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**Blocs interfasciaux échoguidés : applications cliniques pour la gestion de  
la douleur périopératoire chez les chiens**

**Ultrasound-guided interfascial plane blocks: clinical applications for  
perioperative pain management in dogs**

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## Abbreviations

<b>CNS</b>	Central nervous system
<b>ES</b>	Erector spinae
<b>IFP</b>	Interfascial plane
<b>LA</b>	Local anaesthetic
<b>Pm</b>	Psoas minor
<b>PM</b>	Psoas major
<b>QL</b>	Quadratus lumborum
<b>SF-GCMPS</b>	Short Form of the Glasgow Composite Measure Pain Scale
<b>RCT</b>	Randomised clinical trial
<b>SN</b>	Spinal nerve
<b>TAP</b>	Transversus abdominis plane
<b>US</b>	Ultrasound
<b>VB</b>	Vertebral body



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# Summary

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## Summary

This thesis explores the advancements in ultrasound-guided locoregional anaesthesia for perioperative analgesia in dogs, specifically focusing on the interfascial plane blocks. The introduction of these blocks in veterinary practice marks a shift in the approach to locoregional anaesthesia, offering a potentially safer and more effective alternative to traditional techniques like epidural or spinal anaesthesia. The interfascial plane blocks target spaces between fasciae, which are layers of connective tissue that serve as conduits for nerves travelling from the spinal cord to their respective innervation anatomical districts. Unlike traditional peripheral nerve blocks, requiring sonographic identification of nerves, interfascial plane blocks rely on the sonographic identification of the fascial planes and the local anaesthetic distribution, providing a broader area of desensitization.

The thesis begins by discussing the growing interest in interfascial plane blocks in veterinary medicine, driven by the widespread implementation of ultrasonography in modern clinical practice. This advancement has enabled more precise and safer applications of locoregional anaesthesia, which has led to the rapid adoption of these techniques. For instance, the quadratus lumborum block and the erector spinae plane block have gained significant attention due to their ability to provide analgesia to abdomen and spine, respectively, making them suitable for a variety of surgical procedures. These blocks are particularly advantageous in cases where traditional neuraxial techniques may involve a higher risk of complications - including hypotension, motor block, or bleeding, due to potential damage to vessels in the epidural region - especially in patients with comorbidities.

This research aims to fill a gap in veterinary medicine, where the application of interfascial plane blocks in canine species has been predominantly studied in cadaveric models, with limited clinical evidence available to support their efficacy and safety in living patients. Through a series of clinical studies, this thesis provides clinical evidence on the use of these blocks in dogs undergoing various surgical procedures, contributing significantly to the field of veterinary anaesthesia.

The first study evaluates the analgesic efficacy of the quadratus lumborum block using two different concentrations of ropivacaine in dogs undergoing laparoscopic ovariectomy, a common abdominal surgical procedure. The study demonstrates that higher concentration of ropivacaine (0.5%) prolonged the time to the first postoperative rescue analgesia, while lower concentration (0.33%) resulted in a more significant reduction in arterial blood pressure. These findings show that the concentration of local anaesthetic can influence the duration of the analgesic effect of these techniques and highlight the quadratus lumborum block's potential to reduce the use of systemic

opioids, which are associated with various side effects, such as sedation, cardiovascular and respiratory depression, nausea, vomiting and constipation.

The second study explores and compares the analgesic efficacy of the lateral with the latero-ventral approaches for the quadratus lumborum block. The lateral approach was found to be more effective in reducing the need for perioperative rescue analgesics in dogs undergoing laparoscopic ovariectomy. Therefore, it can be recommended as the more effective option for managing perioperative pain in abdominal surgeries, in comparison with the latero-ventral approach.

The third study introduces and evaluates a novel ultrasound-guided technique for catheter placement in the quadratus lumborum plane in canine cadavers, with the goal of providing continuous local anaesthetic administration through the postoperative period. The study assessed the spread of two different volumes of contrast media solution injected throughout the catheters, using computed tomography. The results of this study indicated that the catheter placement technique is feasible in dogs and the use of larger volumes of local anaesthetic resulted in a more extensive spread. This study also included a clinical case series, where the technique was successfully applied in dogs undergoing various abdominal surgeries, demonstrating its potential application in a clinical setting.

The last study investigates the perioperative analgesic effect of the unilateral lumbar erector spinae plane block in dogs undergoing hemilaminectomy for Hansen type I intervertebral disc extrusion, a common spinal surgery in dogs. The study shows that the erector spinae plane block significantly reduces the consumption of both intra- and postoperative systemic analgesics and decreases the incidence of intraoperative cardiovascular complications. This finding supports the use of the erector spinae plane block as a valuable component of multimodal analgesia strategies in spinal surgeries.

While this thesis provides significant evidence supporting the use of interfascial plane blocks for perioperative analgesia in dogs, several areas warrant further investigation. Future studies should assess the impact of these techniques on opioid consumption in dogs undergoing a broader range of surgeries. Furthermore, large-scale, multi-center studies are needed to validate their safety and efficacy. By addressing these gaps, future research will help refine these techniques, ensuring their application in veterinary anaesthesia and improving pain management strategies for surgical patients.

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# Introduction

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## 1. Ultrasound-guided interfascial plane blocks

Thanks to the implementation of ultrasonography in modern clinical practice, interest in a particular branch of locoregional anaesthesia, that studies and develops the so-called interfascial plane (IFP) blocks, has grown exponentially in the last decades. These blocks differ from traditional peripheral nerve blocks in that the target for injection of the local anaesthetic (LA) does not correspond to ultrasound (US)-distinguishable neuronal structures, but to potential spaces situated between opposing sheets of connective tissue, or fasciae, which act as conduits for nerves travelling from the spinal cord to their innervation sites (Elsharkawy et al. 2019; Machi & Joshi, 2019; Chin et al. 2021a). The LA diffuses within the space, desensitising the nerves and inducing a conduction blockade over a large area of the body (Machi & Joshi, 2019; Chin et al. 2021a).

“Fascia” is defined as a sheet of connective tissue that envelops different anatomical structures, such as muscles, bones, nerve structures, and internal organs (Klingler et al. 2014; Adstrum et al. 2017;). Fasciae are typically differentiated in two layers: the superficial fascia, beneath the dermis and the deep fascia, enveloping muscles and neurovascular structures. In particular, the space between the two layers of deep fasciae, acts as a potential communication pathway for nerve structures between different anatomical districts, and that is therefore the target of IFP blocks (; Wilke et al. 2016; Elsharkawy et al. 2019). Histologically, this connective tissue comprises varying layers of organised collagen intermixed with adipose tissue, fibroblasts, and hyaluronic acid (Chin et al. 2021a). In dogs, as in humans, these layers are loosely connected by additional collagen fibres arranged in transverse and/or oblique orientations, acting as scaffolds. This arrangement facilitates hydrodissection during IFP blocks and aids in the spread of the LA solution (Ahmed et al. 2019; Chin et al. 2021a). Functionally, fasciae have traditionally been viewed as shock absorbers that allow muscles to glide past one another and transmit ground forces. They are also thought to play a role in proprioception and muscle coordination, as well as assisting blood and lymphatic flow via a “muscle pump” mechanism (Benjamin 2009; Willard et al. 2012). Some authors consider fasciae as a separate organ, due to their innervation with both sensory and proprioceptive nerve fibres. Although not fully elucidated in veterinary species, this innervation could allow fasciae to become a source of pain when inflamed or constricted (Benjamin 2009; Willard et al. 2012).

IFP blocks are considered alternatives to neuraxial techniques, such as epidural or spinal anaesthesia, to provide regional analgesia to the trunk. The advantages of using this type of blocks are several: first, since the target is superficial and therefore more easily visible and identifiable under US-guidance, IFP are characterized by great simplicity and speed of execution. Distance of the

IFP from important vascular or nerve structures provides good safety to these techniques, as they seem not to be associated with bleeding, epidural haematomas or abscesses and pneumothorax (Chin & Barrington, 2019; Ueshima et al. 2017). In addition, they target spinal nerve (SN) branches at more distal sites than neuraxial techniques. This is considered advantageous since neuraxial techniques can cause undesirable side effects such as hypotension, due to extensive sympathetic block (Holte et al. 2004). Moreover, by guaranteeing a primarily somatic block, there are usually no sequelae and side effects typical of a motor block. Fasciae are often contiguous with each other. Consequently, different approaches to perform the IFP block technique are described, with different outcomes in terms of spread and degree of sensory block achieved (Shao et al. 2022). Unlike neuraxial anaesthesia, this allows the clinician to adjust the block effects by depositing LAs closer to the area of interest. Nevertheless, this branch of locoregional anaesthesia is not entirely free of complications and its efficacy is still subject of research and debate (Lönnqvist & Karmakar, 2019). Indeed, studies in human medicine have shown that IFP blocks are associated with high plasma concentrations of LA (Rahiri et al. 2017). In fact, the clinical efficacy of these techniques is intrinsically linked to the need to inject high volumes of LA in very large anatomical areas, which are therefore more susceptible to absorption of the molecule used. Although this does not appear to be associated with complications related to the toxicity of LA in healthy patients (Børglum et al. 2012), caution must be taken in the presence of co-morbidities (such as renal and cardiovascular disease), although these are the patients who would most benefit from such a locoregional anaesthesia technique (Torup et al. 2012; Ishida et al. 2018).

The mechanism of action of IFP blocks has not been fully understood, and several hypotheses have been proposed (Chin et al. 2021b). Spread of the LA around the nerves within an IFP is widely accepted as leading to sensory block. The extent of this spread and subsequent block may vary depending on several factors, including the bulk flow of the injectate, the specific composition of the fascia, and the concentration and volume of the LA used (Bruggink et al. 2012; Elsharkawy et al. 2018; Chin et al. 2021b). The bulk flow of the injectate is determined by fluid dynamics and the presence of pressure differences (Davis & Kenny 2005). Factors such as the specific IFP, muscle tone, and injection velocity may influence the final spread of the injectate (Elsharkawy et al. 2018). Furthermore, diffusion of the LA across the fascia into surrounding tissues could potentially contribute to the block's effectiveness. Studies have shown that fasciae are not entirely impermeable and that LAs can diffuse across these layers (Chin et al. 2021b). This diffusion might allow the LA to reach nerves that are not directly adjacent to the injection site, providing a broader area of desensitization (Chin et al. 2021a). It has been hypothesized also that part of the analgesic

effect of the IFP blocks could be produced by epidural or paravertebral spread of LA (Chin et al. 2021b, Ueshima et al. 2017). However, the extent and clinical significance of such spread remain highly controversial and will be discussed in more detail later in this thesis. In a cadaveric study conducted on pigs, Otero et al. (2020) observed spread of dye solution in the paravertebral thoracic lymph nodes, after performing the erector spinae (ES) plane block. According to the authors of that study, an immunomodulatory analgesic effect of this block cannot be ruled out. Lastly, systemic absorption of the LA could elicit analgesic effects at distant sites. Following IFP blocks, LAs can be absorbed into the bloodstream and act on the central nervous system (CNS) to provide analgesia (Chin et al. 2021a). This systemic effect is thought to be minimal compared to the action of LA on nerve fibres, but it might still contribute to the overall analgesic profile observed in patients. Overall, while the primary mechanism of action for these blocks is believed to be the spread of LA in the IFP plane, the additional contributions from diffusion across fascia and systemic absorption likely play a role in the block's overall effectiveness.

The first US-guided IFP blocks described in human medicine were the abdominal rectus sheath block (Willschke et al. 2006) and the transversus abdominis plane (TAP) block (Hebbard et al. 2007). These were followed by, among others, the quadratus lumborum (QL) block (Blanco et al. 2007) the serratus plane block (Blanco et al. 2013), the ES plane block (Forero et al. 2016). Interest and utilization of IFP blocks in veterinary medicine have grown significantly over the past decade, as evidenced by the increasing number of research studies and related publications. In canine species, the following techniques are described in cadaveric studies: abdominal and subcostal approaches to the TAP block (Schroeder et al. 2011; Drozdzyńska et al. 2017), the rectus sheath block (St James et al. 2020), the serratus plane block (Freitag et al. 2020), the ES plane block (Ferreira et al. 2019; Portela et al. 2020; Medina-Serra et al. 2020), the QL block (Garbin et al. 2020a, b; Viscasillas et al. 2021a; Alaman et al. 2022a; Marchina-Gonçalves et al. 2022; Marchina-Gonçalves et al. 2023), and the transversus thoracis plane block (Alaman et al. 2021, Alaman et al. 2022b). In this research, we decided to focus on two IFP blocks that attracted great attention and stimulated an explosion of interest in both human and veterinary medicine: the QL block and ES plane block.

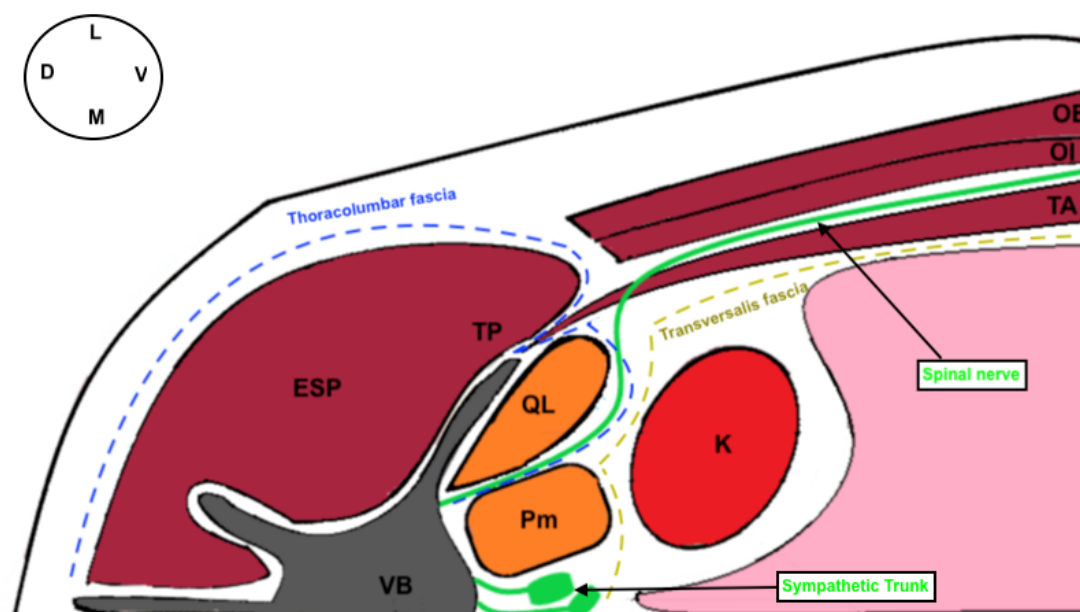
### **1.1 Quadratus lumborum block**

The QL block is an US-guided IFP block used to promote somatic and visceral analgesia to the abdomen (Garbin 2024). It consists of the injection of LA in the thoracolumbar fascia surrounding

the QL muscle, aiming to desensitise the ventral rami of the SNs and the sympathetic trunk. This technique was first described by Blanco et al. (2007) as a modification of the TAP block in humans. Since then, several approaches have been described and the following classification, based on the anatomical location of needle tip placement in relation to the QL muscle, has been proposed: lateral (QL block 1), posterior (QL block 2), and anterior (QL block 3) approaches (Ueshima et al. 2017). The QL block has been implemented in the analgesic management of several abdominal surgeries, such as caesarean section and other gynaecological procedures, small intestine and colon resection, appendectomy, gastrectomy, nephrectomy (Kim et al. 2020; Uppal et al. 2020; Korgvee et al. 2021). In the last few years, this IFP block has been successfully used also for analgesia during femur and hip surgeries, providing a motor-protective effect (Akerman et al. 2018).

