

Locoregional Techniques for Dogs Undergoing Tibial Plateau Leveling Osteotomy: A Literature Review, Anesthesiologist Survey, and Future Directions

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The undersigned, appointed by the dean of the Graduate School, have examined the thesis entitled:

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Leveling Osteotomy: A Literature Review, Anesthesiologist Survey,
and Future Directions**

Presented by Lindsay A. Parker,

A candidate for the degree of Master of Biomedical Science,

And hereby certify that, in their opinion, it is worthy of acceptance.

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I dedicate my thesis to my lifeline for the last nearly 11 years, Mr. Chad Robert Willis. Never the one to tell me to give up on my dreams, you have been my pillar of support throughout veterinary school, 4 internships, working emergency, and my anesthesia residency. Even when I entertained the idea of a second residency, you allowed me to come to my own conclusion that it is in fact, an insane idea.

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LIST OF ABBREVIATIONS

MC, male castrated

FS, female spayed

TPLO, tibial plateau leveling osteotomy

CCLD, cranial cruciate ligament disease

CNS, central nervous system

AMPA, alpha-amino-3-hydroxy-5-methylisoxazole-4-propionic acid

KAI, kainite

NMDA, N-methyl-D-aspartate

CCRP, calcitonin gene-related peptide

ATP, adenosine triphosphate

mGluR, metabotropic glutamate

NK-1, neurokinin-1

TrkB, tyrosine kinase B

BDNF, brain-derived neurotrophic factor

MAC, minimum alveolar concentration

CSF, cerebral spinal fluid

ACVAA, American College of Veterinary Anesthesia and Analgesia

ECVAA, European College of Veterinary Anaesthesia and Analgesia

PNB, peripheral nerve block

LE, lumbosacral epidural

PI, peri-incisional infiltration

ABSTRACT

Over the past several decades there have been significant advancements in our understanding and ability to provide effective analgesia to animals undergoing elective orthopedic surgery through methods that can help us minimize the risk of adverse effects. In dogs, one of the most common elective orthopedic surgeries performed on the pelvic limb is the tibial plateau levelling osteotomy (TPLO) for the treatment of cranial cruciate ligament disease (CCLD). While historically the lumbosacral epidural has been considered the primary method of locoregional therapy for dogs undergoing TPLO, the development of peripheral nerve blocks has been a rapidly growing area of veterinary research. An in-depth knowledge of the pain cycle and ways to intervene in nociception is an immense area of interest in both the human and veterinary worlds. This thesis examines the pain cycle and how protective pain becomes pathologic, along with an exploration of the various pharmaceuticals and locoregional techniques that can be utilized for the lumbosacral epidural, peripheral nerve block, and the peri-incisional infiltration technique. Additional information about locoregional analgesic preferences is gleaned through a survey-based study of board-certified veterinary anesthesiologists. This study demonstrated that newer graduates prefer the use of bupivacaine-dexmedetomidine for peripheral nerve blocks in dogs undergoing TPLO and that analgesic decision-making in the clinical setting is multifactorial. Overall, this research demonstrates that while significant advancements have occurred in the veterinary anesthesia and analgesia, further research into the effectiveness of various techniques as well as the clinical application of these methods is needed.

CHAPTER 1: Introduction and Literature Review

Introduction

The tibial plateau levelling osteotomy (TPLO) is the most common elective surgical orthopedic procedure performed by veterinary surgeons and presents tremendous economic burden for veterinary clients. In 2003, owners spent \$1.32 billion for the medical and surgical treatment of cranial cruciate ligament disease (CCLD).¹ Using the methodology described in the Wilke et al paper, we estimate that the amount spent on CCLD management in 2023 is likely greater than \$4 billion dollars.

The TPLO is an elective orthopedic procedure performed for the treatment of CCLD in dogs, with the goal of restoring joint stability. This procedure involves a curvilinear osteotomy of the proximal tibia and subsequent rotation of the tibial plateau (the contact surface of the joint) to achieve a tibial plateau angle of approximately five degrees. This results in dynamic stabilization, or neutralization of cranial tibial thrust, and ultimately restores translational joint stability in the sagittal plane. As with any orthopedic surgery, patients undergoing a TPLO require adequate and often “multi-modal” analgesia. Peri-operative management may include systemic medications such as non-steroidal anti-inflammatory drugs (NSAIDs) and opioids along with locoregional techniques such as lumbosacral epidural, peripheral nerve blocks, peri-incisional blocks, etc. Recent increases in board-certified veterinary anesthesiologists in private practice specialty hospitals has improved the ability to offer advanced locoregional analgesic techniques for use in dogs undergoing TPLO.

This thesis will provide a review of the peri-operative pain and analgesic methods used in dogs undergoing TPLO. The first section will explore the normal and maladaptive physiology of the pain pathway and analgesic methods used to target different areas of that pathway. The second section will explore the clinical application of these methods in dogs undergoing a TPLO surgery through a survey-based assessment of board-certified veterinary anesthesiologists.

Pain

Normal Physiology and Response to Pain

To select the most appropriate analgesic technique or protocol for an individual patient, a well-rounded understanding of pain physiology is imperative. The general term “painful” is considered an emotional and conscious interpretation of an unpleasant signal causing either actual or potential tissue damage. On the other hand, anesthetized (unconscious) patients having a physiological response to a painful stimulus are “nocicepting” but are unaware of the stimulus.² Activation of specialized neuroreceptors called nociceptors initiate the pain pathway. The process can be divided into five stages: transduction, transmission, modulation, projection, and perception.^{3,4}

With noxious stimuli, such as a skin incision, peripheral nociceptors are activated to initiate an action potential and transduce the physical stimulus of an incision into cellular action potentials.^{3,4} The transmission step of the pain pathway is initiated with the nociceptive signal is carried from the periphery to the spinal cord via afferent nerve fibers, also known as first order neurons.⁵ A noxious stimulus may include either thermal,

mechanical, and/or chemical stimulation.⁵ Three afferent nerve fibers may carry nociceptive signals centrally: A-beta, A-delta, and C fibers.^{3,4} The fibers differ in terms of diameter, myelination, conduction velocity, and threshold which alters the signals transmitted. For instance, while A-beta fibers have a low threshold and normally only respond to non-noxious stimuli, the A-delta fibers have both low and high threshold fibers and have a role in transmission of acute pain. C-fibers are primarily responsible for transmission of dull, chronic pain.^{3,4} In physiologically normal states, only A-delta and C fibers are responsible for transmission of pain signals.⁶ However, central sensitization can result in the functional transformation of A-beta fibers in nociceptive signaling which converts a typically innocuous signal to a painful one. The sensory afferent neurons bring the nociceptive signal to the contralateral side of the dorsal horn of the spinal cord for modulation at the level of the second-order neurons, where the signal may be amplified or inhibited based on release of neurotransmitters.^{3,4} The first order neurons synapse with the second order neurons in the superficial layers of grey matter within the dorsal horn of the spinal cord and is specific depending on the afferent fiber. For example, A delta fibers synapse in the Laminae I and V, C fibers synapse in I and II, and A-beta fibers synapse in Laminae II to V.⁵ With A-delta and C fibers, the dorsal horn laminae releases glutamate, an excitatory neurotransmitter that binds to ligand-gated sodium and calcium channels to activate alpha-amino-3-hydroxy-5-methylisoxazole-4-propionic acid (AMPA), N-methyl-D-aspartate (NMDA), and kainite (KAI) receptors.^{3,4,7,8} Excitatory activity is also modulated by a variety of pre- and postsynaptic opioids (mu, delta, and kappa), noradrenergic, and muscarinic receptors within the spinal cord and the brain.⁵ With stimulation of the AMPA, NMDA, and KAI receptors, the

signal is then projected from the spinal cord to the somatosensory cortex in the brain via an ascending pathway.^{3,4,7,8} The ascending pathways that are important in the continuation of the pain signal include the spinothalamic and trigeminothalamic tract, the spinomedullary and spinobulbar tract, and the spinohypothalamic tract.⁵ However, it is the spinothalamic tract that is most closely associated with pain, temperature, and the itch sensation.⁵ It originates from three distinct regions of the spinal grey matter: spinal dorsal horn Laminae I, and less so from the Laminae IV-V and Laminae VII-VIII.⁵ These populations of spinothalamic tracts are dominated by afferent input from varying primary afferent fibers and thus, can display different patterns of functional activity.⁵ Over 50% of the spinothalamic tract resides within the Laminae I region of the spinal cord. Laminae I spinothalamic cells can be divided into three major classes of modality selective Laminae I spinothalamic cells including nociceptive specific cells, polymodal nociceptive cells, and thermoreceptive specific cells.⁵ Nociceptive specific cells are dominated by A delta fiber input, have small receptive fields, and respond to noxious mechanical or noxious thermal stimuli. They do not respond to innocuous stimuli, only noxious signals.⁵ Polymodal nociceptive cells receive mainly C fiber afferent input and respond to noxious heat (i.e., burning) and cold, as well as pinch sensation from muscles, joints, and/or viscera.⁵ Thermoreceptive specific cells are excited by innocuous cooling and inhibited by skin warming.⁵ Once the signal reaches the thalamus, the signal is integrated and relayed to the somatosensory cortex where it is perceived as pain by the limbic system.⁵ This process occurs through the VMpo, a specific Laminae I spinothalamic cell relay station for signals from the body, including pain.⁵ The VMpo does not exist in non-primates.⁵ Normally, the ascending pain signal via the

spinothalamic tract via Laminae I and the nociceptive specific cells result in transient, localized acute pain perception. The specific mediators, pathways and perceived sensations vary based on tissues involved, stimuli, tissue damage magnitude, and duration of insult. Overall, it is important to remember that pain is associated with multiple ascending pain pathways and leads to activity in multiple regions of the forebrain.⁵ Therefore, pain must be integrated with past experiences and the present context to result in a complete, multidimensional, emotional and conscious pain experience.⁵

