ULTRASOUND-GUIDED FEMORAL AND SCIATIC NERVE BLOCKS IN DOGS

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Thesis submitted for the degree of Masters of Veterinary Medicine to the University of Glasgow
College of Medical, Veterinary and Life Sciences
February 2019

SUMMARY

Femoral and sciatic nerve blocks are an effective method to provide analgesia to the stifle of dogs undergoing orthopaedic surgery. Different modalities can be used to guide location of needle placement at the target nerve such as blind technique, electrolocation and ultrasound-guidance. The method that has demonstrated the most accuracy, speed of block performance and lowest required local anaesthetic volume of injection to achieve a successful nerve block is ultrasound-guidance.

Anatomical studies in dog cadavers have investigated several approaches to the femoral and sciatic nerves; such as the lateral distal iliac approach to the sciatic nerve and ventral suprainguinal approach to the femoral nerve within the iliopsoas muscle. Previous studies have reported injection volumes as low as 0.1 mL kg^{-1} for the femoral, and 0.05 mL kg^{-1} for the sciatic nerve. A cadaver study was undertaken with injection of new methylene blue using the ventral suprainguinal block of the femoral nerve, and the lateral distal iliac approach to the sciatic nerve in six dogs. This preliminary investigation found injection volumes of less than 0.1 mL kg^{-1} at the femoral nerve could provide successful coverage of dye at this location. The volume of injectate at the sciatic nerve could not be reduced below those values previously recommended.

To assess if this finding was replicated in living dogs a clinical trial was undertaken. Healthy dogs scheduled to undergo orthopaedic surgery of the stifle under general anaesthesia were randomised into two treatment groups to receive levobupivacaine; low dose group (LD) of 0.05 mL kg^{-1} for femoral nerve and 0.05 mL kg^{-1} for sciatic nerves and high dose (HD) group 0.1mL kg^{-1} for the femoral and 0.05 mL kg^{-1} for the sciatic nerve. Intraoperative cardiovascular parameters were monitored during surgery, if more than 25 % increase from pre-surgical values was seen rescue analgesia was administered. During the postoperative period dogs were pain scored at regular intervals.

After statistical analysis, groups were found to be similar for preoperative and intraoperative factors, and postoperative pain scores. In both the LD and HD groups it was not possible to completely prevent the noxious response to surgery. In the postoperative period dogs appeared to have good pain relief, with low rescue analgesic requirements. In cases where an intraoperative cardiovascular response had been observed and treated, dogs still had good pain relief up to 10 hours in the postoperative period.

In conclusion, this is the first clinical trial of the ventral suprainguinal femoral nerve block, in combination with the sciatic nerve block. This technique can provide intraoperative analgesia for dogs undergoing orthopaedic surgery of the stifle, but complete sensory blockade was not consistently achieved. However, in cases where an intraoperative cardiovascular response is seen, dogs may still have good pain relief for up to 10 hours in the postoperative period without requirement for further opioid analgesia. Our cadaver study showed volumes less than those previously reported should provide anaesthesia of the femoral nerve, but this was not borne out completely in a clinical trial where several elements of block success (duration and completeness) were tested.

We recommend that cadaver studies be followed up by clinical trials to accurately assess the clinical benefit of locoregional techniques. Due to the inconsistent intraoperative affect we observed, in a clinical setting we recommend using a local anaesthetic injection volume higher than those used in this study, such as 0.2 ml kg^{-1}, when using the ventral suprainguinal approach to the femoral nerve, as per the original reporting of this block, because a higher dose may provide a more consistent affect. Finally, we recommend a clinical trial comparing the ventral suprainguinal approach to the femoral nerve, to other techniques used to block this nerve. This would establish the most effective method to provide sensory blockade at the femoral nerve.

TABLE OF CONTENTS

LIST OF CHAPTERS

LIST OF CHAPTERS CONTINUED

LIST OF TABLES

LIST OF FIGURES

LIST OF FIGURES CONTINUED

ACKNOWLEDGEMENTS

I would like to express my sincerest thanks to Andy Bell for the opportunity to perform this work and for his valuable guidance, encouragement, patience and friendship throughout this work and my residency training at Glasgow Vet School.

I would also like to express my gratitude to Dr Pat Pawson for her teaching, support and guidance throughout this work and my residency.

Thank you to Professor Sandra Corr, William Marshall, Cameron Broom, Elena Addison, Javier Rincon Alvarex and Simone Anesi, for their support and assistance recruiting patients for the clinical trial stage of our study.

I would also like to thank Alan Purvis for his assistance in sourcing cadaver material, without which this project would not have been possible.

Thank you to Chris Miller, Hamaseh Tayari, Ilaria Petruccioni, Tyfane Yamaoka and Eleanor Holden for their patience in letting me take more than my fair share of TPLO cases and their encouragement during tough times.

Finally, I would like to thank my fiancée Chiara Giannasi for her never-ending support and positive attitude, and for letting me study my residency and masters 400 miles apart from each other.

LIST OF ABBREVIATIONS

ABP	Arterial blood pressure
cm	Centimetre
CMPS-SF	Short form composite measure pain scoring assessment
CNS	Central nervous system
ECG	Electrocardiogram
$EtCO_2$	End-tidal carbon dioxide
FÉ-ISO	End-tidal isoflurane
Fixed	Fixed volume group
FN	Femoral nerve
f_R	Respiratory rate
FSNB	Femoral and sciatic nerve block
G	Gauge
USG	Ultrasound-guided group
HD	High dose group
LD	Low dose group
HR	Heart rate
hr	Hour
hr^{-1}	Per hour
IBP	Invasive blood pressure
IM	Intramuscular
IV	Intravenous
kg	Kilogram
kg^{-1}	Per kilogram
LA	Local anaesthetic
mA	Milliamps

mcg	Microgram
mcg kg^{-1} hour^{-1}	Micrograms per kilogram per hour
mcg kg^{-1} minute^{-1}	Micrograms per kilogram per minute
MEAV	Mean effective anaesthetic volume
mg	Milligram
MHz	Megahertz
mL	Millilitre
mm	Millimetre
MSC	Minimum stimulating current
NIBP	Non-invasive blood pressure
NMB	New methylene blue
NSAIDs	Nonsteroidal anti-inflammatory drugs
PNB	Peripheral nerve blocks
PSI	Pounds per square inch
SaN	Saphenous nerve
SD	Standard deviation
SN	Sciatic nerve
SSPCA	Scottish Society for the Prevention of Cruelty to Animals
T0	Cutaneous incision
T1	Incision of the joint capsule
T2	Periosteal stimulus
T3	Osteotomy of the tibia
T4	Cutaneous suture
Tb	15 minutes before the start of surgery
TPLO	Tibial plateau levelling osteotomy
<	Less than
>	More than
≥	More than or equal to

CHAPTER 1: ULTRASOUND-GUIDED FEMORAL AND SCIATIC NERVE BLOCKS IN THE DOG – A LITERATURE REVIEW

Introduction

Pain is classically described as 'an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of tissue damage' (International Association for the Study of Pain, 2015). Surgical stimuli from tissue manipulation and damage activate peripheral nociceptors inducing acute pain. The effects of acute pain can manifest physiologically as tachycardia, arterial hypertension, tachypnoea, cardiac arrhythmias, hyperglycaemia, urinary retention, catecholamine secretion, and decreased immune function (Schroeder, 2013). Use of local anaesthesia is an effective modality of providing perioperative analgesia and preventing pain (Campoy 2012a).

In 2005 Wilke et al. reported that approximately 160,000 canine stifle surgeries are undertaken each year the USA alone, in the nearly 15 years since this study this number is likely to be higher. Research into both the surgical and locoregional anaesthesia techniques for these procedures has been active in recent years. Many novel research studies have investigated peripheral nerve blocks (PNB) of the stifle, such as psoas compartment block from a pre-iliac approach, ventral suprainguinal approach to the femoral nerve, and paravertebral plexus and sciatic nerve blocks (Campoy et al., 2010, 2008; Echeverry et al., 2012; Portela et al., 2013b). This literature review describes those techniques that relate to the locoregional anaesthesia of the stifle, appraises the success rates of each and discusses research opportunities in this area.

Locoregional anaesthesia

Locoregional anaesthesia is the process of depositing local anaesthetic drugs around nerves in the area, or the nerves supplying, the surgical field to prevent noxious stimulus transmission and the pain response during and after surgery. Epidural and spinal anaesthesia use deposition of local anaesthetics in the epidural space, or around the spinal nerves to provide non-specific anaesthesia of nerves arising from the location where injectate is deposited; most commonly in the caudal half of the body. Peripheral nerve blocks (PNB) provide a selective modality to anaesthetise target nerves which innervate specific areas of the body usually a single limb or part of it.

Pharmacology of local anaesthetics

Afferent (sensory) neurons are nerve fibres in the periphery of the body, classified by the types of stimulus they respond to; these may be low threshold or high threshold. Low threshold A-beta myelinated fibres convey touch, vibration and pressure. High threshold myelinated A-delta fibres rapidly convey thermal, chemical, or mechanical nociceptive stimuli and mediate sharp pain. Un-myelinated C-fibres are high threshold but transmit nociceptive stimulus slowly, and are responsible for slow dull or burning types of pain. Efferent (motor) fibres are responsible for muscle control and may be divided into general visceral or general somatic efferent fibres. General somatic efferent fibres innervate skeletal muscle groups and are anaesthetised concurrently with sensory (efferent) fibres, however the duration of motor blockade may not be the same as seen for sensory blockade (Bell, 2018).

Prevention of conduction of nociceptive stimuli from the nociceptor to the central nervous system is the mechanism by which local anaesthetics cause anaesthesia; by inactivation of sodium channels in nerve cell membranes (Martin-Flores, 2013). The axon cell membrane potential is negative, due to a sodium-potassium ATPase pump that transports sodium into the extracellular space and potassium into the cell. Generation of an action potential requires activation of voltage-gated sodium channels causing an influx of sodium into the cell. Voltage-gated sodium channels have three states; 1) activated and open at the start of an action potential, 2) closed allowing the re-polarisation of the cell membrane 3) resting at the point where the resting membrane potential is restored and an action potential can be propagated again. Local anaesthetics bind to voltage-gated sodium channels in their resting state meaning cells will not depolarise, and action potentials cannot be propagated along the axon. This mechanism is responsible for stopping propagation of nociceptive stimuli along the axon (Martin-Flores, 2013). Local anaesthetics can be classified into two groups, aminoesters and aminoamides. In modern practice, the most commonly used group are the aminoamides such as lidocaine, ropivacaine, bupivacaine and levobupivacaine. Regardless of class, the mechanism of action is common to all local anaesthetics.

Potency, onset time and duration of effect are variable between local anaesthetic agents and are dependent on the physical and chemical properties of individual drugs. Lipophilicity determines the ease of which a molecule can penetrate the cell membrane and is a major determinate of potency, with potency increasing with lipophilicity. Classically, an onset time of five to ten minutes and a duration of one to two hours is stated for lidocaine, while bupivacaine and levobupivacaine have an onset of approximately thirty minutes and a duration of four to six hours (Martin-Flores, 2013). However, experimental studies have found that the concentration of the drug also has a significant effect on duration of locoregional anaesthesia. One study compared 0.25, 0.5 and 0.75 % bupivacaine and levobupivacaine, and found that while onset of analgesia was similar, intensity and duration of blockade was significantly shorter with 0.25% than 0.75% bupivacaine and levobupivacaine (Gomez de Segura et al., 2009).

Potentiating local anaesthetics with Adjuvants

Other drugs have been added to local anaesthetics to augment or increase the duration of sensory blockade. Adrenaline has been used for its vasoconstrictive action causing delayed systemic uptake of local anaesthetics and increasing the length of the block. This drug also has an action on alpha adrenoreceptors which has been shown to provide analgesia when used alone for epidurals in human patients (Martin-Flores, 2013).

Alpha-2 adrenoreceptor agonists such as clonidine and dexmedetomidine have been shown to provide spinal and supraspinal analgesia in dogs undergoing pelvic limb surgery. Alpha-2 agonists have an inhibitory effect on transmission of nerve impulses, although the exact mechanism for the effect is not known (O and Smith, 2013). Furthermore, the vasoconstrictive action of these drugs can prolong duration of local anaesthetic blocks.

Bartel et al. (2015) investigated the effect of femoral and sciatic nerve blocks with bupivacaine and dexmedetomidine, compared to bupivacaine and buprenorphine epidurals in healthy dogs undergoing pelvic limb orthopaedic surgery. While under general anaesthesia end-tidal isoflurane (FÉ-ISO), non-invasive blood pressure (NIBP), *f*R (respiratory rate) and heart rate (HR) were monitored. In the postoperative period sedation scores, pain scores, postoperative opioid consumption and urinary retention was observed and recorded. This study found no adverse effects and no significant difference between the groups for any of the observed variables. The results of this study provide evidence that using bupivacaine and dexmedetomidine is a safe treatment option providing perioperative analgesia equal to that of bupivacaine and buprenorphine epidural. However, the study design lacks a bupivacaine only femoral and sciatic nerve block control group which would have been a more clinically useful comparison (Bartel et al., 2015).

O and Smith (2013) investigated three different epidural anaesthesia protocols in healthy dogs undergoing orthopaedic procedures in the pelvic limb. Dogs received bupivacaine alone, bupivacaine and morphine or bupivacaine and dexmedetomidine 4 mcg kg^{-1}. This study recorded FÉ-ISO and decreased the inspired concentration by 0.2 % every ten minutes until gross purposeful movement was noted by the anaesthetists, at which point the depth of anaesthesia was deepened using propofol or 1:1 ketamine and diazepam IV. Postoperative pain scores were recorded for all dogs, and found that scores were higher in the bupivacaine only group when compared to other treatments. Manual expression of the urinary bladder was performed on each patient just prior to cessation of inhalant anaesthesia delivery. No difference in pain scores between the groups was seen in the bupivacaine and morphine, and the bupivacaine and dexmedetomidine groups. However, the bupivacaine and dexmedetomidine group did have a shorter time to urination and longer motor blockade than the other treatment groups. O and Smith concluded using bupivacaine, and dexmedetomidine is an effective treatment to provide perioperative analgesia and reduced the incidence of urinary retention in the postoperative period (O and Smith, 2013). The use of dexmedetomidine is not supported by all studies however. A study assessing the onset and duration of anaesthesia provided by ropivacaine and dexmedetomidine, or ropivacaine alone for femoral and sciatic nerve blocks in dogs found no significant difference in onset or duration of sensory blockade (Trein et al., 2016). Thus, the evidence in the veterinary literature for inclusion of dexmedetomidine for locoregional anaesthesia in dogs is equivocal, further studies are required to fully investigate use of this adjuvant for locoregional anaesthesia.

In humans, the use of dexmedetomidine has also been shown to increase block duration. In one meta-analysis of nine randomised controlled studies investigating brachial plexus blocks (up to 1 mcg kg^{-1}) and epidural (up to 0.2 mcg kg^{-1}) patients treated with dexmedetomidine had an increased duration of sensory blockade and an increase in time to first request of opioid analgesia. The review went on to discuss papers on safety of dexmedetomidine. Demyelination was observed in rabbits when using dexmedetomidine in epidurals (up to 6.1mcg kg^{-1}); although these doses were considerably higher than those used clinically in humans. Although the authors of this review concluded dexmedetomidine is a potential adjuvant for local anaesthesia, they also concluded there is currently insufficient safety data to recommend its use clinically until further safety studies have been carried out (Abdallah and Brull, 2013).

Toxicity and complications

Complications can occur with locoregional anaesthetic techniques, although in veterinary species the exact incidence of morbidity and mortality are not known, they are considered to be rare. Adverse effects when using locoregional anaesthesia include systemic toxicity that may manifest as nystagmus, seizures, hypotension, bradycardia, ventricular tachycardia, nausea, generalised CNS depression, coma and death. Direct nerve damage can also occur is also known to cause sensory and motor deficits (O and Smith, 2013; Martin-Flores, 2013). Delayed hair growth over the site of epidural skin preparation is also reported (Kalchofner Guerrero et al., 2014). Finally, urinary retention is a known secondary effect when using epidural techniques.

Systemic toxicity results from the same mechanism of voltage-gated sodium ion channel inhibition seen in peripheral nerves. Iatrogenic intravascular injection is the most likely event to cause high plasma concentrations and consequently toxicity. For this reason, it is accepted good practice that when injecting local anaesthetics the operator should first aspirate to check for blood in the hub of the needle, to provide an indication if intravascular needle placement has occurred. Should this happen the needle can be slightly withdrawn and replaced, and the process repeated until no blood is seen in the hub of the needle (Trimble and Leece, 2015). Systemic absorption depends on the site of injection. In humans, plasma concentration of local anaesthetic agents is higher with intercostal nerve blocks than epidural, brachial plexus or sciatic nerve blocks (Covino and Vasallo, 1976). One experimental study established the toxic threshold at which seizure activity in dogs was observed after intravenous injection. This was found to be 20.8 mg kg^{-1} for lidocaine, and 4.3 mg kg^{-1} for bupivacaine (Feldman et al., 1989). Maximal injection doses in dogs of 2 mg kg^{-1} for bupivacaine and levobupivacaine and 6 mg^{-1} kg^{-1} for lidocaine are commonly reported in the clinical pharmacology texts (Martin-Flores, 2013).