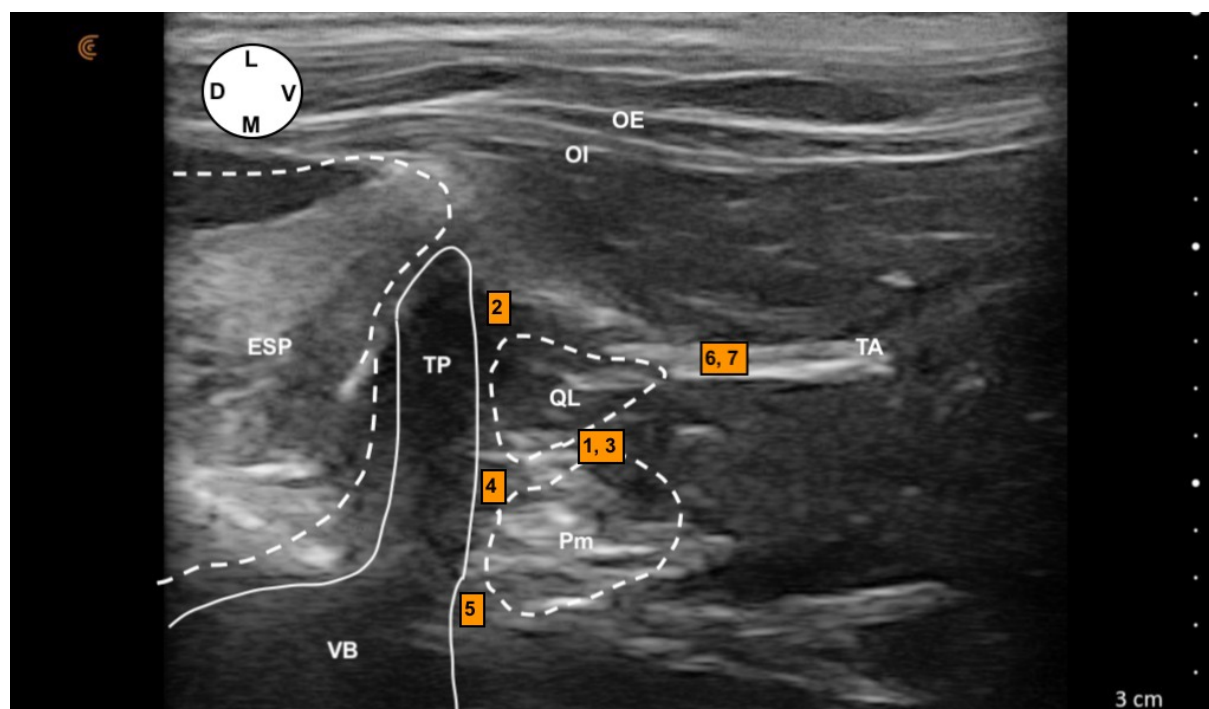
In dogs, the QL muscle is located ventrally to the vertebral bodies (VBs) of the last three thoracic vertebrae and all lumbar vertebrae, reaching caudally the iliac crest. The thoracic and cranial abdominal portions of the QL muscle consists of different bundles attached to the proximal parts of the last two ribs, or the transverse processes of the lumbar VBs. The ventromedial aspect of the QL muscle is in contact with the psoas minor (Pm) muscle, and below the fourth lumbar vertebra, with the psoas major (PM) muscle. Laterally, it is adjacent to the aponeurosis of the transversus abdominis muscle dorsally, and the peritoneum or perirenal fat ventrally. The fasciae surrounding the QL muscle are the thoracolumbar fascia (dorsally), the endothoracic fascia in the thoracic region and the transversalis fascia in the abdominal region (ventrally). The thoracolumbar ventral rami of the SNs between the twelfth thoracic (T12) and third lumbar (L3) vertebra, involved in the somatic innervation of the abdomen, exit the vertebral foramen, and pass through the endothoracic fascia. According to the anatomical study from Garbin et al. (2020a), they travel between the bundles of the QL muscle, or between the QL and Pm muscle. They continue between the aponeurosis of the transversus abdominis muscle or between the transversus abdominis and the obliquus internus abdominis muscles. The visceral innervation of the abdomen is provided by the sympathetic trunk, that is located medio-ventrally to the hypaxial muscles and dorsal to the transversalis fascia. The sympathetic trunk receives ramifications from the rami communicants, after they emerge from the intervertebral foramina and run between the VB and the dorsal aspect of the QL and psoas muscles (Garbin et al. 2020a) (Figure 1).





**Figure 1.** Schematic illustration of a cross section at the level of the first lumbar vertebra (L1) showing the abdominal musculature with the fascia layers surrounding the quadratus lumborum (QL) muscle in a dog. The targets of the QL block (spinal nerve and sympathetic trunk) are represented in green. The yellow dashed line represents the transversalis fascia; the blue green dashed line, the thoracolumbar fascia; the light green dashed line, the ventral layer of the thoracolumbar fascia; ESP, erector spinae muscle; K, kidney; OE, obliquus internus muscle; OI, obliquus internus muscle; Pm, psoas minor muscle; QL, quadratus lumborum muscle; TA, transversus abdominis muscle; TP, transverse process of the vertebra; VB, vertebral body. D, dorsal; M, medial; V, ventral; L, lateral.

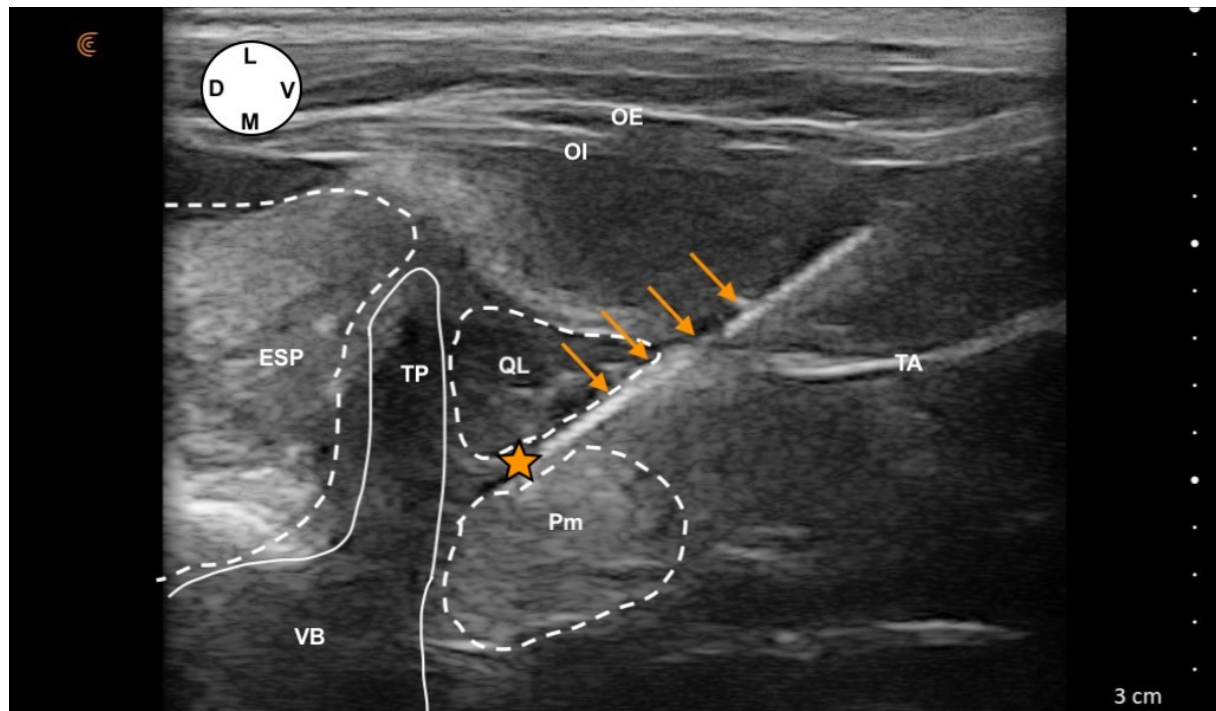
To date, seven cadaveric studies evaluated the spread of injectate in dogs, using different approaches (Garbin et al. 2020a, b; Viscasillas et al. 2021a; Alaman et al. 2022a, Marchina-Gonçalves et al. 2022; Marchina-Gonçalves et al. 2023, Otero et al. 2024) (Figure 2). Garbin (2024) recently proposed a classification, based on the position of the needle tip relative to the QL muscle, during injection: transmuscular, when it is positioned between the QL and Pm muscles (Garbin et al. 2020a, Viscasillas et al. 2021a); dorsal, between the body of the first (L1) or second (L2) lumbar vertebrae and the QL muscle (Alaman et al. 2022a, Marchina-Gonçalves et al. 2022); lateral, between the lateral aspect of the QL muscle and the transverse process of L1 (Garbin et al. 2020b); latero-ventral, between the ventral aspect of the QL muscle and the transversus abdominis muscle (Marchina-Gonçalves et al. 2023). The needle can be advanced in a ventrolateral-to-dorsomedial (Garbin et al. 2020a, b; Alaman et al. 2022a; Marchina-Gonçalves et al. 2022; Marchina-Gonçalves et al. 2023; Otero et al. 2024) or dorsolateral-to-ventromedial direction (Viscasillas et al. 2021a).



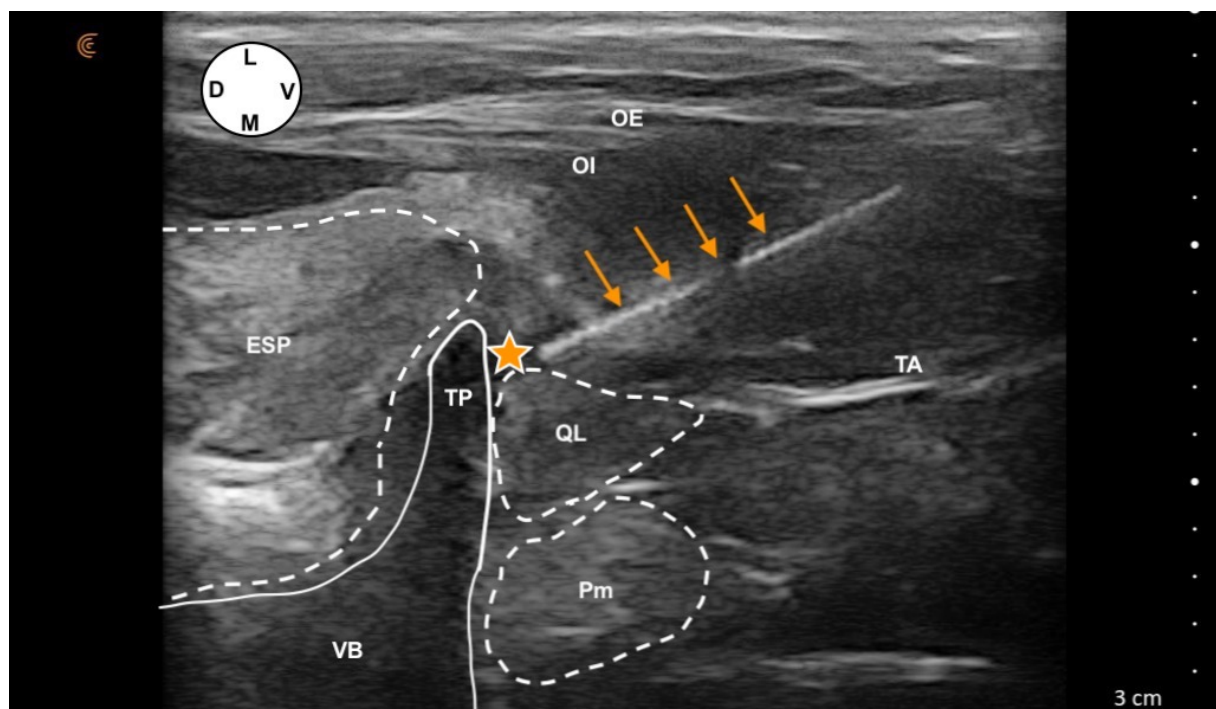
**Figure 2.** Transversal ultrasound image and landmarks for the quadratus lumborum (QL) block and sites of injection of the different approaches described in canine species (numbers). 1, transmuscular approach (Garbin et al. 2020a); 2, lateral approach (Garbin et al. 2020b); 3, transmuscular dorsoventral (Viscasillas et al. 2021a); 4, dorsal (Alaman et al. 2022a); 5, dorsal (Marchina-Gonçalves et al. 2022); 6, lateroventral (Marchina-Gonçalves et al. 2023); 7, lateroventral caudal (Otero et al. 2024). ESP, erector spinae muscle; OE, obliquus externus muscle; OI, obliquus internus muscle; Pm, psoas minor muscle; QL, quadratus lumborum muscle; TA, transversus abdominis muscle; TP, transverse process of the vertebra; VB, vertebral body. D, dorsal; M, medial; V, ventral; L, lateral.

The first study performed in canine cadavers was published by Garbin et al. (2020a). The authors of that study compared the spread of two different volumes of dye-lidocaine solution ( $0.15$  versus  $0.3 \text{ mL kg}^{-1}$ ), injected between the QL and Pm muscles (Figure 3). Anatomical dissections showed that injections with higher volume resulted in consistent staining of the ventral branches of the T13–L3 SNs and the sympathetic trunk. However, the visualization of the IFP between the QL and Pm muscles is not always easily achievable, especially in small and large breed dogs.

In a second cadaveric study, the same authors compared two different approaches, in which the tip of the needle was positioned laterally to the QL muscle (Figure 4): a transversal and a longitudinal QL block, depending on the position of the US probe with respect to the spinal column. The transversal approach resulted in more consistent staining of ventral rami of the SNs and sympathetic trunk, in comparison with the longitudinal one, after injecting  $0.3 \text{ mL kg}^{-1}$  of dye solution (Garbin et al. 2020b).



**Figure 3.** Transversal ultrasound image and landmarks for the transmuscular approach for the quadratus lumborum (QL) block (Garbin et al. 2020a) needle trajectory (arrows) and injection point (star). ESP, erector spinae muscle; OE, obliquus externus muscle; OI, obliquus internus muscle; Pm, psoas minor muscle; QL, quadratus lumborum muscle; TA, transversus abdominis muscle; TP, transverse process of the vertebra; VB, vertebral body. D, dorsal ; M, medial ; V, ventral ; L, lateral.



**Figure 4.** Transversal ultrasound image and landmarks for the lateral approach for the quadratus lumborum (QL) block (Garbin et al. 2020b) needle trajectory (arrows) and injection point (star). ESP, erector spinae

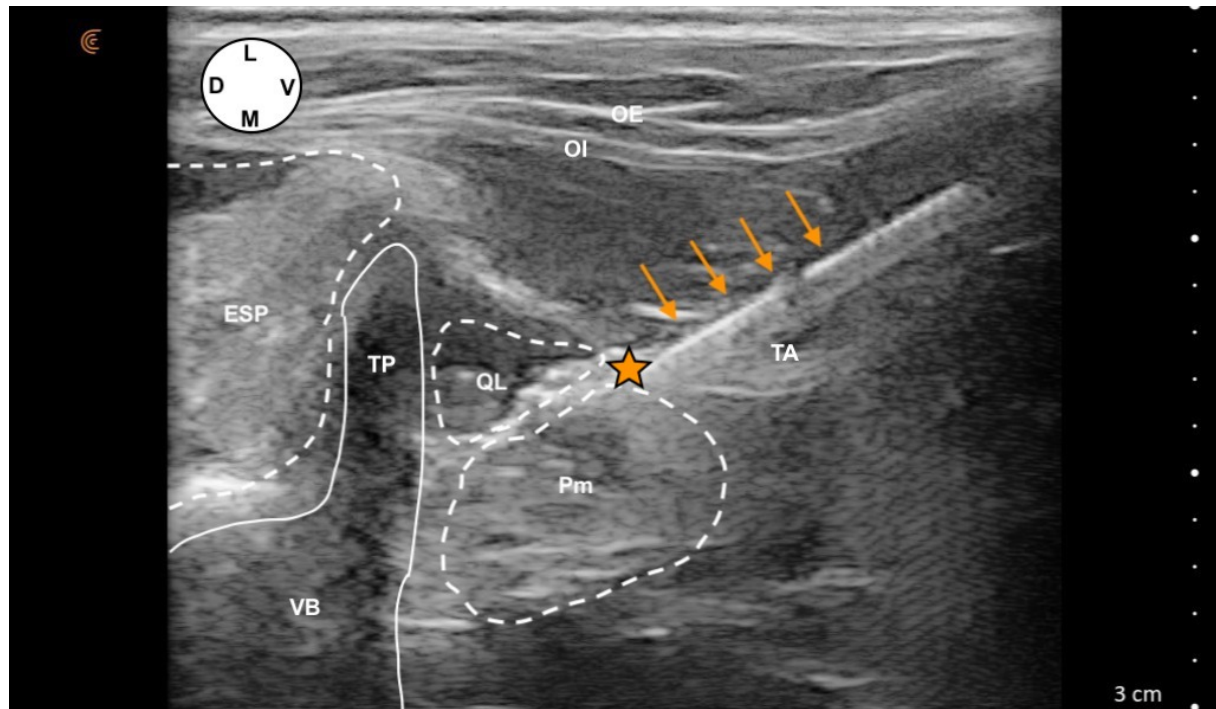
muscle; OE, obliquus externus muscle; OI, obliquus internus muscle; Pm, psoas minor muscle QL, quadratus lumborum muscle; TA, transversus abdominis muscle; TP, transverse process of the vertebra; VB, vertebral body. D, dorsal ; M, medial ; V, ventral ; L, lateral.

