TPLO surgery were enrolled in this study between April 5, 2021, through April 10, 2022.

METHODS
The study population was randomly assigned to either a treatment group receiving PMBT (24 dogs) or a control group (30 dogs). PMBT was performed on the treatment group immediately after induction, and 6 hours, 24 hours, 48 hours, and 8 weeks postoperatively. The control group received sham PMBT (device turned off) at the same time. Evaluation of CRP, CMPS-SF, evidence of SSI, and %WB were evaluated for all dogs 24 hours preoperatively, and then 24 hours, 48 hours, and 8 weeks postoperatively. Owners completed CMPS-SF and subjective evaluations weekly for 8 weeks postoperatively.

RESULTS
No statistically significant differences were found between treatment groups when evaluating CRP, %WB, and CMPS-SF by the clinician and weekly evaluation of the CMPS-SF by owners. Although no statistically significant differences were found in patients developing surgical site infections between treatment groups, SSI was only observed in patients in the control group (5/30, 16.6%). Most were minor/superficial infections (4/30 13.3%), and a single dog (1/30, 3.3%) had a major/deep surgical site infection.

CLINICAL RELEVANCE
Although with promising but not statistically significant differences between groups, surgical site infections may be reduced after PBMT application.

Keywords: PBMT, TPLO, CRP, CCLR, LASER

Photobiomodulation therapy (PBMT), also known as low-level laser therapy, cold laser therapy, or low-intensity laser therapy is increasingly popular in human and animal rehabilitation. It involves the use of a device designed to deliver photochemical rather than thermal energy.[1] PBMT has been used to address inflammation, edema, and chronic joint disorders,[2] to promote healing of wounds,[3] and to treat neurological disorders and pain.[4] The leading theory explaining the basic mechanism of PBMT in the tissues implicates the cytochrome C oxidase as the primary photoreceptor. Once cytochrome C oxidase is stimulated by light, electron transport is accelerated, leading to increased ATP production and thus hastened recovery of injured tissues.[5,6]

Few studies have been done in veterinary medicine evaluating the influence of PBMT before or after surgery.[10–13] The results of the existing studies are controversial.

It is likely that some of the controversies are due to variability in the dosages used to treat the different conditions. The dose recommended to treat

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tissue in animals ranges from 3 to 10 J/cm^2. However, the dose used will depend on manufacturers' recommendations based on the therapeutic goal, skin color, coat color, and surface area.[7,8]

Additionally, PBMT has been used to control inflammatory processes and analgesia without definitive results. Measuring some serum proteins like C-reactive protein (CRP) in blood may help obtain more definitive results. CRP is an acute phase protein for inflammation; it increases 6 hours after tissue injury and eventually will decrease around 48 hours postinjury after a decrease in inflammation.[9]

Some studies have been conducted in dogs with cranial cruciate ligament rupture (CCLR) before and after tibial plateau leveling osteotomy (TPLO) surgery, to evaluate bone healing, percentage weight bearing (%WB), pain evaluation, and wound healing.[10,11]

TPLO surgery is one of the most common surgical techniques to correct CCLR in dogs. Despite good to excellent outcomes in most reports, some patients required prolonged time to recover from lameness or pain. Those patients have longer hospitalization, longer duration of pain medication, or require physical therapy to resolve lameness.

Based on human and veterinary studies, PBMT therapy has been used for preconditioning tissues before surgery to decrease inflammation and increase analgesia, vascularization, and tissue healing.[3,4,12] Rogatko et al (2017) administered a single dose of PBMT to precondition the tissues before TPLO surgery and showed an improvement in peak vertical force (PVF) at 8 weeks compared to the control group.[13]

One of the most common complications after TPLO surgery is the high rate of surgical site infections (SSI; reported as 2.9–25.9%).[14] The use of antibiotics after a TPLO surgery is still controversial since historical evidence does not support antibiotic use after a clean procedure.[15,16] On the other hand, some studies have found that postoperative antibiotics showed some protection against SSI.[17–19] The use of prophylactic antibiotics can lead to resistant strains of bacteria. To the authors' knowledge, no studies have evaluated SSI in TPLO after PBMT.