In addition to systemic effects, direct nerve damage can also result from mechanical trauma of nerves at the injection site. An experimental study in dogs comparing perineural with intraneural injection investigated the direct effect intraneural injection has on peripheral nerves. Dogs were anaesthetised and the sciatic nerve exposed, a 25 g needle was introduced intraneurally or perineurally; then injection of lidocaine and adrenaline was carried out, injection pressure was measured with an inline manometer. Perineural injections had pressures of < 4 pounds per square inch (PSI), whereas intraneural injections gave pressures of 4-25 PSI. Dogs were recovered from anaesthesia and subject to serial neurological assessments. Normal nerve function returned within three hours after all low-pressure injections, however persistent motor deficits were noted for 7 days in all dogs that had undergone injection pressures >25 PSI. After 7 days dogs were euthanised and the sciatic nerve assessed histologically; this showed destruction of the neural architecture and axon degeneration in all nerves receiving high injection pressures (Hadzic et al., 2004). The above study demonstrates potential for severe damage to nerves and provides evidence for the accepted good practice of ensuring resistance is not felt when injecting to prevent intraneural injection.

Another complication that is specific to epidural anaesthesia is urinary retention. Comparison of postoperative urinary retention after epidural or femoral and sciatic nerve block (FSNB) in dogs undergoing pelvic limb surgery was assessed by Campoy et al., (2012a). This study showed a reduction of urinary retention in the FSNB group and is discussed in more detail below. Although the findings of this study were statistically significant, more controlled studies are required to definitively describe the complication rates of these two techniques.

Although severe complications are possible, very few severe adverse events resulting from peripheral nerve block techniques are reported. In a study of 95 dogs, one (1.05%) showed bilateral pelvic limb paralysis one hour after nerve block; these signs were fully resolved five hours after block (Vettorato et al., 2012). Systemic local anaesthetic toxicity, or direct nerve damage may occur when using peripheral nerve blocks or epidural techniques. However, postoperative urinary retention is only reported when epidural anaesthesia is used (Gurney and Leece, 2014).

Anatomy of the hind limb relevant to regional anaesthesia of the stifle joint

Depositing local anaesthetic drugs around the femoral and sciatic nerves can provide local anaesthesia to the entire hind limb distal to the gluteal region (Gurney and Leece, 2014). The hind limb is innervated from the lumbar and sacral plexuses originating from the L3-S2 ventral nerve routes.

The lumbar plexus is composed of nerve routes from L3-L6 and contains six nerves; the ilioinguinal, lateral femoral, femoral (FN), cutaneous, genitofemoral and obturator nerves. The FN arises from L3-L6 vertebrae then runs through the centre of the iliopsoas muscle together with the external iliac artery and vein. The iliopsoas muscle sits within the quadratus lomborum and psoas minor muscles. This group of muscles form a sheath around the femoral nerve called the psoas compartment (Campoy and Mahler, 2013; Dyce, et al., 2002; Gurney and Leece, 2014; Portela et al., 2013b). The FN then exits the iliopsoas muscle and runs through the femoral triangle as seen in figure 1.1.

After exiting the iliopsoas, the FN branches. Authors differ on the location they report branching of the FN into the saphenous nerve (SaN) with Gurney and Leece., (2014) reporting branching into the SaN within the distal iliopsoas. Campoy and Mahler (2013)., and Budras et al., (2007) state the SaN is given off at the level of the femoral triangle. Clinically there is variation between individuals, some branching more proximally in the iliopsoas and some distally to this in the femoral triangle. This has clinical significance when the role of the SaN is considered. The saphenous nerve innervates the medial cutaneous tissues of the hind limb from the stifle to the metatarsus, the sartorius muscle, and contributes to innervation of the stifle joint with the medial articular nerve (Campoy and Mahler, 2013; Dyce et al., 2002). Failure to block the SaN may result in partial failure of the nerve block, as discussed in more detail below. The FN runs through the femoral triangle cranial to the femoral artery and vein in a proximal to distal direction then enters the vastus medialis and rectus femoris muscles (Campoy and Mahler, 2013).

The sacral plexus is made up of nerve routes from L6-S1 and gives off four nerves. The pudendal, caudal cutaneous femoral, gluteal, and sciatic nerves (SN). The sciatic nerve originates from L6, L7 and S1 spinal nerve roots. It passes through the pelvis between the gluteus medius and gluteus profundus muscles and exits through the greater sciatic notch (Figure 1.2). After this, it passes caudally towards the coxofemoral joint and continues between the ischiatic tuberosity and the greater trochanter of the femur. At this point, it is covered by the muscles of the pelvis, with the gluteus profundus deep to-, and the gluteus medius and gluteus superficialis muscles superficial to it (Campoy and Mahler, 2013; Gurney and Leece, 2014). The SN continues distally caudal to the femur between the biceps femoris laterally and the semitendinosus medially; at this point, it divides into the tibial and peroneal nerves (Budras et al., 2007; Campoy and Mahler, 2013; Dyce et al., 2002; Gurney and Leece, 2014).

Innervation of the stifle joint

The medial, cranial and caudal aspects of the stifle are innervated by the medial articular nerve, a branch of the SaN; which originates from the femoral nerve. The posterior and posterior medial aspects of the stifle are supplied by the posterior articular nerve, a branch of the tibial nerve; which originates from the sciatic nerve. Finally, the lateral collateral ligament and lateral joint capsule are innervated by the lateral articular nerve; a branch of the peroneal nerve, which originates from the sciatic nerve (Campoy and Mahler, 2013). This means the main sensory nerves supplying the stifle originate from the sciatic and femoral nerves; sensory blockade of these nerves will provide anaesthesia of the stifle which can facilitate surgery of the joint (Campoy et al., 2012b).

Block modalities

There are four main classes of technique used to facilitate local anaesthetic blocks i.e. facilitating identification of the nerve and the deposition of local anaesthetic in close proximity; blind technique, electrolocation, ultrasound-guidance and a combined ultrasound-guided /electrolocation approach.

Blind technique

Blind approaches require identification of anatomical landmarks to guide the angle and depth of needle placement to reach the target nerve. This modality requires no specialist equipment or training, so is often utilised for superficial techniques such as dental blocks.

Electrolocation

Electrolocation uses a device to create an electrical field around the tip of a needle. As with the blind technique, the needle is passed into the tissue at the anticipated location of the target nerve. When the electrical current surrounding the needle comes into proximity with the nerve it will depolarise, and if it is a motor nerve, the muscle the nerve innervates will contract, this is referred to as a twitch. Electrolocation needles are insulated with the exception of the tip, so only the tissues at the tip are stimulated; giving an accurate indication of their position. The distance of the needle tip from the target nerve is inversely proportional to the current in milliamps (mA) required to elicit the visible twitch seen, as dictated by Coulomb's law. In other words, the electrical current needed to stimulate a nerve is less the closer the needle is to the nerve (Raw et al., 2013).

The needle is placed in the direction of the target nerve using an initial current of 1-1.5 mA. When a twitch by a muscle group innervated by the target nerve is elicited the needle can be moved to improve the intensity of the twitch. At this point the current is gradually reduced until the twitch is absent; the current is subsequently increased to just above the setting where the twitch was lost (this is called the minimum stimulating current [MSC]), and the needle moved to improve the intensity of the muscle contractions. The process is repeated until the twitch is present at 0.4 but lost at 0.2 mA; twitches present at 0.2 mA can indicate intraneural needle placement (Raw et al., 2013).

The benefits of using electrolocation are that the accuracy of needle placement is improved compared to blind technique alone. Furthermore, eliciting a twitch of a muscle innervated by the target nerve provides confirmation the needle tip is near the nerve of interest. However, there are disadvantages to using electrolocation. Unless the needle is placed next to the target nerve on the first attempt the modality necessitates multiple needle passes, this may cause tissue damage especially if the procedure is protracted. Finally, in some cases, close proximity to a nerve as suggested by a strong twitch at a low MSC can be confounded if the needle tip is behind a fascial plane. This will mean the local anaesthetic is deposited close to the nerve but will not contact it (as the facia will obstruct the diffusion of the local anaesthetic) and thus the block will fail.

Recent studies have built on our understanding that close proximity to the target nerve (even when in the same facial plane) may not result in a strong muscular twitch. Portela et al., (2013a) assessed the needle to nerve relationship when using electrolocation. With dogs anaesthetised and the sciatic nerve approached distal to the ischium, electrostimulation of the SN was commenced with a reducing current from 2.0, 1.5, 1.0 and 0.5 mA. The needle to nerve distance was measured with each current using ultrasound. The needle was then moved to contact the nerve and the MSC determined. Finally, the needle was introduced intraneurally with ultrasound guidance to give a needle to nerve contact MSC. The results of this study showed that electrical current decreased as the needle was moved closer to the nerve, as would be expected by Coulomb's law. When the needle contacted the nerve, a motor response could not be reliably achieved; this may mean that the absence of a twitch below 0.4 mA is not a reliable indicator of non-intraneural needle placement (Portela et al., 2013a).

Ultrasound-guidance

Ultrasound-guidance allows real-time visualisation of the needle, and structures such as muscle, nerves, blood vessels and fascia (Seco et al., 2013). This technique uses anatomical landmarks and visualisation of the target nerve, rather than muscular twitches, to confirm needle placement. Ultrasound guidance can be used alone but is most commonly used in combination with electrolocation to visualise then direct the nerve locator needle in the direction of the target nerve. The ultrasonographic appearance of nerves is unique with a hyperechoic outer surface with a hypoechoic centre. This aids identification when several similar structures are in close proximity, such as blood vessels or fascia. Ultrasound offers advantages over electrolocation alone. Needle placement can be more precise due to visualisation of the needle in relation to the target nerve. Likelihood of vessel laceration is less likely because these structures can be directly visualised. With this technique deposition of local anaesthetic can be visualised in real-time, adding the potential to reduce the volume of injectate required to achieve successful sensory blockade (Campoy et al., 2010). Finally, block performance time can be reduced when ultrasound is used in combination with nerve location, compared to that of electrolocation alone (Williams et al., 2003).

Anatomical studies to investigate locoregional approaches to the femoral and sciatic nerves

Anatomical studies are essential to establish the position and landmarks of target nerves. There have been many studies investigating different approaches to the nerves of the hind limb. A measure of success is the length of staining of the target nerve with new methylene blue (NMB) dye, following injection and dissection. It is important at this point to discuss why length of nerve stained is used as measure of success in anatomical studies. Raymond et al. (1989) used an ex-vivo chamber model where the length of nerve exposed to lidocaine was altered while the concentration (38 mg mL^{-1}) of lidocaine was kept the same. Nerve impulses were initiated and measured passing through the nerve to establish the degree of sensory blockade. The minimum length of nerve exposure to local anaesthetics recommended by this study was 2 cm. In vitro studies suggest that shorter lengths of nerve can achieve a successful block; however, the concentration of local anaesthetics needs to be very high. For example, the concentration of local anaesthetics required to block 50% of impulses decreased by half as length was increased from 6 to 25 mm (Raymond et al., 1989). The ≥ 2cm exposure length recommended by this study has become convention to indicate successful nerve staining when attempting locoregional anaesthesia in anatomical studies (Campoy et al., 2008; Echeverry et al., 2012; Gurney and Leece, 2014; Portela et al., 2013b).

Campoy et al. (2010) used ultrasound in combination with electrolocation to perform local blocks of the femoral and sciatic nerves. This anatomical study used a set volume of lidocaine combined with NMB of 0.1 mL kg^{-1} for the FN and 0.05 mL kg^{-1} for the SN. The marker of success was staining ≥ 2cm nerve staining with NMB. A 7-12 MHz linear array ultrasound transducer was used to visualise the target nerves and confirm needle placement in the perineural area. For the femoral nerve, an inguinal approach was used with the limb adducted then scanned ultrasonographically to locate the femoral nerve cranial to the femoral artery. The needle was inserted in plane towards the FN and confirmation of location of the needle was given by eliciting a twitch at an MSC of 0.4 mA, but not at 0.2 mA, lidocaine and NMB solution was then injected (Campoy et al., 2010). Staining of the femoral nerve was > 4 cm in all blocks.

For the sciatic block dogs were positioned in lateral recumbency with the leg to be blocked extended in a neutral position. The gluteal area and the proximolateral aspect of the thigh were clipped and aseptically prepared. Anatomical landmarks of the ischiatic tuberosity and the greater trochanter of the femur were identified, then the probe placed on the lateral aspect of the thigh just distal to these locations. Scanning in short axis showed the structure consistent with the sciatic nerve medial to the biceps femoris fascia and cranial to the fascia of the semimembranosus muscle. A 50 mm needle was inserted in plane with the transducer just distal to the ischiatic tuberosity and advanced in a cranial direction toward the SN (Figure 1.3) until a twitch was elicited (plantiflexion or dorsiflexion of the foot) at a MSC of 0.4 mA but not at 0.2 mA. Lidocaine and NMB 0.05 mL kg^{-1} were injected. The injection was observed in real time. Distance from the transducer to the centre of the sciatic nerve was recorded prior to injection; this was found to be 1.5-1.9 cm. This distance was measured in two of the four dogs, but it was not possible to do sciatic nerve blocks due to requirements of other studies using the same animals. The dogs were then euthanised and dissected. Circumferential staining of sciatic nerves was found to be 2.8 ± 0.3 cm (Campoy et al., 2010).

This study recommended ultrasound-guidance to be an accurate method of depositing local anaesthetic for femoral and sciatic nerve blocks. However, due to small numbers the authors went to on say clinical studies are required to properly assess the technique. Although the findings of this study are a useful foundation for this technique, only four sciatic nerve blocks were undertaken, with only three of these being successful.

Echeverry et al., (2012) undertook an anatomical study using an ultrasound-guided suprainguinal approach to the femoral nerve (Figure 1.4) to inject 0.3 mL kg^{-1} of NMB. This study found the volume of 0.3 mL kg^{-1} provided 6.2 (5-6.8) cm of circumferential staining. This study went to attempt the block in healthy live dogs neurological deficits were found after injection of 0.2 ml kg^{-1} lidocaine, but this was not assessed in a clinical context. Campoy et al. 2008 used a volume of 0.1, 0.2 and 0.4 mL kg^{-1} for an electrolocation approach to the FN in the psoas compartment and found no statistical difference between the injection volumes and the likelihood to achieving a successful staining of ≥ 2 cm (Campoy et al., 2008). Although Echeverry., (2012) and Campoy., (2010) recommend injection volumes of 0.3 and 0.1 mL kg^{-1} of NMB respectively may be sufficient to stain the FN in the psoas compartment, neither injection volume was small enough to give an indication of a lower threshold which may be used.

Portela et al., (2013b) conducted an anatomical and clinical study investigating a novel lateral pre-iliac approach to the femoral nerve in the psoas compartment. This study was conducted in 3 parts.

The cadaver study used dissection of the FN from the thigh through the femoral triangle, to the origin of the nerve to establish its path. This dissection enabled selection of anatomical landmarks for the approach to the femoral nerve in the psoas compartment. Next, the study used electrolocation of the FN in the psoas compartment to elicit a twitch of the quadriceps and extension of the stifle at 0.5 mA but not at 0.2 mA; 0.1 mL kg^{-1} of lidocaine and NMB was then injected in the left and right psoas compartments of two dogs. Following euthanasia, dissection and measurement of femoral nerve circumferential staining was 7.25 (6-8) cm; no staining at the intervertebral foramina was noted (Portela et al., 2013b).

Campoy et al. (2008) undertook a study investigating the volume needed to achieve successful staining of the lumbar plexus and sciatic nerve in the dog. The study used electrolocation with a lateral approach to the lumbar plexus at the level of the fifth lumbar vertebrae, 1-2 cm lateral to the midline. The measure of success was staining ≥ 2 cm. Dogs were randomised into groups, anaesthetised, blocks carried out then euthanised and dissected immediately. For the lumbar plexus, block dogs received either 0.1, 0.2 or 0.4 mL kg^{-1} lidocaine and NMB. No statistically significant difference in staining with change in volume of injectate was observed. However, more dogs in the 0.1 and 0.2 mL kg^{-1} group had insufficient staining of the femoral nerve compared to only one partial staining (1 cm) in the 0.4 mL kg^{-1} group. This study recommended using 0.4 mL kg^{-1} of dye to achieve a successful staining of the femoral nerve within the psoas compartment.

The study noted an epidural staining in 8.7% (n = 2) of dogs using this approach. Furthermore, traces of dye were found in the abdominal cavity of two dogs. There was concern that clinical use of this approach has the potential for epidural leakage, which may cause anaesthesia of the contralateral limb and sympathetic blockade in the hindlimbs which may lead to hypotension (Campoy et al., 2008; Otero and Campoy, 2013).

This study also investigated a lateral distal ischiatic approach to the sciatic nerve immediately proximal to the greater trochanter of the femur and the ischiatic tuberosity (Campoy and Mahler, 2013). Lidocaine and methylene blue 0.05, 0.1 and 0.25 mL kg^{-1} respectively were administered. All volumes provided successful staining in all but two individuals. Seven out of eight dogs in the 0.25 mL kg^{-1} group had staining in excess of 4 cm. Due to successful staining in all groups, this study recommended using 0.05 mL kg^{-1} to block the sciatic nerve at this location using a nerve locator (Campoy et al., 2008).

In summary, anatomical studies provide the basis for assessing location of target nerves, their anatomical interaction with fascia, muscle and vessels, and give an indication if techniques merit assessment in a clinical context.