Viscasillas et al. (2021a) performed a transmuscular QL block advancing the needle with a dorsolateral-to-ventromedial direction in canine cadavers. A volume of 0.2 mL kg<sup>-1</sup> of a mixture of iomeprol and methylene blue was injected. Results showed staining of the ventral rami of the SNs from T13 to L4, similarly to the high-volume solution used by Garbin et al. (2020a).

The dorsal QL block was described in two different studies, in which the injection was performed between the VB of L1 or L2 and the QL muscle (Marchina-Gonçalves et al. 2022; Alaman et al. 2022a). Marchina-Gonçalves et al. (2022) demonstrated that a high volume of injectate (0.6 mL kg<sup>-1</sup>) resulted in staining of the sympathetic trunk within T10 and L4, and ventral rami of the SNs between L1 and L3. Similarly, 0.5-mL kg<sup>-1</sup> of methylene blue consistently stained the ventral rami of the SNs between T13–L3 SNs and the sympathetic trunk from the T11–L3 vertebrae (Alaman et al. 2022a). However, both studies showed spread of injectate to the epidural space (Marchina-Gonçalves et al. 2022; Alaman et al. 2022a).

The QL block can be challenging to perform, when deep injections targets are selected, such as with the approaches described by Garbin et al. (2020a), Alaman et al. (2022a) and Marchina-Gonçalves et al. (2022). At this level, the vicinity of the aorta, the caudal vena cava, and abdominal organs can pose some difficulties in performing the block. Recently, a novel latero-ventral approach for the QL block has been proposed, in which the injection site is more superficial and away from important anatomical structures (Marchina-Gonçalves et al. 2023) (Figure 5). According to the authors, this approach might be safer and easier to perform. However, the latero-ventral approach failed to produce a consistent spread of injectate towards the sympathetic trunk, suggesting that it might not provide visceral pain relief to the abdomen (Marchina-Gonçalves et al. 2023).

Recently, Otero et al. (2024) described a caudal QL block approach, in which the injection is performed laterally to the QL muscle at the level of L6. Following the injection of 0.3 mL kg<sup>-1</sup> of methylene blue solution, this technique resulted in a solution spread, staining a median (range) of 3 (2-4) SNs, between L3 and L6. According to the authors of that study, this technique appears to be feasible for providing analgesia and a motor protective effect after surgical procedures involving the hindlimbs.



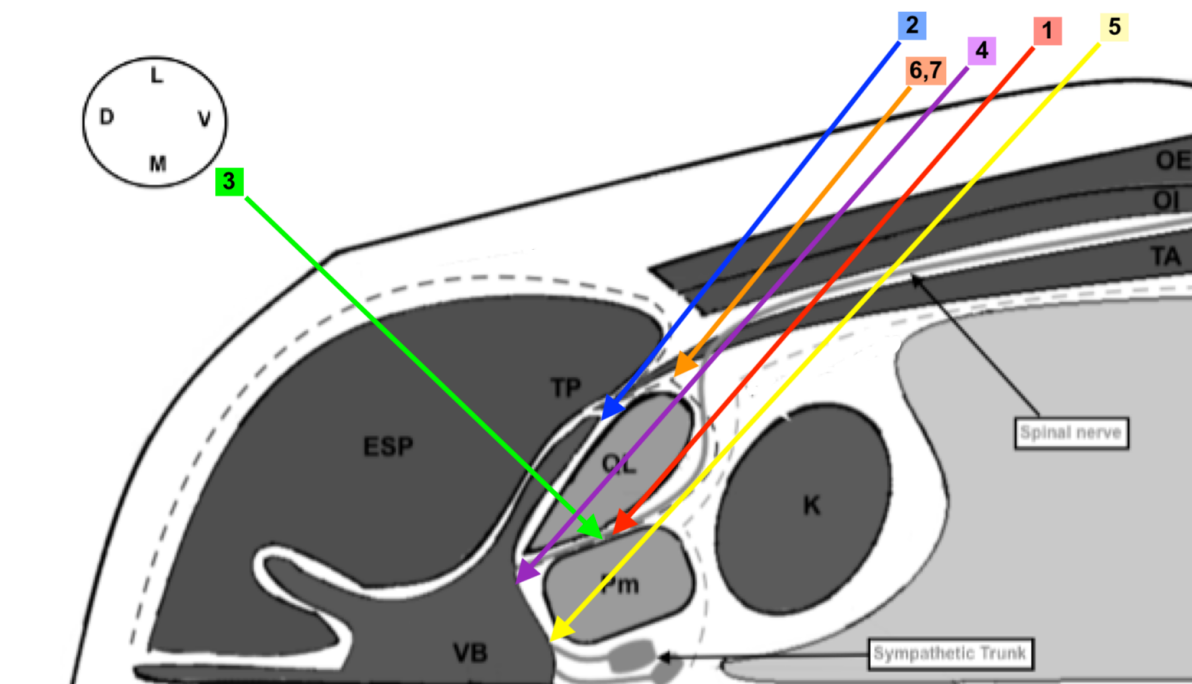
**Figure 5.** Transversal ultrasound image and landmarks for the latero-ventral approach for the quadratus lumborum (QL) block (Marchina-Gonçalves et al. 2023), needle trajectory (arrows) and injection point (star). ESP, erector spinae muscle; OE, obliquus externus muscle; OI, obliquus internus muscle; PM, psoas minor muscle QL, quadratus lumborum muscle; TA, transversus abdominis muscle; TP, transverse process of the vertebra; VB, vertebral body. D, dorsal ; M, medial ; V, ventral ; L, lateral.

Targets, approaches, volumes, needle trajectories, and staining of the ventral rami of the SNs and the sympathetic trunk, as reported in the aforementioned cadaveric studies, are summarised in Table 1. Figure 6 illustrates the needle trajectories of the different approaches.

**Table 1.** Cadaveric studies describing the different approaches for the quadratus lumborum (QL) block in canine species.

Authors	Vertebral body	Approach	Volume	Needle trajectory	Spinal nerves	Sympathetic trunk
Garbin et al. 2021a	L1	Transmuscular	0.15 versus 0.3 mL kg <sup>-1</sup>	Ventrolateral to dorsomedial	T13-L3 (higher volume)	T13-L3 (higher volume)
Garbin et al. 2021b	L1	Lateral	0.3 mL kg <sup>-1</sup>	Ventrolateral to dorsomedial	T12-L3	T11-L2

Viscasillas et al. 2021a	L1	Transmuscular	0.2 mL kg <sup>-1</sup>	Dorsolateral to dorsomedial	T13-L4	Not reported
Marchina-Gonçalves et al. 2022	L1	Dorsal	0.6 mL kg <sup>-1</sup>	Ventrolateral to dorsomedial	L1-L3	T10-L4
Alaman et al. 2022a	L2	Dorsal	0.3 versus 0.5 mL kg <sup>-1</sup>	Ventrolateral to dorsomedial	T13-L3 (higher volume)	T11-L3 (higher volume)
Marchina-Gonçalves et al. 2023	L1	Latero-ventral	0.6 mL kg <sup>-1</sup>	Ventrolateral to dorsomedial	T13-L7	-
Otero et al. 2024	L6	Latero-ventral	0.3 mL kg <sup>-1</sup>	Ventrolateral to dorsomedial	L3-L6	L3-L6



**Figure 6.** Schematic illustration of a cross section at the level of the first lumbar vertebra (L1) showing the abdominal musculature with the fascia layers surrounding the quadratus lumborum (QL) muscle in a dog. Each arrow reflects the needle trajectory described by cadaveric studies: 1, transmuscular approach (Garbin et al. 2020a); 2, lateral approach (Garbin et al. 2020b); 3, transmuscular dorsoventral (Viscasillas et al. 2021a); 4, dorsal (Alaman et al. 2022a); 5, dorsal (Marchina-Gonçalves et al. 2022); 6, lateroventral (Marchina-Gonçalves et al. 2023); 7, lateroventral caudal (Otero et al. 2024). ESP, erector spinae muscle; K, kidney; OE, obliquus internus muscle; OI, obliquus internus muscle; Pm, psoas minor muscle; QL, quadratus lumborum muscle; TA, transversus abdominis muscle; TP, transverse process of the vertebra; VB, vertebral body. D, dorsal; M, medial; V, ventral; L, lateral.



To perform this IFP block, the animal is placed in lateral recumbency, with the side to be desensitised uppermost. The latero-dorsal aspect of the abdomen should be clipped and aseptically prepared before injection. The US transducer is positioned caudally and parallel to the proximal aspect of the last rib, with the transducer marker slightly titled in a dorso-cranial direction, to correctly visualize the transverse process of L1, the QL, Pm and ES muscles. The transverse process appears as a hyperechoic structure with an acoustic shadow beneath it. The QL muscle is usually located ventrally to the transverse process, and it is slightly hypoechoic, in comparison with the ES plane and the Pm muscles. The ES muscles are seen dorsally and laterally to the transverse processes. The Pm muscle is located ventromedially to the QL muscle, and the IFP is a thin hyperechoic line between them (Garbin 2024). After injection, an anechoic pocket should be visualised between the QL and Pm muscles, the ventral aspect of the transverse process of L1 and the QL muscle, or between the VB of L1 and the QL muscle, depending on the approach used.

At the beginning of this research project, only one case-series had assessed the analgesic efficacy of QL block in dogs (Viscasillas et al. 2021b). The authors of that study investigated the spread and analgesia of 0.4 mL kg<sup>-1</sup> a 0.25% bupivacaine/iohexol solution in female dogs undergoing ovariohysterectomy, using a transmuscular dorsal approach (Viscasillas et al. 2021a). CT images revealed that the injectate covered a median (range) of 3 (2–5) vertebrae, indicating that the spread along the QL plane in live dogs was comparable to that in canine cadavers. Pain scores were maintained below a score of 4 out of 24 up to four hours, using the Short Form of the Glasgow Composite Measure Pain Scale (SF-GCMPS) in the postoperative period.

In human medicine, complications associated with the QL block include hematoma formation (Visoiu & Pan, 2019), muscle weakness, and lumbar motor impairment (Wikner, 2017). Additionally, hypotension secondary to bilateral QLB has been reported in two case reports (Almeida & Assuncao, 2018; Sá et al. 2018). In veterinary medicine, complications of bilateral QLB in dogs include transient respiratory arrest and retroperitoneal hematoma (Herrera-Linares & Martinez, 2022; Chiavaccini et al. 2023).

## **1.2 Erector spinae plane block**

The US-guided IFP block that roused the greatest interest in the last few years, both in human and veterinary medicine is undoubtedly the ES plane block. It consists in injecting LA into the IFP between the transverse process of thoracic or lumbar vertebrae and the ES muscles. The most

reliable target of this technique is constituted by the medial and lateral branches of the dorsal rami of the SNs (Tran et al. 2022, Lim et al. 2023). Therefore, this IFP block has been successfully implemented in multimodal analgesic regimens for patients undergoing thoraco-lumbar or lumbar spine surgeries (Viderman et al. 2022; Tran et al. 2022). However, since the ES plane block was first described by Forero et al. in 2016, its therapeutic effect has been attributed also to its diffusion into the epidural and paravertebral space and staining of the ventral rami of the SNs (Otero et al. 2020). These findings are still subject of debate, and recent cadaveric studies did not confirm such results (Ivanusic et al. 2018; Aponte et al. 2019; Lim et al. 2023).

The ES plane block has been utilised in a variety of clinical scenarios, including anatomical areas not innervated by the dorsal branches of the SNs, such as the thoracic and abdominal cavities. Some authors have suggested it holds significant promise for postoperative analgesia in humans, even describing it as a “magic bullet” (Chin & Barrington, 2019). However, it is important to approach these claims with caution. While recent systematic reviews and meta-analyses have reported benefits such as reduced postoperative opioid consumption, lower pain intensity, decreased postoperative nausea and vomiting, and prolonged time to first rescue analgesia following thoracic and abdominal surgeries (Dost et al, 2022; Gao et al, 2022), there is still scepticism regarding its mechanism of action and scope of effectiveness. Lönnqvist et al. (2021) raised significant concerns about the evidence base for the ES plane block, renaming it the “RIP II block,” symbolising its potential decline in popularity similar to the now abandoned interpleural block. Few randomized controlled trials (RCTs) have been conducted, and additional high-quality studies are necessary to establish robust conclusions about its indications, efficacy, and safety (Lönnqvist et al. 2021; Pawa et al. 2023).

In dogs, each SN splits into several primary branches, after exiting the spinal canal: meningeal branch, a communicating branch (*ramus communicans*), a dorsal primary ramus, and a ventral primary ramus. The most proximal branch is the meningeal, situated just beyond the dorsal root ganglion. It comprises sensory axons and postganglionic sympathetic axons that innervate the dura mater, dorsal longitudinal ligament, and vertebral canal blood vessels (Hermanson, 2020). The existence of the meningeal branch in dogs, however, is debated (Forsythe & Ghoshal, 1984). The *ramus communicans* connects with the sympathetic trunk and carries visceral afferent and efferent axons to and from visceral structures (Hermanson, 2020). The dorsal rami of the SNs divide into a medial and lateral branch. The medial branches pass through the longissimus and terminates into the multifidus muscle, innervating the multifidus, rotatores, longissimus, spinalis, and semispinalis



muscles, as well as the vertebrae, ligaments, and dura mater. The lateral branch travels through the longissimus and iliocostalis muscles, supplying innervation to the iliocostalis muscles and the skin of the dorso-lateral aspect of the trunk (Hermanson, 2020). This pattern is consistent, except for the last three or four lumbar segments, where a clear separation of medial and lateral branches does not occur (Hermanson, 2020). There have also been reports of an intermediate branch from the dorsal ramus that innervates the longissimus muscle in the thoracolumbar region of dogs, though its presence is inconsistent (Forsythe & Ghoshal, 1984). Additionally, the lateral branches of the thoracic and lumbar dorsal rami of the SNs provide cutaneous branches (Hermanson, 2020).

The ES muscle group extends from the cervical region to the sacrum, occupying the space between the spinous and transverse processes of cervical, thoracic, and lumbar vertebrae. The muscles included in this group are the longissimus, spinal, and iliocostalis muscles, all covered by the thoracolumbar fascia. Anatomical variations occur in the thoracic, thoracolumbar, and lumbar portions of the spine in dogs, and several cadaveric studies have investigated these differences (Ferreira et al. 2019, Portela et al. 2020, Medina-Serra et al. 2020, Cavalcanti et al. 2022).

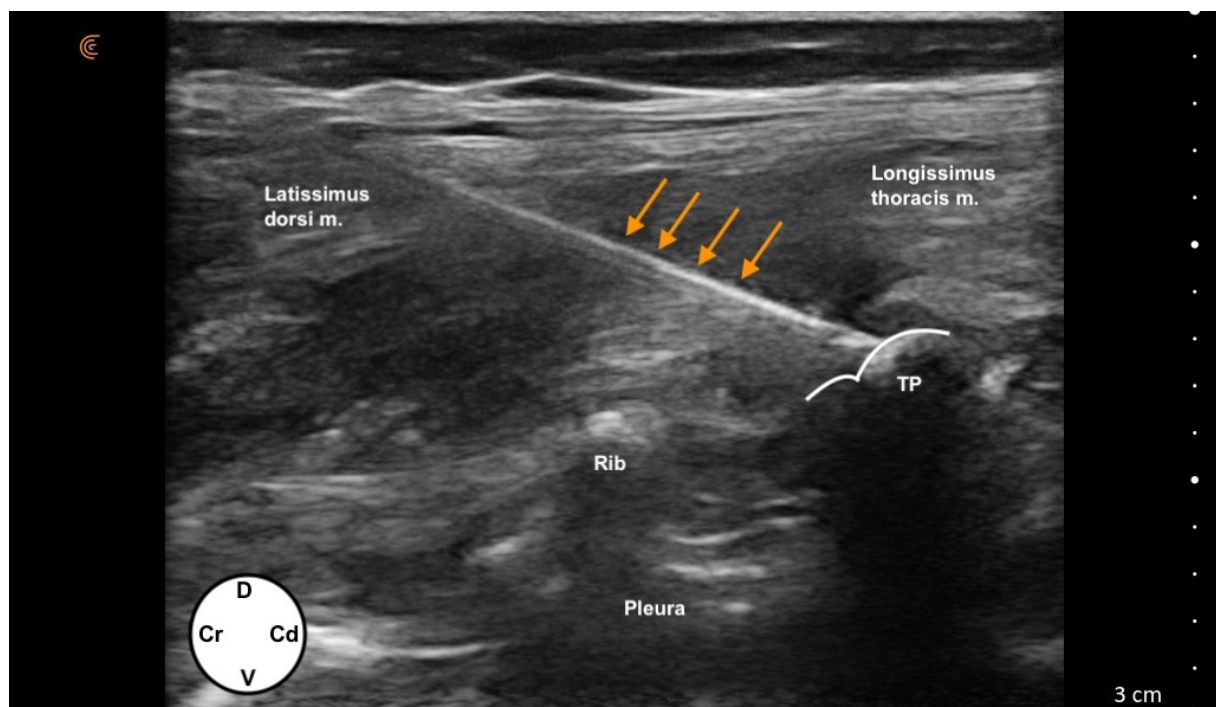
The thoracic portion of the canine spine has been investigated in two cadaveric studies (Ferreira et al. 2019, Portela et al. 2020). According to the anatomical dissections performed by Portela et al. (2020), the thoracolumbar fascia is a robust fibroelastic structure, anchored dorsally to the spinous processes and laterally to the transverse processes and the dorsolateral aspect of the ribs. A portion of the thoracolumbar fascia is positioned between the longissimus thoracis and iliocostalis thoracis muscles, attaching to the transverse processes of the thoracic vertebrae. The longissimus thoracis muscle is connected to the dorsolateral sides of the transverse processes, lying above them, the thoracolumbar fascia, and the proximal parts of the ribs. Within the intertransverse space, the longissimus thoracis muscle rests on the levatores costarum muscles. A thin connective tissue layer, seemingly originating from the thoracolumbar fascia, is situated between the longissimus thoracis and levatores costarum muscles. The rotatores and multifidus muscles are located medially to the longissimus thoracis muscles. The dorsal branches of the SNs travel dorsally between the multifidus and levatores costarum muscles, where they split into medial and lateral branches. The lateral branches enter the ES plane from the medial side of the levatores costarum muscles, running laterally across the dorsal surface of this muscle and the iliocostalis thoracis muscle, and are covered dorsally by the longissimus thoracis muscle. These lateral branches pierce through the thoracolumbar fascia and continue as the dorsal cutaneous branches. The medial branches, after separating from the dorsal branches of the SNs, proceed dorsocaudally between the multifidus and

longissimus thoracis muscles along with branches of the dorsal intercostal arteries. A connective tissue partition, continuous with the thoracolumbar fascia, levatores costarum, external intercostal muscles, and internal intercostal membrane, is observed between the ES plane and thoracic paravertebral space. No clear anatomical connection between the ES plane and paravertebral space was found.