Abnormal Response to Pain

While physiological pain is considered protective, maladaptive pain from a prolonged or excessive insult is considered pathological. Pathological pain may arise from tissue damage itself (inflammatory pain) or nerve injury (neuropathic pain).⁹ Hyperalgesia, or an exaggerated pain response, may develop depending on the magnitude and severity of the initial injury. Allodynia may also arise, which occurs when a normally non-noxious stimulus becomes noxious.⁹ This maladaptive pain may result from inadequate analgesia prior to surgery, following a severe and/or chronic pain insult, or trauma (i.e., fracture, soft tissue injury). There are four categories of hyperalgesia: 1) peripheral sensitization, 2) central sensitization, 3) primary hyperalgesia, and 4) secondary hyperalgesia.^{3,8}

- i. *Peripheral sensitization* occurs when the sensory nerve endings of the A-delta and C fibers become hyperexcitable to external stimuli due to tissue damage or inflammation in a localized area.¹⁰ When these peripheral nociceptors become sensitized, it leads to an overall lowered pain threshold and increased pain perception secondary to the release of various inflammatory mediators,

such as neutrophils, mast cells, macrophages, platelets, lymphocytes including hydrogen ions, histamine, prostaglandins (PGE₂), cytokines (IL-1, IL-6, IL-8), tumor necrosis factor- α , endocannabinoids, neurotrophins, and neuropeptides (substance P, calcitonin gene-related peptide (CGRP), bradykinin).⁹ These inflammatory mediators, often referred to as “sensitizing soup”, can activate nociceptors and enhance their respective sensitivity to touch, heat, cold, and pressure (i.e. normally non-noxious stimuli). This sensitivity enhancement is achieved by activating nociceptors, lowering the overall activation threshold of high-threshold nociceptors, and further release of inflammatory mediators that promote hypersensitivity of nociceptors.⁹

- ii. Central sensitization occurs secondary to the abnormal nociceptive activation of A-beta fibers as result of severe injuries causing sustained electrical signal input to the dorsal horn of the spinal cord that amplify nociceptive signaling.⁴ Central sensitization may also result in CNS plasticity, which refers to the sensory memory of a painful experience and results in a more painful, intense perception of a similar nociceptive insult. Plasticity and central sensitization are more challenging to treat due to amplification of signals, resulting in the phenomenon called “allodynia” which is a prolonged and amplified response to what would normally be a non-noxious stimulus in A-beta afferent nerve fibers.^{3,7,8} The main mechanism for central sensitization includes: NMDA receptor-mediated sensitization, disinhibition, and glial-neuronal interactions.⁹

NMDA receptor-mediated sensitization occurs following the activation of nociceptors and release of excitatory neurotransmitters including glutamate,

substance P, CCRP, and adenosine triphosphate (ATP) in the dorsal horn of the spinal cord.⁵ This process leads to the activation of normally silent NMDA glutamate receptors, leading to calcium influx and enhancement of the noxious stimuli transmission.⁵ The central sensitization, or wind-up phenomenon, occurs when there enough stimulation to remove the magnesium block of the NMDA receptors, thereby making the receptors more available for glutamate activation.⁵ Disinhibition leads to central sensitization secondary to uncontrolled and untreated tissue injury causing loss of the “gate-controlling” inhibitory interneurons within the substantia gelatinosa of Laminae II and resulting in increased projection to the thalamus.⁵ Glial-neuronal interactions may also result in central sensitization. Glial cells include the microglia and astrocytes.⁵ The microglia normally act as central nervous system residing macrophages; they aggregate at the site of injured peripheral nerve termination in the dorsal or ventral horn, release inflammatory cytokines, and brain-derived neurotrophic factor (BDNF) which result in enhancement of the nociceptive signal.⁵ The astrocytes contribute to central sensitization by helping maintain the continuous excitatory state.⁵

The use of pre-emptive analgesia, or analgesia provided prior to continuously painful insult (i.e., orthopedic surgery), can significantly reduce the risk of central sensitization by preventing sustained afferent input of nociception and alteration to the CNS plasticity. Such techniques may include the use of systemic analgesic medications and locoregional techniques. Unfortunately, once central sensitization has occurred it is a very difficult

phenomenon to treat where higher doses of systemic opioids and ketamine are typically needed to reduce the hyperexcitability of dorsal horn neurons with reduced signal inhibition.¹⁰ Clinically, some veterinarians will prescribe “pain holidays” for their patients with suspected central sensitization, which is when patients are hospitalized and treated with continuous rate infusions of various analgesics to overcome.

iii. Primary hyperalgesia describes sensitization at the site of primary injury due to inflammatory mediators including serotonin, bradykinin, proteases, cytokines, prostaglandins, histamine, and nerve growth factor which result in the increased sensitivity of the nerve ending to thermal and mechanical stimuli.^{3,7,8} Primary hyperalgesia is a consequence of peripheral sensitization.⁹

iv. Secondary hyperalgesia describes increased sensitization in areas adjacent to the primary site of injury (i.e. away from primary site of injury) and is due to central sensitization via activation of NMDA, metabotropic glutamate (mGluR), neurokinin-1 (NK-1) and tyrosine kinase B (TrkB) receptors in the dorsal horn of the spinal cord.^{3,7,8}

Treatment of Perioperative Pain

When considering the pain pathway, there are multiple levels that one may interfere with the transduction, transmission, modulation, and perception of pain. Basic strategies may include systemic administration of medications (such as opioids, non-steroidal anti-inflammatories) or locoregional therapies, including local or topical, perineuraxial, neuraxial or regional blockades.

Pharmaceuticals for Locoregional Blocks

Primary Medications

Sodium Channel Blocking Agents:

Local anesthetics are the only class of analgesics that can block pain transmission and prevent central sensitization by preventing the repeated stimulation of primary afferent neurons.^{6,11} When given as part of a peripheral nerve block, local anesthetics interrupt the transmission of sensory nociceptive signals by preventing the signal from being perceived by the CNS as pain but can maintain motor control.¹² For example, the saphenous nerve has only sensory components and blockade of this nerve will result in analgesia without impairing motor function in the pelvic limb.¹² When administered epidurally however, both sensory and motor innervation are both interrupted temporarily.

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Local anesthetics transiently (i.e. reversibly) block the generation and propagation of nerve signals by interfering with sodium channel function.¹² This is achieved primarily through voltage gated sodium channel blockade and the inhibition of action potential generation by preventing nerve cell membrane depolarization.^{12,13,14} The mammalian receptor site that results in the local anesthetic effects resides within the inner pore of the sodium channel.¹⁵ These agents also block voltage dependant potassium and calcium channels, but with lower affinity.¹² The physicochemical properties of local anesthetics dictate how effectively the drug moves from the site of application and asserts its effect on the nervous system and the rest of the body. The major physicochemical

properties that influence the duration of effect include lipophilicity, protein binding, and vasoactivity.¹²

Lipophilicity determines a local anesthetic drug's potency as well, as a more lipophilic drug is able to diffuse across a bilipid neuron cell membrane layer more effectively than a lipophobic drug, and thereby have increased access to the inner sodium channel. A local anesthetic's partition coefficient is a primary determinant of lipophilicity, otherwise the percentage of the drug that exists in a neutral, non-ionized state at physiological pH.¹² An ionized, conjugated base state drug molecule cannot cross the bilipid neuronal cell membrane layer. Among the more common local anesthetic agents used in small animal medicine, the degree of lipophilicity is as follows: bupivacaine > ropivacaine > lidocaine.^{11,12,16,17} The use of long-acting anesthetic agents, such as ropivacaine or bupivacaine, is the foundation of success for locoregional blocks with up to 8 hours of blockade.¹⁸ The increased degree of lipophilicity delays the onset of effect and therefore the time to onset of effect is the reverse ranking, with lidocaine having the shortest to time of neuronal blockade.¹² Clinically however, the use of longer acting local anesthetic agents appear to provide sustained analgesia that is not only beneficial intraoperatively, but also carries over into the post-operative period.¹² The most recent addition to the local anesthetic realm is liposomal bupivacaine, which claims up to 72 hours duration of action.¹⁹ Liposomal bupivacaine utilizes the use of spherical microscopic vesicles composed of liposomal encased bupivacaine molecules.²⁰ The liposomal delivery system functions as a depot, as vesicles are gradually released and degraded by the body system.¹³ Due to the lipophilicity of liposomal bupivacaine, it has a biphasic absorption phase with an initial peak at 1 hour post administration and a second

peak at 12-36 hours later.²⁰ However clinically, many veterinarians choose to combine local anesthetics such as lidocaine with bupivacaine, or bupivacaine with liposomal bupivacaine to manipulate onset time and duration of action. Other ways to manipulate the onset and duration of action of local anesthetics is the use of adjuvant medications, which are discussed under the section “Secondary Medications.”