Clinical studies to assess efficacy of femoral and sciatic nerve blocks

Campoy et al., (2012a) carried out a clinical study assessing the efficacy of bupivacaine FSNB compared to morphine and bupivacaine epidurals in dogs scheduled to undergo tibial plateau levelling osteotomy (TPLO) under general anaesthesia. Dogs were anaesthetised then randomised to one treatment group. This study used an inguinal approach to the femoral nerve. Sciatic nerve blocks were achieved using a proximal approach as described above by Campoy et al. (2008). Electrolocation was used to confirm needle placement close to the target nerve, and a volume of 0.1 mL kg^{-1} 0.5 % bupivacaine was used for both femoral and sciatic blocks. For epidural anaesthesia, the study used 0.5 mg kg^{-1} bupivacaine and 0.1 mg kg^{-1} morphine (made up to a total volume 0.2 mL kg^{-1} by diluting with 0.9% saline). Success of each treatment was assessed using intraoperative haemodynamic stability, postoperative pain scores, opioid consumption and incidence of urinary retention. If hypertension or tachycardia were detected rescue analgesia was administered. This study reported dogs treated with epidurals had significantly lower intraoperative FÉ-ISO and mean arterial blood pressure (MAP), but significantly higher postoperative opioid consumption and incidence of urinary retention. This study recommended femoral and sciatic nerve blocks as an alternative to epidural anaesthesia, due to the reduction in incidence of urinary retention and postoperative opioid requirement this technique can offer (Campoy et al., 2012a).

Caniglia et al. (2012) also assessed the perioperative analgesia provided by FSNB or epidural with bupivacaine. This study found that intraoperative and postoperative requirement for rescue analgesia was similar in both groups, concluding that FSNB provided analgesia similar to epidural techniques. These studies set the foundation that local anaesthetic blocks can provide equal analgesia to epidurals.

Further to the above study, Campoy et al., (2012b) published a case series of 10 dogs undergoing procedural sedation for orthopaedic surgeries of the stifle and tibia. Dogs were sedated using propofol and dexmedetomidine by intravenous infusion, without endotracheal intubation. All dogs received FSNB using ultrasound-guidance combined with electrolocation using the technique described by Campoy et al. (2012a) injecting 0.1 mL kg^{-1} 0.5 % bupivacaine. Cardiovascular parameters including NIBP, *f*R and HR, administering rescue opioid analgesia if these values increased more than 20 % above baseline. None of the dogs displayed signs of breakthrough noxious stimulus during surgery, and supplementary opioid analgesia was not required until ten hours after recovery from anaesthesia. This study provides further evidence for the validity for use of ultrasound and electrolocation for femoral and sciatic nerve blocks (Campoy et al., 2012b)

After the anatomical study of the lateral pre-iliac approach to the femoral nerve in the psoas compartment by electrolocation Portela et al., (2013) went on to assess the effect of the block in a clinical trial. Fifteen dogs were treated using a lateral pre-iliac approach to the FN in the psoas compartment and a sciatic block as described by Campoy et al., 2008. Both blocks used 0.1 mL kg^{-1} of 0.5% ropivacaine. The study monitored FÉ-ISO, IBP, *f*R, HR and postoperative pain scores, giving additional opioid analgesia if values increased more than 25% from baseline. No cardiovascular response was observed in 13/15 dogs. The study recommended the lateral pre-iliac approach to the femoral nerve in the psoas compartment is possible using electrolocation and provides effective analgesia for dogs undergoing orthopaedic surgery on the stifle (Portela et al., 2013b).

This paper had a good sequential study design, with the basic cadaver dissection followed by in an in-vivo phase of the study providing a foundation for the clinical trial. This initial proof of concept gave the authors a good understanding of the technique, and justification that the project should be taken to clinical trial. However, the study used only one type of local block and had no control group. Thus, further studies are needed to assess the effectiveness of this block compared to other techniques of hind limb local anaesthesia.

The literature suggests ultrasound-guided femoral and sciatic nerve blocks, with or without electrolocation, can provide effective perioperative analgesia for orthopaedic surgery in the stifle of dogs. Injectate volumes of 0.05 mL kg^{-1} for sciatic and 0.1 mL kg^{-1} for femoral nerve blocks are effective although higher volumes have also been recommended. However, at this time no studies have investigated the use of lower volumes than 0.05 mL kg^{-1} for the SN and 0.1mL kg^{-1} for FN. Ultrasound-guided injection of 0.2 mL kg^{-1} provided successful staining of the FN within the psoas compartment as found by the anatomical study by Echeverry et al., (2012). However, this novel approach to the FN has not been assessed in a clinical trial and warrants further investigation.

We hypothesise that ultrasound-guidance would allow reduction of the volume of NMB required to achieve successful staining of the target nerve, below the minimum volumes currently recommended.

CHAPTER 2: ULTRASOUND-GUIDED FEMORAL AND SCIATIC NERVE BLOCKS IN THE DOG – A CADAVER STUDY

Introduction

Femoral and sciatic nerve blocks are an effective method to provide perioperative analgesia to dogs undergoing orthopaedic surgery of the stifle joint (Campoy et al., 2012a; Caniglia et al., 2012; Portela et al., 2013b). The lateral distal ischiatic approach to the sciatic nerve with ultrasound-guidance as reported by Campoy et al. (2010) has been shown to provide effective analgesia to the stifle joint when combined with an inguinal approach to the femoral nerve. The ultrasound-guided ventral suprainguinal approach to the femoral nerve within the psoas compartment reported by Echeverry et al., (2012) has shown encouraging results in cadaver based pre-clinical studies. This approach to the femoral nerve facilitates sensory blockade prior to branching of the saphenous nerve, and can offer the advantage of a more complete nerve block to the stifle for patients undergoing surgery of this region (Campoy and Mahler, 2013; Dyce, et al., 2002).

Before undertaking clinical trials, cadaver studies indicate whether novel approaches or alterations to established techniques are likely to be successful (Campoy et al., 2008; Portela et al., 2013b). Assessment of successful injection location in cadaver studies is achieved with new methylene blue, with subsequent dissection of the area to assess the length of circumferential staining of the target nerve of ≥ 2 cm. Visualisation of circumferential spread of injectate around the target nerve is recommended as the marker of success when using ultrasound guidance for nerve block placement (Echeverry et al., 2012; Marhofer et al., 2014). In cadavers the lowest volumes of injectate reported for the ultrasound-guided suprainguinal approach to the femoral nerve is 0.2 mL kg^{-1}, and for the sciatic nerve 0.05 mL kg^{-1}, however volumes less than this have not been investigated (Campoy et al., 2010; Echeverry et al., 2012). When compared to electrolocation, human studies have found ultrasound-guidance has the advantages of reduced block placement time, increased accuracy of needle placement, shortened onset times, and reduced volume of local anaesthetic required to achieve a successful nerve block (Campoy et al., 2010; Williams et al., 2003). The aim of this study was to assess if ultrasound-guidance would allow reduction of the volume of NMB required to achieve successful staining of the target nerve, below the minimum volumes currently recommended.

Materials and methods

The study was approved by the University of Glasgow School of Veterinary Medicine Research Ethics Committee reference number 49a/15. Six non-client owned dog cadavers of various breeds were enrolled. Cadavers were obtained from the Scottish Society for the Prevention of Cruelty to Animals (SSPCA) after euthanasia for reasons unrelated to musculoskeletal or neurological disorders. The age of cadavers was not reported when cadavers were received from the SSPCA. Exclusion criteria were bodyweight less than 10 kg, trauma or advanced autolysis of the cadaver tissues. Each dog had two limbs, one of each received a fixed volume (Fixed) and the other the ultrasound-guided volume (USG) of injectate; this was randomised using GraphPad Prism (GraphPad Software, Inc. La Jolla, CA, USA. Cadavers were frozen at -20° Celsius then thawed for 24 hours prior to commencing investigations.

Sciatic Nerve

Cadavers were placed in lateral recumbency with the leg to be blocked uppermost in a neutral position. Hair was clipped over the gluteal and the proximal caudolateral thigh region; the skin was cleaned, and ultrasound gel applied over the lateral thigh region. An operator (the author) who was experienced in the use of ultrasound-guided locoregional anaesthesia carried out all nerve blocks. Ultrasonographic scanning of the sciatic nerve was performed using a Mindray 75L38EA 5-10 MHz linear ultrasound transducer with a Mindray DP-30Vet diagnostic ultrasound imaging system (Mindray Bio-Medical Electronics, Nanshan, Shenzhen, China). Once a transverse plane view of the sciatic nerve was obtained, the depth, gain, and focus position was adjusted to give optimal image quality to visualise the target nerve. An in-plane lateral distal ischiatic approach the sciatic nerve using the method described by Campoy et al., 2010 (Figure 1.3) with an insulated an echogenic locoregional anaesthesia needle (Stimuplex 50 mm 22 G, B. Braun Medical Ltd, Sheffield UK).

Treatment groups were as follows. The Fixed group received a set volume of 0.05 mL kg^{-1} NMB for the sciatic nerve block. In the USG group the stop point for the injection was decided by visualisation of circumferential anechoic echogenicity around the target nerve of approximately 2-5 mm, referred to as a doughnut sign (Figure 2.1) by the person carrying out the nerve block (the author) who was blinded to the volume of injection; Injection was carried out at a slow rate by another investigator (the supervisor). New methylene blue 2 % (Methylene Blue Hydrate; Janssen Pharmaceuticals, Geel, Belgium) was used as injectate for all blocks as reported by Campoy et al., (2008). After the doughnut sign had been visualised the volume needed to achieve this was recorded in each limb.

Femoral Nerve

Hair was clipped and skin cleaned over the caudal abdomen and lumbar regions. A transverse ultrasonographic image of the psoas compartment was then obtained, and image quality optimised to visualise the target nerve as stated above. The in-plane ventral suprainguinal approach to the femoral nerve as described by Echeverry et al., (2012) was used (Figure 1.4). The same equipment described above for the sciatic block was used for femoral nerve blocks. The Fixed group received a set volume of 0.1 mL kg^{-1} NMB for the femoral nerve block. In the USG group, the stop point for the injection was decided by visualisation of a doughnut sign by the person carrying out the nerve block, who was blinded to the volume of injection. Injection of NMB was carried out at a slow rate by another investigator and the volume of injectate used in each limb recorded.

Immediately after blocks were performed the skin on the lateral thigh was incised, and the biceps femoris was removed to enable visualisation of the sciatic nerve and surrounding structures (Figure 2.2). Then the ventral aspect of the lumbar region was dissected to expose the psoas muscle and visualise the femoral nerve (Figure 2.3). Nerves were dissected and removed from cadavers before the length of circumferential staining was measured. Success was deemed as circumferential staining of the target nerve with NMB $\geq$ 2 cm, deemed sufficient to produce a sensory blockade (Raymond et al., 1989).

Data analysis

Statistical analysis was carried out using SPSS (IBM Corporation, Armonk, New York, USA). The volume of injectate and length of circumferential staining were analysed using student t-test. Results are reported as mean ± standard deviation. The level of significance was set at $p < 0.05$.

Results

Mean cadaver body mass was 19.5 (± 5.2) kg. Intraneural injection was not encountered in any of the nerves blocked.

Sciatic Nerve

The volume of NMB injected was 0.05 mL kg^{-1} in the Fixed group, and 0.04 (± 0.28) mL kg^{-1} in the USG group (Figure 2.4), volumes were not significantly different between groups ($p = 0.67$). Staining was 5.9 (± 3.01) cm in the Fixed group, and 5.7 (± 1.18) cm in the USG group (Figure 2.5) and demonstrated no significant difference ($p = 0.514$). Staining obtained for all sciatic nerves in the Fixed and USG groups was >2 cm.

Femoral Nerve

The volume of NMB injected was 0.1 mL kg^{-1} in the Fixed group, and 0.06 (± 0.02) mL kg^{-1} in the USG group (Figure 2.6) with a significant difference between groups ($p = 0.01$). Staining was 5.9 (± 3.41) cm in the Fixed group, and 5.7 (± 2.15) cm in the USG group (figure 2.7) showing no significant difference ($p = 0.93$). Staining obtained for all femoral nerves in the Fixed and USG groups was >2 cm.

Discussion

It was not possible to reduce the volume of NMB required to achieve successful staining of the sciatic nerve using ultrasound-guidance. However, for the femoral nerve ultrasound-guidance enabled significantly less volume to achieve circumferential staining of ≥ 2 cm. The mean volume of injection was not significantly different between the Fixed and USG groups for the sciatic nerve despite ultrasonographic visualisation of the target nerve and doughnut sign. We conclude that for sciatic nerves it is not possible to reduce the volume of NMB using ultrasound-guidance beyond 0.05 mL kg^{-1} in agreement with Campoy et al., 2008. Staining of all nerves was > 2 cm which is considered sufficient to produce a sensory blockade (Raymond et al., 1989). However, because none of the sciatic nerves had < 2 cm of staining, it may be possible to use an even lower than the set volume of 0.05 mL kg^{-1} NMB to achieve successful staining.

In the original study investigating the ventral suprainguinal approach to the femoral nerve, Echeverry et al., (2012) found a set volume of 0.3 mL kg^{-1} provided 6.2 (5-6.8) cm of circumferential staining in cadavers. However, after block placement in healthy dogs this study reported the block could be effective with volumes as low as 0.2 ml kg^{-1}. The volumes are considerably larger than those used in this study; however, the length of staining observed is similar. When using a lateral pre-iliac approach to the femoral nerve in the psoas compartment by electrolocation Portela et al., (2013b) found 0.1 mL kg^{-1} of lidocaine and NMB provided average staining of 7.25 (6-8) cm. These lengths are greater than those found in the study reported here, with 0.1 mL kg^{-1} providing an average of 5.9 cm of circumferential staining; although it should be noted that both previously reported studies achieved successful staining of ≥ 2 cm. Deposition of NMB within the psoas compartment to achieve staining of the femoral nerve was used in the study described here, and that by Portella et al., (2013b). However, Portella et al., (2013b) used a lateral pre-iliac approach using electrolocation in vivo, rather than cadavers with ultrasound guidance as in the current study. This may be relevant because spread of injectate in cadavers could be different than it is in living animals, which could effect clinical efficacy of the nerve block techniques being assessed.

The study reported here found ultrasound-guidance facilitated a reduction in the volume of NMB to successfully stain the femoral nerve. Studies in the human literature have demonstrated reduction of mean effective anaesthetic volume (MEAV) when using ultrasound-guidance compared to electrolocation (Casati et al., 2007; McNaught et al., 2011). When placing interscalene brachial plexus blocks with 0.5 % ropivacaine, MEAV was significantly lower at 0.9 mL when using ultrasound-guidance then when using peripheral nerve stimulation at 5.4 mL (McNaught., 2011). Casati et al., (2007) found a 43% reduction of MEAV for femoral nerve blocks in humans when comparing ultrasound-guidance and electrolocation. Finally, a 37% reduction of MEAV when using ultrasound-guidance compared to electrolocation for sciatic nerve blocks has been shown (Danelli et al., 2009). Studies investigating the reduction of MEAV for locoregional anaesthesia in the veterinary literature are lacking at the time of writing.

The use of MEAV is an important method to refine PNB techniques. As injectate volume reduces, the accuracy of needle placement at the target nerve must increase. Effectiveness of local anaesthetic blocks can be assessed by the speed of onset and duration of sensory blockade. Duration of blockade is influenced by higher concentration of local anaesthetic at the target nerve, but not a larger volume (Fenten et al., 2015; Gomez de Segura et al., 2009). A previous study in humans found when using 1 or 1.5 % mepivacaine for axillary brachial plexus blocks, a higher drug concentration was associated with longer duration, but not a higher volume (Fenten et al., 2015). Classically, higher volumes of local anaesthetic were used when accuracy of needle placement close to the target nerve could not be achieved consistently. More recent studies have demonstrated accuracy of injectate placement is more likely to influence effectiveness of sensory blockade (Casati et al., 2007; McNaught et al., 2011). Furthermore, when using drugs with cardiotoxic potential, such as bupivacaine and levobupivacaine, larger volumes may increase the likelihood for systemic toxicity (Feldman et al., 1989). Therefore, the increased accuracy and reduced volume of injection facilitated by ultrasound -guidance may not only improve block effectiveness, but also safety for patients.

Evaluation of the target nerve for circumferential staining of ≥ 2 cm was stated as the measure of success in this study, and has been used by other authors (Campoy et al., 2008; Echeverry et al., 2012; Portela et al., 2013b). The convention to use this marker of success is due to pre-clinical research identifying this length of local anaesthetic coverage is necessary to prevent action potential propagation along the nerve axon (Raymond et al., 1989). For this reason, the 'doughnut sign' is used to provide an endpoint of ultrasound-guided volume of local anaesthetic placement. However, more recent clinical studies suggest that circumferential coverage of the target nerve with local anaesthetic is not required to achieve successful sensory blockade. In a study of ulnar blocks in humans Marhofer et al., (2014) found that despite circumferential spread of LA in only 67% of cases, the block success rate was 90% independent of whether the 'doughnut sign' was observed or not. This finding brings into question whether the 'doughnut sign' should be used as an end-point for the volume of injectate of local anaesthetic in clinical studies and needs further evaluation in the veterinary literature.

Side effects of placement of peripheral nerve blocks include direct nerve injury and intraneural injection. A specific adverse effect of psoas compartment blocks is the risk of epidural migration of injectate. Campoy et al., (2008) identified epidural spread NMB in 8.7% of dogs (n = 2/28 when using 0.2-0.4 mL kg^{-1} for a paravertebral approach to the lumbar plexus block of dog cadavers. Clinically in a study of 95 dogs, one (1.05%) showed bilateral pelvic limb paralysis one hour after nerve block; these signs were fully resolved five hours after block (Vettorato et al., 2012). To fully assess if epidural migration of NMB had occurred in the current study, laminectomy would have been required, this is a limitation and would be useful to include in future work.

At the time of writing, no studies have reported the use of the ventral suprainguinal approach to the femoral nerve in clinical practice. Clinical evaluation of this technique in combination with the lateral post iliac approach to the sciatic nerve is warranted to assess if this combination of blocks can provide effective analgesia to the stifle during orthopaedic surgery in dogs.

Conclusion

In summary, ultrasound-guidance reduces the volume of NMB required to achieve successful staining of the femoral nerve within the psoas compartment using a suprainguinal approach. As yet this block has not been reported clinically, with the evidence base present for this block, a clinical trial is now warranted to investigate this approach in clinical practice.