The canine lumbar spine, evaluated by Medina-Serra et al. (2020), presents several differences, when compared with the thoracic portion of the spine. First, lumbar vertebrae have shorter spinal processes, which are slightly cranially sloped, in comparison with the thoracic ones. In addition, they have longer bodies and transverse processes, cranially and slightly ventrally directed. The first four lumbar vertebrae present accessory processes, that are absent on L5 and L6. Finally, each cranial articular process presents mamillary processes (Hermanson 2020a). At the lumbar level, the longissimus lumborum and iliocostalis lumborum muscles fuse into a thick mass, with the iliocostalis lumborum lying close to the transverse processes and the longissimus lumborum positioned medial to the iliocostalis lumborum and lateral to the spinal processes. The dorsal branches of the SNs are visible within this muscle mass, arborizing within the longissimus lumborum and iliocostalis lumborum. The transverse processes are covered by the deep layer of the thoracolumbar fascia, which, along with the intertransverse connective tissue, creates a clear separation between the epaxial and hypaxial musculature. The longissimus lumborum muscle is enveloped by a dense aponeurosis acting as a retinaculum, which also covers the multifidus and sacrocaudalis dorsalis lateralis muscles. Notably, the lumbar region lacks the spinalis muscle. The multifidus muscle in this area is larger than its thoracic counterpart, originating from the articular processes and running laterally to the spinal processes, just ventral to the supraspinous ligament.

The thoracolumbar section of the spine, between T11 and L2, is known as a region of anatomical transition. In this area, the transverse processes of the caudal thoracic vertebrae gradually decrease in size, while the mamillary processes increase as the vertebrae transition into the lumbar region (Cavalcanti et al. 2022, Herrera-Linares et al. 2024). In this region, the multifidus and longissimus muscle cover the dorsal and lateral aspects of the mamillary processes, respectively. Here, the medial branches of the dorsal rami of the SNs run with a caudodorsal direction, in contact with the vertebral lamina and the base of the mamillary process of the vertebra immediately caudal to their intervertebral foramen of origin. These branches are covered by the multifidus and longissimus lumborum muscles. The lateral branches caudal to T11 bifurcate into the longissimus lumborum muscle shortly after originating from the dorsal rami of the SNs (Cavalcanti et al. 2022).

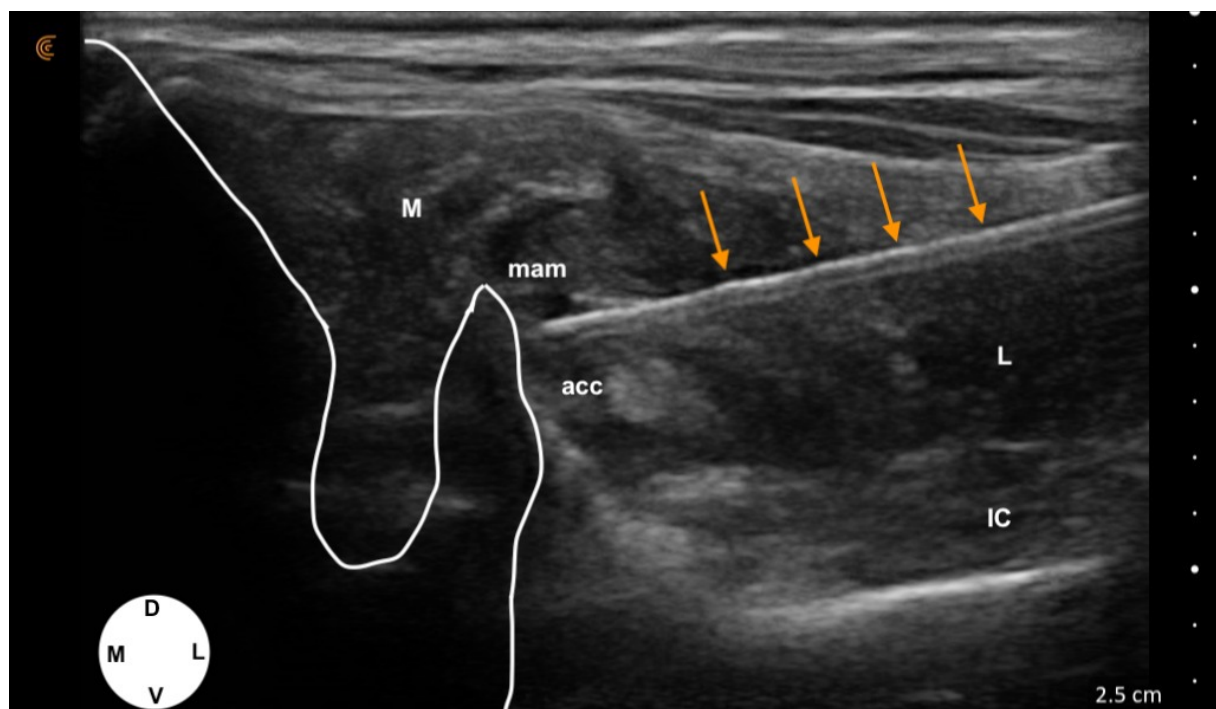
A longitudinal approach for the ES plane block was first described for the thoracic portion of the spine in two different studies (Ferreira et al. 2019; Portela et al. 2020), with only minor variations between the techniques. The US probe is placed in a sagittal orientation, laterally to the dorsal midline, to obtain a parasagittal view of the transverse process of the thoracic vertebra. Once an irregular shape resembling an armchair profile, corresponding to the lateral edge of the transverse process, is visualized, a needle is introduced in-plane through the epaxial muscles, following a cranial-to-caudal direction, until its tip is in contact with the dorsolateral aspect of the transverse process (Figure 8). A volume between 0.3- and 0.6- mL kg<sup>-1</sup> can be injected, and its distribution is observed between the longissimus thoracis muscle and the transverse processes of the thoracic vertebrae. According to the results of one of the studies, it is possible to desensitize a median of 4 medial branches and 4 lateral branches of the dorsal rami of the SNs using this approach (Portela et al. 2020).



**Figure 8.** Ultrasound image and landmarks for the thoracic longitudinal approach for the erector spinae plane (ESP) block and needle trajectory (arrows) at the level of the thoracic vertebrae. TP: transverse process. D, dorsal ; V, ventral ; Cr, cranial ; Cd, caudal.

In the cadaveric study of Medina-Serra et al (2020) a transversal approach was compared to the longitudinal one, in the lumbar portion of the spine. Using this approach, the US transducer is

positioned at the level of the spinous process of L4, perpendicular to the spine. Then, the transducer is moved caudally until the accessory process of L4 and the mamillary processes of L5 are visualized. Using an in-plane technique, the needle is advanced in a latero-medial direction until the needle tip comes into contact with the lateral aspect of the mamillary process above the accessory process of L4 (Figure 9). After injecting a volume of 0.4 mL kg<sup>-1</sup> of contrast dye solution, the transversal approach resulted in a consistent stain of two dorsal rami of the SNs, showing a multisegmental spread involving a median (range) of 2 (2-3) dorsal rami of the SNs.



**Figure 9.** Ultrasound image and landmarks for the lumbar transversal approach for the erector spinae plane (ESP) block and needle trajectory (arrows) at the level of the lumbar vertebrae: Acc, accessory process of the lumbar vertebra; IC, iliocostalis lumborum muscle; L, longissimus lumborum muscle; M, multifidi muscle; Mam, mamillary process. TP: transverse process. D, dorsal ; V,ventral ; Cr, cranial ; Cd, caudal.

Cavalcanti et al. (2022) published finally another cadaveric study, questioning which approach guarantees a better spread of injectate at the level of the thoracolumbar spine, between T11 to L2. The results of that study seem to recommend performing the transversal approach as described by Medina-Serra et al. (2020) in the thoracolumbar area caudal to T11. The authors of that study suggested that the gradual anatomic transformation in the thoracolumbar spine is responsible for these differences in spread characteristics after the two approaches of the ES plane block.

The main application for the ES plane block reported in veterinary medicine is to provide perioperative analgesia during spinal surgeries, such as hemilaminectomy. Benefits of the ES plane block were described in case reports (Zannin et al. 2020, Rodriguez Mulet et al. 2021) and retrospective studies where this block was performed uni- and bilaterally, as part of a multimodal analgesic approach (Portela et al. 2021, Viilman et al. 2022). In the two retrospective studies, the thoracic approach for the ES plane block has been proved to effectively reduce perioperative opioid consumption and intra- and postoperative complications, when compared to a standard opioid-based analgesic protocol. As in human medicine, the ES plane block has been used in procedures beyond its "credible" application also in veterinary medicine: it has been performed as part of a multimodal analgesic approach in dogs undergoing thoracotomy, in combination with epidural administration of morphine and opioid premedication (Gómez Fernández et al. 2021), to treat visceral abdominal pain caused by acute pancreatitis in a dog (Bartholomew & Ferreira, 2021) and in dogs submitted to sternotomy, in combination with dexmedetomidine infusion (Ferré et al. 2022).

In human literature, ES plane block demonstrated an excellent safety profile and is associated with low risk of complications (De Cassai et al. 2021, Oezel et al. 2022). Some of the reported potential complications include pneumothorax, lower extremity weakness, motor block, due to spread of local anaesthetic to either the lumbar plexus or epidural space, and LA systemic toxicity (De Cassai et al. 2019; Tulgar et al. 2019, 2020; Saadawi et al. 2021). In dogs, three cases of sinus arrest have been reported following ES plane block (Sambugaro et al. 2022; Viilmann et al. 2022).

## **2. Local anaesthetics**

LAs work by reversibly inhibiting the generation and transmission of electrical impulses in nerves, leading to sensory and motor block. Most LAs are tertiary amine compounds that are not water-soluble. Therefore, they are often formulated as hydrochloride salts to improve their solubility in water. Their action depends on their different lipid solubility, ionization constant (pKa), and extent of protein binding. The potency of a LA is determined by its lipid solubility, which promotes its ability to diffuse through the nerve sheath. The onset time of a LA also depends on its lipid solubility, along with its pKa. The degree of protein binding influences the duration of action; drugs with a higher affinity for proteins remain attached to the lipoproteins in the blocked nerve for a longer period, resulting in a more prolonged effect (Otero & Portela, 2022; Rioja Garcia, 2024).

## 2.1 Classification

Local anaesthetic agents can be classified in various ways, including by their duration of action or their chemical structure. Chemically, LAs are categorized as either ester-linked or amide-linked, based on the nature of their intermediary chain. A LA molecule typically consists of a lipophilic aromatic group, an intermediate chain, and a hydrophilic amino group at the end of the chain. The nature of the intermediary chain is crucial for classification according to chemical structure (Rioja Garcia, 2024).

### 2.1.1 Ester-linked local anaesthetic agents

Ester-linked local anaesthetic agents have an intermediary chain that includes an ester group ( $\text{COO-CH}_2$ ), classifying them as amino-esters. These agents are less commonly used in clinical settings due to their typically shorter duration of action, which is attributed to their rapid hydrolysis by plasma cholinesterases. Examples of amino-ester linked local anaesthetics include cocaine, procaine, tetracaine, and benzocaine (Rioja Garcia, 2024; Martin-Flores & Lorenzutti, 2024).

### 2.1.2 Amide-linked local anaesthetic agents

Amide-linked local anaesthetic agents feature an intermediary chain composed of an amide group ( $\text{NH-CO-CH}_2$ ). These agents are widely used in clinical practice due to their chemical properties, which make them well-suited for medical use. Examples of amide-linked local anaesthetics include lidocaine, ropivacaine, and bupivacaine (Rioja Garcia, 2024; Martin-Flores & Lorenzutti, 2024).

## 2.2 Mechanism of action

From a pharmacological perspective, LAs are primarily recognised as ion channel blockers, targeting voltage-gated sodium ( $\text{Na}^+$ ) channels. They also interact with voltage-dependent potassium ( $\text{K}^+$ ) and calcium ( $\text{Ca}^{2+}$ ) channels, although with less affinity (Komai & Dowell, 2001). Research suggests that LAs may also influence intracellular pathways associated with G-protein coupled receptors (Hollmann et al. 2001). This broad range of molecular interactions could account for some of the adverse and toxic effects LAs can have on various organ systems. The key mechanism through which local anaesthesia is achieved involves blocking the inward flow of  $\text{Na}^+$  ions through voltage-gated

Na<sup>+</sup> channels, thereby preventing membrane depolarisation and subsequent nerve excitation and signal transmission (Fozzard et al. 2005). Na<sup>+</sup> channels, which are gated pathways for sodium ions, operate in three distinct states: resting, open, and inactivated. These states depend on the membrane potential and timing. When the membrane is at its resting potential, the channel is mostly in a resting state. Upon depolarisation, the channel opens to permit Na<sup>+</sup> ions to pass through, but after a few milliseconds, it closes into an inactivated state, allowing the membrane to repolarise. Once repolarisation is complete, the channel returns to its resting state (Catterall et al. 2000).

Clinically, LAs exhibit a differential blockade, where sensory, motor, and autonomic fibers are affected to varying degrees. This phenomenon occurs because small, unmyelinated fibers (C fibers) and thinly myelinated fibers (A $\delta$  fibers), responsible for pain and temperature sensation, are more susceptible to LAs than larger, myelinated motor fibers (A $\alpha$  fibers) (Matthews & Rushworth, 1957; Franz & Perry, 1974; Ford et al. 1984; Gokin et al. 2001). However, differential blockade is not solely determined by fiber size. Factors such as myelination, the length of nerve exposed to LA, and the concentration used also contribute. This property is particularly useful in perioperative analgesia, as it allows for pain relief while preserving motor function, facilitating faster recovery and mobility (Otero & Portela, 2018, Rioja Garcia, 2024; Martin-Flores & Lorenzutti, 2024).

Another significant mechanism by which LAs work is known as decremental conduction. This term refers to the reduced ability of consecutive nodes of Ranvier to propagate an impulse when a LA is administered (Condouris et al. 1976). This mechanism explains how an impulse can be interrupted even if none of the nodes is entirely non-responsive (Raymond et al. 1989), as seen with low LA concentrations. When LA concentrations block 74–84% of Na<sup>+</sup> conductance at successive nodes, the impulse amplitude progressively diminishes until it falls below the threshold (Fink, 1989). Higher LA concentrations that block sodium conductance at three consecutive nodes will completely halt impulse propagation. This principle explains why using small-volume/high-concentration of LA solutions leads to more extensive and longer-lasting blocks compared to large-volume/low-concentration solutions, despite the same overall drug dosage (Portela et al. 2010; Fenten et al. 2015; Tayari et al. 2017). When LAs are administered via the central neuraxis (epidural or intrathecal routes) or systemically, they may also exert analgesic effects at the spinal cord level, in addition to their primary mechanisms. For instance, LAs can inhibit other ion channels, such as K<sup>+</sup> or Ca<sup>2+</sup> channels, in the dorsal horn of the spinal cord, potentially altering central sensory processing and contributing to their pain-relieving properties (Olschewski et al. 2009).