The objective of the present study is to determine the effect of PBMT in adult, client-owned dogs of any breed or sex, with a diagnosis of cranial cruciate ligament rupture undergoing TPLO surgery, on measurement of CRP in blood, percentage of %WB, a short form of a composite Glasgow pain score[20] (CMPS-SF) in-hospital and in-home, and incidence of surgical site infections.

Our null hypothesis was that there would not be statistically significant differences postoperative between groups in %WB, CRP, and CMPS-SF by owner or clinician, and risk of SSI.

Methods

Study design

A blinded, randomized, placebo-controlled prospective study was conducted at the Veterinary Health Center, College of Veterinary Medicine, at Kansas State University from April 2021 to April 2022. All study procedures were reviewed and approved by the Kansas State University Institutional Animal Care and Use Committee (IACUC #4500). Between the dates of April 2021 and April 2022, a consent form was provided to the dog owners and signed before enrolling their animals in the study. All patients had confirmed cranial cruciate ligament rupture (CCLR) as determined by physical examination by the attending orthopedic surgeon or small animal surgery resident.

Eligibility

Inclusion criteria consisted of client-owned dogs of any breed or sex, older than 1 year of age, with a diagnosis of CCLR, enrolled during their initial visit at the Veterinary Health Center. Standard lateral and craniocaudal radiographs were performed under sedation followed by TPLO surgery with any of the following variations: arthrotomy, arthroscopy, partial meniscectomy, and meniscal release.

Exclusion criteria included results of a preoperative complete blood count and serum chemistry demonstrating systemic illness or any other reason to avoid NSAID medication such as historical gastrointestinal signs or inability of the owners to give oral NSAIDs. Aggressive or anxious temperament that might interfere with stance analysis and subjective pain scoring, or neurologic disease confirmed by 1 of the clinical investigators were also grounds for exclusion.

Sample size determination

Rogatko et al 2017,[13] using a single dose of PBMT preoperative, reported better peak vertical force (PVF) at 8 weeks; the mean static %WB was 39.6% (±SD 4.7%) in patients that received laser treatment compared 28.9% ± 2.6% for patients in the sham group ($P < .01$). In another study evaluating PVF at 8 weeks after TPLO and PBMT, authors reported a mean of 52% ± 11% on the PBMT group and 48% ± 7% on the control group resulting in a not statistically significant difference.[10] Considering this data from the literature, and assuming a mean difference in static %WB of 5% between treatment groups (40% static %WB for the control and 45% static %WB for the treatment group), a standard deviation of 5 and 7% for the control and treatment groups, respectively, a power of 80%, and alpha of 0.05, the number of patients needed per group was predicted to be 25, for a total of 50 patients.[10,13] Sample size was calculated using a 2-sample means test assuming unequal variances in standard software (Stata17.0 SE; StataCorp LLC).

Enrollment, treatment groups, and outcome measurements

After enrollment, a randomization technique was performed using Microsoft Excel (2018) to assign patients to the treatment or control groups. For statistical analysis, the animal was deemed the experimental unit.

A Class IV, 980/810 nm gallium-aluminum-arsenide diode laser (CTX SmartCoat TM, Companion Animal Health) was used for all treatments.

A profile for each patient was entered into the software included with the device to note species, body weight, area to treat, coat color and length, skin color, and condition to treat. The software then generated a protocol defining the power and duration of the application. Animals in the control group had a sham treatment with the device turned off but moved in a similar pattern for the calculated duration. Patients were treated after shaving their fur for surgery.

PBMT was performed on the medial and lateral aspect of the distal femur and proximal tibia using back-and-forth movements in contact with the skin from proximal to distal and distal to proximal in a constant movement for the predetermined time of the treatment in all patients assigned to the treatment group. The laser energy was administered through a handpiece with a circular 4.7 cm diameter (2.21 cm^2) spot size using a power setting of 10 W and passed in continuous motion over an area of 12.7 cm X 20.3 cm for 2.1 minutes delivering a total of 1300 J (5 J/cm2) to the medial and then repeated on the lateral aspect of the knee.