Protein binding also determines the duration of action for local anesthetic agents. For example, bupivacaine and ropivacaine have greater protein binding compared to that of lidocaine.^{11,12} It is only the unbound fraction that can exert pharmacological action.¹² Vasoactivity is an important factor of duration of action as the uptake of the local anesthetic drug into systemic circulation is delayed if the local tissue is either avascular or if local vasoconstriction is induced.¹² While local anesthetics cause vasoconstriction at low doses, this class of drugs will result in vasodilation at higher doses. The potency of vasoconstriction is influenced by lipophilicity primarily, but is also influenced by drug potency, pKa, and molecular weight.¹²

Adverse effects of local anesthetics occur secondary to systemic absorption, with neurotoxicity and cardiovascular effects being of primary concern.¹² The most severe toxicity results from intravascular injection, particularly with bupivacaine, where death may occur from calcium channel blockade in cardiomyocytes and cardiac arrest.^{21,22} The only treatment available for inadvertent intravascular injection of potentially lethal local anesthetics (i.e. bupivacaine) is lipid emulsion.²³ It is also possible for toxicity to develop following administration of large volume local tissue infiltration of local anesthetic drug(s).²³

Opioids:

The use of opioids as premedication and post-operative analgesia is common in veterinary medicine. When considering the pain pathway, opioids can interfere with nociception transmission at the level of modulation and perception by hyperpolarizing membranes and preventing the onset of action potentials in neurons.^{24,25}

There are three opioids receptor types that have been recognized: mu, kappa, and delta.^{24,25} The receptors for opioids are transmembrane G-protein coupled and are found throughout the body, including the brain, spinal cord, chemoreceptor trigger zone, gastrointestinal tract, synovium, urinary tract, leukocytes, uterus, and others.^{24,25} Activation of these receptors, results in varied degrees of hyperpolarization of postsynaptic neurons and provides analgesia.^{24,25} Beyond the receptor class, opioids can be further classified by the effect they cause, such as a concentration or dose-response effect.^{24,25} For example, a full agonist produces a dose dependent increase of effect, until a maximum stimulation of the receptor occurs.^{24,25} While a partial agonist similarly results in a dose dependent effect, the maximum stimulation is less than that of the pure mu agonist.^{24,25} The potency of opioids does not describe the duration of effect or efficacy, but more so describes the relative dose needed to elicit a response (i.e., analgesia).^{24,25}

Significant side effects of opioids arise from the supraspinal effects of this drug class including sedation, nausea, vomiting, inappetence, ileus, dysphoria, bradycardia, and respiratory depression.^{24,25} Sedation and impaired cognitive function results secondary to CNS depression following binding to opioid receptors in the brain and

thereby reducing neuronal activity.^{24,25} Nausea and vomiting may occur through the vomiting reflex with stimulation of the chemoreceptor trigger zone (CTZ) in the brain via dopamine release.^{24,25} Aspiration pneumonia as a sequela to vomiting may also occur. Ileus and subsequent constipation may result secondary to opioid receptor binding in the gastrointestinal tract.^{24,25} This opioid binding diminishes smooth muscle contractions resulting in slowed transit time and reduced bowel movements, leading to constipation.^{24,25} Respiratory depression, or hypoventilation, occurs through opioid receptor binding in the brainstem, which reduces the sensitivity of the respiratory center to arterial carbon dioxide partial pressures.^{24,25} Moreover, the use of opioids requires rigorous control drug logs and trained personnel to dose these medications appropriately. With the on-going opioid crisis in North America, the future veterinary use of opioids may be extremely limited due to increased opioid regulations and reduced supply making the use of such products overly expensive. The trend of “opioid-free anesthesia” is a growing area of research in veterinary medicine and there is a focus on expanding the knowledge and use of locoregional techniques for veterinary patients.

The addition of opioids including morphine, tramadol, fentanyl, and buprenorphine, to local anesthetics has conflicting evidence on whether duration of a local block is affected. The addition of morphine to a lidocaine/epinephrine axillary block in human medicine resulted in comparable post-operative pain scores to the control group of lidocaine/epinephrine.²⁶ Additionally, the patients from the treatment group had approximately half the post-operative rescue analgesia requirements of the control group.²⁶ The mechanism of action for this apparent improved analgesia with opioid adjuvants is thought to be due to inhibition of synaptic transmission via G protein-coupled opioid

receptors.²⁷ The addition of 200 mg of tramadol to an axillary block of lidocaine/epinephrine for patients undergoing hand surgery experienced an almost a twice as long onset of sensory block compared to the control group (16 +/- 7 minutes vs 9 +/- 3 minutes).²⁸ However, once the 200 mg tramadol group achieved sensory block the duration of the block and time for first rescue analgesia was significantly longer compared to the control group and the other treatment group receiving 100 mg tramadol additive.²⁸ It was determined that the benefits of the addition of 200 mg tramadol were limited by the slow onset of sensory block.²⁸ While the prolonged duration of sensory blockade using tramadol as a locoregional adjuvant and its subsequent reduced post-operative analgesia requirements has been proven multiple times, the slower onset time has been disputed and may be a reflection of study design.^{28, 29, 30, 31} The mechanism of action of the addition of tramadol to local anesthetics, central vs peripheral, has not yet been determined definitively.²⁸ As with most locoregional adjuvant medications, there are conflicting studies that report lack of enhanced analgesic effects with tramadol.³² The noted difference may be secondary to study design, power, or technique.

The addition of fentanyl to locoregional blocks has also had conflicting studies as an adjuvant for axillary brachial plexus blocks in humans. While Fletcher et al concluded that there was no clinical benefit to the addition of fentanyl to lidocaine, Nishikawa et al found an improved success rate of axillary block with the addition of fentanyl, but prolonged onset of sensory blockade.^{33,34} The prolonged onset of sensory block was attributed to the decrease of pH from fentanyl.³⁴

In contrast to pure μ receptor opioids, the addition of partial μ agonist buprenorphine to local anesthetics exhibits a potent blockade of the voltage-gated sodium channel subtypes and C-fiber receptor agonists.²⁷ Moreover, buprenorphine has been found to have anti-hyperalgesic effects that are more pronounced and longer lasting than the analgesic effects.³⁶ The use of buprenorphine as an adjuvant to maxillofacial locoregional blockades enhance the analgesic duration with one study achieving analgesic effects to up to 96 hours was observed but there were inconsistent minimum alveolar concentration (MAC) sparing effects.³⁷ This is a similar reflection in human medicine, where the addition of buprenorphine to local anesthetic for dental block resulted in a statistically and clinically significant three-fold increase in post-operative analgesia duration.³⁸ Interestingly when added to lidocaine for dental surgery, buprenorphine was shown to have minimal effect on post-operative pain score and duration of post-operative analgesia without any difference in rescue analgesia requirements between treatment and control group.³⁹ The benefits of adding buprenorphine to local anesthetics also appears to apply to interscalene, axillary brachial plexus, and sciatic nerve blocks in human medicine, where the duration of nerve block action was prolonged, and the block efficacy was enhanced.^{40,41,42,43}

Secondary Medications (i.e. Additives)

Dexmedetomidine:

The addition of an alpha-2 agonist, such as dexmedetomidine, has shown to prolong the duration of peripheral nerve block action by providing additional analgesia and local vasoconstriction without affecting motor function.⁴⁴⁻⁵³ Several human and veterinary studies have investigated the effect of dexmedetomidine on the onset and

duration of action of different local anesthetics, including lidocaine and ropivacaine, and the majority have concluded that the addition of the alpha-2 agonist resulted in faster onset and prolonged nerve blockade resulting in lower post-operative rescue analgesia requirements.⁴⁴⁻⁵³ Acquafredda et al found that addition of dexmedetomidine to lidocaine prolonged the duration of a peripheral nerve block by 2.5 times.⁴⁴ Interestingly, systemically administered dexmedetomidine also prolonged local anesthetic block by 1.5 times and reduced the need for post-operative rescue analgesia in the first 4 hours.⁴⁴ A meta-analysis of 3149 human patients demonstrated the combination of dexmedetomidine and local anesthetics increased the duration of post-operative analgesia for approximately 5 hours.⁵⁴ Researchers have suggested that 1 mcg/kg best “minimal effective dose” when compared to 0.5 mcg/kg and 2 mcg/kg of dexmedetomidine in order to avoid potential adverse effects (i.e. bradycardia, hypotension), whilst capitalizing on analgesic potential.^{48,51} The enhanced block has been postulated to be likely due to the sensitivity of the peripheral nerve extrinsic blood supply to adrenergic stimuli.^{45,46} The local effects of alpha-2 agonist induced vasoconstriction reduces systemic uptake of the local anesthetic, which also prolongs the duration of sensory blockade.^{45,46} Additionally, by blocking the hyperpolarization active cation current during the late repolarization period, dexmedetomidine can prolong analgesia duration and extend nerve hyperpolarization.⁵⁵

Epinephrine:

Epinephrine is a well-established additive for local anesthetics in human and animal medicine, due to its vasoconstrictive effects on the peripheral nerve vasculature resulting in prolonged duration of block.^{46,56-60} In rats the application of 2% lidocaine

reduced peripheral nerve blood flow to 81%, while the combination of 2% lidocaine and epinephrine further reduced blood flow to 20% of baseline.⁵⁶ This reduction in peripheral nerve blood flow is like that following application of a pneumatic tourniquet.⁶¹ The resulting vasoconstriction is suspected to prolong block by reducing clearance of the local anesthetic and is inferred by lower plasma concentrations of local anesthetic when combined with epinephrine.⁴⁶ The duration of effect appears to be limited when epinephrine is added to lidocaine, with alpha adrenergic receptor stimulation being documented only during the first 10 minutes of application when applied to a rat sciatic nerve.⁶⁰ When compared to dexmedetomidine as a peripheral nerve block adjuvant, perineural dexmedetomidine at a dose of 1 mcg/kg resulted in similar prolonged duration of complete blockade and time to first pain sense as 200 mcg of epinephrine.⁶² There was no significant difference between the dexmedetomidine and epinephrine treatment groups.⁶² However, because systemic uptake effects of epinephrine including tachycardia, hypertension, and arrhythmias, dexmedetomidine was suggested to be the safer alternative with similar benefits to peripheral nerve block.⁶²