CHAPTER 3: ULTRASOUND-GUIDED FEMORAL AND SCIATIC NERVE BLOCKS IN THE DOG - A CLINICAL TRIAL

Introduction

Femoral and sciatic nerve blocks have been demonstrated to provide effective perioperative analgesia to dogs undergoing orthopaedic surgery to the stifle joint (Campoy et al., 2012a; Caniglia et al., 2012; Portela et al., 2013b). In humans ultrasound-guidance offers the advantages of increased accuracy of injectate deposition in the region of the target nerve, faster block performance time, and reduced volume of local anaesthetic required to achieve successful sensory blockade (Casati et al., 2007; Williams et al., 2003). Using lower volumes of local anaesthetics, and thus total dose administered, reduces the potential of encountering systemic toxicity of drugs such as bupivacaine and levobupivacaine (Feldman et al., 1989).

In dogs the volume of local anaesthetic currently recommended to provide neurological blockade to the stifle are as low as 0.1 mL kg^{-1} for the femoral nerve within the psoas compartment, and 0.05 mL kg^{-1} for the sciatic nerve (Campoy et al., 2010). The preceding cadaver study investigating the ventral suprainguinal approach to the femoral nerve found significantly lower volumes than 0.1 mL kg^{-1} provided successful staining of the nerve. It also suggested volumes lower than those currently recommended may be effective at providing sensory blockade of the femoral nerve. However, cadaver studies may not be equal to living tissues due to non-functioning vasculature, and tissue changes post mortem. For this reason, it is vital to undertake a clinical trial to assess if the findings from the cadaver study are borne out in a clinical context.

The aims of this study were;

1) To determine, based on the findings of the cadaver study, whether lower volumes of injectate could provide intraoperative haemodynamic stability and postoperative analgesia.
2) To evaluate if a clinical refinement of the ventral suprainguinal femoral nerve block using 0.05 mL kg^{-1} levobupivacaine is equal at providing intraoperative haemodynamic stability and postoperative analgesia compared to standard volumes of 0.1 mL kg^{-1}.

Materials and methods

Animals

The study was approved by the University of Glasgow School of Veterinary Medicine Research Ethics Committee reference number 43a/16. The study was prospective, randomised, blinded and controlled. To give an 80% power to detect a significant (alpha 0.05) difference in proportions between groups, in terms of requirement for additional analgesia intraoperatively, 10 dogs were recruited into each group. This was based on preliminary results showing the proportion of dogs not requiring additional analgesia following nerve block is very high (0.9), but low in those receiving blocks which are not effective (0.4).

Healthy dogs (American Society of Anesthesiologists status 1 and 2) admitted for tibial plateau levelling osteotomy (TPLO) at the University of Glasgow Small Animal Hospital were enrolled into the study with prior informed owner consent. Exclusion criteria were evidence of cardiovascular disease, bodyweight less than 8 kg or more than 45 kg, neurological disease, clotting disorders, skin infection at the proposed puncture sites or concurrent treatment with medication except nonsteroidal anti-inflammatory drugs (NSAIDs). Pre-operative assessment comprised of clinical examination and a short-form composite measure pain scoring assessment (CMPS-SF [see Appendix 1]) was carried out by the same individual (Reid et al., 2007).

Anaesthesia

Pre-medication consisted of acepromazine (ACP 2 % solution; Novartis Animal Health UK Ltd, Camberley, UK) 0.02 mg kg^{-1} and methadone (Comfortan 1% solution; Dechra Veterinary Products Limited, Shrewsbury, UK) 0.3 mg kg^{-1} administered by intramuscular injection in the epaxial muscles 30 minutes before induction of anaesthesia. An intravenous cannula (Biovalve Safe; Vygon Ltd, Swindon, UK) was placed in the left or right cephalic vein and was present throughout the anaesthetic. Induction of anaesthesia was achieved with propofol (PropoFlo Plus 1 % emulsion; Zoetis UK, Tadworth, UK) administered by intravenous (IV) route until dogs were anaesthetised and endotracheal intubation with a cuffed endotracheal was possible. Isoflurane (Isoflurane-Vet 100 %; Boehringer-Ingelheim, Bracknell, UK) in oxygen was delivered for maintenance of anaesthesia by a breathing system appropriate to the dog's body mass. Hartmann's solution (Vetivex 11 solution; Dechra Veterinary Products Limited, Shrewsbury, UK) was infused at 5 mL kg^{-1} hr^{-1} IV. Dogs were monitored throughout the anaesthetic with capnography, ECG (electrocardiogram), non-invasive blood pressure monitoring, pulse oximatery and end-tidal anaesthetic agent monitoring using a multiparameter monitor (Datex-Ohmeda S5; Datex-Ohmeda Ltd, Hatfield, UK). End-tidal anaesthestic agent monitoring was calibrated before and during the data collection period by a trained technician to ensure no drift in FÉ-ISO was encountered. If animals were not currently treated with NSAIDs, meloxicam (Metacam, 0.5 % solution; Boehringer-Ingelheim, Bracknell, UK) 0.2 mg kg^{-1} was administered by subcutaneous injection before recovery from anaesthesia. If dogs were currently treated with NSAIDs treatment was continued postoperatively.

Defined intervention protocols to deal with complications were established as follows. If movement or an extremely light plane of anaesthesia was observed propofol (1mg kg^{-1} IV) would be administered. Hypoventilation defined as end-tidal carbon dioxide ($EtCO_2$) > 8 kPa (Dugdale, 2007) would be treated with intermittent positive pressure ventilation with the aim of maintaining $EtCO_2$ within the normal range 4.6-6 kPa. Hypotension defined as mean arterial blood pressure (MAP) < 60 mmHg (Gaynor et al., 1999) with heart rate (HR) < 60 beats per minute would result in atropine (10 mcg kg^{-1} IV) administration. Mean arterial blood pressure < 60 mmHg and HR > 140 results in Hartman's solution (10 mL kg^{-1} IV) administered over 15 minutes. If hypotension was still present despite the above treatment the vasoconstrictor metaraminol (2 mcg kg^{-1} IV) would be administered.

Nerve block procedure

After induction of anaesthesia the leg to be operated on was prepared for surgery by clipping of body hair, and skin prepared aseptically using chlorhexidine. One operator experienced in the use of ultrasound-guided locoregional anaesthesia carried out all nerve blocks. Ultrasonographic scanning of the sciatic nerve was performed using a Esaote 7-10 MHz linear ultrasound transducer and ultrasound system (My Lab 20 Plus: Esaote, Genoa, Italy). Once a transverse plane view of the sciatic nerve was obtained depth, gain, and focus position was adjusted to give optimal image quality to visualise the target nerve. A lateral distal ischiatic approach to the sciatic nerve was performed (Figure 1.3) using the method described by Campoy et al., (2010) with an insulated echogenic locoregional anaesthesia needle (Stimuplex 50-120 mm 22 G, B. Braun Medical Ltd, Sheffield UK). For femoral nerve blocks a transverse ultrasonographic image of the psoas compartment was then obtained (Figure 3.1) and image quality optimised to visualise the target nerve as stated above. The in-plane ventral suprainguinal approach to the femoral nerve (Figure 1.4) as described by Echeverry et al., (2012) was used.

Dogs were randomised into two groups using GraphPad Prism (GraphPad Software, Inc. La Jolla, CA, USA) to receive one of two treatments. The low dose group (LD) received femoral nerve blocks using 0.05 mL kg^{-1}, and sciatic nerve blocks using 0.05 mL kg^{-1} levobupivacaine 0.5 % (5 mg ml^{-1}). The high dose group (HD) received femoral nerve blocks using 0.1mL kg^{-1} and sciatic nerve blocks using 0.05 mL kg^{-1} levobupivacaine. The operator performing the nerve blocks was unaware of the volume of injectate; blinding was achieved as follows. Group allocation was not divulged to the operator. After visualisation of the target nerve, confirmation of accurate needle placement was achieved by injecting increments of 0.1 mL levobupivacaine (maximum of 0.05 ml kg^{-1}) which gave visualisation of injectate spread around the target nerve. When the operator was satisfied that needle placement was optimal, the display of the ultrasound machine was turned out of sight and another operator would complete the injection volume as dictated by the treatment group. Injection was performed at a slow rate.

Efficacy evaluation of the nerve block

Intraoperative period. Intraoperative monitoring of the patient was carried out by one experienced anaesthetist unaware of treatment group. Baseline heart rate (HR), respiratory rate (f_R), mean arterial blood pressure and FÉ-ISO were recorded 15 minutes before the start of surgery (Tb), then at cutaneous incision (T0), incision of the joint capsule (T1), periosteal stimulus (T2), osteotomy of the tibia (T3) and cutaneous suture (T4). If HR, f_R or MAP were noted to increase more than 25% above baseline, fentanyl (Fentadon; Dechra Veterinary Products Limited, Shrewsbury, UK) (2 mcg kg^{-1} IV) was administered. If these elevations were persistent 10 minutes after fentanyl administration, an additional dose of fentanyl was given. If after a further 10 minutes cardiovascular elevation persisted, a fentanyl infusion (0.2 mcg kg^{-1} min^{-1} IV) would be administered. Total amount of intraoperative fentanyl administration was calculated by dividing the total amount of fentanyl administered during surgery (hours), then dividing again by body mass (kg).

Postoperative period. Recovery from anaesthesia was scored using a numerical categorical score (See Appendix 1) by the same anaesthetist unaware of group, lowest score 0, highest score 6. If persistent scores (for more than 3 minutes) of 5-6 were observed dexmedetomidine (0.5 mcg kg^{-1} IV) would be administered. Pain scoring was carried out using the short form composite measure pain scale (See Appendix 1) at 0, 1, 2, 4, 6, 8 and 10 hours after recovery from anaesthesia by trained personnel unaware of the intraoperative efficacy of the nerve block; if pain scores were > 5/20 (if the patient was not ambulatory) or 6/24 rescue analgesia was administered (methadone 0.3 mg kg^{-1} IV).

Data analysis

Data analysis was conducted using SPSS statistics (SPSS; IBM Corporation, Armonk, New York, USA). Data was analysed for normality of distribution using Shapiro–Wilk tests and then appropriate parametric (T-test and ANOVA) or non-parametric (Mann–Whitney U test) statistical testing was applied.

Groups were assessed for similarity for sex, age, body mass, pre-operative CMPS-SF, time from pre-medication to induction of anaesthesia, total anaesthetic time and total surgical time and analysed using the Student's T-Test. Intraoperative HR, *f*R, MAP, FÉ-ISO and postoperative CMPS-SF were assessed using repeated measures analysis of variance (RM-ANOVA). Time to first rescue analgesia was assessed using Kaplan-Meier analysis. Total postoperative methadone doses were compared using Mann-Whitney U Test. Categorical values were compared between groups using Fisher's exact tests. Results are reported as mean ± standard deviation. The level of significance was set at $p < 0.05$.

Results

Twenty dogs were recruited to the study (LD *n* = 10, HD *n* = 10). Breeds of the dogs were as follows. LD group: Beagle (*n* = 1), Boxer dog (*n* = 1), Crossbreeds (*n* = 1), Flat Coated Retriever (*n* = 1), Golden Retriever (*n* = 1), Miniature Poodle (*n* = 1), Labrador (*n* = 2) Staffordshire Bull Terriers (*n* = 2). HD group: Bernese Mountain Dog (*n* = 1), Boxer dog (*n* = 1), Crossbreed (*n* = 2), English Springer Spaniel (*n* = 1), Jack Russell Terrier (*n* = 2), Labrador (*n* = 3).

The groups were not different in terms of sex, age, body mass, pre-operative NSAID treatment, pre-operative CMPS-SF, time from pre-medication to induction of anaesthesia (Table 1). All nerve blocks were performed successfully in both groups, with visualisation of local anaesthetic spread next to the target nerve observed in all cases. The volume of local anaesthetic injected at the femoral nerve was delivered as per the study protocol (1.2 ± 0.40) versus (2.88 ± 1.0) mL kg^{-1} in the LD and HD groups, (p = 0.000), as seen in Table 1.

Total anaesthetic time was (219 ± 34) versus (243 ± 29) minutes in the LD and HD groups respectively with no significant difference observed between groups ($p = 0.133$). Total surgical time was (120 ± 29) versus (128 ± 28) minutes in the LD and HD groups respectively with no significant difference observed between groups ($p = 0.633$).

Intraoperative HR, *f*R, MAP and FÉ-ISO (Table 2) were not significantly different between groups. All intraoperative time points were analysed by repeated measures ANOVA, the dose of local anaesthetic had no significant effect on HR ($p = 0.19$), *f*R, ($p = 0.375$), MAP, ($p = 0.38$), or FÉ-ISO requirement ($p = 0.172$).

Requirement for intraoperative analgesia (Table 3) was not significantly different between groups at any time point. Total intraoperative fentanyl administration was not found to be statistically different between groups ($p = 0.84$). No fentanyl infusions were required in any group as no single animal had persistent cardiovascular parameter elevation ten minutes after a second dose of fentanyl.

Minor complications were as follows; One dog in each group required an intravenous bolus of Hartmann's solution (10 mL kg^{-1}) during preparation for surgery due to heart rate of more than 140 BPM and MAP < 60 mmHg; MAP in both dogs was observed to be in the normal range after this. Two dogs in each group required mechanical ventilation due to high respiratory rate and to ensure adequate volatile anaesthetic agent uptake prior to starting surgery. Recovery from anaesthesia was of good quality in all dogs with scores of 1.7 (± 1.34) versus 1.50 (± 1.27) in the LD and HD groups respectively, with no significant difference observed ($p = 0.343$). Administration of dexmedetomidine was not required in either group as no dog had a recovery score persistently in category 5 or 6. All 20 dogs completed the study without major complications.

Postoperative composite measure pain scores over the first 10 hours after recovery from anaesthesia are reported in Table 4a. Pain scores were not significantly different between groups as assessed by repeated measures ANOVA ($p = 0.085$) (Figure 3.2). Total number of postoperative methadone doses were similar between groups ($p = 0.393$). Dogs receiving rescue analgesia remained in the analysis. When the last observation carried forward method was used (the first pain score over the threshold requiring rescue analgesia is carried forward to the other measurement times) no significant difference in postoperative pain score was found using a repeated measures ANOVA ($p = 0.12$) (Figure 3.3).

Using survival analysis, the time to first rescue analgesia was estimated as 7.4 (95% CI = 4.4 – 10.3) and 10.4 (95% CI = 8.3 – 12.4) hours in the LD and HD groups respectively. This was not significantly different between groups ($p = 0.146$) (Figure 3.4). The pooled time to rescue for both groups was 8.9 (95% CI 6.9 – 10.8) hours.

Discussion

This clinical trial is the first study to assess local anaesthetic blockade by the ventral suprainguinal approach to the femoral nerve (in combination with the sciatic nerve) in dogs undergoing stifle surgery. The majority of dogs in both groups had successful nerve blocks (complete absence noxious response to surgical stimulus), but neither group had sensory blockade sufficient to entirely prevent the nociceptive barrage of surgery. For those dogs that required intraoperative rescue analgesia we would have expected them to show behavioural signs of pain after pre-operative methadone had worn off and the only other analgesia present was a NSAID. However, during the postoperative period both groups appeared to have sufficient pain relief with blockade of the femoral and sciatic nerves.

This novel approach to the femoral nerve has not been reported in a clinical context previously. Theoretically, local anaesthetic deposition around the femoral nerve within the psoas compartment has the advantage of providing sensory blockade proximal to branching of the saphenous nerve, which is postulated to facilitate a more complete nerve block to the stifle. Neither volume of local anaesthetic used in this study was able to completely obtund the nociceptive barrage of surgery as a number of intraoperative doses of fentanyl as rescue analgesia were required in each group. There are several possible explanations for this finding; 1) insufficient local anaesthetic injection volume at the femoral and/or sciatic nerves, 2) additional sensory nerve supply to the stifle which may not be blocked using the methods used this in this study, 3) block placement failure, 4) cardiovascular elevation thresholds were not specific for a noxious response during surgery.

Insufficient local anaesthetic injection volume around the femoral nerve is a possible cause for the lack of complete prevention of the sympathetic response during surgery. Local anaesthetic injection volume recommended by Echeverry et al., (2012) for the ventral suprainguinal approach to the femoral nerve was 0.2 mL kg^{-1}, with which sensory deficits were observed in experimental dogs; but this was not assessed in a clinical context. Local anaesthetic volumes of 0.05-0.1 mL kg^{-1} were used in the study reported here, which is significantly less than that recommended by Echeverry et al., (2012). However, due to the sufficient (> 2 cm) circumferential staining seen during our cadaver study, we suspect the volume was sufficient to facilitate local anaesthetic blockade of the femoral nerve. Although the findings of the cadaver study supported the hypothesis that volumes as low as 0.05 mL kg^{-1} could provide successful blockade of the femoral nerve, it is possible that distribution of injectate in living animals may not replicate that seen in cadavers due to non-functioning vasculature and post-mortem tissue changes. It is also possible the volume of local anaesthetic deposited at the sciatic nerve was too low. However, the sciatic volume used in this study was the same as that recommended by previous studies where intraoperative nociceptive response was not observed during stifle surgery (Campoy et al., 2012b).