Evaluations of the patients occurred preoperatively, at 24 and 48 hours postoperatively, and again at 8 weeks postoperatively. The data was obtained by the same clinician who was blinded to the treatment group. The data was gathered as follows.

The IDEXX Catalyst® CRP Test (IDEXX Laboratories) utilizing gold nanoparticles to measure antigen was used to measure CRP in blood. A lithium heparin container with 600–800 µL of whole blood was utilized in-house using a Catalyst® one (IDEXX Laboratories). A PetSafe Stance Analyzer (LiteCure LLC, Companion Animal Health) 38" L X 24" W X 1.75" H, was used to measure the percentage of weight bearing in all 4 limbs on all the patients. Five measurements were collected at each time point and the highest and lowest values were eliminated to yield an average for the 3 remaining values.

A modified short form of a Composite Measure Pain Scale (CMPS-SF)[20] was used for all the patients. The same scale was used by 1 member of the owner's family, at home, weekly for 8 weeks. The forms evaluated by the owner were returned to the hospital at the 8-week recheck. Two questions were added to the CMPS-SF regarding the appearance of the surgical site, and which medications the patient was taking during the time of the evaluation. The owners were instructed that the same individual was to complete the evaluations during the next 8 weeks to minimize variability in measurements.

Surgical site infections (SSI) were evaluated based on the CDC guidelines.[21] The CDC defines SSI as present when there is a purulent discharge from the surgical site or patients are showing clinical signs such as fever, localized pain, or tenderness. SSI are divided into superficial, where only skin and subcutaneous tissue are involved, and deep where fascia, muscle organ/space are involved.[21,22] If the owners noticed a discharge from the surgical site, they were asked to visit their primary care veterinarian for a complete evaluation. When the veterinarian confirmed purulent material coming from the surgical site, antibiotics were prescribed.

Day 0 baseline evaluations—During intake, patients underwent a complete physical and orthopedic examination. A baseline CMPS- SF was performed by the primary author (OAC), who was blinded as to the treatment group, objective stance data was obtained, and blood was drawn from the jugular vein for a complete blood count, chemistry, and CRP. Radiographs were also obtained.

Day 1 (day of surgery) evaluations—Patients were premedicated and then placed under general anesthesia. Anesthetic protocols were at the discretion of the boarded anesthesiologist in charge. A standard surgical preparation protocol for a TPLO surgery was performed. The first treatment of PBMT was done after clipping the surgical area. After PBMT was completed, patients received an ultrasound-guided femoral and sciatic nerve block with ropivacaine HCl 1 mg/kg (Somerset Therapeutics, LLC). A standard TPLO was performed either by a ACVS diplomate surgeon or a supervised small animal surgery resident according to a previously described technique.[23] A partial meniscectomy was performed if a meniscal tear was found during medial parapatellar mini-arthrotomy; no meniscal releases were performed. For postoperative pain control, hydromorphone 0.08 mg/kg (hydromorphone HCL by Hykma) was administered subcutaneously every 4 hours for the first 24 hours along with a single dose of carprofen 2.2 mg/kg SC once (Rymadil; Zoetis), after the first day, opioids and NSAID were switched to oral codeine 1.4 mg–2.0 mg/kg PO every 8 hours (West-Ward), carprofen 2.2 mg/kg PO every 12 hours (Rymadil; Zoetis). Six hours after surgery, a second PMBT was performed. The individuals performing the laser or placebo treatments did not participate in any evaluations of the study subjects.

Day 2 and 3 (24- and 48-hours postoperative) evaluations—Twenty-four and 48 hours after surgery, the dogs received either PBMT or placebo treatment, CRP blood test, CMPS-SF, and stance analysis. The patients were discharged from the hospital 48 hours after the surgery. A modified short form of a composite measure pain scale (CMPS-SF) was given to the owners with the addition of 2 questions to evaluate the surgical site.