Ketamine:

There is conflicting data on the efficacy of ketamine as an adjuvant. When administered epidurally in humans, 30 mg of ketamine has been shown to increase the duration of regional anesthesia and post-operative analgesia.^{63,64} In contrast, the same dose of ketamine in a local block has not proven to be effective in terms of prolonging and/or expediting onset of peripheral nerve block and alternatively has resulted in a 67% incidence of adverse side effects including a reported unpleasant feeling, bad dreams, hallucination, altered short-term memory, distortion of body image, drowsiness, anxiety,

headache, dizziness, and nausea.⁶⁵ While the adverse side effects were not observed, likely due to difference in dosage, a similar lack in analgesic effects were found in a study using 0.5 mg/kg ketamine as a locoregional adjuvant in paravertebral blocks in female patients undergoing modified radical mastectomy.³² In human studies where the peripheral administration of ketamine has shown effective analgesia, it has been used as incisional infiltration and appears to be dependent on the presence of local inflammation.^{66,67} It has been postulated that the efficacy of ketamine depends on perineurium disruption, to gain access to the NMDA receptors and thus can only exert local analgesic action in inflamed tissues and not at a nerve plexus that is distant from the surgical site.⁶⁵ Interestingly, a randomized, double-blind, placebo-controlled comparative analgesic study of pre-incisional ketamine administered either subcutaneously or intravenously for patients undergoing open cholecystectomy concluded that a 2 mg/kg dose of subcutaneous infiltration ketamine or a 1 mg/kg dose of intravenous ketamine given at 15 minutes prior to surgical incision provided adjunctive analgesia during the first 24 hours post-operatively based on visual analog scale and rescue analgesic consumption.⁶⁸ Similar results were indicated with pre-incisional subcutaneous infiltrated ketamine for circumcision surgery.⁶⁹ However, both studies made clear that the subcutaneous ketamine needed to be precisely infiltrated along the planned incision which indicates that a surgeon would need to not divert from the planned incision for its success.^{68,69} These findings suggest that ketamine may best be used as a lumbosacral epidural and/or peri-incisional infiltration adjuvant, rather than for peripheral nerve block.

Common Locoregional Delivery Methods

Given the on-going opioid epidemic in the USA, the ability of the veterinary community to have access to and provide opioids for our patients is becoming increasingly difficult as opioid supply is limited to combat human addiction and overdose.⁷⁰ In late 2018, approximately 83% of surveyed veterinarians reported difficulty in ordering opioids the previous 6 months, specifically hydromorphone, morphine, fentanyl, and oxymorphone.⁷⁰ Many veterinarians (41%) also reported that the shortage resulted in significant difficulty in providing appropriate analgesia to their patients.⁷⁰ This finding emphasizes the importance of utilizing and continuing research with locoregional techniques and medications in veterinary patients. Commonly utilized locoregional techniques for pelvic limb surgeries in dogs include lumbosacral epidural, peripheral nerve block, intraarticular injection, and/or peri-incisional infiltration with local anesthetic. While it is typically primary surgeon decision on the use of intra-articular injection or peri-incisional infiltration, it is the anesthesiologist who may elect between the choice of lumbosacral epidural or peripheral nerve block for pelvic limb surgeries. Utilizing the knowledge of anatomy and dermatomes, locoregional anesthesia and analgesia can minimize nociceptive signaling. However, each technique offers benefits and disadvantages.

Lumbosacral Epidural:

The administration of a lumbosacral epidural requires advanced training and success can be dependent on patient positioning, body condition and presence of underlying axial skeleton abnormalities (i.e., hemivertebrae, stenosis, etc.). Once the L7-S1 space is palpated manually, the technique requires minimal equipment beyond sterile

gloves and a spinal needle.⁷¹ There are multiple methods to confirm needle placement including hanging drop and loss of resistance.⁷¹ The epidural space has liposomal stores and is the potential space between the dura mater and the wall of the vertebral canal.⁷¹ The subarachnoid space sits below the epidural space and has cerebral spinal fluid (CSF) present.⁷¹ Medications for anesthetizing the spinal cord may be administered in either the epidural or subarachnoid space, although recommended total volume of medication differs due to risk of local anesthetics travelling too far cranially in the subarachnoid space and anesthetizing the diaphragm.⁷¹ In either placement, the administration of local anesthetics results in transient motor and sensory blockade to both pelvic limbs, as well as urinary retention.⁷¹ However, these side effects may be mitigated with the use of morphine only lumbosacral epidural.⁷² In addition to urinary retention, other adverse effects of lumbosacral epidural may include neurotoxicity, infection, delayed hair growth, hypotension and bradycardia, inadvertent intravascular injection, pruritus, and delayed hair growth and/or color.⁷¹ While the anesthetist may use indicators such as relaxed anal tone and reduced blood pressure following lumbosacral epidural administration as an indicator of success, it is not until noxious stimulation (generally intraoperatively) that the effectiveness of a lumbosacral epidural can be truly determined.⁷¹ Even with ideal administration of a lumbosacral epidural, there can be uneven distribution of medication, often referred to as “patchy distribution”.⁷¹ Some anesthesiologists promote the placement of the planned surgical side dependently so that theoretically the medication administered epidurally will settle over the nerve roots of the surgical leg via gravity.^{73,74} To date, this remains controversial and there are no studies to prove this as an effective technique.^{73,75} However, the use of higher volume (0.2 ml/kg) has shown to result in

homogenous spread regardless of positioning.^{73,75,76} Common medications used for lumbosacral epidural include local anesthetic agents and opioids, while ketamine, alpha 2 agonists, and liposomal encapsulated bupivacaine have also been described, they are not currently used clinically in veterinary medicine.

Peripheral Nerve Blocks:

With the focal administration of local anesthetic to the peripheral nerves, dogs maintain motor to both limbs and sensory control of the contralateral limb. In a 2015 study by McCally et al comparing bupivacaine administered as an epidural, femoral nerve block, or femoral/sciatic nerve block in dogs undergoing unilateral TPLOs, it was found that the peripheral nerve blocks provided short-term postoperative analgesia comparable to lumbosacral epidurals.⁷⁷

There is ongoing debate in the anesthesia community over which technique is better for peripheral nerve block: ultrasound or nerve stimulator. The choice of technique may be limited due to experience and availability of equipment. Potential complications that may occur with peripheral nerve block includes hematoma, local anesthetic toxicity, and nerve injury.⁷⁸ Due to the significant decrease of major central nervous system local anesthetic toxicity, Orebaugh et al championed the combined use of ultrasound with a nerve stimulator to improve the efficacy and safety of block.⁷⁹ In fact, the use of ultrasound for peripheral nerve blocks was delayed until the early 2000s due to lack of suitable ultrasound machines for locoregional block administration.⁸⁰ With recent technological advances small, portable and financially affordable ultrasound machines are more readily available.⁸⁰ The advantages of ultrasound guided peripheral nerve block

is that anatomical structures (including nerves and important blood vessels) can be easily identified, making the insertion and placement of the needle prior to deposition of the local anesthetic safer and allows safer re-positioning of the needle to avoid important structures.⁸⁰ Additionally, the administration of the local anesthetic can be visualized in real-time to ensure it is accurately deposited within the nerve sheath as opposed to the blind redirection of insulated needles with nerve stimulation, which may decrease block performance and increase patient discomfort.⁸⁰ The added benefit of this real-time visualization is that if the nerve can be visualized via ultrasound, it may be blocked anywhere along its pathway.⁸⁰ Once the anatomical structures are identified, the peripheral nerve block can be efficiently delivered with reduced onset time, increased success, and reduced complication rate.⁸⁰ Due to the variability in available equipment for peripheral nerve block, training with both ultrasound and nerve stimulator for peripheral nerve block is important for anesthesiologists to avoid the disadvantage of not having experience with one or the other technique and entering a practice that only has one option.