Additional sensory nerve supply to the stifle which may not be blocked using the methods used this in this study, which manifests as nociceptive response during surgery, is another possible cause for the noxious response observed in dogs from both treatment groups. The nerves which innervate the stifle are the medial articular nerve (a branch of the SaN) and the posterior articular nerve, a branch of the tibial nerve, which is itself a branch of the sciatic nerve (Campoy and Mahler, 2013). The medial articular nerve occasionally receives nerve fibres from the obturator nerve (Gurney and Leece, 2014). The ventral suprainguinal approach to the FN, and the lateral distal ischiatic approach to the SN do not block the obturator nerve; thus, this may be the cause of inconsistent nociceptive response in cases observed in this study. At T1 (incision of the joint capsule) rescue analgesia was required in 10/20 dogs, at this point in surgery the stifle joint is distracted which may contribute to the noxious response observed, and could indicate that the medial nerve inconsistently receives fibres from the obturator nerve, and is a cause behind this finding. The obturator nerve can be blocked in combination with the femoral nerve within the psoas compartment, as described by Tayari et al., (2017). It would have been beneficial to use this approach in an attempt to obtain a more complete sensory blockade; however, this study was published after the study design of this clinical trial was conceived.

Block placement failure is a possible reason why noxious response was observed during surgery in this study. It is conceivable that some of the animals in this study may not have received local anaesthesia accurately as nerve location was not used concurrently with ultrasound, and due to the technical difficulty of the ventral suprainguinal block. However, we consider this unlikely for two reasons; in the complimentary cadaver study 100 % of nerves were stained accurately by the same operator, and both the femoral and sciatic nerves were successfully visualised in all dogs prior to injection of levobupivacaine.

The final reason we can consider for observation of noxious response during surgery in both groups is that intervention thresholds for cardiovascular elevation were too low, i.e. a 25 % increase above baseline values was not specific and overly sensitive for detection of nociceptive stimulus. Intraoperative increase in HR, f_R and MAP to indicate noxious stimulus has been used by many authors, however, the level indicative of nociception is not agreed upon. A 10 % increase was used by Caniglia et al., 2012, whereas Adami et al., (2016) and Tayari et al., (2017) used thresholds of 20 % above baseline. Portela et al., (2013a) used a 25 % increase from baseline values which is in agreement with the present study. We suspect that a 25 % increase in HR, f_R and MAP are the most lenient of the thresholds previously used, and give the best chance of successful sensory blockade being an outcome. However, there is no convention of what percentage increase in cardiovascular parameters above baseline should be used in studies of this type to indicate noxious stimulus and requirement for rescue analgesia. Furthermore, the above studies all had different pre-anaesthetic medication and anaesthetic maintenance protocols between them, therefore meaningful comparison is not possible.

When block success (those dogs that did not require intraoperative rescue analgesia) is compared to other studies we can see a difference to those observed in the clinical trial reported here. Block success in the LD group was (n = 4/10) and in the HD group (n = 3/10). Portela et al., (2013) had (n = 13/15) success rate for a lateral pre-iliac approach to the femoral nerve and sciatic nerve blocks using 0.1 mL kg^{-1} of 1% lidocaine for each block, with 13/15 dogs having a successful nerve block. It should be noted this study used a higher volume of local anaesthetic for sciatic nerve blocks than the current study, 0.1 mL kg^{-1} versus 0.05 mL kg^{-1} respectively. Therefore, in the present study our blocks were not sufficient to provide an equal measure of intraoperative stability as has been observed by Portela et al., (2013).

Another method to assess if peripheral nerve blocks are successful is total intraoperative fentanyl administration. A retrospective clinical study by Vettorato et al., (2012) suggested total intraoperative fentanyl administration of less than 1.25 ± 0.75 mcg kg^{-1} $hour^{-1}$ indicates a successful nerve block, and greater than 2.1 mcg kg^{-1} $hour^{-1}$ to be an indication of block failure. This measure of block success was also used by Tayari et al., (2017) when investigating a combined approach to the femoral, obturator, and sciatic nerve within the psoas compartment of dogs undergoing stifle surgery. In the study described here, intraoperative fentanyl requirement was not significantly different between groups ($p = 0.45$) 1.62 mcg kg^{-1} $hour^{-1}$ versus 1.48 mcg kg^{-1} $hour^{-1}$ for the LD and HD groups respectively. For both groups the total fentanyl administration lies within the equivocal range, i.e. being considered neither completely successful (< 1.25 ± 0.75 mcg kg^{-1} $hour^{-1}$), or completely failed (> 2.1 mcg kg^{-1} $hour^{-1}$). When individual dog total fentanyl administration is considered, the numbers of dogs in each group give a clearer picture. The number of dogs with total fentanyl administration below 1.25 ± 0.75 mcg kg^{-1} $hour^{-1}$ in the LD group was ($n = 4/10$) and the HD group was ($n = 3/10$). The number of dogs with total fentanyl administration above 2.1 mcg kg^{-1} $hour^{-1}$ in the LD group was ($n = 3/10$) and the HD group was ($n = 4/10$). This finding corelates with the number of dogs that were considered to have had a successful nerve block as defined by intraoperative cardiovascular stability, and backs up the finding that intervention thresholds used in our study were appropriate. As this is the first clinical trial assessing the ventral suprainguinal approach to the femoral nerve, there is no other data to benchmark the likely success rates for this block. Further studies comparing this approach to the femoral nerve with other more established techniques (such as the inguinal approach, and the lateral pre-iliac approach) may give an indication of which technique provides the most reliable anaesthesia of the femoral nerve during orthopaedic surgery of the stifle (Campoy et al., 2010; Portela et al., 2013b).

Postoperative analgesia was found to be good in both groups, irrespective of whether intraoperative locoregional blockade had been successful in preventing nociceptive stimulation or not. The vast majority of dogs (LD n = 7/10, HD n = 9/10) had adequate analgesia and did not require rescue opioid treatment up to 10 hours after recovery from anaesthesia. This finding was encouraging and is in agreement with similar studies which used the CMPS-SF to assess postoperative analgesia requirement was used (Bini et al., 2018; Campoy et al., 2012b, 2012a; Tayari et al., 2017). Kaplin-Meier survival analysis showed with 95% confidence that when this protocol is used for dogs having TPLO surgery rescue analgesia is needed 6.9-11 hours after surgery (Figure 3.4). Survival time to first methadone administration in dogs after TPLO surgery and FSNB was retrospectively assessed by Bini et al., (2018); these authors reported the time to first methadone administration (as dictated by CMPS-SF) was 9.3 (3.1-23) hours after block placement, which is similar to the observation found in the study reported here.

It was not possible to find statistically significant difference between groups for postoperative analgesia requirement when all pain scores were considered (Table 4a and Figure 3.2) or when the last observation carried forward method was used (Table 4b and Figure 3.3).

The complementary cadaver study suggested lower volumes than those previously reported should provide anaesthesia of the femoral nerve within the psoas compartment. Mean effective anaesthetic volume is the volume of local anaesthetic required to produce surgical locoregional anaesthesia and may be reduced when ultrasound-guidance is used. (Di Filippo et al., 2016). Several studies in humans have demonstrated this effect with reduction of MEAV by 83 % for brachial plexus blocks (McNaught et al., 2011), 43 % for femoral nerve blocks (Casati et al., 2007) and 37 % for sciatic nerve blocks (Danelli et al., 2009). These findings agree with the results of the study described here, where volumes of 0.05 versus 0.1 mL kg^{-1} mL kg^{-1} were equal at providing successful intraoperative and post-operative analgesia. The reason ultrasound-guidance can facilitate reduction of MEAV is real time visualisation of the target nerve and surrounding structures, enabling accurate needle positioning close to the target nerve. Additionally, spread of local anaesthetic solution can be assessed in real time (Casati et al., 2007).

Circumferential coverage of the target nerve is not required to achieve successful sensory blockade, however the reasons for this finding are not fully understood (Marhofer et al., 2014). The ≥ 2 cm circumferential coverage of the target nerve with local anaesthetic solution or NMB reported by Raymond et al., (1989), has been used by several studies in the veterinary literature and is the benchmark to which cadaver studies define success or failure when evaluating novel nerve blocks or alterations to existing methods (Campoy et al., 2008; Echeverry et al., 2012; Portela et al., 2013b). Raymond et al., (1989) used an ex-vivo chamber model where the length of nerve was altered while the concentration 38 mg mL^{-1} of lidocaine was kept the same. Nerve impulses were initiated and measured passing through the nerve to establish the degree of sensory blockade. Thus, the minimum length of nerve exposure to circumferential local anaesthetic drugs that is recommended by Raymond et al., (1989) was 2 cm. However, application of ex-vivo research in clinical cases may not see these findings entirely borne out. Although the cadaver study provided an indication that volumes less than those currently recommended would provide effective analgesia, a clinical trial was required to assess this in a clinical context.

It is possible the findings of the clinical trial reported here are not valid to predict a clinical outcome. This may be due to insufficient power to detect a difference where one in fact exists, known as type 2 error (Leslie, 2011). As part of the study design for this project a power calculation was undertaken which determined that 10 dogs in each group would provide an 80 % chance of avoiding a type 2 error. Similar studies of FSNB have used group sizes between 7 and 11 dogs in each group (Campoy et al., 2012b, 2012a; Portela et al., 2013b; Tayari et al., 2017). The fact that similar projects have used group sizes comparable to those used here does not rule out the possibility our study was under powered, however it does indicate our findings are comparable to those of previous work. A power calculation was not undertaken prior to the cadaver study due to the precedent that small group numbers had successfully been used in previously reported studies, which may be a limitation of this work. However, in the cadaver study six dogs were used, this is comparable or more power than previously reported anatomical studies where between 2 and 6 dogs were used, which indicates the data has sufficient power to be relied upon (Campoy et al., 2010; Echeverry et al., 2012; Portela et al., 2013b; Tayari et al., 2017)..

Limitations of the study are that postoperative assessment for skin irritation at the puncture site or neurological dysfunction at 2-6 weeks after surgery was not included as part of the study protocol, as has been reported by similar studies (Adami et al., 2016; Portela et al., 2013b; Tayari et al., 2017). Furthermore, the severity of the lameness prior to surgery was not recorded which may have been different between the treatment groups. Were this study to be repeated several areas could be refined to provide a more comprehensive data output such as; including preoperative lameness severity assessment, postoperative assessment for skin reaction over the site of needle insertion, and postoperative assessment of neurological dysfunction at 2-6 weeks after surgery, as has been undertaken by previous studies in this area.

Conclusion

The ventral suprainguinal approach to the femoral nerve block, in combination with the sciatic nerve block, can provide intraoperative analgesia to the stifle, but complete sensory blockade is not consistently achieved. However, in cases where an intraoperative cardiovascular response is seen, dogs may still have good pain relief up to 10 hours in the postoperative period without requirement for further opioid analgesia.

Our cadaver study showed volumes less than those previously reported should provide anaesthesia of the femoral nerve, but this was not borne out completely in a clinical trial where several elements of block success (duration and completeness) were tested. We recommend that cadaver studies be followed up by clinical trials to accurately assess the clinical benefit of locoregional techniques. Due to the inconsistent intraoperative affect we observed, in a clinical setting we recommend using a local anaesthetic injection volume of 0.2 ml kg^{-1} when using the ventral suprainguinal approach to the femoral nerve, as per the original reporting of this block, because a higher dose may make provide more consistent affect. Finally, future work in this area comparing the ventral suprainguinal approach to the femoral nerve, to other techniques used to block this nerve would be useful. This would establish the most effective method to provide sensory blockade at the femoral nerve.

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TABLES

Table 1. Group details of twenty dogs undergoing tibial plateau levelling osteotomy treated with femoral and sciatic nerve blocks.

	LD	HD	
	Mean (SD)	**Mean (SD)**	***p* =**
Sex (n)	F = 8 M = 2	F = 4 M = 6	0.073
Age (months)	80.9 (31.4)	66.0 (23.6)	0.246
Body mass (kg)	23.8 (7.8)	28.8 (10.1)	0.232
Pre-operative NSAID treatment	7 (0.48)	7 (0.48)	0.000
GCMPS-SF – before surgery	1 .6 (1.2)	1.8 (0.9)	0.691
Time from pre-medication to IoA (min)	34.1 (9.3)	32.5 (3.5)	0.617
Femoral nerve block volume (mL)	1.20 (0.40)	2.88 (1.00)	0.000

Key: CMPS-SF = composite measure pain scale – short form; LD = Low Dose Group; HD = High Dose Group; *p* = probability; SD = standard deviation; mL = millilitre; n = number.

Table 2.

Intraoperative haemodynamic variability in twenty dogs undergoing tibial plateau levelling surgery treated with femoral and sciatic nerve blocks. No statically significant difference was observed between groups

		15 minutes before surgery	Start of surgery	Incision of joint capsule	Periosteal stimulus	Osteotomy	Cutaneous suture
		Tb	T0	T1	T2	T3	T4
	Group	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
HR	LD	90.3 (18.8)	89.6 (17.7)	97 (22.3)	78.1 (10.2)	77.4 (14.7)	83.7 (11.9)
	HD	75.7 (21.6)	78 (16.0)	90.9 (19.1)	71.2 (16.7)	70.0 (16.1)	77.4 (12.5)
MAP	LD	73.4 (6.2)	83.3 (25.5)	93.9 (24.7)	80.3 (16.2)	79.3 (11.8)	83.2 (7.5)
	HD	76.4 (10.4)	83.8 (13.7)	97.3 (15.7)	87.1 (10.0)	83.4 (10.2)	90.5 (7.1)
fR	LD	11.6 (2.6)	13.0 (4.7)	15.1 (6.7)	11.2 (3.1)	10.2 (2.9)	10.4 (4.1)
	HD	13.0 (5.0)	14.0 (7.7)	17.7 (10.0)	11.3 (4.3)	11.5 (3.6)	13.2 (3.3)
FÉ-ISO (%)	LD	1.16 (0.06)	1.1 (0.08)	1.15 (0.07)	1.1 (0.05)	1.7 (0.09)	1.18 (0.12)
	HD	1.20 (0.12)	1.2 (0.12)	1.20 (0.10)	1.1 (0.09)	1.1 (0.03)	1.1 (0.04)

Key: HR = heart rate, *fR* = respiratory rate; MAP = mean arterial blood pressure; FÉ-ISO = end-tidal isoflurane; LD = Low Dose Group; HD = High Dose Group; SD = standard deviation; Tb = 15 minutes before start of surgery; T0 = start of surgery; T1 = incision of joint capsule; T2 = periosteal debridement; T3 = tibial osteotomy; T4 = cutaneous suture.

Table 3.

Patients requiring fentanyl administration after femoral and sciatic nerve block, and total intraoperative fentanyl administration

	LD	HD	
	Patients requiring fentanyl administration	**Patients requiring fentanyl administration**	***p***
Fentanyl required T1 (incision of joint capsule)	5	5	0.672
Fentanyl required T2 (periosteal debridement)	1	2	0.5
Fentanyl required T3 (osteotomy)	6	6	0.675
Fentanyl required T4 (cutaneous suture)	0	1	0.5
Total intraoperative fentanyl administration mg kg^{-1} $hour^{-1}$ [Mean (SD)]	1.62 (1.69)	1.48 (1.34)	0.84

Key: LD = Low Dose Group; HD = High Dose Group; mg kg^{-1} $hour^{-1}$ = micrograms per kilo per hour; *p* = probability;

SD = standard deviation; T1 = incision of joint capsule; T2 = periosteal debridement; T3 = tibial osteotomy; T4 = cutaneous suture.

Table 4a.

Median (range) for postoperative composite measure pain scores (CMPS-SF) for 20 dogs after TPLO surgery and femoral and sciatic nerve blocks. No statically significant difference was observed between groups

	0 Hours	1 Hour	2 Hours	4 Hours	6 Hours	8 Hours	10 Hours	*p*
LD	1.5 (0-11)	2 (0-4)	2.5 (1-6)	3.5 (1-14)	3 (2-6)	3 (1-5)	2.5 (1-5)	
HD	1 (0-3)	2 (0-3)	1.5 (1-6)	2 (1-4)	2 (0-8)	2 (0-5)	2 (1-4)	0.085

Key: LD = Low Dose Group; HD = High Dose Group; *p* = probability.

Table 4b.

Median (range) for postoperative composite measure pain scores (CMPS-SF) with last observation carried forward for 20 dogs after TPLO surgery and femoral and sciatic nerve blocks. No statically significant difference was observed between groups

	0 Hours	1 Hour	2 Hours	4 Hours	6 Hours	8 Hours	10 Hours	*p*
LD	1.5 (0-11)	2.5 (0-11)	3 (1-11)	3.5 (1-11)	4.5 (2-11)	5 (1-11)	4.5 (1-11)	
HD	1 (0-3)	2 (0-3)	1.5 (1-6)	2 (1-6)	2 (0-8)	2.5 (0-8)	2.5 (1-8)	0.121

Key: LD = Low Dose Group; HD = High Dose Group; *p* = probability.