Eight-week evaluations—Owners of all the study patients were asked to return at 8 weeks after TPLO surgery for a recheck. This evaluation consisted of a complete physical and orthopedic examination, stance analysis, blood drawn for a CRP blood test, and a pain evaluation using the CMPS-SF, all performed by the original clinician (OAC). Radiographs of the stifle were performed utilizing the same sedation as during the preoperative study. After radiographs were finished, patients received either PBMT or placebo treatment and the study was deemed completed.

Masking

The investigator (OAC) measuring and recording all outcome measurements as well as the statistician (NC) were blinded to treatment allocation status.

Statistical analysis

Descriptive statistics (mean, median, SD, and range) for age, weight, and a frequency table for reproductive status were computed by treatment group. To confirm whether randomization balanced out signalment factors, age, and weight were compared between treatment groups using a t test, and reproductive status by treatment group using a χ^2 test.

Descriptive statistics or frequency tables were also computed for all outcome measurements (CRP values, %WB, pain based on clinician, and based on owner's assessment, and surgical site infections) by treatment group and by the time of measurement (preop, 24 hours, 48 hours and 8 weeks; for pain assessed by the owner time was categorized as follows: 1, 2, 3, 4, 5, 6, 7, and 8 weeks).

The effect of the treatment group on CRP values was estimated in a linear mixed effects model which included fixed effects of the treatment group (control vs treatment), time measurement (preop, 24 hours, 48 hours, and 8 weeks), and the 2-way interaction between treatment group and time of measurement. The dependent variable consisted of logarithmic-base 10 CRP values (CRP values were log-transformed to meet the normality assumption). A Newton-Raphson Optimization procedure and residual pseudolikelihood estimation were fitted. An unstructured covariance structure was included to account for repeated measures. A Tukey *P*-value adjustment for multiple comparisons was implemented. Residual diagnostics were assessed graphically. Outcome values were back-transformed for reporting and interpretation (model-adjusted mean CRP values and SEM are depicted along with corresponding *P*-values).

The effect of the treatment group on %WB values was estimated in a generalized linear mixed effects model. Fixed effects of the treatment group (control vs treatment), time measurement (preop, 24 hours, 48 hours, and 8 weeks), and the interaction between the treatment group and time were included. The outcome consisted of %WB values divided by 100, to transform it into a continuous proportion. A beta distribution, logit link, Newton-Raphson Optimization procedure, residual pseudolikelihood estimation, and Kenward Roger degrees of freedom adjustment were fitted. An unstructured covariance structure was included to account for repeated measures. A Tukey *P*-value adjustment for multiple comparisons was implemented.

The frequency (number and %) of surgical site infections by treatment group, and overall, was computed. An exact logistic regression was fitted to compare the proportion of surgical site infections by treatment group; odds ratio (OR) and corresponding *P*-value were reported.

Pain as evaluated by the clinician, and by the owner was recorded using the CMPS-SF. There are no reports on grading pain such as mild, moderate, or severe with this form. The pain score is the sum of the rank scores for the test's 6 categories; the maximum pain score possible is 24. The total CMPS-SF score has been shown to be a useful indicator of analgesic requirement and the recommended analgesic intervention level is 6/24; as such, pain scores were categorized into 2 categories; observations when patients had a pain score equal to or lower than 6 (as in "analgesia not required"), and observations when patients had scores equal or higher than 7 ("analgesia is required"). Similarly, given all pain measurements as assessed by the clinician at 8 weeks were zeros, and all pain measurements as assessed by the owner after 4 weeks were zeros, for data analysis purposes, time measurements at 48 hours and 8 weeks were combined when evaluating pain recorded by the clinician, and observations from weeks 4 to 8 were combined when evaluating pain recorded by the owner.