Peri-incisional Blocks:

Peri-incisional blocks, or “wound infiltration”, involves the sterile injection of local anesthetic directly into the surgical field.⁸¹ This technique is popular due to the low cost, efficiency, ease of application, and lack of requirement for specialty equipment.⁸¹ The infiltration is directed into the fascia, skin, subcutaneous tissue, muscle, and/or parietal peritoneum.⁸² The use of shorter (i.e. lidocaine) or longer (i.e. ropivacaine, bupivacaine) have been shown to reduce post-operative pain scores, need for rescue analgesics, and reduce duration of hospitalization.⁸¹ Liposomal bupivacaine presents an

intriguing option for locoregional therapy used in human and veterinary medicine. The encapsulation of drugs into multivesicular liposomes provides a sustained drug release upon administration.⁸³ There are limited studies exploring the use of liposomal bupivacaine beyond its labelled use in veterinary medicine, but more research is done every year to investigate the efficacy and safety of this drug used in an off-label manner. Limited studies may also be reflective on drug availability, as liposomal bupivacaine is currently only licensed for use within the United States. Presently, liposomal bupivacaine is only licensed for use as an incisional block following TPLOs in dogs and/or peripheral nerve block in cats post-onychectomy for up to 72 hours of local anesthesia and analgesia.¹⁹ The safety of using liposomal encapsulated bupivacaine as a peripheral nerve block for the brachial plexus in rabbits and dogs has been previously investigated and concluded that the medication is well tolerated up to 30 mg/kg and the only adverse effect was minimal to mild granulomatous inflammation of the adipose tissue around the nerve roots in 29% of the tested dogs.⁸⁴ Presently, there is no published clinical study regarding the use of liposomal bupivacaine as a peripheral nerve block for dogs undergoing pelvic limb surgery. However, in human medicine the use of liposomal bupivacaine for peripheral nerve blocks has been extensively researched with partial sensory and motor block of greater than 24 hours at the highest doses examined.⁸⁵ Furthermore, comparative studies of bupivacaine versus liposomal encapsulated bupivacaine in a pooled analysis from 9 double-blind studies representing 5 different surgical procedures found that liposomal bupivacaine was significantly associated with lower cumulative pain scores at 72 hours post-operatively, as well as delayed first rescue analgesia requirements and overall lower rescue opioid needs.⁸⁶

Summary

Epidurals present adverse side effects including urinary retention and prolonged motor blockade. While transient, these effects do result in increased post-operative patient care requirements with bladder care and extended hospitalization, which increases client cost and risk of patient infection. Peripheral nerve block for pelvic limb surgeries allows desensitization of the lumbosacral plexus and has been proven to be equally efficacious as lumbosacral epidural in terms of minimum alveolar concentration (MAC) sparing of isoflurane, minimized rescue analgesia requirement intra- and post-operatively.⁸⁷ The key difference between the techniques is the lack of urine retention and motor blockade with peripheral nerve block, which allows patients to have shorter hospitalization, reduce opioid usage, and a quicker return to weight bearing on the operated limb. By blocking the afferent nerve impulse with preoperative peripheral nerve block, thereby preventing the transduction of a nociceptive stimulus, the total amount of intraoperative opioids and inhalant anesthetic requirements is reduced, thereby minimizing potential side effects.⁸⁷ These described benefits make the use of peripheral nerve block an attractive option for veterinary anesthesiologists and surgeons alike. The investigation into the locoregional preferences of board-certified anesthesiologists may reveal trends for methods and medications that warrant further investigation into developing such techniques.

CHAPTER 2: Pelvic limb anesthesia and analgesia in dogs undergoing tibial plateau leveling osteotomy (TPLO): A survey of board-certified anesthesiologists

Introduction

One of the most common elective orthopedic procedures performed in dogs is the tibial plateau leveling osteotomy (TPLO) for dogs with cranial cruciate ligament disease (CCLD). The current economic impact of CCLD to dog owners is not fully known; however, in 2003 it was found to be approximately \$1.32 billion USD.¹ It is possible that the financial impact is higher today.

The TPLO is the preferred surgical procedure of board-certified veterinary surgeons for dogs with CCLD.⁸⁸ The use of effective perioperative anesthesia and analgesia is paramount for any surgical procedure, including the TPLO. While numerous studies have evaluated perioperative anesthesia and analgesia in dogs undergoing TPLO, there is no consensus on the ideal management strategy. To date, no study has reported on the anesthesia and analgesia preference of board-certified veterinary anesthesiologists of the American College of Anesthesia and Analgesia (ACVAA) and European College of Veterinary Anaesthesia and Analgesia (ECVAA) in dogs undergoing TPLO.

Therefore, the primary objective of this study is to report on the anesthesia and analgesia preferences of board-certified veterinary anesthesiologists when overseeing the perioperative care of dogs undergoing a TPLO. We hypothesized that training (ACVAA or ECVAA), time from board-certification, and employment sector would influence the

choice of peripheral nerve block (PNB), lumbosacral epidurals (LE), or peri-incisional infiltration (PI) as the primary locoregional method for dogs undergoing TPLO.

Materials and Methods

Using Qualtrics software, an online-electronic survey was designed by the authors with the targeted population of Diplomates of the American College of Anesthesia and Analgesia (ACVAA) and of the European Veterinary Anaesthesia and Analgesia (ECVAA). All authors approved of the survey questions and design prior to its availability to the anesthesia colleges. This study was approved by the institutional review board at University of Missouri (#381772) and was conducted according to the tenets of the Declaration of Helsinki. At the time of survey, there were a total of 300 ACVAA Diplomates⁸⁹ and 200 ECVAA Diplomates⁹⁰ who were provided online survey access through a link emailed by their specific specialty list-serves. The electronic survey was developed to investigate the anesthetic and analgesic preferences for dogs undergoing tibial plateau leveling osteotomy (TPLO) procedures. The survey contained a total of 18 questions that included multiple choice questions, rank order questions, and an open-ended conclusion question. The survey was designed using online commercial software (Qualtrics, Provo, Utah).

The survey was initiated, and responses collected between September 2021 and October 2021. An email was sent to diplomate-specific list-serves by their respective colleges explaining the survey content and purpose of our investigation, with an embedded link to access the online survey. The survey included questions about demographics, time since board-certification, and preference of locoregional technique between PNB, LE, PI, other, or none. Following selection of locoregional preference,

respondents were asked questions specific for that technique including administration, perceived success, preferred medications. Respondents were also asked to rank PNB, LE, and PI with regards to rescue analgesia requirements intra-operatively, post-operatively, adverse effects, risks, and duration of action. A free-form comment section was made available for respondents to justify their choices. While most questions required a response in order to advance through the remainder of the survey, some questions were designed to allow multiple selections such as preference of medications for given locoregional technique. Therefore, questions had variable response totals depending on whether multiple, or any, selections were made. Incomplete surveys were discarded. Survey settings were set as to prevent multiple responses from a single anesthesiologist.

Completed surveys were tabulated and the data was exported for analysis using computerized software (Microsoft Excel for Mac, Version 16.64; Microsoft, Redmond, Washington). Descriptive statistics were calculated and summarized in tabular format. The study hypotheses were tested using the Fisher's exact test due to a low number of responses in some categories. Additionally, due to a low number of respondents that were dual-boarded by both the ACVAA and ECVAA (n=3), data reporting and comparisons between college Diplomates was performed between those who were ACVAA-only and those with ECVAA board-certification. Response characteristics such as training (ACVAA or ECVAA), time from board-certification (<1yr, 2-5yr, 6-10yr, 11-20yr, >20yr) and employment sector (academia, private practice, government, locum, retired) were evaluated for association with preferred locoregional method [peripheral nerve block (PNB), lumbosacral epidurals (LE), or peri-incisional infiltration (PI)]. All analyses

were performed with statistical software (Stata/SE 17.0, StataCorp, College Station TX) and were two-sided with significance set at $p < 0.05$.

Results

A response rate of 28% was achieved with a total of 141 completed surveys obtained from a possible total of 500 ACVAA and ECVAA Diplomates at the time of survey.^{89,90} Overall, 69% (97/141) of respondents were board-certified by only the ACVAA and 31% (44/141) had ECVAA board-certification (Table 1). Of the ACVAA Diplomates, 1 respondent had additional board certification by the American College of Veterinary Emergency and Critical Care. Of those ECVAA board-certified Diplomates, 3 respondents were also board-certified by the ACVAA. The majority of respondents (65%; 92/141) had been board-certified in anesthesia and analgesia within the last 10 years (Table 1). Respondents were predominantly located in the United States (56%; 79/141) followed by Europe/UK (26%; 37/141), Canada (9%; 13/141), Australia/New Zealand (6%; 8/141), Asia (2%; 3/141), and the Middle East (<1%; 1/146). Most of the respondents worked in private practice (52%; 74/141) followed by academia (45%; 64/141), were retired (1%; 2/141), or worked primarily as a locum (<1%; 1/141) (Table 1).

Most Diplomates (52%; 71/141) supervised at least 1-5 TPLO/week with an additional 34% (48/141) supervising 6-10 TPLO/week. Very few reported supervising 11-20 TPLO/week (8%; 11/141) or >20 TPLO/week (5%; 7/141). Of those that reported supervising 1-5 TPLO/week (n=71), 63% (45/71) were in academia as compared to 34% (24/71) private practice, 1% locums (1/71) and 1% retired Diplomates (1/71). Of the 48

Diplomates that reported supervising 6-10 TPLO/week, 65% (33/48) worked in private practice as compared to 35% (17/48) from academia. Only 11 Diplomates reported supervising 11-20 TPLO/week (91% (10/11) private practice and 9% (1/11) academic) and very few (n=6) reported supervising >20 TPLO/week (100% (6/6) private practice). Most dogs were discharged one day post-operatively (72%; 102/141), however a small percentage of respondents (5%; 7/141) indicated that they did not know when TPLO dogs were discharged post-operatively.

Preferred locoregional method:

Anesthesiologists preferred PNB (79%; 111/141) over LE (21%; 29/141) or PI (<1%; 1/141). No respondent selected that they preferred no locoregional technique. However, there was no association ($p=0.283$) between locoregional method and those with ACVAA or ECVAA board certification. There was a significant association ($p<0.001$) between preferred locoregional method and time from board certification (Table 2) with 74% (82/111) of those board-certified within the last 10 years preferring PNB over LE (38%; 11/29), those board-certified over 10 years ago preferring LE (62%; 18/29) over PNB (26%; 29/111), and only those board-certified >20 years ago preferring PI (100%; 1/1). Employment sector was also significantly associated ($p=0.003$) with preferred locoregional method (Table 2). Most Diplomates in both academia (73%; 47/64) and private practice (86%; 64/74) preferred PNB. However, more Diplomates in academia (27%; 17/64) preferred LE over those in private practice (12%; 9/74). Those in locum-based practice and retired Diplomates uniformly preferred LE (100%; 3/3).

