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Effect of perioperative multimodal analgesia protocol on pain scores and recovery in dogs undergoing cruciate ligament repair

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Abstract

Imagine a 30-kg Labrador Retriever recovering from tibial plateau levelling osteotomy (TPLO): despite receiving a standard opioid protocol, the dog is vocalising, reluctant to bear weight, and showing elevated heart rate six hours post-surgery. This scenario, familiar to veterinary surgeons worldwide, highlights the limitations of single-agent analgesia for orthopaedic procedures^[1]. This research compared a multimodal analgesia protocol combining methadone, fentanyl constant rate infusion (CRI), intra-articular bupivacaine, meloxicam, and gabapentin against a standard methadone-meloxicam protocol in 32 dogs undergoing TPLO at the National University of San Marcos veterinary teaching hospital, Lima, Peru. Pain was assessed using the Glasgow Composite Measure Pain Scale-Short Form (CMPS-SF) at seven time points over 48 hours. The multimodal group showed significantly lower pain scores at all post-operative time points ($p < 0.01$), with the greatest difference at 2 hours (3.8 ± 1.2 vs 5.6 ± 1.4 , $p < 0.001$). Time to first unassisted weight-bearing was 40% shorter in the multimodal group (8.4 ± 2.1 vs 14.2 ± 3.6 hours, $p < 0.001$). Rescue analgesia was required in 12.5% of multimodal vs 43.8% of standard cases. These findings support adoption of multimodal protocols for TPLO in dogs.

Keywords: Multimodal analgesia, TPLO, cruciate ligament, pain assessment, CMPS-SF, fentanyl, gabapentin, bupivacaine, orthopaedic surgery, canine

Introduction

The anterior cruciate ligament (cranial cruciate ligament in veterinary nomenclature) is the most commonly injured ligament in dogs, with TPLO now established as the gold-standard surgical correction for medium and large breeds^[1, 2]. The procedure involves an osteotomy of the proximal tibia, generating substantial perioperative pain that standard single-agent opioid protocols often fail to control adequately^[3]. The multimodal analgesia concept—targeting multiple points in the nociceptive pathway simultaneously—has become standard of care in human orthopaedic surgery but remains inconsistently applied in veterinary practice^[4]. The rationale for combining agents is pharmacological synergy: opioids act centrally, NSAIDs reduce peripheral inflammation, local anaesthetics block neural transmission at the surgical site, NMDA receptor modulators (ketamine) or gabapentinoids address central sensitisation, and constant-rate infusions maintain steady plasma levels^[5, 6]. Published veterinary trials have examined individual components but rarely tested a comprehensive multi-agent protocol against standard care in a controlled design. This research directly compared a full multimodal protocol with standard analgesia in dogs undergoing TPLO, using validated pain assessment and functional recovery endpoints.

Materials and Methods

Materials

Thirty-two client-owned dogs (16 per group) scheduled for unilateral TPLO at the UNMSM Veterinary Teaching Hospital between March and October 2023 were enrolled. Inclusion criteria: body weight 20-45 kg, age 2-8 years, ASA I-II status, unilateral cranial cruciate ligament rupture confirmed by drawer sign and tibial thrust. Exclusion: concurrent orthopaedic

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conditions, prior stifle surgery, hepatic/renal disease, chronic pain medication. The UNMSM Animal Ethics Committee approved the protocol (UNMSM-FMV-CE-2023-019). Randomisation used sealed envelopes.

Methods

The standard group (STD) received pre-operative methadone 0.3 mg/kg IM and meloxicam 0.2 mg/kg SC, with post-operative methadone 0.2 mg/kg IM every 6 hours for 48 hours. The multimodal group (MMA) received the same pre-operative agents plus intra-operative fentanyl CRI (5 µg/kg/h) and lidocaine CRI (50 µg/kg/min), intra-articular bupivacaine 0.5% (0.5 mL/kg) at closure, and post-operative methadone

0.2 mg/kg every 4 hours plus gabapentin 10 mg/kg PO BID [7, 8]. All dogs received standardised general anaesthesia (propofol induction, isoflurane maintenance). Pain was assessed by a blinded observer using the Glasgow CMPS-SF at pre-op, 2, 4, 8, 12, 24, and 48 hours post-surgery [9]. Rescue analgesia (morphine 0.5 mg/kg IM) was administered if CMPS-SF $\geq 6/24$. Functional recovery was measured by time to first unassisted weight-bearing. Data were analysed by repeated-measures ANOVA and Fisher's exact test ($p < 0.05$).