## **2.3 Most commonly used local anaesthetics for interfascial plane blocks**

Bupivacaine, levobupivacaine and ropivacaine are commonly used LAs in veterinary practice, particularly for peripheral nerve blocks in dogs. Both have distinct profiles that make them suitable for specific clinical applications, and both are commonly used for IFP injections.

### **2.3.1 Bupivacaine**

Bupivacaine is one of the most widely used LAs. Despite its relatively slow onset, which typically takes 20 to 30 minutes, bupivacaine provides a significantly longer duration and analgesic effects compared to lidocaine, lasting from 3 to 10 hours. This LA is particularly lipophilic and is approximately four times more potent than lidocaine. Clinically, bupivacaine is frequently used for nerve blocks and neuraxial anaesthesia across a variety of concentrations (ranging from 0.06% to 0.75%), allowing for the development of differential block, especially when lower concentrations are applied. However, bupivacaine is known for its higher cardiotoxicity compared to other LAs, which is why it is not used for topical anaesthesia or intravenous regional anaesthesia (Martin-Flores & Lorenzutti, 2024; Rioja Garcia, 2024).

### **2.3.2 Levobupivacaine**

Levobupivacaine offers a noteworthy clinical and pharmacokinetic profile. As a single-enantiomer formulation, it excludes the R (+) isomer present in racemic bupivacaine, which is associated with CNS and cardiovascular risks. This exclusion gives levobupivacaine a higher therapeutic index than bupivacaine while still providing a long duration of action, lasting between 240 and 360 minutes. Its onset and duration of action are comparable to those of bupivacaine, making it a preferred option for locoregional analgesia in canine patients (Martin-Flores & Lorenzutti, 2024; Rioja Garcia, 2024).

### **2.3.3 Ropivacaine**

Ropivacaine is an amino-amide LA with a duration of action lasting up to six to eight hours, depending on the concentration used (Rioja Garcia, 2024). Structurally related to bupivacaine, ropivacaine is marketed as the pure S (–)-enantiomer, which reduces the cardiotoxic risks associated with the R (+)-enantiomer. Compared to bupivacaine, ropivacaine is less lipophilic, potentially limiting its penetration into larger motor fibres. This feature may result in a reduced motor blockade while still providing effective sensory block, thereby aiding in early postoperative mobility. However, clinical outcomes can vary (Kuthiala & Chaudhary, 2011).



Ropivacaine, slightly less potent than bupivacaine, is available in concentrations up to 1%. It shares similar clinical applications with bupivacaine, including use in infiltrative, peripheral nerve, epidural, and intrathecal blocks, and has a comparable onset of action. It also exhibits a biphasic effect on peripheral vasculature, inducing vasoconstriction at concentrations below 0.5% and vasodilation at concentrations above 1% (Kuthiala & Chaudhary, 2011). Due to its lower cardiotoxicity and neurotoxicity compared to bupivacaine, ropivacaine is considered a safer option (Martin-Flores & Lorenzutti, 2024).

## **2.4 Local anaesthetic systemic toxicity**

LAs can elicit significant adverse effects, such as the local anaesthetic systemic toxicity (LAST), a severe and potentially life-threatening condition. It primarily affects the CNS and cardiovascular system, and occurs when plasma concentrations of LAs exceed the threshold for systemic toxicity (Eva Rioja, 2024 ; Audette et al. 2024 ; Fischer & Martin-Flores, 2024). This can result from overdose due to miscalculation or excessive cumulative administration, inadvertent intravascular injection, impaired metabolism or elimination, as seen in hepatic, renal, or cardiovascular insufficiencies (Thomson et al. 1971, Thomson et al. 1973). The toxic effects arise due to unintended bloc of Na<sup>+</sup> channels in excitable tissues, particularly in the CNS and myocardium. While LAST symptoms in humans usually occur after approximately one minute after injection of LA, some cases may present over 15 minutes later, thus it is important to closely monitor patients after performing locoregional anaesthesia techniques (Neal et al. 2018). Local anesthetics differ significantly in their potential to induce systemic toxic effects, with this tendency generally aligning with their efficacy in nerve blockade (Mather, 2010). Highly lipid-soluble agents, such as bupivacaine, exhibit greater systemic toxicity compared to those with lower lipid solubility, like lidocaine. Additionally, S (–)-enantiomers, such as levobupivacaine and ropivacaine, are associated with a lower toxicity profile than their R (+)-enantiomer counterparts or the racemic mixtures of both (Feldman et al. 1989; Rutten et al. 1989; Santos & De Armas, 2001).

### **2.4.1 Central nervous system toxicity**

CNS toxicity typically manifests before cardiovascular signs (Santos & De Armas, 2001), except in cases of bupivacaine overdose, where sudden cardiac arrest may occur without preceding neurological symptoms. Early signs include lethargy, dizziness, nystagmus, and muscular twitching.

As toxicity progresses, generalised seizures may develop due to the depression of cortical inhibitory pathways, allowing unopposed excitatory neuronal activity. At higher plasma concentrations, CNS depression, coma, and respiratory arrest may ensue (Eva Rioja, 2024 ; Fischer & Martin-Flores, 2024). In conscious dogs, the mean dose required for convulsive activity is 22 mg kg<sup>-1</sup> for lidocaine, 4.3 mg kg<sup>-1</sup> for bupivacaine and 4.9 mg kg<sup>-1</sup> for ropivacaine (Fischer & Martin-Flores, 2024).

### **2.4.2 Cardiovascular toxicity**

Compared to CNS toxicity, cardiovascular involvement is more critical, as it may lead to fatal arrhythmias and cardiovascular collapse. The severity depends on the specific LA used: lidocaine overdose typically results in hypotension and bradycardia due to myocardial depression. Bupivacaine and ropivacaine toxicity induce sudden ventricular tachycardia, fibrillation, and cardiac arrest, which are often refractory to standard resuscitative measures (Fischer & Martin-Flores, 2024). ECG changes associated with LAST include widening of the QRS complex and T-wave inversion, prolongation of the P-R interval, leading to conduction block, ventricular premature complexes progressing to ventricular fibrillation (Chang et al. 2000 ; Beecroft & Davies, 2010). Cardiovascular toxicity is often dose-dependent. In anaesthetised dogs, the doses of lidocaine, bupivacaine, levobupivacaine, and ropivacaine capable to induce cardiovascular collapse in dogs were 127, 22, 27, and 42 mg kg<sup>-1</sup>, respectively (Groban et al. 2001).

### **2.4.3 Treatment**

When signs of LAST appear, administration of the LA must be discontinued immediately. The primary treatment approach is supportive, prioritising oxygenation and ventilation. If required, the trachea should be intubated, and the patient should be mechanically ventilated to prevent or reverse hypoxaemia, hypercapnia, and acidosis, all of which exacerbate toxicity (Neal et al. 2018). Seizures should be managed using benzodiazepines. The severity of cardiovascular toxicity depends on the specific LA used. Lidocaine and mepivacaine generally induce mild and reversible cardiovascular effects that can be managed with positive inotropes and fluid therapy. However, bupivacaine and other long-acting local anaesthetics are associated with severe arrhythmias, including ventricular tachycardia and fibrillation, which are often resistant to conventional treatment. In such cases, cardiopulmonary resuscitation must be initiated promptly, with defibrillation if necessary. Low doses of epinephrine are recommended to avoid exacerbating arrhythmias and metabolic derangements (Neal et al. 2018). Vasopressin should be avoided due to its negative impact on cardiac output and tissue perfusion (Di Gregorio et al. 2009). Lidocaine, Ca<sup>2+</sup>

channel blockers, and beta-blockers should not be administered as their cardiodepressant effects may be exacerbated. Amiodarone is the preferred treatment for ventricular arrhythmias associated with LAST (Weinberg et al. 2002).

Intravenous lipid emulsion therapy, such as Intralipid® 20%, is now recognised as a first-line treatment for LAST, particularly in cases of refractory cardiac arrest (Eva Rioja, 2024; Fischer & Martin-Flores, 2024). Its mechanisms of action include the sequestration of lipophilic anaesthetics in the bloodstream, reducing their tissue availability, and enhancing myocardial function through a direct inotropic effect, which improves cardiac output and perfusion (Fernandez et al. 2011). This therapy facilitates redistribution of LAs from the heart and brain to muscle and liver for metabolism and detoxification. Studies have demonstrated its efficacy in reversing cardiovascular collapse, with significant survival benefits in animal models (Fettiplace and McCabe 2017). Intralipid® 20% is usually administered as an intravenous bolus of 1.5 mL kg<sup>-1</sup>, followed by infusion at 0.25 - 0.5 mL kg<sup>-1</sup> min<sup>-1</sup>.

In conclusion, US-guided IFP blocks have gained increasing attention in veterinary medicine as a potential alternative to traditional locoregional anaesthesia techniques. While their anatomical basis and injection approaches have been extensively described, their clinical application remains insufficiently investigated. Key aspects, such as analgesic efficacy and safety profile in alive patients, require further evaluation. A deeper understanding of these techniques is essential to optimize their use in veterinary practice and improve perioperative pain management in dogs. Building on existing cadaveric studies, this research project aims to provide new evidence on their clinical applicability, contributing to the refinement of multimodal analgesic strategies in veterinary anaesthesia and analgesia.



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Aims

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## Aims

The aim of this PhD thesis is to investigate the clinical application and efficacy of IFP blocks for perioperative analgesia in dogs undergoing various surgical procedures. This research seeks to address the significant gap in veterinary medicine regarding the practical use of IFP blocks, moving beyond cadaveric studies to provide robust clinical evidence through RCTs. The thesis is structured around four individual studies, each contributing to the collective understanding and validation of these analgesic techniques.

The primary issue in veterinary medicine is the limited number of randomized clinical trials providing concrete evidence regarding the efficacy and mechanisms of IFP blocks. Most current knowledge is derived from cadaveric studies, which, while valuable, do not fully translate to clinical practice. This PhD thesis aims to fill this critical gap by conducting RCTs that can offer definitive evidence on the clinical utility of these blocks in alive patients. By achieving these aims, this research will significantly advance the field of veterinary anaesthesia and analgesia, providing veterinarians with evidence-based techniques to improve perioperative pain management in dogs. The outcomes of these studies will not only validate the use of IFP blocks in clinical settings but also potentially set new standards for perioperative analgesia in veterinary medicine.

**Study 1:** This study was performed in collaboration with the Veterinary Teaching Hospital of the University of Pisa (Italy). The aim of study 1 was to investigate the effectiveness of the lateral QL block (Garbin et al. 2021) performed using two different concentrations of ropivacaine (0.5% and 0.33%) at prolonging the time to the first postoperative rescue analgesia in dogs undergoing laparoscopic ovariectomy, and to compare these blocks with a systemic opioid-based protocol. We also investigated the impact of the QL block on the arterial blood pressure. We hypothesized that ropivacaine 0.5% would result in a longer-lasting postoperative analgesic effect and a more significant reduction in the arterial blood pressure versus ropivacaine 0.33%.

**Study 2:** The second RCT was performed in collaboration with the Veterinary Teaching Hospital of the University of Teramo (Italy). It aimed to compare the perioperative analgesic efficacy of QL block performed using two different approaches: lateral (Garbin et al. 2021) or latero-ventral (Marchina-Gonçalves et al. 2023) in female dogs undergoing laparoscopic ovariectomy. We hypothesised that the lateral approach would result in fewer dogs requiring perioperative rescue analgesics in comparison with the latero-ventral approach.

**Study 3:** The third study, performed at the Veterinary Teaching Hospital of the University of Liege, aimed to describe an US-guided technique for placing catheters for LA administration in the QL IFP in canine cadavers, to assess the spread of two different volumes (0.3 *versus* 0.6 mL kg<sup>-1</sup>) per side of contrast media solution injected through the catheters using computed tomography, and to describe the outcomes of five dogs undergoing different abdominal surgeries, in which catheters bilaterally placed in the QL IFP were included in a multimodal postoperative analgesic plan. We hypothesized that this technique is feasible in dogs and that using a higher volume of injectate would result in greater spread along the vertebral bodies.

**Study 4:** Finally, study 4 investigated the perioperative analgesic effect of the unilateral lumbar ES plane block (Medina-Serra et al. 2021) performed with ropivacaine in dogs undergoing thoracolumbar or lumbar hemilaminectomy for Hansen type I intervertebral disc extrusion at the Veterinary Teaching Hospital of the University of Liege. We hypothesized that unilateral ES plane block performed with ropivacaine would decrease the consumption of intra- and postoperative systemic analgesics and reduce the occurrence of intraoperative cardiovascular complications.



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# Experimental Section

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# Experimental Section

## Study 1:

Postoperative analgesic effect of bilateral quadratus lumborum block (QLB) for canine laparoscopic ovariectomy: comparison of two concentrations of ropivacaine

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## Abstract

**Objective** The aim of this study was to evaluate the effect of the transverse quadratus lumborum block (QLB<sub>LQL-T</sub>) on time to the first postoperative rescue analgesia in dogs submitted to laparoscopic ovariectomy (LO).

**Material and methods** A total of twenty-three female dogs were included. Dogs were randomly assigned to receive a bilateral QLB<sub>LQL-T</sub>, performed either with 0.3 mL kg<sup>-1</sup> ropivacaine 0.5% [group QLB<sub>0.5%</sub> ( $n = 8$ )] or with ropivacaine 0.33% [group QLB<sub>0.33%</sub> ( $n = 8$ )] or a fentanyl-based protocol [group No-QLB ( $n = 7$ )]. Dogs were premedicated intravenously (IV) with fentanyl 5 mcg kg<sup>-1</sup>, general anaesthesia was induced IV with propofol and maintained with sevoflurane. Invasive mean arterial pressure (MAP) values were recorded five minutes before and five minutes after performing the QLB<sub>LQL-T</sub>. The short-form of the Glasgow composite measure pain scale was used every hour after extubation, and methadone 0.2 mg kg<sup>-1</sup> was administered IV when pain score was  $\geq 5/24$ . Kolmogorov–Smirnov test, ANOVA test combined with Tukey post hoc test, Student’s T-test and Chi-square test were used to analyse data;  $p < 0.05$ .

**Results** Time from QLB<sub>LQL-T</sub> to the first rescue analgesia was significantly longer in QLB<sub>0.5%</sub> than in group QLB<sub>0.33%</sub> and No-QLB. MAP pre- and post-block decreased significantly only in group QLB<sub>0.33%</sub>.

**Conclusions and clinical relevance:** bilateral QLB<sub>LQL-T</sub> with a volume of 0.3 mL kg<sup>-1</sup> of ropivacaine prolonged the time to the first postoperative methadone administration and reduced the pain scores in female dogs undergoing LO, in comparison with dogs receiving a systemic fentanyl-based analgesic protocol. In addition, ropivacaine 0.5% provided longer postoperative analgesic effect in comparison with ropivacaine 0.33%.

**Keywords:** analgesia, dog, quadratus lumborum block, laparoscopic ovariectomy, ultrasound-guided locoregional anaesthesia

## Introduction

Laparoscopic ovariectomy (LO) is currently considered the gold standard for neutering female dogs [Fernandez-Martín et al. 2022] thanks to the advantages over the traditional laparotomic technique, such as reduced surgical trauma, lower perioperative pain, and decreased hospitalization times [Devitt et al. 2005, Davidson et al. 2004, Culp et al. 2009]. In the absence of complications, dogs have been discharged between 8 and 12 h after surgery [Wormser et al. 2016]. To permit such a prompt discharge, effective perioperative analgesia is essential to reduce the occurrence of uncontrolled post-surgery stress responses, including immunosuppression, overstimulation of the sympathetic nervous system, and anorexia [Romano et al. 2016]. Locoregional anaesthesia (LRA) can provide a more stable anaesthetic plane due to the sparing effect on inhalant anaesthetic drugs and a reduction in the use of intra- and postoperative opioids [Wormser et al. 2016, Romano et al. 2016, Tayari et al. 2022].