The effect of the treatment group on the probability of patients requiring analgesia (with pain assessed by the clinician) was estimated in a generalized linear mixed effects model. Fixed effects of treatment group (control vs treatment), time measurement (preop, 24 hours, 48 hours to and 8 weeks), and the 2-way interaction between treatment group and time of measurement were included. The outcome consisted of the probability of patients requiring analgesia (those with pain scores equal or greater than 7, as per the clinician's assessment, compared to those with scores less than 7 [not requiring analgesia]). A binary distribution, logit link, Newton-Raphson Optimization procedure, residual pseudolikelihood estimation, and Kenward Roger degrees of freedom adjustment were fitted. A first-order autoregressive (ar(1)) covariance structure was included to account for repeated measures. A Tukey *P*-value adjustment for multiple comparisons was implemented.

Similarly, the effect of the treatment group on the probability of patients requiring analgesia (with pain assessed by the owner) was estimated in a generalized linear mixed effects model. Fixed effects of the treatment group (control vs treatment), time measurement (1 week, 2 weeks, 3 weeks, and 4 to 8 weeks), and the 2-way interaction between the treatment group and time of measurement were included. The outcome consisted of the probability of patients requiring analgesia (those with pain scores equal or greater than 7, as per owner's assessment, compared to those with scores less than 7 [not requiring analgesia]). This model was fitted as described above. An alpha level of 0.05 defines statistical significance.

Results

A total of 54 client-owned dogs completed the study. The overall mean (SD) for age was 5.54 (2.41) years old; age did not significantly (P = .18) vary by treatment group; the mean age was 6.03 years (2.54 years) for individuals in the treatment group and 5.14 years (2.27 years) for individuals in the control group. Overall mean body weight was 35.17 kg (9.86 kg). There were no statistically significant differences in body weight between treatment groups (P = .22); mean body weight was 33.33 kg (8.39 kg)

for individuals in the treatment group and 36.64 kg (10.81 kg) for patients in the control group. Thirty-one patients were spayed females, 2 were intact females, and 21 were castrated males. There was a statistically significantly higher proportion of castrated males (54.2%, 95% CI 34.2–71.1%) than females in the treatment group, compared to the control group, where the proportion of castrated males was 26.7% (95% CI 10.8–42.5%) (P = .04). The treatment PBMT group consisted of 24 patients and the control group included 30 patients.

Percentage weight bearing and CRP

Descriptive statistics for CRP values and %WB, overall, by treatment group, by time measurement, and by both treatment group and time measurement are presented **(Table 1)**.

Overall, the model-adjusted mean CRP values were considered normal preoperatively on both treatment and control groups, with its highest value at 24 hours, followed by a decrease at 48 hours postsurgery. The treatment-by-time interaction was not statistically significant (P = .21), the treatment group was not significant (P = .13), but CRP values significantly varied (P < .001) by time measurement. Specifically, mean CRP values were statistically significantly higher at 24 hours than preoperatively (P < .001), and compared to 8 weeks (P < .001), and mean CRP values at 48 hours were statistically significantly higher than preoperatively (P < .001) and at 8 weeks (P < .001; **Table 2**).

As observed with CRP values, for model-adjusted mean %WB, the treatment-by-time interaction was not statistically significant (P = .26), the treatment group was not significant (P = .78), but the time measurement was significant (P < .001). Mean %WB was significantly higher preoperatively than at 48 hours (P = .04), and mean %WB at 8 weeks was statistically significantly higher than at 24 hours (P < .001), and at 48 hours (P = .0001; **Table 3**).

Pain scale based on clinician and owners' evaluations

A frequency table of proportion (and %) of patients where analgesia was required (pain scores ≥ 7) as per clinician's and owner's assessments, by both treatment group and time measurement, is presented elsewhere **(Supplementary Table S1)**.

Table 1—Descriptive statistics for CRP values and %WB by both treatment group and time of measurement.