Figure 1.1. Dissection of the femoral triangle of the left pelvic limb of a dog cadaver showing the course of the femoral and saphenous nerves

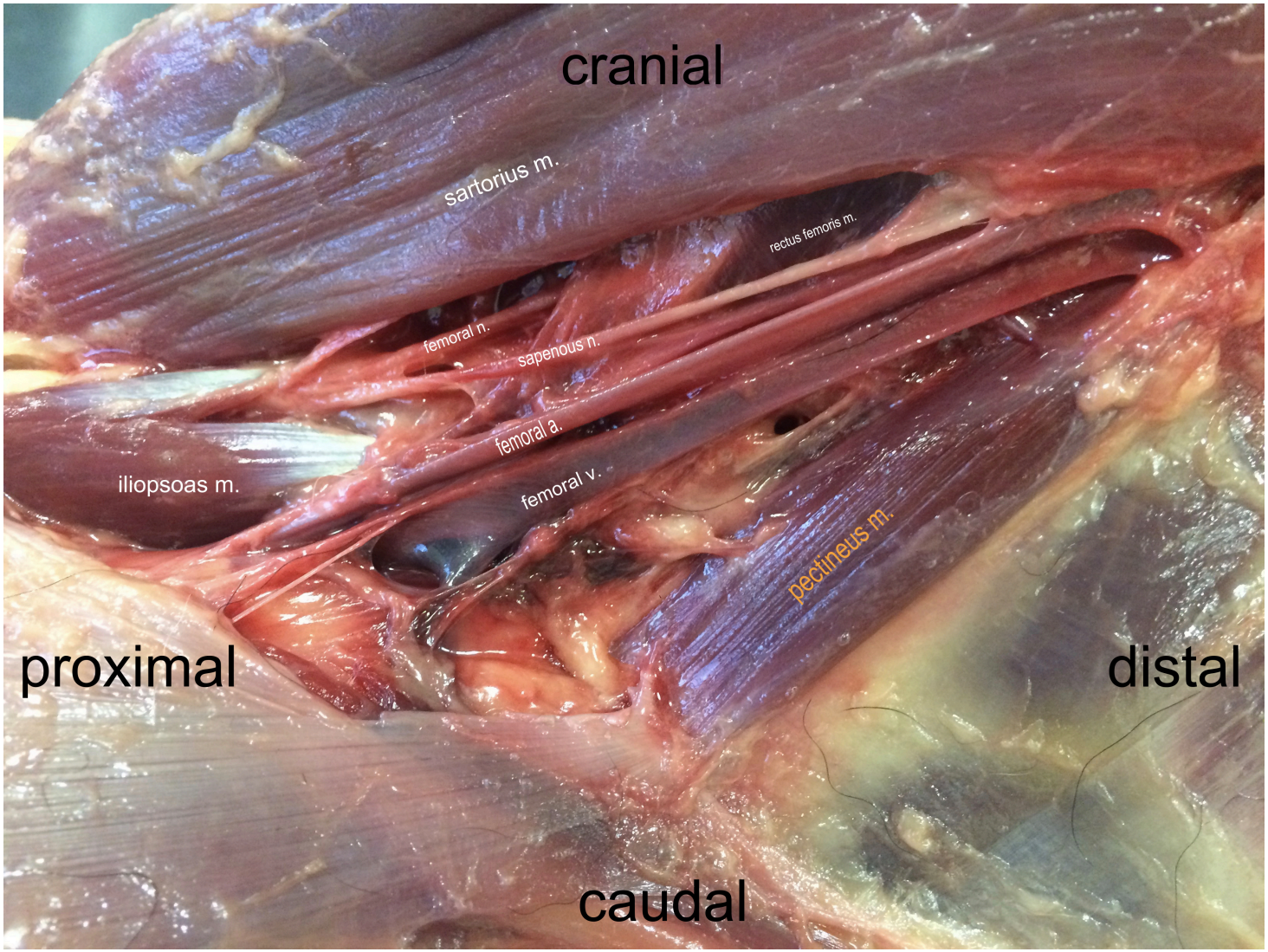


Figure 1.2

Dissection of the lateral aspect of the thigh of a dog cadaver showing the course of the sciatic nerve. Note the quadriceps muscle has been removed.

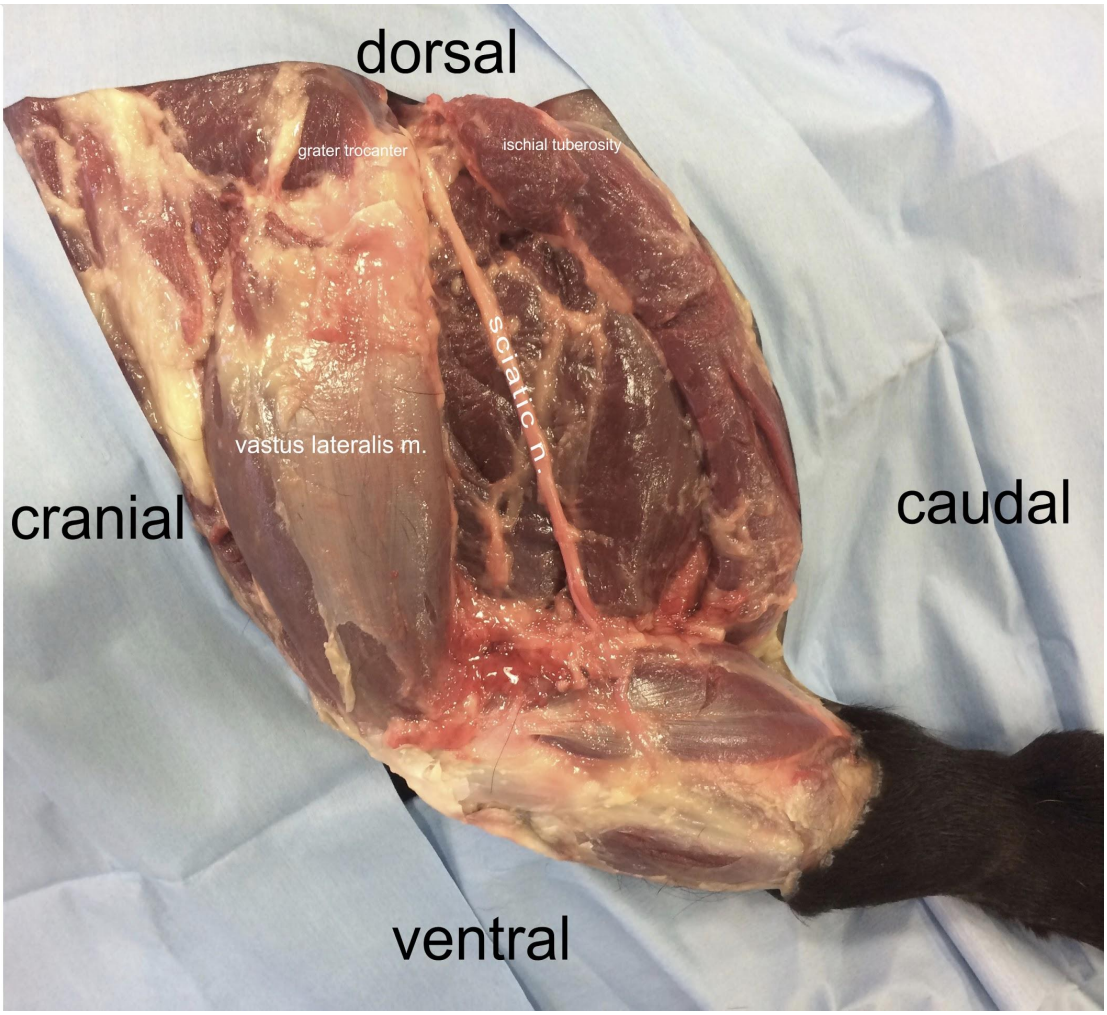


Figure 1.3.

Ultrasound-guided lateral distal ischiatic approach to the sciatic nerve in the left pelvic limb of a dog, using in plane technique to guide needle insertion. As described by Campoy et al., (2010).

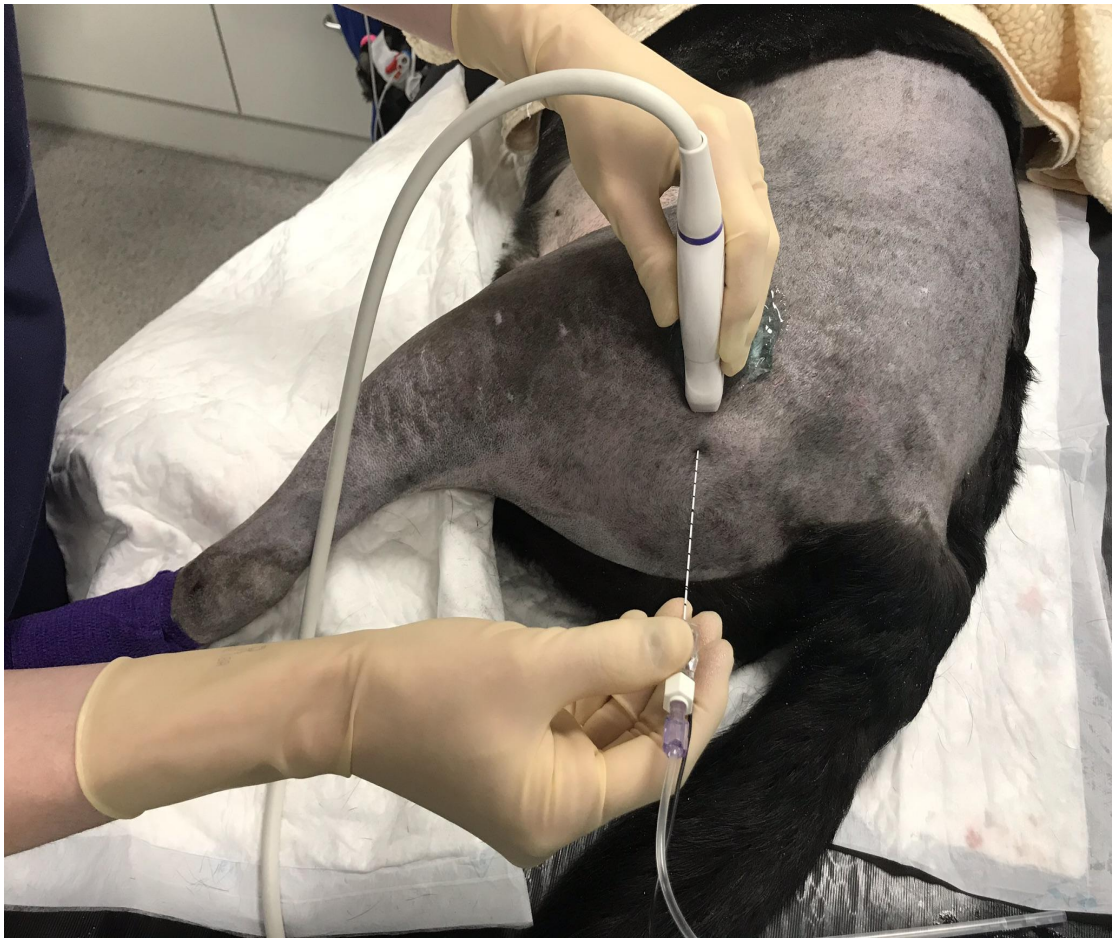


Figure 1.4.

Ultrasound-guided ventral suprainguinal approach to the left femoral nerve within the psoas compartment using in-plane technique as described by Echeverry et al., (2012).

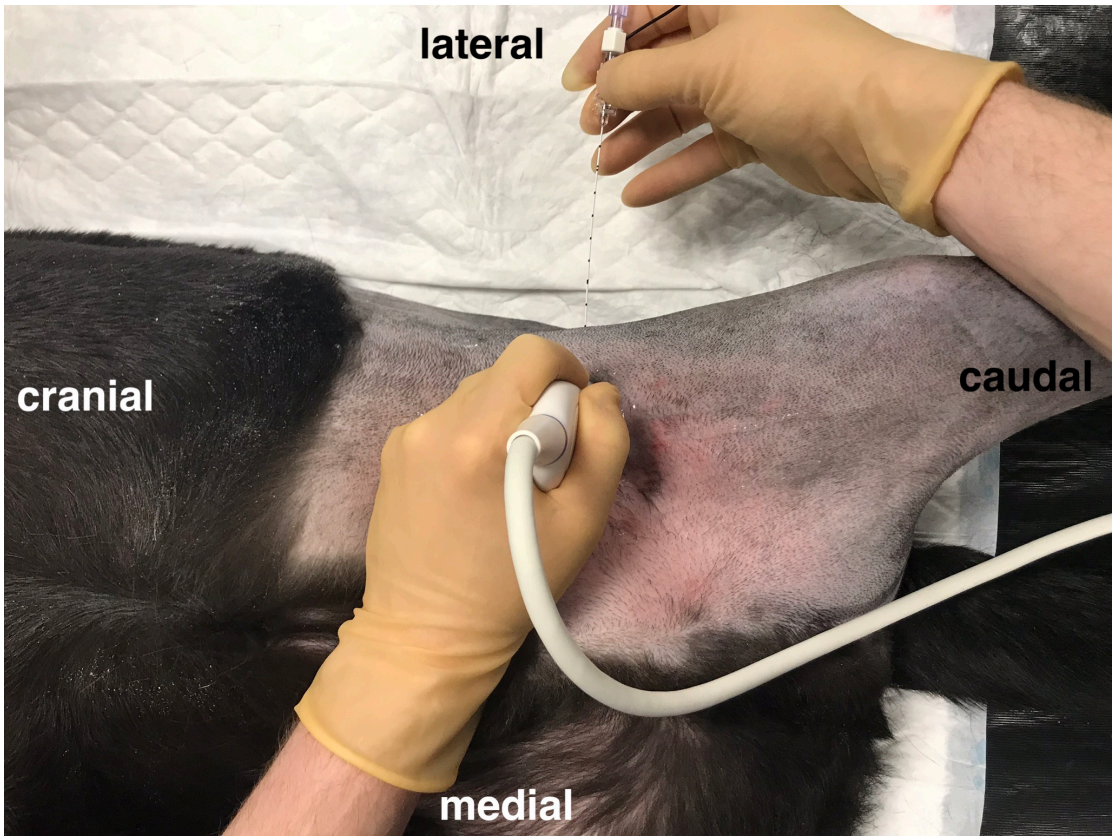
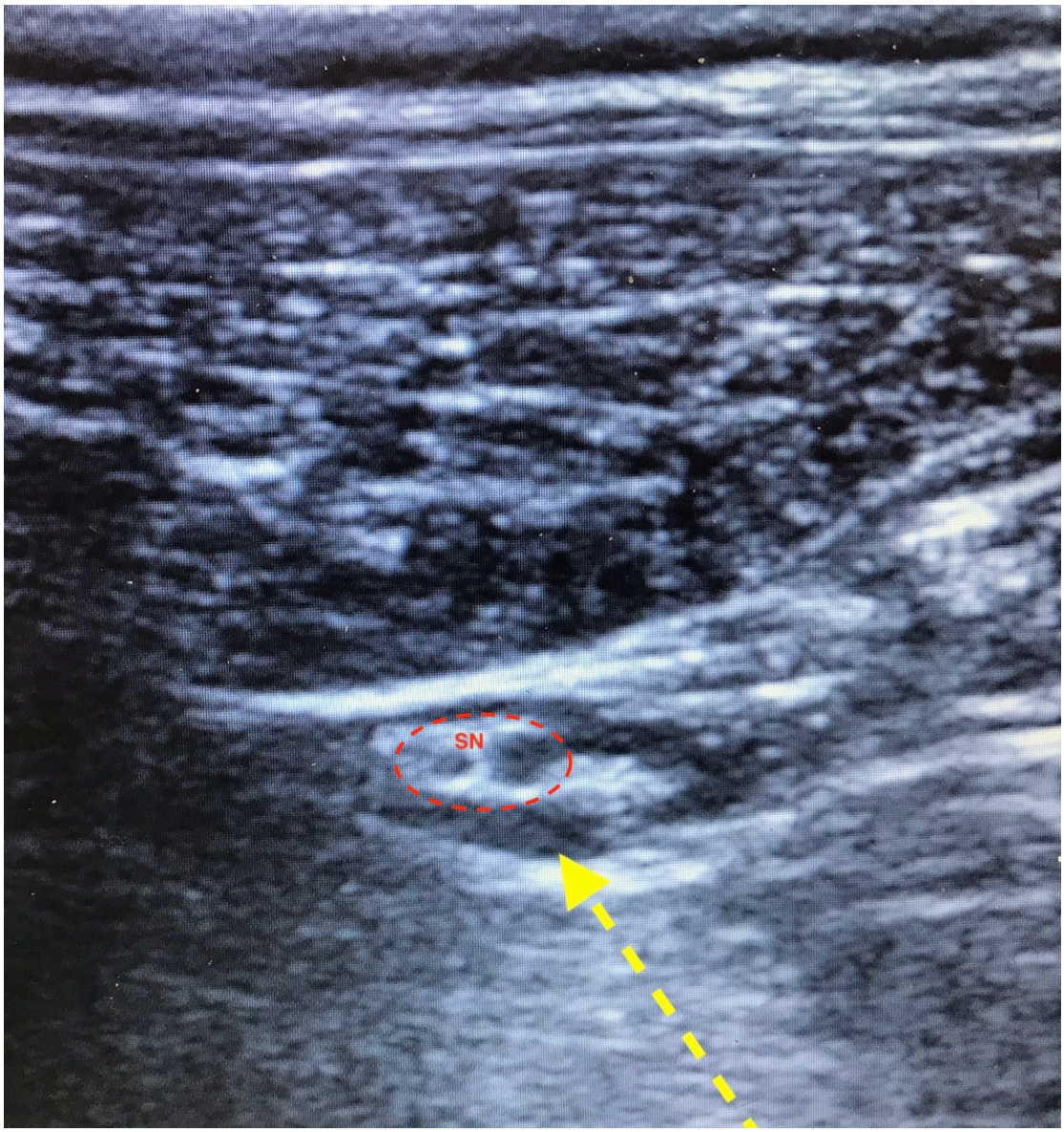


Figure 2.1.

Ultrasonographic image of the sciatic nerve demonstrating circumferential deposition of NMB around the target nerve referred to as a ‘doughnut sign’. Note that the external surface of the nerve is hyperechoic, with an anechoic centre, this is the typical ultrasonographic appearance of a nerve.



Key SN = sciatic nerve with dashed outline. Arrow = anechoic fluid surrounding the nerve.

Figure 2.2.