Implementation of ultrasonography in modern LRA has led to a rapid growth in the use of so-called interfascial plane blocks (IFPBs) [Chin et al. 2017]. This class of blocks are relatively easy to perform safely and are considered as the minimally invasive evolution of locoregional anaesthesia [Machi et al. 2019]. Among them, the ultrasound (US)- guided transversus abdominis plane (TAP) block aims to desensitize the thoracolumbar ventral rami of the spinal nerves (VRSN) and to provide somatic analgesia of the abdominal wall and peritoneum [Castañeda-Herrera et al. 2017]: it has been proposed as part of a multimodal analgesic approach for dogs undergoing LO [Paolini et al. 2022, Espadas-Gonzales et al. 2022]. However, the US-guided quadratus lumborum block (QLB) has been shown to provide both somatic and visceral analgesia to the abdomen in both human and veterinary medicine [Chin et al. 2017, Machi et al. 2019, Viscasillas et al. 2021a], leading several authors to prefer the QLB to the TAP block [Liu et al. 2020]. The target for the QLB is the fascia surrounding the quadratus lumborum (QL) muscle where the VRSN and the sympathetic trunk, respectively responsible for the somatic and visceral innervation of the abdomen, lie. Garbin et al. described two lateral approaches in which the tip of the needle was positioned laterally to the QL muscle: a transversal (QLB<sub>LQL-T</sub>) and a longitudinal (QLB<sub>LQL-L</sub>) block, depending on the position of the US probe with respect to the spinal column [Garbin et al. 2020a, Garbin et al. 2020b]. Several other approaches have been evaluated in canine cadaveric studies [Garbin et al. 2020a, Garbin et al. 2020b, Alaman et al. 2021, Viscasillas et al. 2021b, Marchina-Goncalves et al. 2022a, Marchina-Goncalves et al. 2023]. Results showed a consistent spread of the injectate towards the VRSN between the first (L1) and fourth (L4) lumbar vertebrae, while spreading to the caudal thoracic vertebrae was less frequent. A

variable spread of injectate solution along the sympathetic trunk between the thirteenth thoracic (T13) and the third lumbar (L3) vertebrae has also been reported [Garbin et al. 2020a, Garbin et al. 2020b, Alaman et al. 2021, Viscasillas et al. 2021b, Marchina-Goncalves et al. 2022, Marchina-Goncalves et al. 2023].

In human medicine, hypotension secondary to bilateral QLB has been reported in two case reports [Almeida et al. 2018, Sà et al. 2018]. In veterinary medicine, transient respiratory arrest and retroperitoneal hematoma have been described as complications of bilateral QLB in dogs [Herrera-Linares et al. 2022, Chiavaccini et al. 2023]. Currently, there is only one published case series regarding the analgesic efficacy of bilateral QLB in dogs undergoing ovariohysterectomy [Viscasillas et al. 2021a]. To the author's knowledge, at the moment there are no randomized blinded studies in the veterinary literature regarding the use of QLB in dogs undergoing LO.

This study aimed to investigate the effectiveness of the QLB<sub>LQL-T</sub> performed using two different concentrations of ropivacaine (0.5% and 0.33%) at prolonging the time to the first postoperative rescue analgesia in dogs undergoing LO, and to compare these blocks with a systemic opioid-based protocol. We also investigated the impact of the QLB<sub>LQL-T</sub> on the arterial blood pressure. We hypothesized that ropivacaine 0.5% would provide a longer-lasting postoperative analgesic effect and produce a greater reduction in the arterial blood pressure versus ropivacaine 0.33%.

## Material and Methods

Twenty-four female dogs of different breeds, ages, and weights, undergoing LO at the Veterinary Teaching Hospital of the University of Pisa, were enrolled in the study. The Consolidated Standards of Reporting Trials (CONSORT) guidelines were applied [Schulz et al. 2020]. Ethical approvals were obtained from the competent authorities (Nr. 25/2020). By signing the informed consent document, the owner agreed to enrol their dog in the study. Prior to anaesthesia, each dog underwent a clinical examination, including body condition score (BCS) on a nine-point scale [LaFlamme et al. 1997] and a complete haematological, biochemical, and coagulation screening. Based on the findings of the preoperative evaluation, only dogs with an American Society of Anaesthesiologists (ASA) status 1, with a BCS ranging between 3 and 6 out of 9 were included in the study. Other exclusion criteria included problematic behaviour, skin infection, or irritation at the site of the QLB<sub>LQL-T</sub>, and administration of any anti-inflammatory drugs within 24 h prior to surgery.

**Preoperative Management.** On the day of surgery, the following anaesthetic protocol was applied to all dogs: after intravenous catheter insertion into one of the cephalic veins, a bolus of 5 mcg kg<sup>-1</sup> of fentanyl (Fentadon, 50 mcg mL<sup>-1</sup>, Eurovet Animal Health B.V., Bladel, The Netherlands) was administered intravenously (IV) and lactated Ringer's (RL) solution (Ringer Lattato, B. Braun S.p.a. Vet Care, Milan, Italy) at 5 mL kg<sup>-1</sup> h<sup>-1</sup> was initiated. After five minutes of pre-oxygenation by mask, general anaesthesia was induced with propofol (Propovet multidose, 10 mg mL<sup>-1</sup>, Zoetis Italia S.r.l., Rome, Italy) IV to effect, until endotracheal intubation was feasible. The endotracheal tube was connected to a rebreathing system and anaesthesia was maintained with sevoflurane (Sevoflo, Ecuphar S.r.l., Milan, Italy) in an oxygen–air mixture with a fraction of inspired oxygen (FIO<sub>2</sub>) of 0.6. A fraction of expired sevoflurane concentration (FE'Sevo) was initially set between 2 and 2.3%. Each dog was positioned in lateral recumbency. An arterial catheter was inserted at the level of the dorsal pedal artery and connected to a pre-calibrated transducer, zeroed to atmospheric pressure, positioned at the level of the right atrium and connected to a multi-parameter monitor (Mindray Beneview T5, Mindray Medical Italia S.r.l., Milan, Italy) for invasive blood pressure measurement.

The hair in the abdomen and flank of each dog was clipped in the same way, to prevent recognition during the postoperative pain assessment. Dogs were randomly allocated into three groups: dogs in group QLB<sub>0.5%</sub> received a bilateral QLB<sub>LQL-T</sub> with 0.3 mL kg<sup>-1</sup> of ropivacaine (Naropina, 10 mg mL<sup>-1</sup>, Aspen Pharma Trading Limited, Verona, Italy) 0.5% per side (total dose 3 mg kg<sup>-1</sup>); dogs in group QLB<sub>0.33%</sub> received the same block with 0.3 mL kg<sup>-1</sup> of ropivacaine 0.33% per side (total dose 2 mg kg<sup>-1</sup>);

dogs in the control group (No-QLB) received a systemic fentanyl-based analgesic protocol and no LRA. The anaesthetists in charge of intraoperative monitoring (C.D.F. or G.F.T.) were unaware of the concentration of ropivacaine used, though they were aware of the group No-QLB, for ethical reasons. Simple sequence randomization for 24 numbers divided into three columns was performed using the online website [www.random.org](http://www.random.org) (accessed on 1 July 2020). All blocks were performed by the same anaesthetist (M.D.) using an along visual axis technique [Di Franco et al. 2021] with a dedicated veterinary ultrasound system (Sonosite S II Veterinary Ultrasound System, Fujifilm Italia S.p.a., Milan, Italy) and a linear ultrasound probe (HFL50, 15–6 MHz Linear Transducer). The QLB<sub>LQL-T</sub> was performed as described by Garbin et al. [2020b] using an 85 mm echogenic needle for nerve blocks (Visioplex, Vygon Italia S.r.l., Padua, Italy). For each side (right and left), before performing the QLB<sub>LQL-T</sub> and five minutes after infusion, invasive mean arterial pressure (MAP) values were recorded. A five-minute interval was used after changing the recumbency prior to the MAP measurement and the next block. Time from the execution of the block to starting of surgery ( $T_{B-S}$ ) was also recorded.

**Intraoperative Management.** Subsequently, dogs were transported to the operating room and connected to an anaesthetic workstation (Avance CS<sup>2</sup>, GE Healthcare, Bensalem, PA, USA). Volume-controlled ventilation was set to maintain end-expiratory CO<sub>2</sub> (EtCO<sub>2</sub>) between 35 and 45 mmHg. During anaesthesia, heart rate (HR), peripheral arterial hemoglobin saturation (SpO<sub>2</sub>), systolic, mean, and diastolic invasive arterial blood pressures (SAP, MAP, DAP), respiratory rate (fR), EtCO<sub>2</sub>, and FE'Sevo were continuously monitored and recorded every five minutes. All dogs were operated by the same surgeon, using the two-port LO technique, with transabdominal suspension suture for ovarian traction [Devitt et al. 2005]. Sevoflurane was regulated to maintain a surgical anaesthetic plane, defined as absence of palpebral reflex and voluntary movements, and a mild jaw tone [Grubb et al. 2020].

HR and MAP registered five minutes before the start of the surgery were recorded as T0 and considered as baseline. A 20% increase in the cardiovascular variables from the corresponding values at T0 was considered as a sign of nociception [Wenger et al. 2005] and a bolus of 2.5 µg kg<sup>-1</sup> of fentanyl was administered IV. In case variables did not return to T0 within five minutes, fentanyl infusion was started at an increasing rate between 2 and 15 mcg kg<sup>-1</sup> h<sup>-1</sup> until return to basal values. The management of intraoperative nociception for dogs in group No-QLB was conducted as for any other procedure performed in our institution, in which LRA is not used; a bolus of 2.5 µg kg<sup>-1</sup> of fentanyl was administered IV at T0, then a fentanyl infusion was started at a rate between 2 and 15 mcg kg<sup>-1</sup> h<sup>-1</sup> to maintain HR and MAP within 20% of baseline values during surgery [Romano et al.



2016]. In the QLB<sub>0.5%</sub> and QLB<sub>0.33%</sub> groups, the time of administration of fentanyl, if necessary, and the surgical step responsible for the nociception response were recorded. The following were considered surgical steps of LO: S<sub>1</sub>, placement of the drapes and Backhaus forceps; S<sub>2</sub>, skin incision; S<sub>3</sub>, introduction of the trocars and insufflation of the abdomen; S<sub>4</sub>, traction of the first ovary; S<sub>5</sub>, cauterization of the first ovary; S<sub>6</sub>, traction of the second ovary; S<sub>7</sub>, cauterization of the second ovary; S<sub>8</sub>, deflation of pneumoperitoneum and extraction of the trocars; S<sub>9</sub>, suturing of the skin.

In case of hypotension (MAP < 60 mmHg), 5 mL kg<sup>-1</sup> of Ringer lactate was administered IV over five minutes. If hypotension persisted, dopamine (Dopamina Hospira, 200 mg mL<sup>-1</sup>, Hospira Italia, Naples, Italy) infusion was started at 5 mcg kg<sup>-1</sup> min<sup>-1</sup> and increased by 0.5 mcg kg<sup>-1</sup> min<sup>-1</sup> every five minutes until the MAP was above 60 mmHg. In presence of bradycardia (HR < 60 bpm) and concomitant hypotension, atropine (Atropina Solfato 1 mg mL<sup>-1</sup>, A.T.I. Azienda terapeutica veterinaria S.r.l., Naples, Italy) at 20 mcg kg<sup>-1</sup> was administered IV. At the end of surgery, administration of sevoflurane was interrupted and, when the dog returned to spontaneous ventilation, mechanical ventilation was stopped. Each dog was then moved to the recovery room and tracheal extubation was performed once the swallowing reflex returned. The duration of anaesthesia and surgery and time from the block to starting of surgery were recorded.

**Postoperative Management.** One hour after extubation, an anaesthetist (C.D.F. or G.F.T.), different from the one performing the block and the one monitoring the intraoperative phase and blinded to the treatment allocation, performed the pain assessment using the short-form Glasgow Composite Measure Pain Scale (SF-GCMPS) [Reid et al. 2007] every hour up to 8 h starting from the QLB<sub>LQL-T</sub> execution. In case of a score  $\geq 5/24$ , methadone (Semfortan, 10 mg mL<sup>-1</sup>, Dechra, Turin, Italy) 0.2 mg kg<sup>-1</sup> IV and carprofen (Rimadyl, 50 mg mL<sup>-1</sup>, Zoetis Italia S.r.l., Rome, Italy) 2 mg kg<sup>-1</sup> were administered IV, and the postoperative pain monitoring for the purposes of this study was interrupted. If the score was <5/24, up to 720 min of assessment, only carprofen 2 mg kg<sup>-1</sup> IV was administered, and the study monitoring was stopped. The time from the block to the first postoperative methadone administration, if necessary, was recorded and compared between groups.

**Statistical Analysis.** The sample size calculation with an alpha of 0.05 and power of 80%, to detect a difference of 120 min in the time for the first postoperative methadone administration between group QLB<sub>0.5%</sub> and group QLB<sub>0.33%</sub>, resulted in a minimum of seven dogs for each group. The calculation was done considering a mean duration of analgesia from ropivacaine 0.33% of about 550  $\pm$  80 min [Tayari et al. 2017]. We decided to enrol eight animals for each group, to face any eventual

losses of dogs or higher standard deviation. These criteria gave a minimum number for each group of seven. Data were analysed for distribution with a Kolmogorov–Smirnov test. Data not normally distributed were described by the median and range, while those normally distributed were described by the mean and standard deviation. An analysis of variance (ANOVA) test with a Tukey post hoc test was used to compare duration of anaesthesia, surgery, and time from the block to the first postoperative rescue methadone, amongst the three groups. For pre- and post-block MAP values in the two groups that received the QLB<sub>LQL-T</sub>, a Student's T-test was used for paired data. For HR, fR, SAP, MAP, FE'Sevo values, an ANOVA test for repeated data was used to evaluate the trend inside each group. A Chi-square test was performed to evaluate fentanyl boluses in groups receiving the QLB<sub>LQL-T</sub> and the use of vasoactive drugs in the three groups.  $p < 0.05$ .

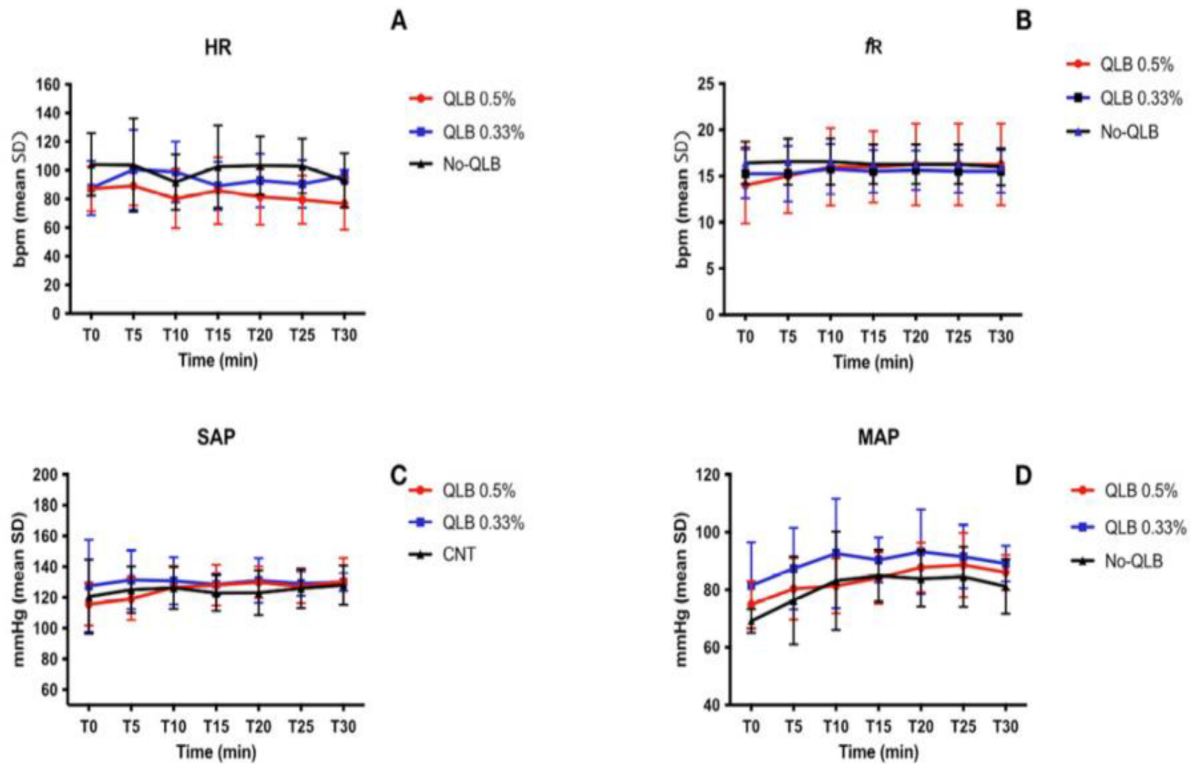
## Results

Twenty-three ASA I female dogs undergoing LO were included the study: one dog from group No-QLB was excluded because of conversion of the procedure into a laparotomic surgery due to intraoperative hemorrhage. Demographic data,  $T_{B-S}$ , duration of anaesthesia, and duration of surgery are summarized in Table 1. Median BCS was 4.5 (4–5) in all groups.