		Treatment group by time measurement							
		Treatment	Control	Treatment	Control	Treatment	Control	Treatment	Control
Variable, unit	Statistic	Preoperative		24 hours		48 hours		8 weeks	
CRP, mg/dL	Mean	0.48	0.29	7.03	7.30	6.75	6.60	0.39	0.33
	Median	0.40	0.20	7.00	7.20	7.55	7.00	0.20	0.20
	SD	0.34	1.14	1.75	1.67	1.95	2.05	0.55	0.29
	Range	0.10–1.20	0.10–0.70	3.90–9.30	2.70–9.50	2.30–9.00	1.90–10.00	0.10–2.70	0.10–1.20
%WB	Mean	11.67	10.80	5.92	8.90	8.57	7.81	13.65	13.48
	Median	12.00	10.50	3.50	9.50	7.00	8.00	13.00	13.00
	SD	4.83	5.48	6.09	5.83	6.12	6.17	6.81	7.54
	Range	0.00–20.00	2.00–22.00	0.00–23.00	0.00–22.00	0.00–21.00	1.00–26.00	1.00–25.00	0.00–31.00

CRP = C-reactive protein. %WB = Percent weight bearing.

Table 2—Model-adjusted means (±SEM) for CRP values by treatment group and time of measurement.

	Time measurement				
Treatment group	Preoperative	24 hours	48 hours	8 weeks	Overall
Treatment	0.38 (1.11)	6.80 (1.10)	6.40 (1.11)	0.27 (1.12)	1.45 (1.05)
Control	0.27 (1.10)	7.06 (1.10)	6.21 (1.10)	0.25 (1.11)	1.30 (1.05)
Overall	0.32 (10.7)[a]	6.93 (1.07)[b]	6.30 (1.07)[b]	0.26 (1.08)[a]	

Linear mixed model included fixed effects for treatment group (P = .13), time measurement (P < .001), and the treatment group-by-time measurement interaction (P = .21), and an unstructured covariance structure to account for repeated measures. Means with different superscripts indicate significant differences (comparisons between columns).

See Table 1 for the key.

Table 3—Model-adjusted %WB (±SEM) by treatment group and time of measurement.

	Time measurement				
Treatment group	Preoperative	24 hours	48 hours	8 weeks	Overall
Treatment	12.17 (1.34)	7.10 (1.13)	8.96 (1.20)	13.65 (1.41)	10.18 (0.65)
Control	10.80 (1.11)	9.89 (1.13)	7.82 (1.02)	7.82 (1.02)	11.62 (0.58)
Overall	11.47 (0.87)[ac]	8.39 (0.82)[b]	8.37 (0.78)[ab]	13.83 (0.97)[c]	

Generalized linear mixed model (beta distribution and logit link) included fixed effects for treatment group (P = .78), time (P < .001), and the treatment-by-time interaction (P = .26), and an unstructured covariance structure to account for repeated measures. Means with different superscripts indicate significant differences (comparisons between columns).

Table 4—Model adjusted mean percentage (±SEM) of patients when analgesia was required (pain scores >7) as per clinician's assessment by treatment group and time measurement.

	Time measurement			
Treatment group	**Preoperative**	**24 hours**	**48 hours and 8 weeks**	**Overall**
Treatment	4.17 (4.14)	20.83 (8.41)	6.68 (3.72)	8.56 (3.39)
Control	10.00 (5.55)	16.67 (6.90)	3.79 (2.62)	8.73 (2.84)
Overall	6.50 (3.66)[ab]	18.66 (5.40)[a]	5.04 (2.24)[b]	

Generalized linear mixed model (binary distribution and logit link) included fixed effects for treatment group (P = .97), time (P = .03), and the treatment-by-time interaction (P = .59), and an ar(1) covariance structure to account for repeated measures. Means with different superscripts indicate significant differences (comparisons between columns).

Table 5—Model adjusted mean percentage (±SEM) of patients when analgesia was required (pain scores >7) as per owner's assessment by treatment group and time measurement.