Peripheral Nerve Block (PNB):

Those respondents that preferred PNB as a locoregional technique (n=111) were then asked additional questions regarding their preference of technique, preference of nerves to block, drug preference, and perceived effectiveness:

- *Technique Preference:* 44% (49/111) of respondents preferred to use a combination of nerve stimulation with ultrasound guidance during PNB. Respondents who utilized only a single piece of equipment preferred ultrasound guidance (35%; 39/111) over nerve stimulation only (21%; 23/111). No respondent indicated the use of a blind technique or anatomical method as their preferred technique.
- *Nerve Blockade Preference:* The preferred sites of nerve blockade were the proximal femoral nerve with sciatic nerve (52%; 58/111), saphenous nerve with sciatic nerve (40%; 44/111), iliopsoas approach to femoral nerve combined with sciatic nerve (4%; 4/111), sciatic nerve with saphenous nerve and lateral cutaneous nerve (2%; 2/111), proximal femoral nerve only (<1%; 1/111), saphenous nerve with sciatic and obturator nerves (<1%; 1/111), and lumbar plexus with iliopsoas approach to femoral nerve (<1%; 1/111).
- *Anesthetic/Analgesic Preference:* The use of bupivacaine only (42%; 48/114) was preferred over other possible options including bupivacaine with additive (31%; 35/114), ropivacaine only (18%; 21/114), ropivacaine with additive (4%; 5/114), mixed local anesthetics (4%; 4/114), or lidocaine with additives (<1%; 1/114). No respondent preferred lidocaine only, liposomal encapsulated bupivacaine only, or liposomal encapsulated bupivacaine with additives.

Medications chosen as additive for local anesthetic agents included dexmedetomidine (85%, 35/41), medetomidine (5%; 2/41), morphine (5%; 2/41), epinephrine (2%; 1/41), and ketamine (2%; 1/41). Respondents who preferred bupivacaine with an additive (n=35) selected an alpha-2 agonist most of the time (91%; 32/35), with dexmedetomidine as the most preferred option (86%; 30/35). Of those who preferred mixing anesthetic agents (n=4), 50% (2/4) indicated a preference for bupivacaine with lidocaine.

- *Perceived Effectiveness*: Most anesthesiologists (78%; 87/111) who preferred PNB responded that it was effective 81-100% of the time. The remainder of respondents indicated PNB effectiveness of 61-80% (20%; 22/111) or 41-60% (2%; 2/111). No diplomate responded that their effectiveness was less than or equal to 40%.

Lumbosacral Epidural (LE):

Those respondents that preferred LE as a locoregional technique (n=29) were then asked additional questions regarding their drug preference and perceived effectiveness rate:

- *Anesthetic/Analgesic Preference*: The preferred medication for LE was the combination of bupivacaine with opioid (79%; 23/29). Other medications included ropivacaine with opioid (10%; 3/29), lidocaine with opioid (7%; 2/29), or opioid only (3%; 1/29).
- *Perceived Effectiveness*: Most anesthesiologists (55%; 16/29) who preferred LE responded that it was effective 81-100% of the time. Interestingly, those who had been boarded for less than 5 years indicated less confidence in LE

with an effectiveness of 61-80% (83%; 5/6). The remainder of Diplomates (55%; 16/29) reported a an 81-100% efficacy, while 41% (12/29) reported a 61-80% efficacy, and 3% (1/29) a 41-60% efficacy.

Peri-Incisional Infiltration (PI):

One respondent (n=1) selected PI as their preferred method with a perceived effectiveness of 1-20% and the preferred medication was liposomal encapsulated bupivacaine. Additionally, all Diplomates (n=141) were asked to grade the efficacy of PI as a sole means of primary locoregional method for dogs undergoing TPLO: 75% (106/141) reported a 1-20% efficacy, 10% (14/141) reported a 21-40% efficacy, 8% (11/141) reported a 41-60% efficacy, 5% (7/141) reported a 61-80% efficacy, and 2% (3/141) a 81-100% efficacy.

Duration of action, side effects, and risk:

Participants (n=141) were asked survey questions about observed adverse side effects, perceived duration of action, and risk associated with each technique, and perceived effectiveness of their preferred technique (Table 3):

- *Adverse Side Effects:* Most respondents (75%; 106/141) indicated that PNB had fewer less desirable side effects as compared to PI (21%; 30/141) and LE (4%; 5/141).
- *Perceived Effectiveness and Duration of Action:* Most respondents favored PNB for effectiveness and noted that it required less intra-operative rescue analgesia (57%; 80/141) and less post-operative rescue analgesia (54%;

76/141). Most (54%; 76/141) noted that LE provided the best duration of analgesia.

- *Perceived Risk:* The majority of respondents (59%; 83/141) noted that PI had less risk as compared to PNB (21%; 30/141) and LE (20%; 28/141).

Use of Post-Operative Analgesics:

Injectable analgesics administered in the immediate post-operative period (n=141) included non-steroidal anti-inflammatories (93%; 131/141 (NSAIDs)), opioids (91%; 128/141), ketamine (10%; 14/141), dexmedetomidine (6%; 8/141), lidocaine (4%; 5/141), corticosteroids (3%; 4/141), and injectable gabapentin (<1%; 1/141). Oral analgesics prescribed post-operatively for TPLO dogs included NSAIDS (94%; 132/141), gabapentin (37%; 52/141), opioids (28%; 39/141), acetaminophen with codeine (13%; 18/141), corticosteroids (3%; 4/141), amantadine (2%; 2/141), and cannabinoids (<1%; 1/141). There were 3% (4/141) of respondents that were unaware of what medications were prescribed post-operatively. Respondents were allowed to indicate multiple medications for both injectable and oral post-operative medications.

Subjective Rationale for Treatment or Technique Choice:

When given the voluntary opportunity to justify the selections made throughout the survey, those who responded indicated that multiple factors were taken into consideration by respondents. Overall, 38% (54/141) of survey respondent provided additional voluntary information regarding the justification of their survey choices. Some anesthesiologists (7%; 4/54) commented that their selection depended on whether the dog was undergoing a single session bilateral TPLO, for which an LE would be their

preferred locoregional technique. Those same respondents indicated a preference for PNB in dogs undergoing a unilateral TPLO. Animal size was another consideration for some respondents, with 28% (15/54) commenting that LE was preferred in smaller dogs and PNB for larger dogs. Additionally, the impact of prolonged motor blockade and urinary retention in dogs after LE was noted by 39% (21/54) to negatively impact post-operative care. Furthermore, 7% (4/54) indicated that the necessity of student and house officer training (i.e., veterinary technicians, veterinary students, interns, specialty interns, and residents) was a factor that influenced treatment or technique. Multiple respondents (37%; 20/54) indicated that a combination of PNB+PI or LE+PI was their overall preferred anesthesia and analgesia choice for TPLO dogs—with liposomal encapsulated bupivacaine indicated by all (100%; 20/20) as the preferred PI agent. Interestingly, some respondents (7%; 4/54) noted that their analgesia/anesthesia preference did not always align with surgeon preference and that the perceived pressure to expedite surgical anesthesia resulted in them choosing less time-consuming methods over their preferred method of analgesia/anesthesia.

Discussion

In this study, Diplomates of the ACVAA and ECVAA were surveyed to explore their anesthesia and analgesia preferences for the treatment of dogs undergoing TPLO. The hypothesis that board-certification college (i.e., ACVAA or ECVAA) is associated with preferred locoregional treatment method was rejected. However, the hypotheses that time from board-certification and employment location would be associated with locoregional treatment methods were accepted.

Overall, peripheral nerve blockade (PNB) was the locoregional method preferred by 79% of all Diplomates. Although PNB is considered a moderately challenging technique that may be more time-consuming than LE, surveyed anesthesiologists in this report responded that, despite any perceived challenges, a major benefit was the maintenance of contralateral motor function and more rapid post-operative ambulation (39%). However, 28% of respondents who elected to justify their choices indicated that LE was their preference for smaller dogs while PNB was their choice for larger dogs. For dogs undergoing single session bilateral TPLO procedures, 7% of anesthesiologists specifically commented that LE was their preferred locoregional technique. Interestingly, despite ranking LE as the most advantageous locoregional method for duration of analgesia, most surveyed anesthesiologists selected PNB as the technique least prone to require intraoperative or post-operative rescue analgesia. Additionally, 75% of Diplomates responded that PNB presented the least number of adverse effects. Regarding intra-operative management, surveyed anesthesiologists responded that the use of PNB avoided the hypotensive effects of LE, as the administration of a local anesthetic to the epidural space exerts a sympatholytic effect which consequentially may lead to hypotension. Additionally, 39% surveyed anesthesiologists felt that PNB was beneficial to reduce the burden of post-operative patient care for technician staff including moving large patients and performing bladder care due to secondary urinary retention observed with LE. Given the current climate of perpetual veterinary technician shortages, this insight is an important consideration that could help limit contribution to potential burn-out of veterinary technicians.

Most anesthesiologists were employed in either private practice (52%) or academia (45%). Veterinary anesthesiologists practicing in either of those settings largely favored PNB over other methods. A greater percentage of those in private practice (86%) preferred PNB as compared to those in academia (73%). Interestingly, those in academia more commonly reported preferring LE (27%) as compared to those in a private practice setting (12%). The reason for this is not fully elucidated from this study but 7% of respondents indicated necessity of training requirements and/or clinical exposure in an academic setting. While the training of house officers occurs frequently in private practice, there are a larger number of student-learners present in an academic setting and can include veterinary technicians, veterinary students, interns, specialty interns, and residents—leading to an environment where technique diversity for teaching purposes is critically important. Furthermore, the desire to provide teaching opportunities with various procedures may influence equipment availability and impact the use of techniques such as PNB, which requires more specialized equipment.