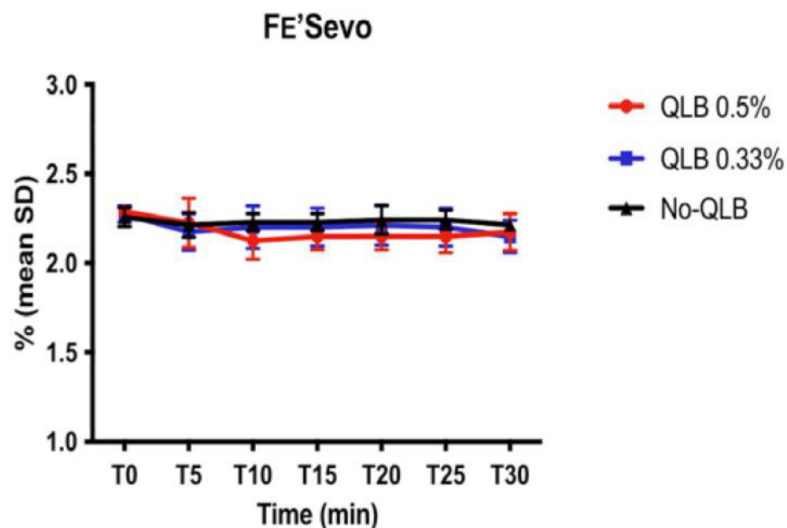
**Table 1.** Demographic data, time from the block to the starting of surgery ( $T_{B-S}$ ) (minutes), duration of anaesthesia and surgery (minutes). Results are presented as mean and standard deviation. QLB<sub>0.5%</sub>, quadratus lumborum block with ropivacaine 0.5% (n = 8); QLB<sub>0.33%</sub>, quadratus lumborum block with ropivacaine 0.33% (n = 8); No-QLB, systemic fentanyl-based analgesic protocol (n = 7).

Group	Age (Months)	Weight (kg)	$T_{B-S}$ (Minutes)	Duration Anaesthesia (Minutes)	Duration Surgery (Minutes)
QLB <sub>0.5%</sub>	20 ± 12	29 ± 6	29 ± 6	107 ± 17	35 ± 13
QLB <sub>0.33%</sub>	21 ± 13	27 ± 5	27 ± 5	98 ± 33	35 ± 11
No-QLB	24 ± 12	30 ± 4	-	101 ± 17	39 ± 10

MAP values five minutes before ( $78 \pm 14$  mmHg) and after ( $76 \pm 11$  mmHg) the block in group QLB<sub>0.5%</sub> were not statistically different ( $p = 0.18$ ), while a significant decrease ( $p = 0.002$ ) in MAP five minutes after the block (from  $76 \pm 12$  mmHg to  $63 \pm 8$  mmHg) was recorded in group QLB<sub>0.33%</sub>. Regarding the intraoperative values of HR, SAP, MAP,  $f_R$ , FE'Sevo, no significant differences between T0 and the other intraoperative values for the three groups were detected (Figure 1A–D and Figure 2).



**Figure 1.** (A) mean values and standard deviation (SD) of intraoperative heart rate (HR) (beats per minute, bpm); (B–D) mean values and SD of respiratory rate (fR), systolic (SAP) and mean arterial pressure (MAP). QLB<sub>0.5%</sub>, quadratus lumborum block (QLB<sub>LQL-T</sub>) with ropivacaine 0.5%; QLB<sub>0.33%</sub>, quadratus lumborum block (QLB<sub>LQL-T</sub>) with ropivacaine 0.33%. No-QLB, systemic fentanyl-based analgesic protocol.



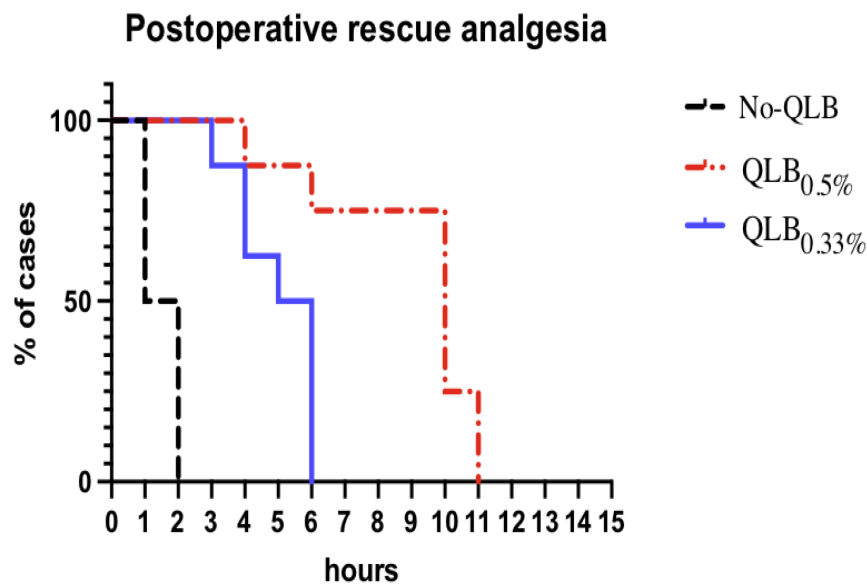
**Figure 2.** Mean values and standard deviation (SD) of fraction of expired sevoflurane (FE'Sevo). QLB<sub>0.5%</sub>, quadratus lumborum block (QLB<sub>LQL-T</sub>) with ropivacaine 0.5%; QLB<sub>0.33%</sub>, quadratus lumborum block (QLB<sub>LQL-T</sub>) with ropivacaine 0.33%. No-QLB, systemic fentanyl-based analgesic protocol.

One bolus of fentanyl was administered in 6/8 patients in group QLB<sub>0.5%</sub> and in 7/8 patients in group QLB<sub>0.33%</sub>. No dogs in group QLB<sub>0.5%</sub> and QLB<sub>0.33%</sub> required fentanyl infusion. All dogs in group No-QLB received one bolus plus infusion of fentanyl (mean rate of  $5.7 \pm 3.2$  mcg kg<sup>-1</sup> h<sup>-1</sup>), to maintain the physiological variables within 20% of baseline values during surgery. Data regarding the distribution of intraoperative rescue fentanyl administration in group QLB<sub>0.5%</sub> and QLB<sub>0.33%</sub> are summarized in the Table 2.

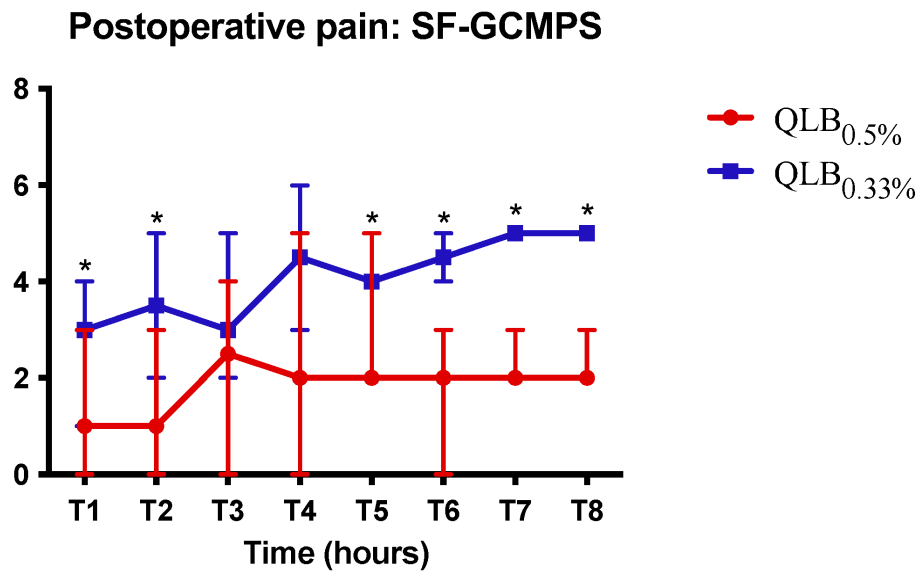
**Table 2.** Distribution of intraoperative rescue fentanyl boluses (2.5 mcg kg<sup>-1</sup>), during the specific surgery steps in the two groups receiving the quadratus lumborum block (QLB<sub>LQL-T</sub>). QLB<sub>0.5%</sub>, QLB<sub>LQL-T</sub> with ropivacaine 0.5%; QLB<sub>0.33%</sub>, QLB<sub>LQL-T</sub> with ropivacaine 0.33%. S<sub>1</sub>, placement of the drapes and Backhaus forceps; S<sub>2</sub>, skin incision; S<sub>3</sub>, introduction of the trocars and insufflation of the abdomen; S<sub>4</sub>, traction of the first ovary; S<sub>5</sub>, cauterization of the first ovary; S<sub>6</sub>, traction of the second ovary; S<sub>7</sub>, cauterization of the second ovary; S<sub>8</sub>, deflation of pneumoperitoneum and extraction of the trocars; S<sub>9</sub>, suturing of the skin.

Group	Dog	Distribution of intraoperative rescue fentanyl boluses								
		S <sub>1</sub>	S <sub>2</sub>	S <sub>3</sub>	S <sub>4</sub>	S <sub>5</sub>	S <sub>6</sub>	S <sub>7</sub>	S <sub>8</sub>	S <sub>9</sub>
QLB <sub>0.5%</sub>	1	x								
	2		x							
	3			x						
	4			x						
	5							x		
	6							x		
	7									
	8									
QLB <sub>0.33%</sub>	1	x								
	2	x								
	3			x						
	4			x						
	5			x						
	6						x			
	7							x		
	8									

One dog in group QLB<sub>0.5%</sub> and one in group QLB<sub>0.33%</sub> required dopamine, while no one needed atropine. Four out of 7 dogs in group No-QLB received dopamine and 2/7 dogs received atropine. Time from the block to the first postoperative methadone administration in group QLB<sub>0.5%</sub>, was  $612 \pm 164$  min and was significantly longer than group QLB<sub>0.33%</sub> ( $316 \pm 113$  min) ( $p = 0.002$ ) and group No-QLB ( $59 \pm 24$  min) ( $p < 0.0001$ ) (**Figure 3**); postoperative analgesia in the group QLB<sub>0.33%</sub> was significantly longer than No-QLB ( $p = 0.0016$ ). Postoperative pain scores were significantly different between the QLB groups at T1, T2, T5, T6, T7 and T8 ( $p = 0.007$ ) with lower pain scores registered in group QLB<sub>0.5%</sub> (**Figure 4**). No complications occurred in the postoperative period in any dog.



**Figure 3.** Kaplan–Meier analysis of time (hours) to first postoperative rescue analgesia required in a percentage (%) of cases in the three groups. QLB<sub>0.5%</sub>, quadratus lumborum block (QLB<sub>LQL-T</sub>) with ropivacaine 0.5%; QLB<sub>0.33%</sub>, quadratus lumborum block (QLB<sub>LQL-T</sub>) with ropivacaine 0.33%. No-QLB, systemic fentanyl-based analgesic protocol.



**Figure 4.** Median values and range of postoperative pain scores, short-form Glasgow Composite Measure Pain Scale (SF-GCMPS). QLB<sub>0.5%</sub>, quadratus lumborum block (QLB<sub>LQL-T</sub>) with ropivacaine 0.5%; QLB<sub>0.33%</sub>, quadratus lumborum block (QLB<sub>LQL-T</sub>) with ropivacaine 0.33%. No-QLB, systemic fentanyl-based analgesic protocol. \* Significant difference between the two groups ( $p < 0.05$ ).

## Discussion

The present study demonstrated that bilateral QLB<sub>LQL-T</sub> with a volume of 0.3 mL kg<sup>-1</sup> of ropivacaine 0.5% provides prolonged time until first postoperative rescue analgesia and reduced pain scores in female dogs undergoing LO, in comparison with dogs receiving the same block using ropivacaine 0.33% and dogs receiving a systemic fentanyl-based protocol. Surprisingly, results of this study indicated that ropivacaine 0.33% produced a more important reduction in the mean arterial blood pressure than ropivacaine 0.5%.

In our study, QLB<sub>LQL-T</sub> significantly prolonged the time to the first postoperative administration of methadone in comparison with group No-QLB. This finding is well documented in veterinary medicine, where the implementation of LRA led to a reduction in perioperative opioid requirements, improved quality of recovery, decreased morbidity, and hospitalization times [Portela et al. 2010, Tayari et al. 2017, Viscasillas et al. 2021a]. Furthermore, the block performed with ropivacaine 0.5% delayed the first postoperative administration of methadone and reduced pain scores in comparison with ropivacaine 0.33%. These data support the hypothesis that the higher the concentration of LA, the higher the quality and duration of the block obtained, as already reported in the literature [Portela et al. 2010, Fenten et al. 2015, Tayari et al. 2017]. In a previous study, dogs receiving the QLB (0.4 mL kg<sup>-1</sup> per side of bupivacaine 0.25%, 2 mg Kg<sup>-1</sup>), undergoing laparotomic ovariohysterectomy, were found to require the first post-operative methadone administration four hours after surgery [Viscasillas et al. 2021a]. This result does not differ much from ours. In our study, dogs in group QLB<sub>0.33</sub> (0.3 mL kg<sup>-1</sup> per side of ropivacaine 0.33%, 2 mg Kg<sup>-1</sup>) and QLB<sub>0.50%</sub> (0.3 mL kg<sup>-1</sup> per side of ropivacaine 0.5%, 3 mg kg<sup>-1</sup>) required rescue analgesia approximately 5 and 10 h after the execution of the block, respectively. Despite different surgeries, approaches and LAs were evaluated, it is possible to speculate that the delayed first postoperative methadone administration found in our study was produced by higher concentrations of ropivacaine used.

The TAP block, in combination with intercostal blocks or alone, has been recently proposed as part of multimodal analgesic protocols in dogs undergoing LO [Paolini et al. 2022, Espadas-Gonzalez 2022]. Paolini et al. and Espadas-González et al. reported relatively no dogs required postoperative opioid administration up to 24 h post-surgery in both studies [Paolini et al. 2022, Espadas-Gonzalez 2022]. Instead, the QLB<sub>LQL-T</sub> in our study delayed the first postoperative methadone administration up to a maximum of about 11 h, when ropivacaine 0.5% was used. However, the premedication protocols administered in those studies included a combination of methadone, dexmedetomidine,



and ketamine or a combination of methadone and dexmedetomidine, respectively [Paolini et al. 2022, Espadas-Gonzalez 2022]. In addition, all dogs received meloxicam IV at the end of the surgery. In our study, we designed an anaesthetic protocol to reduce possible interferences due to other drugs. In our opinion, the decision to administer only fentanyl IV in premedication and the delayed administration of carprofen in the postoperative period allowed us to assess more precisely the perioperative analgesic effect of the QLB<sub>LQL-T</sub>. According to this study design, a pain score higher than or equal to 5/24 was used as cut-off value for the administration of postoperative rescue methadone, despite a score of 6/24 is suggested [Reid et al. 2007]. This decision was based on the author's intention to treat pain as soon the analgesic effect of ropivacaine started to decrease, taking in account that dogs in our study received only fentanyl in premedication. Similarly, Viscasillas et al. used a cut-off of 4/24 in their study [Viscasillas et al. 2021a].

In human medicine, hypotension secondary to bilateral QLB has been described in two case reports [Almeida et al. 2018, Sà et al. 2018]. The authors speculated that this complication was related to a bilateral paravertebral extension of the QLB leading to an associated sympathetic block, resulting in a long-lasting vasodilation. In our study, we registered a reduction in MAP in the five minutes following the execution of the block in both groups, which could be due to a certain degree of sympatholysis and splanchnic vasodilation. However, this complication did not last. Surprisingly, the reduction in MAP was statistically significant only when ropivacaine 0.33% was used. Experimental studies conducted in animals have shown that ropivacaine is able to elicit a vasoconstriction response directly proportional to the concentration used [Burmester et al. 2005, Timponi et al. 2006, Wienzek et al. 2007]. The same results have also been achieved in clinical studies [39]. Since vasoconstriction decreases the systemic absorption of local anaesthetic (LA), we might speculate that the vasoconstriction induced by ropivacaine was less important in group QLB<sub>0.33%</sub> than in group QLB<sub>0.5%</sub>. Consequently, the systemic absorption of the drug may have been greater in subjects receiving ropivacaine 0.33%, resulting in a transitory reduction in MAP.