	Time measurement				
Treatment group	**1-week**	**2-week**	**3-week**	**>4-week**	**Overall**
Treatment	16.67 (8.89)	11.11 (7.50)	5.56 (5.46)	1.12 (1.13)	6.01 (2.49)
Control	26.92 (8.80)	16.00 (7.42)	8.00 (5.49)	1.61 (1.14)	9.09 (2.60)
Overall	21.35 (6.56)[a]	13.37 (5.43)[a]	6.68 (3.99)[ab]	1.35 (0.83)[b]	

Generalized linear mixed model included fixed effects for treatment group (P = .41), time (P < .001), and the treatment-by-time interaction (P = .99), and an ar(1) covariance structure to account for repeated measures. Means with different superscripts indicate significant differences (comparisons between columns).

When estimating the model-adjusted mean percentage of patients when analgesia was required (for those patients with pain scores equal or greater than 7), as per the clinician's evaluation, the treatment-by-time interaction was not statistically significant (P = .59), the treatment group was not statistically significant (P = .97), but time measurement was statistically significant (P = .03). Mean percentage of patients when analgesia was required was statistically significantly higher at 24 hours postoperatively than at 48 hours or 8 weeks postoperatively (P = .04; **Table 4**).

For model-adjusted mean percentage of patients when analgesia was required (for those patients with pain scores equal or greater than 7), as per the owner's evaluation, the treatment-by-time interaction was not statistically significant (P = .99), the treatment group was not significant (P = .41) but the time of measurement was statistically significant (P < .001). The mean percentage of patients when analgesia was required was statistically significantly higher at 1 week compared to 4 weeks or greater (P = .001), and at 2 weeks compared to 4 weeks or greater (P = .01; **Table 5**).

Surgical site infections

There were 5 (5/30; 16.6%) patients with surgical site infections on the control group; 4 of those patients had minor/superficial site infections who responded to 1 round of antibiotics. One of the patients developed a major surgical site infection for which the TPLO plate had to be removed 6 months after the surgery. There were no infections reported on the treatment group at the moment of the study. The odds of patients experiencing surgical site infections in the control group were 6.08 times greater than the odds of patients experiencing surgical site infections in the treatment group; however, this association was not statistically significant (OR [median unbiased estimate] = 6.08; 95% CI 0.78 - +Inf; P = .09).

Discussion

In the present study, we failed to reject our null hypothesis and no statistically significant differences were found between treatment groups when evaluating gait analysis, CRP, or pain scores evaluated by the clinician or the owners. These measurements, however, significantly varied over time. Renwick et al (2018),[11] when evaluating the influence of PBMT after TPLO surgery did not find differences between groups on osteotomy healing on a radiographic scale, time cessation of NSAID, and wound healing by owner questionnaires. They only found differences in terms of improvement in the gait section of the adjusted Canine orthopedic Index (COI).[11]

Results after PBMT are still controversial. Many of the published studies have been in vitro or have been experimental, making it harder to extrapolate results into meaningful clinical outcomes.[5,6]

As mentioned on the introduction the dosages recommended for PBMT to treat tissue in animals range from 3 to 10 J/cm^2.[7,8] During this study we decided to follow the recommendations of the manufacturer entering the specifications for each patient such as body weight, skin color, coat color, and the option short for the length of the fur. However, during the revision of the administered doses to the patients the author found that all the patients received the same dose of PBMT. The reason why the device decided to give the same dose to each patient remains unknown.

In the present study, we rejected our null hypothesis while evaluating SSI between groups. Five (16.6%) patients in the control group developed a surgical infection compared to no patients in the treatment group. Based on the CDC guidelines, 4 of those patients developed a superficial SSI infection where antibiotics were prescribed to resolve clinical signs. One of those

5 patients presented a deep SSI where the plate had to be removed 6 months after TPLO surgery. Upon bacterial culture of the site and implant, we were able to isolate *Staphylococcus Pseudointermedius*.