The preferred location of peripheral nerve blockade varied in this report with respondents indicating the use of several solitary sites, as well as a combination of sites. The combined femoral and sciatic technique was preferred (52%) followed by the saphenous nerve with sciatic nerve (40%). Interestingly when comparing the perceived efficacy of the PNB and LE, 77% of surveyed anesthesiologists indicated a >80% confidence in their PNB effectiveness while only 55% indicated similar confidence with LE. The reason for the perceived lower efficacy of LE is not fully elucidated in this study but it may be secondary to inherent differences in technique. Ultrasound guidance with PNB allows direct visualization of block administration and loss of nerve stimuli is

demonstrated with a nerve stimulator when there is appropriate drug administration—providing immediate feedback to the clinician regarding the accuracy of medication delivery to the target site. Alternatively, when using LE the confirmation of appropriate delivery of treatment is most often determined by monitoring for a response to nociceptive stimuli, which often occurs during the surgical procedure. However, respondents in this study noted that LE was preferred in cases of a single-session bilateral TPLO due to a single site of treatment that would result in anesthesia of both pelvic limbs.

Anesthesiologists reported that the use of ultrasound guidance was preferred over the use of a nerve stimulator when performing PNB. Interestingly, there is debate within the veterinary anesthesia community over which of these two techniques is superior for PNB. Due to reduced central nervous system local anesthetic toxicity, Orebaugh et al.,⁷⁹ championed the combined use of ultrasound with a nerve stimulator to improve the efficacy and safety of PNB. A preference for combined techniques was reflected in this report with 44% of anesthesiologists surveyed preferring the combined use of ultrasound with a nerve stimulator. However, access to equipment may play a role in technique choice, with some respondents commenting that lack of access to an ultrasound resulted in the use of a nerve stimulator. An advantage of ultrasound guided PNB is that anatomical structures (including nerves and important blood vessels) can be easily identified, making the insertion and placement of the needle prior to deposition of the local anesthetic safer and allowing safer re-positioning of the needle to avoid important structures.⁸⁰ Additionally, accurate deposition of local anesthetic may improve reliability and duration of block, as well as decrease patient discomfort as blind redirection of the

needle is eliminated.⁸⁰ The added benefit of this real-time visualization is that if the nerve can be visualized via ultrasound, it may be blocked anywhere along its pathway.⁸⁰ Once the anatomical structures are identified, the PNB can be efficiently delivered with reduced onset time, increased success, and reduced complication rate.⁸⁰ Due to the variability in available equipment for PNB, training with both ultrasound and nerve stimulator for PNB is important for anesthesiologists to avoid the disadvantage of not having experience with one or the other technique and entering a practice that only has one option.

Bupivacaine was the preferred anesthetic for all treatment methods. The use of bupivacaine-only was preferred for PNB, bupivacaine with an opioid for LE, and only liposomal encapsulated bupivacaine was selected for use with peri-incisional infiltration. No respondents selected lidocaine as their drug of choice of local anesthetic for PNB and very few respondents who preferred LE opted for its use (7%), which is secondary to the short duration of action of lidocaine (1-2 hours) compared to the extended duration of bupivacaine (up to 8 hours).¹³ Dexmedetomidine was the most commonly reported additive for PNB for those using bupivacaine, ropivacaine, and lidocaine. Both human and veterinary studies have investigated the effect of dexmedetomidine on the onset and duration of action of different local anesthetics and have concluded that the addition of the alpha-2 agonist results in faster onset of action and prolonged nerve blockade which leads to lower post-operative rescue analgesia requirements.⁴⁴⁻⁵³ A previous study found that addition of dexmedetomidine to lidocaine prolonged the duration of a PNB by 2.5 times and systemically administered dexmedetomidine appeared to prolong the block by 1.5 times while also reducing the need of post-operative rescue analgesia in the first 4

hours.⁴⁴ Additionally, the local effects of alpha-2 agonist induced vasoconstriction reduces systemic uptake of the local anesthetic, thereby prolonging the duration of sensory blockade.^{45,46} Other drugs reported by respondents as additives for PNB included medetomidine, morphine, epinephrine, and ketamine.

The lack of veterinary anesthesiologist preference for the use of peri-incisional blockade (PI) as a sole means of locoregional anesthesia in dogs undergoing TPLO is not surprising. When all Diplomates were questioned, the overwhelming majority (74%) believed that PI as a sole means of providing locoregional anesthesia was only effective less than 20% of the time. This reported lack of preference for PI may reflect the focus of veterinary anesthesiologist in managing TPLO cases and their attention to providing long-acting pre-emptive analgesia as compared to that provided for primarily in the post-operative period. Interestingly, 37% of respondents commented that they believed the combination of an effective PNB or LE along with the use of a peri-incisional block liposomal encapsulated bupivacaine at the end of surgery as a PI in dogs undergoing TPLO was highly beneficial, but that this was a surgeon-based decision. One hundred percent of the respondents who indicated this combination indicated a preference for liposomal encapsulated bupivacaine.

Surgeon influence was reported to play a role in the treatment choices of veterinary anesthesiologists. Seven percent of respondents in this survey commented that their preferred choice of locoregional method was not always the same as the surgeon's and in some cases, they made treatment decisions to avoid conflict with surgeons who preferred one method over another. Additionally, perceived time pressure secondary to

surgeon-influence was reported to impact treatment choice leading Diplomates to potentially select techniques based on rapidity of administration and not personal preference. One of the most prevalent comments made by anesthesiologists was the influence of patient body size on their preference between a LE or PNB. Due to the challenges of smaller anatomy, LE was suggested as the preferred locoregional technique for smaller dogs by 28% of respondents who elected to justify their choices. The prolonged motor blockade commonly observed post-LE was deemed not an issue, since smaller patients could theoretically have manual bladder care and be carried outside for urination and defecation as opposed to larger patients. PNB was deemed preferable for larger dogs due to reduced motor blockade, and the maintenance of motor function would result in less burden for the post-operative nursing staff. Occasionally surgeons will elect to perform bilateral TPLO procedures, and anesthesiologists indicated that in this situation they would select LE regardless of size due to the effective anesthesia and analgesia administered for both pelvic limbs using a singular injection that negates need for repositioning. Overall, the choice of locoregional technique is a multifactorial decision. A veterinary anesthesiologist's decision when selecting a locoregional technique for a dog undergoing a TPLO can be impacted by any of the previously discussed areas as well as their personal training history and the educational requirements of potential house officers, technicians, and students. A combination of locoregional techniques, whether it was PNB+PI or LE+PI was indicated as the overall preferred method by 37% of respondents who indicated this in the free-form comment section as the combination choice was not offered in this survey. Moreover, 100% of those

respondents indicated a preference of liposomal encapsulated bupivacaine as their choice of PI.

Nonsteroidal anti-inflammatory drugs (NSAIDs) were the preferred injectable (92%) and oral (93%) post-operative medication used by anesthesiologist. This is not surprising based on their established and approved use in post-operative pain as well as the management of both acute and chronic pain.⁹¹ The use of opioids was much more common in injectable form (92%) as compared to oral (25%) and may reflect the lack of effective oral options.⁹²⁻⁹⁶ However, in this study 37% of Diplomates reported the use of oral gabapentin or pregabalin for post-operative TPLO patients despite a lack of evidence to support its efficacy in ameliorating post-operative pain in dogs after TPLO. Interestingly, some Diplomates reported that while gabapentin is commonly prescribed post-operatively for TPLO dogs that this decision is most often made by the primary surgeon.

There are limitations of this study that should be considered. While the hypothesis may be considered a broad statement, however there was concern that a possible low response rate could occur given the survey design and we wanted to maintain a testable hypothesis. Additional limitations include the response rate and accessibility of the study to board-certified anesthesiologists as it assumes all have easy and readily available access to email and internet to complete the study. However, the response rate in this study is within the range of previously published studies.⁹⁸ Statistical testing was complicated by a low number of responses in some categories necessitating the use of the Fisher's exact test. The results of this initial survey study can be used to help guide future

research, allowing more robust statistical methods for comparative purposes. In this study, treatment efficacy and success were the subjective opinion of respondents. The use of objective measures to assess efficacy is ideal but is beyond the scope of this study. Moreover, the impact of animal size on choice of locoregional technique was not assessed. While some respondents did indicate a combination of locoregional techniques, we did not evaluate the combination of locoregional techniques specifically as we were more interested in preferred singular locoregional technique.

Overall, Diplomates of ACVAA and ECVAA prefer PNB as the singular locoregional method of pelvic limb anesthesia in dogs undergoing TPLO. The choice of locoregional analgesia is associated with time from board-certification and employment sector. A greater percentage of newer Diplomates and those in private practice prefer PNB while a larger percentage of more senior Diplomates and those in academia prefer LE. It is possible that this difference reflects a generational shift within Diplomates of the ACVAA and ECVAA. Or it may simply be related to an improved recognition of PNB techniques regarding perceived superior rescue analgesia sparing effects, improved impact on post-operative care, and reduced adverse effects as compared to LE. In the future, as more PNB approaches are described and taught in residency programs, it is reasonable to assume that PNB may remain the preferred choice of veterinary anesthesiologists for pelvic limb anesthesia in dogs undergoing TPLO. Regardless, a diplomate's preference in locoregional analgesia for dogs undergoing TPLO may be a combination of techniques and is overall complex and multifactorial which includes perceived effectiveness along with education, training requirements, and perceived time pressure. Most notably in this study, the possibility of veterinary surgeons influencing an

anesthesiologist's treatment choice resulting in the potential use of a less preferred treatment method or one perceived as less effective, cannot be overlooked. A focus on peri-operative collaboration and strengthening the surgeon-anesthesiologist relationship should be encouraged and may be one of the most critical components necessary to ensure optimal peri-operative patient care.⁹⁹⁻¹⁰³ Further research is warranted in this area.