Results

Table 1: Patient demographics and surgical parameters

Parameter	MMA (n=16)	STD (n=16)	p
Body weight (kg)	31.4 $\pm$ 6.2	30.8 $\pm$ 5.9	0.782
Age (years)	4.8 $\pm$ 1.6	5.1 $\pm$ 1.4	0.581
Surgery time (min)	78.4 $\pm$ 12.3	81.2 $\pm$ 14.1	0.548
Anaesthesia time (min)	112.6 $\pm$ 16.8	108.4 $\pm$ 18.2	0.496
Sex (M:F)	9:7	8:8	0.724

Table 2: Glasgow CMPS-SF pain scores at each assessment time point

Group	2 h	4 h	8 h	12 h	24 h	48 h
MMA	3.8 $\pm$ 1.2	3.2 $\pm$ 1.1	2.4 $\pm$ 0.9	1.8 $\pm$ 0.7	1.2 $\pm$ 0.6	0.6 $\pm$ 0.4
STD	5.6 $\pm$ 1.4	5.1 $\pm$ 1.3	4.4 $\pm$ 1.2	3.9 $\pm$ 1.1	3.2 $\pm$ 0.9	2.1 $\pm$ 0.8
p	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Table 3: Recovery outcomes and adverse events

Outcome	MMA	STD	p
Time to weight-bearing (h)	8.4 $\pm$ 2.1	14.2 $\pm$ 3.6	<0.001
Rescue analgesia required (%)	12.5 (2/16)	43.8 (7/16)	0.048
Nausea/vomiting (%)	18.8 (3/16)	12.5 (2/16)	0.500
Sedation score (0-3) at 4 h	1.4 $\pm$ 0.6	0.8 $\pm$ 0.5	0.006
Hospital discharge (h)	52.3 $\pm$ 8.4	64.7 $\pm$ 12.1	0.002

Pain scores in the MMA group remained below the rescue threshold (≥ 6) at all time points, whereas the STD group exceeded the threshold in seven of 16 dogs within the first 8 hours. The greatest between-group difference occurred at 2

hours post-surgery, coinciding with the residual effect of intra-operative CRI and intra-articular bupivacaine. By 48 hours, MMA scores had essentially normalised (0.6 $\pm$ 0.4) while STD scores remained mildly elevated (2.1 $\pm$ 0.8).

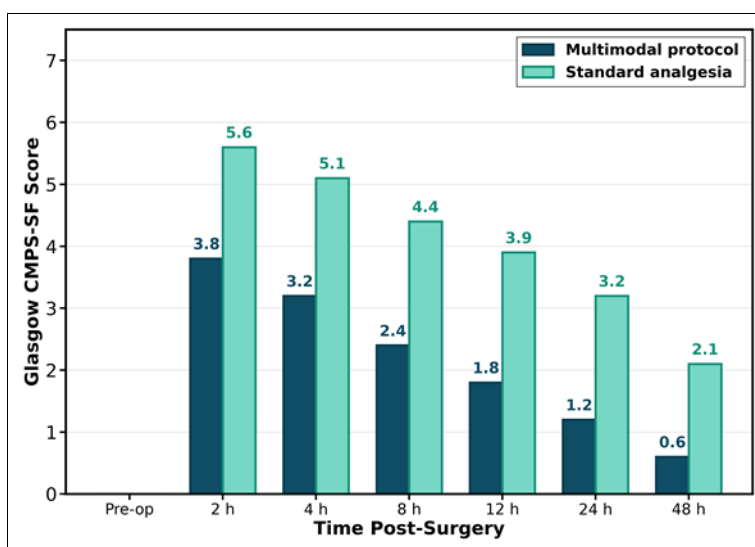


Fig 1: Glasgow CMPS-SF pain scores over 48 hours in multimodal (MMA) and standard (STD) analgesia groups