SSI were analyzed in this study due to a historically high rate after TPLO surgery in several reports. Surgical site infection rates after TPLO range from 2.9% up to 25.9%.[14]. Theories about the development of SSI after TPLO surgery include thermal bone necrosis, prolonged surgery, and anesthesia times, micromotion at the osteotomy site, and limited soft tissue coverage.[24,25] If we analyzed those theories, we could see that in general the probable cause of SSI is the diminished or interruption of blood supply to the surgical site during the surgery or recovery time. PBMT is purported to help reduce healing times photoactivating cellular mechanisms, reducing edema, promoting fibroblast proliferation, and collagen synthesis.[25–27] Therefore, it is possible that PBMT minimized the risk of SSI. Although no statistically significant (or borderline significant) differences were found on patients developing surgical site infections between treatment groups, surgical site infections were only observed in patients in the control group. Likely, significance was not achieved given the small effective sample size (n = 5); nonetheless this finding is promising from a clinical and prognostic standpoint and warrants further research.

No statistically significant changes were found when evaluating CRP between treatment groups; however, CRP significantly varied over time. CRP is an acute phase protein (APPs) that can be used as a marker of systemic inflammation. All the patients in the study had a normal preoperative CRP between 0 to 1.0 mg/dL. To report the influence of CRP in this study, preoperative values and postoperative values were taken. All the patients had a normal preoperative CRP indicating that none of the patients had a significant systemic inflammation that could affect the outcome of the surgery. The maximum value of CRP was at 24 hours after surgery. CRP values started to decrease at 48 hours postsurgery. This behavior was first reported by Löfgvist et al (2018), where serum CRP was run in patients after TPLO and a maximum peak was recorded at 24 hours after TPLO to then start declining. Patients who maintained abnormal (higher) levels of CRP at 6 days postsurgery where consistent of having a surgical site infection.[9] On a study in humans by Zwiri et al (2022), no statistically significant differences were found on patients with temporomandibular disorder in the groups treated with PBMT vs traditional conservative treatment such as diet and stress counseling and a hot towel therapy.[27]

Freitas et al 2001, when evaluating the effect of 830 nm LASER light using CRP levels did not found any difference between treatment group and control groups after removing the lower wisdom tooth.[28]

Based on the knowledge of the author (OAC) there are no reports of PBMT and the evaluation of CRP in Veterinary Medicine. Therefore, this may be the first study evaluating it, finding a lack of significance in patients which are treated with PBMT after TPLO surgery.

While measuring %WB, Rogatko et al[13] found that a single dose of preoperative PBMT was associated with a statistically significant improvement in PVF for dogs undergoing TPLO on the operated limb 8 weeks postoperative. During the present study, we did not find statistically significant difference while evaluating %WB between groups at the different times. These results are similar than Kennedy et al, which showed not statistically significant differences between LLLT group and the control group on PVF at 8 weeks after TPLO surgery.[10] During evaluation of pain by the clinician and by the owners no statistically significant difference was found in our study similar at the same study from Kennedy et al, mentioned above during the evaluation of pain using a modified Glasgow composite scoring system by the clinician and the owners using the CBPI scale where no statistically significant difference was found between groups.

Study limitations include the variability in surgical outcomes arising from several surgeons performing the TPLO surgeries. Even though TPLO is a well-described and commonly performed surgery, there are some differences on the surgical technique inherent to each surgeon. Similarly, it is possible that misclassification of some of the outcomes occurred, however, because the clinician (as well as the owners) conducting all measurements was blinded to treatment allocation, bias would likely be nondifferential. Schnidl et al (2001), in a review of low-intensity laser studies, noted that one of the most common limitations in the literature is the lack of double-blinded protocols.[29] In our study, not only the clinician but the statistician was completely blinded to minimize bias. Although this study involved only client-owned animals, we consider this study group is representative of adult client-owned dogs elsewhere, as it included dogs of different breeds, reproductive status, and ages (older than 1 year of age).

In conclusion, although not conclusive, PBMT may reduce surgical site infections after TPLO surgery. The use of PBMT is still controversial as this study showed there are no significant differences in outcomes between PBMT and the control group after TPLO surgery. We reject our null hypothesis finding not statistically significant differences when evaluating %WB, CRP, or pain scale by owners and clinicians. There is still a long path to show efficacy of PBMT on clinical outcomes.

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Supplementary Materials

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