CHAPTER 3: Conclusion

Considering the ongoing national opioid shortage, it is becoming more imperative to employ multi-modal anesthesia and analgesia techniques to minimize opioid usage whilst maintaining gold standard patient care. While lumbosacral epidurals may be considered the traditional choice for regional anesthesia and analgesia for the pelvic limbs, research into peripheral nerve blocks has opened additional locoregional approaches to consider. This is a particularly important area of research given the risk of complications following an epidural which may prolong hospitalization, increase client cost, and increase risk of nosocomial infection. The overall financial impact of employing peripheral nerve blockade appears to be of limited concern in veterinary medicine. A financial impact study revealed that while combined ultrasonography and nerve stimulation guided peripheral nerve blocks for stifle procedures did impact anesthesia cost, those patients had a reduced need for intra-operative and post-operative analgesia and lower anesthetic complications.¹⁰⁴ For these reasons, it is important to continue exploring this area in veterinary medicine with well-designed clinical trials exploring the use of alternative medications for locoregional therapy in veterinary patients.

In the first chapter of this study, the role of pain and the amelioration of pain through various pharmaceutical methods was explored. The application of such methods is vital in multi-modal analgesia, and for the prevention of sensitization. The application of these pharmaceuticals through various means, including lumbosacral epidural, peripheral nerve block and peri-incisional infiltration, were also briefly compared. While considered the tradition locoregional technique, lumbosacral epidurals also present

adverse side effects including urinary retention and prolonged motor blockade. While transient, these effects do result in increased post-operative patient care requirements such as bladder care and extended hospitalization, which increases client cost and risk of patient infection. By blocking the afferent nociceptive impulse with preoperative peripheral nerve block, the transduction of a nociceptive stimulus is interrupted prior to the signal reaching the spinal cord for modulation.⁸⁷ The development of the peripheral nerve block for pelvic limb surgeries allows desensitization of the lumbosacral plexus and has been proven to be equally efficacious as lumbosacral epidural in terms of MAC sparing of isoflurane, minimized rescue analgesia requirement intra- and post-operatively.⁸⁷ The key difference between the techniques is the lack of urine retention and motor blockade with peripheral nerve block, which allows patients to have shorter hospitalization, reduce opioid usage, and a quicker return to weight bearing on the operated limb.⁸⁷ Overall, further investigation and research into the development of locoregional blocks and the medications used is of great benefit to our veterinary patients and those undergoing TPLO.

In the second chapter of this study, a survey-based study of board-certified anesthesiologists investigated locoregional anesthesia and analgesia preferences for use in dogs undergoing tibial plateau levelling osteotomy (TPLO) procedures. The study revealed that a significant proportion of veterinary anesthesiologists preferred distal femoral (saphenous) and sciatic peripheral nerve blocks (52%) performed with combined ultrasound and nerve stimulation guidance (44%) using non-additive bupivacaine (43%) or dexmedetomidine as the preferred additive to bupivacaine (91%).¹⁰⁵ Compared to lumbosacral epidurals and peri-incisional infiltration, anesthesiologists felt that peripheral

nerve blocks resulted in lower overall analgesic requirements (intra-operatively (57%) and post-operatively (54%)) and lower adverse effects (75%).¹⁰⁵ Interestingly, 37% of respondents indicated that they ultimately prefer a combination of locoregional techniques, either a peripheral nerve block or lumbosacral epidural, with liposomal encapsulated bupivacaine as a peri-incisional infiltration.¹⁰⁵ No respondent indicated that they used liposomal bupivacaine as a peripheral nerve block agent.¹⁰⁵

The use of liposomal encapsulated bupivacaine is primarily restricted to the USA and therefore the majority of the research is US-based. The main advantage of liposomal bupivacaine is the described duration of analgesia of “up to 72 hours”.¹⁹ The product is much more expensive than conventional bupivacaine, which is common choice for locoregional blocks due to its duration of action of 8 to 12 hours.¹⁰⁶ This apparent prolonged analgesia has led to the assumption that liposomal bupivacaine may be superior to bupivacaine. While initial studies were suggestive of this, newer publications have since reported that the two agents are at least comparable clinically although there are concerns with study design and lack of recording significant parameters, such as time to effect and mixing of local anesthetic agents.¹⁰⁷⁻¹⁰⁸ However, through personal communication with the primary investigator, it was indicated that liposomal bupivacaine without additive takes approximately 24 hours to have clinical effect¹⁰⁷ which is consistent with pharmacokinetic and clinical studies. Given the expense associated with liposomal bupivacaine, it may not be clinically worthwhile to use the medication in this off-label manner and increase client and hospital cost unnecessarily.¹¹⁰ There is currently no research investigating the use of liposomal bupivacaine as a peripheral nerve block for saphenous-sciatic block compared to traditional bupivacaine-dexmedetomidine and

labelled use of liposomal bupivacaine as a peri-incisional block. It has been established that the addition of dexmedetomidine to local anesthetics prolongs the duration of block by 2.5 times, which brings the approximated duration to about 30 hours post-administration.⁴⁴

Traditionally, lumbosacral epidurals have been the preferred locoregional therapy for dogs undergoing pelvic limb surgery. Although the technique requires level of training not dissimilar to peripheral nerve block administration, lumbosacral epidurals result in bilateral motor and sensory blockade to the pelvic limbs and results in urinary retention that requires enhanced post-operative nursing care.⁷¹ Moreover, this technique risks hemorrhage, infection and air embolism at the level the central nervous system.⁷¹ Moreover, this locoregional can result in uneven distribution of anesthesia and analgesia.⁷¹ Peripheral nerve blocks avoid motor blockade and provide transient sensory blockade when administered in close proximity to the nerves that innervate the stifle, the femoral and sciatic nerves.⁷⁸ The financial implication of peripheral nerve blocks and equivalent analgesia to lumbosacral epidurals warrants further research in this area.

Summary and Future Direction

Ultimately, this research determined that board-certified anesthesiologists have numerous techniques and mediations available to them to ensure adequate analgesia in patients undergoing a TPLO. Their preferred methods, as determined in this research, is the administration of bupivacaine-dexmedetomidine as a peripheral femoral and sciatic nerve block. Survey respondents also indicated a preference for the concurrent use of

liposomal encapsulated bupivacaine as a peri-incisional block administered at the time of incision closure.¹⁰⁵ However, based on recent comparative literature in human and veterinary medicine, the application of liposomal encapsulated bupivacaine may not be clinically superior to the traditional use of bupivacaine-dexmedetomidine as a peripheral nerve block. Interestingly, the combined use of bupivacaine-dexmedetomidine as a peripheral nerve block and concurrent peri-incisional infiltration with liposomal encapsulated bupivacaine pharmacokinetically appears to result in a predictable and systemic additive exposure without signs of toxicity.¹¹¹ Based on the findings in this report, it is clear that further research, including well-designed clinical trials, are warranted to help improve our understanding of perioperative pain and to help optimize the management of pain in dogs undergoing TPLO.

TABLES

Table 1. Demographics of Survey Respondents.

Diplomate Demographics <i>(n=141)</i>	
Specialty College	
ACVAA ¹	69%
ECVAA ²	31%
Time of Board Certification	
<1 year	13%
1-5 years	27%
6-10 years	25%
11-20 years	23%
>20 years	12%
Employment Sector	
Private Practice	52%
Academia	45%
Retired	1%
Locum	<1%
Employment Location	
US	56%
Europe/UK	26%
Canada	9%
Australia/NZ	6%
Asia	2%
Middle East	<1%

1 = includes (1) diplomate with additional ACVECC certification
 2 = Includes (3) ECVAA Diplomates with additional ACVAA certification

Table 2. Associations between the locoregional method of pelvic limb anesthesia in dogs undergoing TPLO and specialty college, time of board certification, and employment sector.

	Percentage of Respondents			
	PNB	LE	PI	Measure of Association
Specialty College				
ACVAA (n=97)	75%	24%	1%	p=0.283
ECVAA (n=44)	86%	14%	0%	
Time of Board Certification				
<1 year (n=19)	74%	26%	0%	p<0.001
1-5 years (n=39)	97%	3%	0%	
6-10 years (n=35)	86%	14%	0%	
11-20 years (n=32)	66%	34%	0%	
>20 years (n=16)	50%	44%	6%	
Employment Sector				
Private Practice (n=74)	87%	12%	1%	p=0.003
Academia (n=64)	73%	27%	0%	
Retired (n=2)	0%	100%	0%	
Locum (n=1)	0%	100%	0%	

Table 3. Risks, side effects, and perceived duration of action of PNB, LE, and PI when used as the sole locoregional method of pelvic limb anesthesia in dogs undergoing TPLO.

	Percentage of Respondents (<i>n=141</i>)		
	PNB	LE	PI
Lower risk	21%	20%	59%
Lower intra-op rescue	57%	42%	1%
Lower post-op rescue	54%	41%	5%
Lower adverse side effects	75%	4%	21%
Best duration of action	38%	54%	8%

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