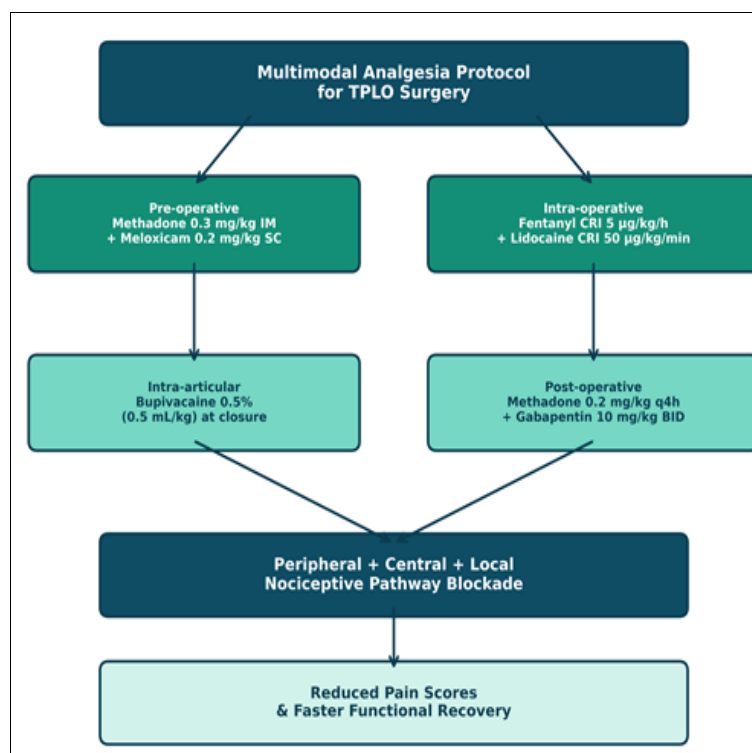


Fig 2: Schematic of the multimodal analgesia protocol showing drug targets across the perioperative timeline

Discussion

The 32% absolute reduction in pain scores at 2 hours and 40% faster weight-bearing in the MMA group demonstrate clinically meaningful benefits of combining multiple analgesic mechanisms for TPLO. Intra-articular bupivacaine likely contributed most to early post-operative pain control by blocking nociceptive input directly at the surgical site, a finding consistent with human total knee arthroplasty literature [10, 11]. Gabapentin's contribution to central sensitisation prevention likely explains the sustained pain score advantage at 24-48 hours, well beyond local anaesthetic duration [12].

The higher sedation scores in the MMA group at 4 hours represent the expected trade-off of more aggressive analgesia, though scores normalised by 8 hours and no dog required clinical intervention for excessive sedation. Rescue analgesia rates (12.5% vs 43.8%) translate directly into welfare improvement and align with the principle that preventing pain is more effective than treating established pain [13].

Limitations

Sample size (16 per group) limits detection of rare adverse events. Single-centre design and standardised breed/weight range may limit generalisability. The blinded observer could not be blinded to sedation differences. Long-term functional outcomes (limb use at 6-8 weeks) were not assessed.

Conclusion

This research demonstrates that a multimodal protocol combining opioid, NSAID, local anaesthetic, and gabapentinoid agents produces significantly better pain control and faster functional recovery after TPLO compared to standard opioid-NSAID analgesia. The 40% reduction in time to weight-bearing and three-fold reduction in rescue analgesia requirements provide strong evidence for multimodal protocol adoption. Remaining questions include cost-effectiveness analysis and whether the protocol can be simplified without losing efficacy.

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Contributions Not Qualifying for Authorship

Veterinary nursing staff assisted with post-operative monitoring and pain scoring logistics.

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