Dissection of the left pelvic limb of a dog showing staining of the sciatic nerve. Note the biceps femoris has been removed to allow visualisation of the sciatic nerve and surrounding structures. Green line shows the course of the locoregional anaesthesia needle

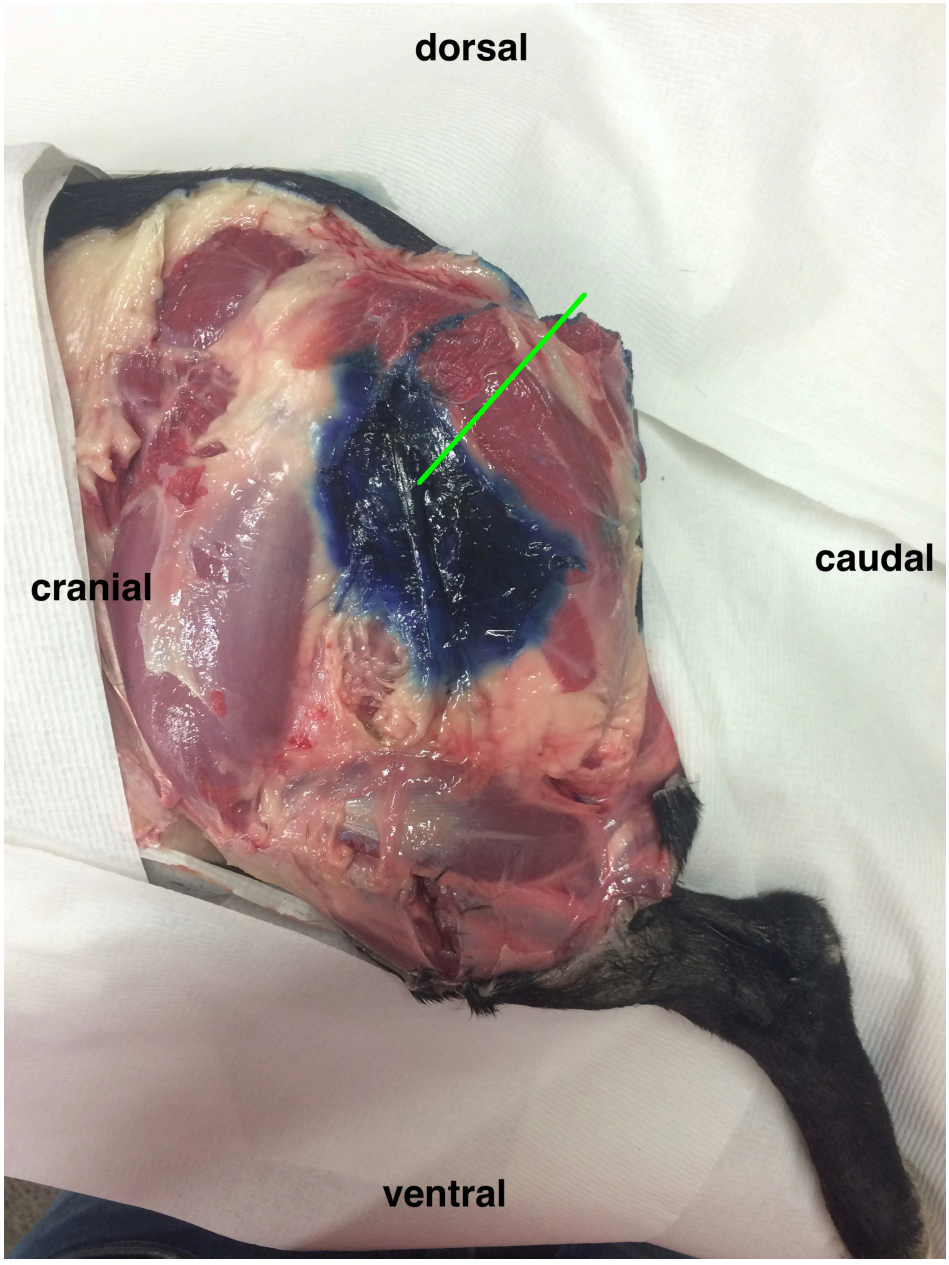


Figure 2.3.

Dissection of the psoas compartment showing the path of the femoral nerve. Note the psoas muscle has been dissected to allow visualisation of the nerve.

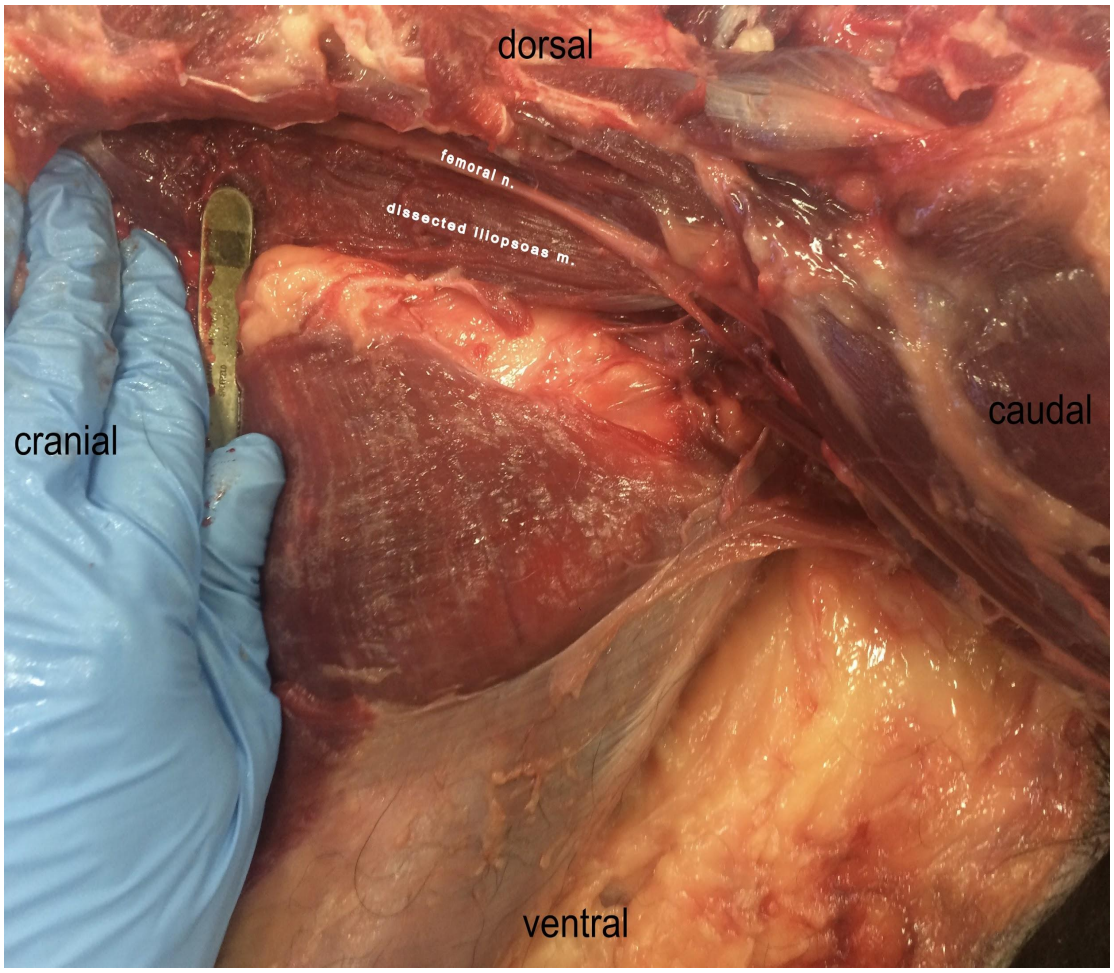
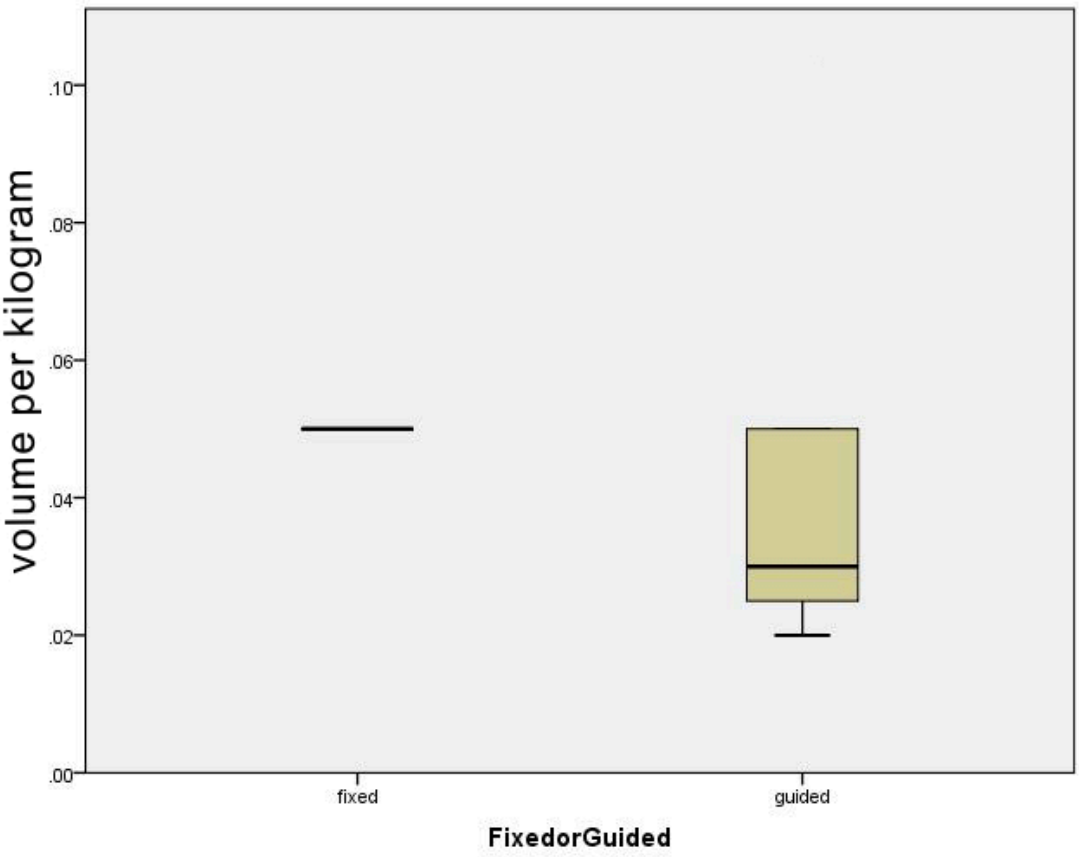


Figure 2.4.

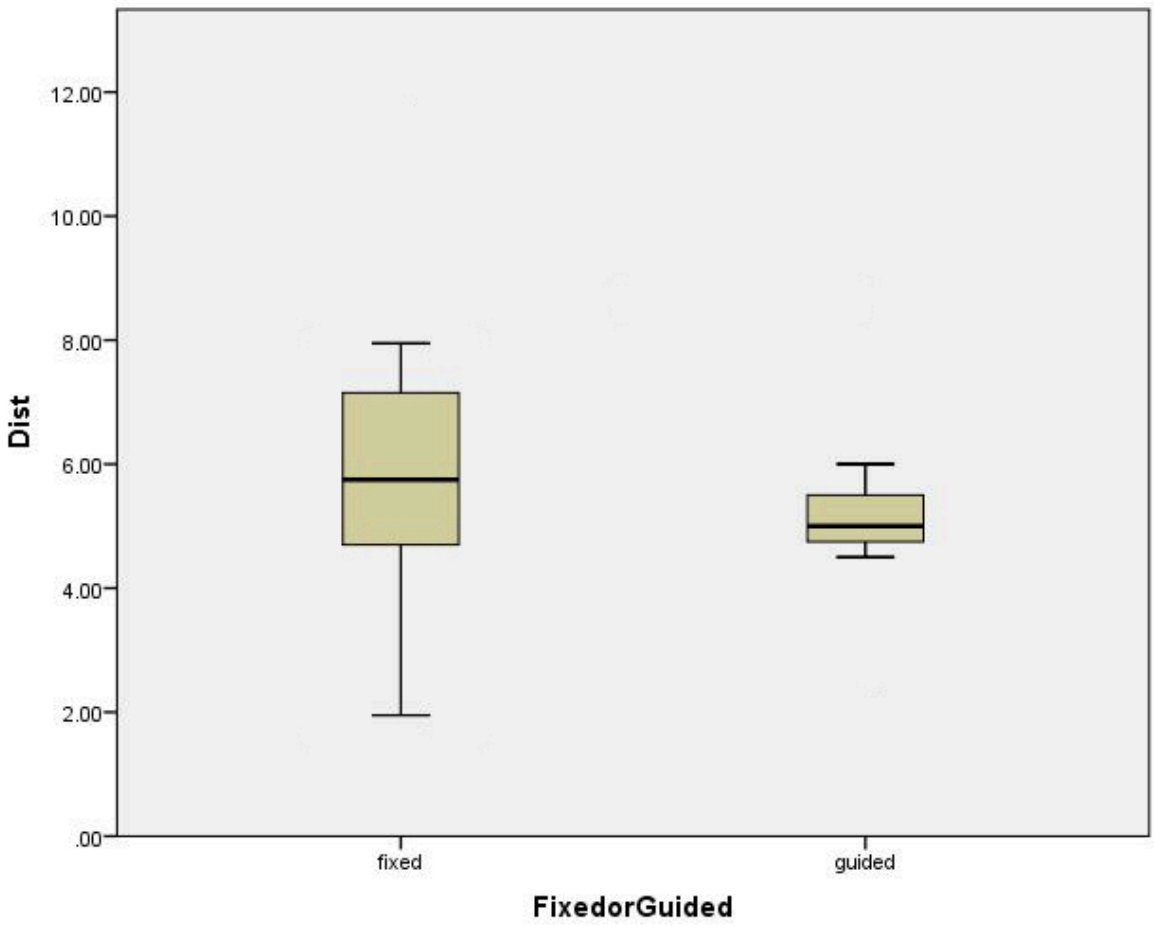
Boxplot the mean volume of NMB injected for sciatic nerves was 0.05 mL kg^{-1} in the fixed group, and 0.04 mL kg^{-1} in the USG. Volumes were not significantly different between groups (p = 0.67).



Key: USG = ultrasound-guided; NMB = new methylene blue; volume per kilogram (mL kg^{-1})

Figure 2.5.

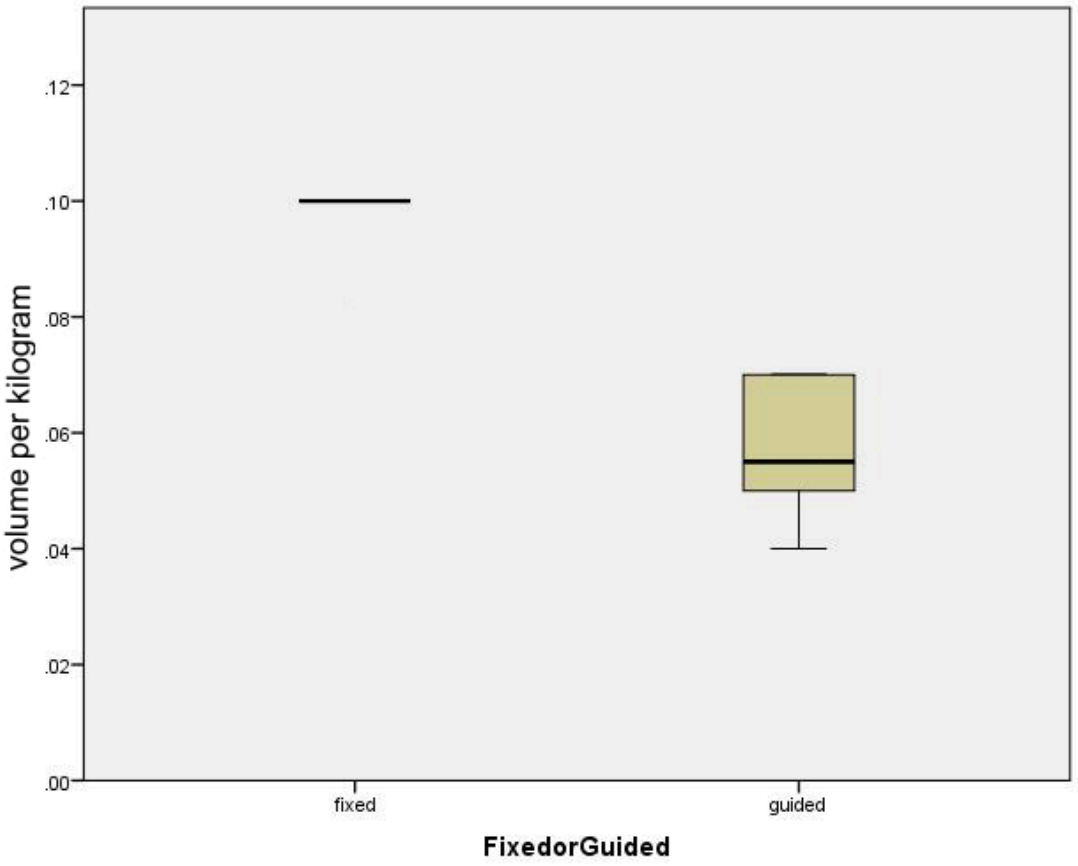
Boxplot showing length of stained sciatic nerve with new methylene blue was 5.9 cm in the Fixed group, and 5.7 cm in the USG group, and demonstrated no significant difference (p = 0.514).



Key: cm = centimetre; Fixed = fixed volume group; NMB = new methylene blue; USG = ultrasound-guided

Figure 2.6

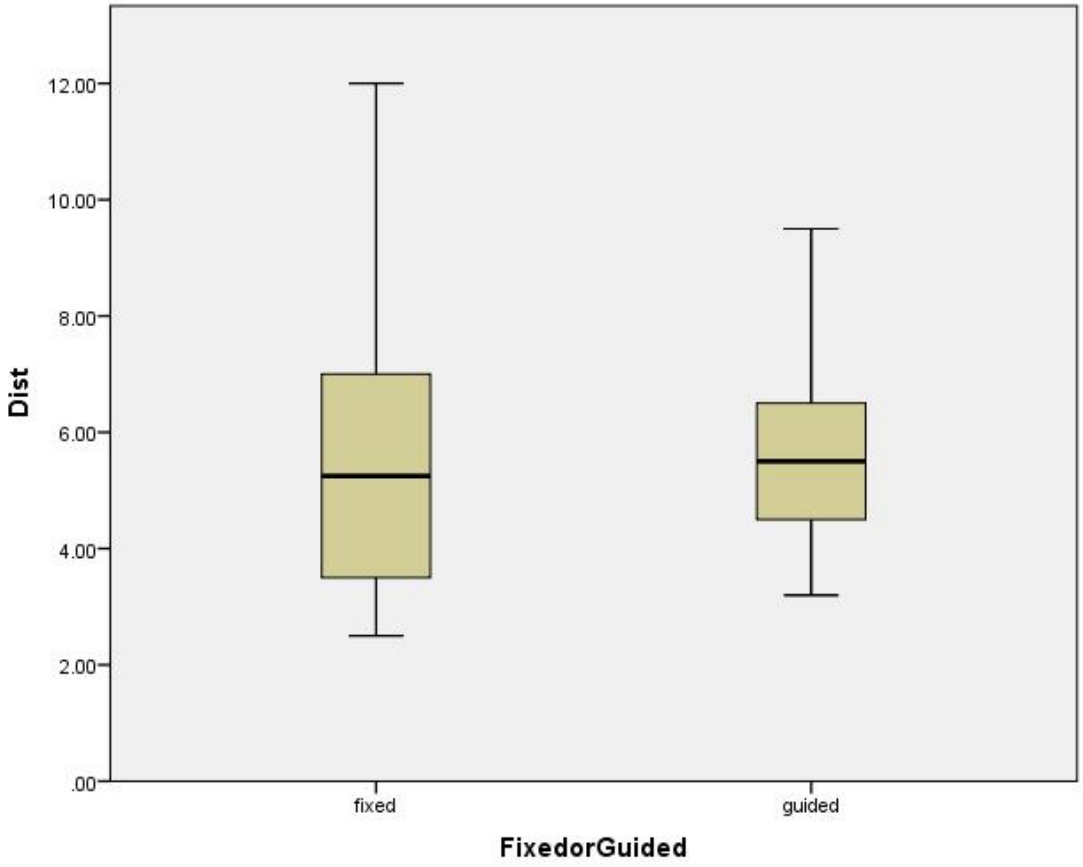
Boxplot showing mean volume of new methylene blue injected for the femoral nerve was 0.1 mL kg^{-1} in the Fixed group, and 0.06 mL kg^{-1} in the USG group and with a significant difference between groups (p = 0.01). The volume required in the USG group was significantly less than that used in the Fixed group.



Key: Fixed = fixed volume group; USG = ultrasound-guided group

Figure 2.7.

Boxplot showing average staining of the femoral nerve was 5.9 cm in the Fixed group, and 5.7 cm in the USG group showing no significant difference (p = 0.93), thus distance was equal for both groups, with all nerves having more than or equal to 2 cm of staining (this would be considered to be sufficient to provide an effective nerve block if done in a living animal).



Key: cm = centimetre; Fixed = fixed volume group; NMB = new methylene blue; USG = ultrasound-guided

Figure 3.1

Transverse ultrasonographic image of the femoral nerve within the psoas compartment obtained using the ventral suprainguinal approach as described by Echeverry et al., (2012). The iliopsoas is outlined in a dashed white line, with the femoral nerve outlined in yellow. A blood vessel is outlined in red.

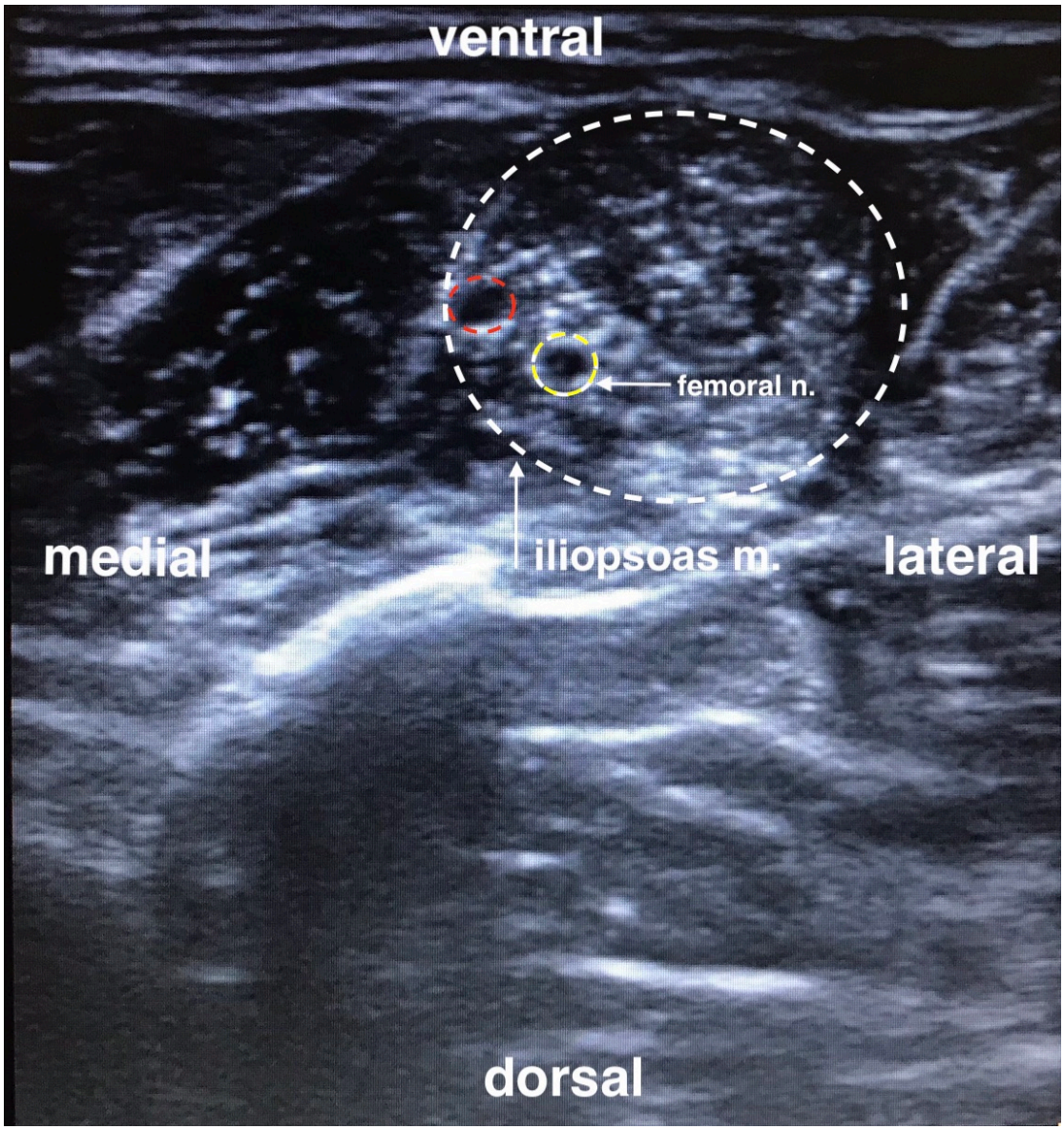
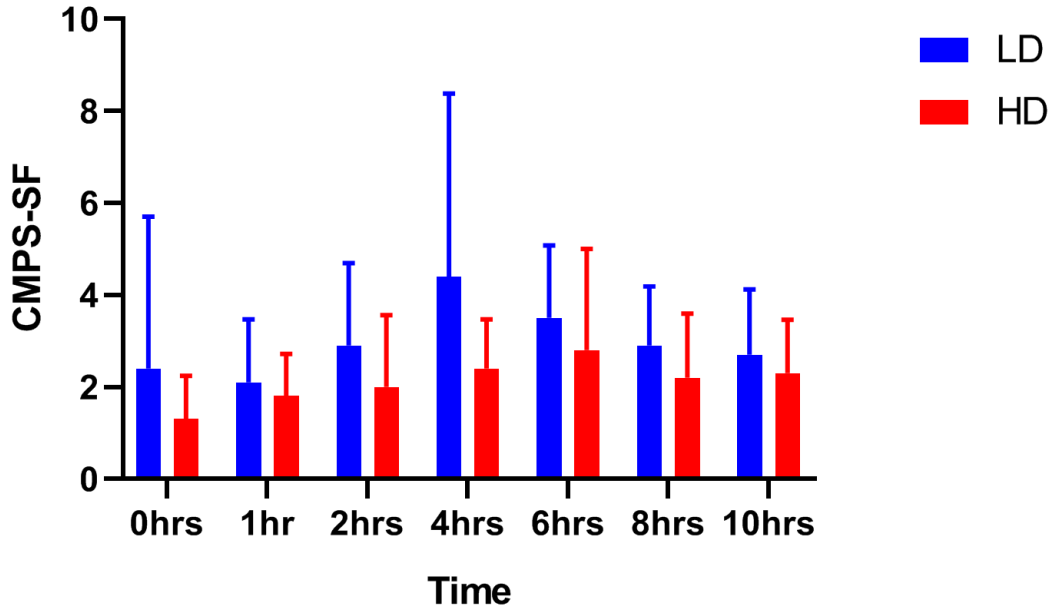


Figure 3.2.

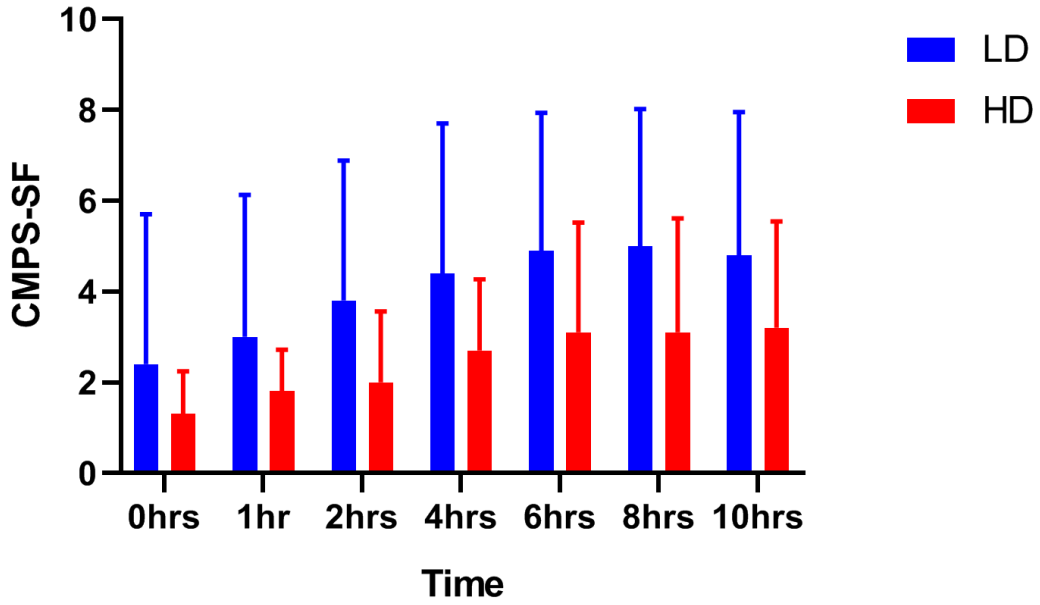
Chart showing postoperative composite measure pain scores in 20 dogs after TPLO surgery, depicting that there was no significant difference in CMPS-SF scores in the first 10 hours after surgery.



Key: hrs = hours; CMPS-SF = short form composite measure pain scale. LD = low dose group; HD = high dose group.

Figure 3.3

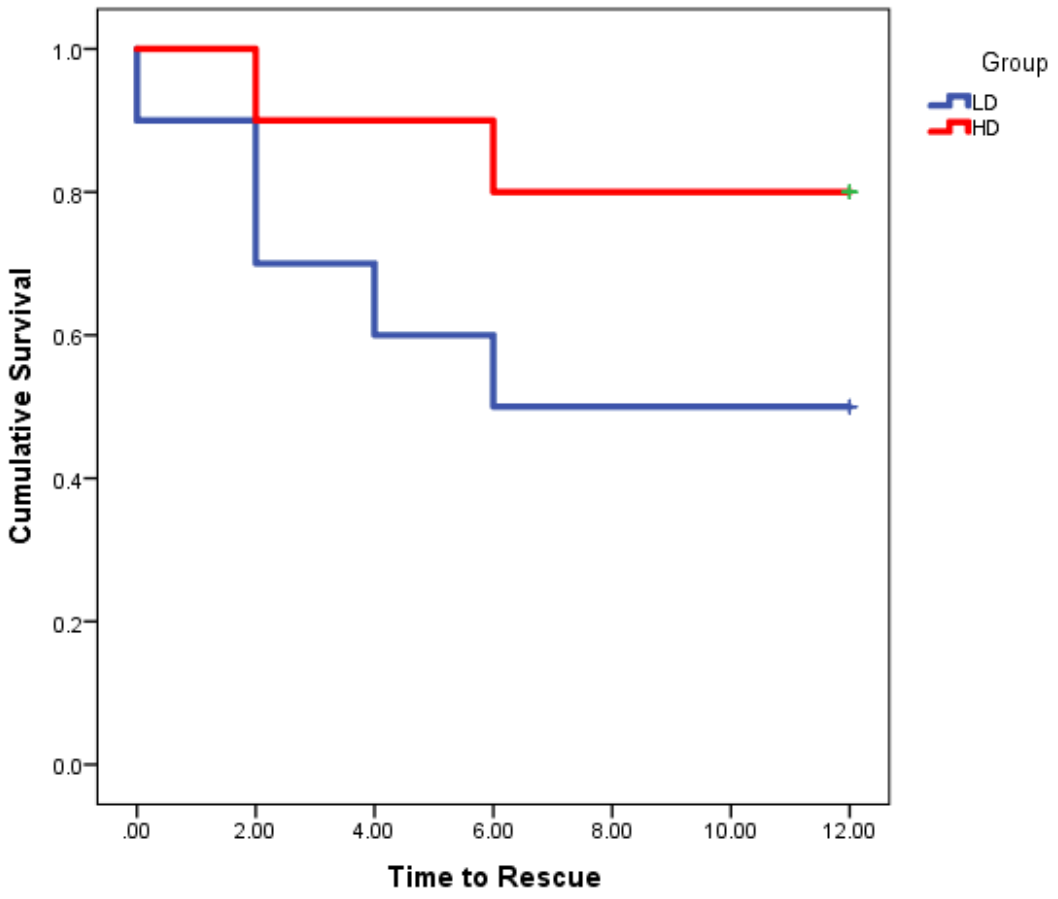
Chart showing postoperative composite measure pain scores in 20 dogs after TPLO surgery when using the last observation carried forward method. Although there is a trend for the LD group to have higher CMPS-SF scores in the first 10 hours after surgery, this was not statistically significant.



Key: hrs = hours; CMPS-SF = short form composite measure pain scale. LD = low dose group; HD = high dose group

Figure 3.4

Kaplan Meier survival analysis for time to first rescue analgesia requirement in 20 dogs, (10 HD and 10 LD) after TPLO surgery. No statistical significance was found between dogs in the LD or HD groups.



Key: hrs = hours; CMPS-SF = short form composite measure pain scale. LD = low dose group; HD = high dose group

APPENDIX 1

SHORT FORM OF THE GLASGOW COMPOSITE PAIN SCALE

Dog's name _____

Hospital Number _____ **Date** / / **Time**

Surgery Yes/No (delete as appropriate)

Procedure or Condition_____

_____

In the sections below please circle the appropriate score in each list and sum these to give the total score.

A. Look at dog in Kennel

Is the dog?

(i)

Quiet	0
Crying or whimpering	1
Groaning	2
Screaming	3

(ii)

Ignoring any wound or painful area	0
Looking at wound or painful area	1
Licking wound or painful area	2
Rubbing wound or painful area	3
Chewing wound or painful area	4

In the case of spinal, pelvic or multiple limb fractures, or where assistance is required to aid locomotion do not carry out section **B** and proceed to **C**
Please tick if this is the case ☐ then proceed to C.

B. Put lead on dog and lead out of the kennel.

When the dog rises/walks is it?

(iii)

Normal	0
Lame	1
Slow or reluctant	2
Stiff	3
It refuses to move	4

C. If it has a wound or painful area including abdomen, apply gentle pressure 2 inches round the site.

Does it?

(iv)

Do nothing	0
Look round	1
Flinch	2
Growl or guard area	3
Snap	4
Cry	5

D. Overall

Is the dog?

(v)

Happy and content or happy and bouncy	0
Quiet	1
Indifferent or non-responsive to surroundings	2
Nervous or anxious or fearful	3
Depressed or non-responsive to stimulation	4

Is the dog?

(vi)

Comfortable	0
Unsettled	1
Restless	2
Hunched or tense	3
Rigid	4

Total Score (i+ii+iii+iv+v+vi) = _____

Simple descriptive score for quality of recovery following anaesthesia. Modified from Jiménez et al., (2011)

Category	Description
1	Easy transition to alertness, coordinated movement
2	Fairly easy transition, holds head up, no body movement attempted
3	Some incoordination, does not startle, generally quiet
4	Limited muscle control, startles, may paddle or whine
5	Uncoordinated whole-body movements, startles, vocalizes
6	Emergence delirium, thrashing, cannot easily restrain