Intraoperative HR, SAP, MAP,  $f_R$ , FE'Sevo, did not show statistically significant differences between the three groups. Our study design aimed to reduce possible interferences due to other drugs except for the QLB<sub>LQL-T</sub> on the anaesthetic and analgesic plane. This finding may suggest that the QLB<sub>LQL-T</sub> with ropivacaine 0.5% and 0.33% provided a similar anaesthetic and analgesic plane to a systemic fentanyl-based analgesic protocol. However, although the difference was not statistically significant, dogs in groups receiving QLB<sub>LQL-T</sub> suffered less cardiovascular complications than dogs in group No-QLB, as reported in the literature [Grubb et al. 2020, Tayari et al. 2022].

Nine out of sixteen dogs required intraoperative rescue fentanyl in groups QLB during  $S_1$ ,  $S_2$ , and  $S_3$ . This result supports the notion that, during a minimally invasive surgery such as LO, the insufflation of the peritoneal cavity corresponds to an important nociceptive somatic stimulation, as reported in human medicine [Umano et al. 2021]. The canine abdominal wall is innervated by the VRSN between the ninth thoracic (T9) and L3 vertebrae [Castañeda-Herrera et al. 2017]. Garbin et al. reported that QLB<sub>LQL-T</sub> performed with 0.3 mL kg<sup>-1</sup> did not produce a consistent spread to the caudal thoracic VRSN, responsible for the innervation of the cranial portion of the abdominal wall [Garbin et al. 2020b]. However, we decided to use 0.3 mL kg<sup>-1</sup> because a higher volume in group QLB 0.5% would have exceeded 3 mg kg<sup>-1</sup> of ropivacaine [Grubb et al. 2020b]. Therefore, our results seem to confirm findings from previous cadaveric study [Garbin et al. 2020b]. Four out of eighteen dogs required intraoperative rescue fentanyl during  $S_6$  and  $S_7$ . Ovaries in female dogs are innervated by fibres from the sympathetic trunk portion between T13 and the second lumbar (L2) vertebrae [Boscan et al. 2011], consistently stained by the QLB<sub>LQL-T</sub> in a previous cadaveric study [Garbin et al. 2020b]. However, an important limitation of the study needs to be addressed. According to this study design, a bolus of 2.5 mcg kg<sup>-1</sup> of fentanyl IV was administered in presence of nociception, in 9/16 dogs during  $S_1$ ,  $S_2$ , and  $S_3$ . Considering the short duration of surgery in our study ( $35 \pm 13$  and  $35 \pm 11$  in group QLB<sub>0.5%</sub> and group QLB<sub>0.33%</sub>, respectively), and taking in account that plasma fentanyl concentrations decrease only after 20 min after IV administration [Sano et al. 2006], it is not possible to exclude that the rescue analgesia administered during the first steps of the LO mitigated the cardiovascular response during the visceral stimulation.

Based on the results of our study, QLB<sub>LQL-T</sub> seemed to produce a reduction in the requirement of intraoperative rescue fentanyl, in comparison with a group receiving a systemic fentanyl-based analgesic protocol. However, the anaesthetists in charge of the intraoperative monitoring were aware of the group No-QLB due to ethical issues, which could bias the results. Despite this, no statistically significant differences were found regarding the intraoperative rescue fentanyl consumption between group QLB<sub>0.5%</sub> and QLB<sub>0.33%</sub>, suggesting that QLB<sub>LQL-T</sub> performed with ropivacaine 0.5% and 0.33% provides the same intraoperative analgesic efficacy. This finding has been already reported in previous studies [Portela et al. 2010, Fenten et al. 2015, Tayari et al. 2017]. This information could be clinically useful, especially when an animal with comorbidities (cardiac, renal, or hepatic diseases) may equally benefit from an IFBP and from a reduction in the total amount of LA administered [Tayari et al. 2017].

In their study, Viscasillas et al. found that only 1/10 dog receiving the QLB required intraoperative rescue analgesia during laparotomic ovariohysterectomy [Viscasillas et al. 2021a]. The results of this study greatly differ from ours. However, a different approach to the QLB was performed [19], a different LA and volume were used and, most importantly, a substantially different premedication (medetomidine 20 mcg kg<sup>-1</sup> intramuscularly and meloxicam 0.2 mg kg<sup>-1</sup> subcutaneously) was administered. Considering the analgesic effect and duration of the drugs used in their study [Murrell et al. 2005, Bendinelli et al. 2019], it is not possible to exclude that the difference in rescue analgesia requirement between these two studies was dependent on drugs administered in premedication, rather than the QLB technique.

The present study has several limitations which need to be addressed. First, the study was based on a small sample of animals, and dogs were recruited from the population of a single Veterinary Teaching Hospital, which may limit generalization of the results. Second, as already mentioned, the anaesthetists in charge of the intraoperative monitoring were aware of the group No-QLB, leading to a possible bias: ideally, a negative control group should have received QLB<sub>LQL-T</sub> with saline solution; however, this was not considered ethically feasible in our institution. Third, despite all blocks being performed by the same operator, the success of any LRA technique is operator-dependent and it is influenced by the difficulty of the technique performed. It is not possible to rule out that different results would be obtained if blocks were performed in a higher number of dogs by different anaesthetists. Part of these limitations would be addressed by designing a multicentric study. Fourth, the decision to assess postoperative pain for a limited number of hours after the block execution did not allow in some cases (particularly in group QLB<sub>0.5%</sub>) to identify the exact moment when the first postoperative methadone administration was needed and the total consumption of postoperative methadone. However, LO is considered a day-hospital surgical procedure and postoperative hospitalization is not always essential [Wrmser et al. 2016]; for this reason, we limited the post-operative time monitoring.

In conclusion, bilateral QLB<sub>LQL-T</sub> with a volume of 0.3 mL kg<sup>-1</sup> of ropivacaine prolonged the time to the first postoperative methadone administration and reduced the pain scores in female dogs undergoing LO, in comparison with dogs receiving a systemic fentanyl-based analgesic protocol. In addition, ropivacaine 0.5% provided a longer postoperative effect in comparison with ropivacaine 0.33%, despite no differences being found in the intraoperative period between the two concentrations. Results of this study also suggests that ropivacaine 0.33% produce a more important reduction in the arterial blood pressure than ropivacaine 0.5%, during the first five

minutes after performing the block. However, this effect did not extend into the intraoperative period.

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# Experimental Section

## Study 2:

Comparative study between lateral *versus* latero-ventral quadratus lumborum block for perioperative analgesia in canine laparoscopic ovariectomy

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## Abstract

**Objective** To compare the perioperative analgesic effect of lateral versus latero-ventral quadratus lumborum block (QLB) in dogs undergoing laparoscopic ovariectomy.

**Study design** Randomised, blinded clinical study.

**Animals** A total of 15 client-owned female dogs undergoing laparoscopic ovariectomy.

**Methods** Animals were randomly assigned to receive a bilateral QLB, performed with 0.3 mL kg<sup>-1</sup> ropivacaine 0.5%, either with lateral (group L<sub>QLB</sub>, n = 7) or latero-ventral approach (group LV<sub>QLB</sub>, n = 7). Dogs were premedicated intramuscularly with methadone 0.2 mg kg<sup>-1</sup> and dexmedetomidine 3 µg kg<sup>-1</sup>. General anaesthesia was induced intravenously (IV) with propofol and maintained with isoflurane. Cardiovascular and respiratory variables were continuously monitored and recorded every 5 minutes during surgery. Fentanyl 3 µg kg<sup>-1</sup> was administered IV if there was a 20% increase in heart rate and/or mean arterial pressure from previous values recorded 5 minutes before. Meloxicam 0.2 mg kg<sup>-1</sup> was administered IV to all dogs during recovery. The short-form of the Glasgow Composite Pain Scale was used hourly for 8 hours post-QLB. Methadone 0.2 mg kg<sup>-1</sup> was administered IV when pain score was ≥ 6/24. A chi-square test compared the number of dogs requiring intraoperative rescue fentanyl. A Friedman test with a Dunn's post hoc was used to evaluate the trend in postoperative pain scores within each group, and a Mann-Whitney test compared scores between the groups at each time point; p < 0.05.

**Results** Significantly fewer dogs required intraoperative rescue fentanyl in group L<sub>QLB</sub>, than in group LV<sub>QLB</sub>. No dog required postoperative rescue methadone and there were no significant differences in pain scores.

**Conclusions and clinical relevance** Bilateral QLB performed with lateral approach reduced the number of dogs requiring intraoperative rescue analgesia in comparison with the latero-ventral approach. No differences were detected postoperatively, possibly due to the confounding effects of methadone, dexmedetomidine, and meloxicam.

## Introduction

The quadratus lumborum block (QLB) is an ultrasound (US)- guided interfascial plane (IFP) block used to promote somatic and visceral analgesia to the abdomen (Garbin et al. 2020a, b; Marchina-Gonçalves et al. 2021, 2023; Viscasillas et al. 2021a, b; Alaman et al. 2022; Degani et al. 2023). It consists of the injection of local anaesthetic in the thoracolumbar fascia surrounding the quadratus lumborum muscle, aiming to desensitize the ventral rami of the spinal nerves (VRSNs) and the sympathetic trunk. Cadaver studies evaluated the spread of injectate using different approaches (Garbin et al. 2020a, b; Marchina-Gonçalves et al. 2021, 2023; Viscasillas et al. 2021a; Alaman et al. 2022). Garbin (2024) recently proposed a nomenclature for their classification, based on the position of the needle tip during injection: transmuscular, when it is positioned between the quadratus lumborum and psoas muscles (Garbin et al. 2020a; Viscasillas et al. 2021a); dorsal, between the body of the first lumbar (L1) or second lumbar (L2) vertebrae and the quadratus lumborum muscle (Marchina-Gonçalves et al. 2021; Alaman et al. 2022); and lateral, between the lateral aspect of the quadratus lumborum muscle and the transverse process of L1 (Garbin et al. 2020b). Overall, the QLB resulted in a consistent staining of the VRSNs between L1 and the third (L3) lumbar vertebrae, with maximal spreading observed between the thirteenth thoracic (T13) and fourth lumbar (L4) vertebrae, as well as around the sympathetic trunk between T13 and L3 (Garbin 2024).

The QLB can be challenging to perform, especially when deep injection targets are selected, such as with the approaches described by Garbin et al. (2020a), Marchina-Gonçalves et al. (2021), and Alaman et al. (2022). At this level, the vicinity of aorta, caudal vena cava and abdominal organs can pose some difficulties in performing the block. Recently, a novel latero-ventral approach for the QLB has been described, in which the injection site is more superficial and away from important anatomical structures (Marchina-Gonçalves et al. 2023). According to the authors of that study, this approach might be safer and easier to perform. However, the latero-ventral approach failed to produce a consistent spread of injectate towards the sympathetic trunk, suggesting that it might not provide visceral pain relief to the abdomen (Marchina- Gonçalves et al. 2023).

According to the results of the latest systematic reviews and meta-analysis published in human medicine, it remains unclear whether the injection position of the needle affects the analgesic efficacy of the QLB (Kim et al. 2020; Uppal et al. 2020; Korgvee et al. 2021). Furthermore, the exact mechanism of action of the IFP blocks is still the subject of debate. Several authors hypothesized that the analgesic effect of these locoregional anaesthesia techniques could be produced not only

by direct blockade of peripheral nerve fibres but also by the systemic effect secondary to the vascular absorption of local anaesthetic (Lönnqvist & Karmakar 2019; Chin et al. 2021). Evidence demonstrating the analgesic efficacy of the QLB in dogs is described in one case series and one randomised clinical trial (RCT) (Viscasillas et al. 2021b; Degani et al. 2023). In a previous study, the lateral approach described by Garbin (2021) was found to be effective in reducing the perioperative opioid consumption when compared with a systemic fentanyl-based protocol, in female dogs undergoing laparoscopic ovariectomy (Degani et al. 2023). To the best of our knowledge, studies comparing the analgesic effect of different approaches for the QLB in dogs undergoing abdominal surgery are lacking in literature.

This RCT aimed to compare the perioperative analgesic efficacy of a bilateral QLB performed using two different approaches (lateral or latero-ventral) in female dogs undergoing laparoscopic ovariectomy. We hypothesized that the lateral approach would result in fewer dogs requiring perioperative rescue analgesics in comparison with the latero-ventral approach.

## Material and Methods

This blinded RCT was approved by the Scientific Ethics Committee of the University of Teramo, protocol number 2727 with the date 29/01/2024. The Consolidated Standards of Reporting Trials (CONSORT) guidelines have been followed (Schulz et al. 2010). By signing the informed consent document, owners agreed to enrol their dog in the study. A total of 15 female dogs with an American Society of Anaesthesiologists (ASA) status 1, undergoing laparoscopic ovariectomy, were enrolled. Prior to anaesthesia, each dog underwent a complete physical examination, including body condition score (BCS) on a nine-point scale evaluation (Laflamme 1997), and routine blood tests screenings (haematology and serum biochemistry). Exclusion criteria included age of less than 6 months, aggressive behaviour, skin infection at the site of the QLB, and administration of corticosteroids or non-steroidal anti-inflammatory drugs (NSAIDs) within 24 hours prior to surgery.

**Preoperative management:** Pain assessment was performed using the Short Form of the Glasgow Composite Measure Pain Scale (SF-GCMPS) (Reid et al. 2007) on admission, to obtain baseline values. Premedication consisted of an intramuscular injection of methadone  $0.2 \text{ mg kg}^{-1}$  (Semfortan  $10 \text{ mg mL}^{-1}$ ; Eurovet Animal Health, The Netherlands) and dexmedetomidine  $3 \mu\text{g kg}^{-1}$  (Dextroquillan  $0.5 \text{ mg mL}^{-1}$ ; Fatro, Italy). Approximately 15 minutes later, a 20-gauge intravenous (IV) catheter was aseptically inserted into one of the cephalic veins and lactated Ringer's solution at  $5 \text{ mL kg}^{-1} \text{ hour}^{-1}$  was initiated. After 5 minutes of preoxygenation by mask (SurgiVet Pet Oxygen Masks; Tri-Med Medical Supplies, UK), general anaesthesia was induced with propofol (Propovet  $10 \text{ mg mL}^{-1}$ ; Zoetis, Italy) IV to effect, until endotracheal intubation (Rusch; The Sheridan, NC, USA) was feasible. The endotracheal tube was connected to an anaesthetic workstation (Fabius, Dräger, Italy) via a circle breathing system (Flextube; Intersurgical, UK), and anaesthesia was maintained with isoflurane (Isoflo; Zoetis) delivered in oxygen/air mixture with a fraction of inspired oxygen (FIO<sub>2</sub>) of 60%.

Immediately after induction, dogs were connected to a multiparametric monitor (M3046-M2; Philips, Italy) and the following physiological variables were continuously monitored and recorded every 5 minutes, during anaesthesia: heart rate (HR), peripheral arterial haemoglobin saturation (SpO<sub>2</sub>), respiratory rate (fR), and systolic, mean and diastolic arterial blood pressures (SAP, MAP, DAP), measured invasively via a 20-gauge peripheral catheter placed in one of the dorsal pedal arteries. The end-expiratory carbon dioxide concentration (P<sub>E</sub>'CO<sub>2</sub>) and the end-tidal isoflurane concentration (F<sub>E</sub>'Iso) were monitored with an infrared gas analyser (M3016 Measurement Server Extension; Philips), which was calibrated in accordance with the manufacturer instructions, before

each anaesthesia. The hair on the abdomen and flank of each dog was clipped and the skin was aseptically prepared. All dogs were administered a bilateral QLB with 0.3 mL kg<sup>-1</sup> of ropivacaine (Ropivacaine hydrochloride 10 mg mL<sup>-1</sup>; Galenica Senese, Italy) 0.5% per side (3 mg kg<sup>-1</sup> in total). Dogs were randomly allocated into two groups using block randomization (<https://www.random.org>, accessed on 1 October 2023): group L<sub>QLB</sub>, QLB performed as described by Garbin et al. (2020b), and group LV<sub>QLB</sub>, QLB performed as described by Marchina- Gonçalves et al. (2023). All blocks were performed by the same anaesthetist (MD), equally trained in both techniques. A 100 mm insulated needle for nerve blocks (Stimulplex; B Braun, Italy) and a 14 MHz high-frequency linear transducer (L7HD3VET; Clarius Mobile Health, BC, Canada), connected to a touchscreen tablet (iPad Air, fifth generation; Apple, CA, USA), were used. The anaesthetist in charge of intraoperative monitoring (AP) and the surgeon (ABi) were blinded to group allocation. Time to perform the block, considered as the interval between the start of the scanning and the end of injection, as well as time from the block to starting of surgery, were recorded.

**Intraoperative management:** Dogs were moved to the operating room and volume-controlled ventilation was initiated to maintain PE'CO<sub>2</sub> between 35 and 45 mmHg (4.6-5.9 kPa). All dogs were operated on by the same surgeon, using a modified Hasson technique (Bianchi et al. 2021). FE'Iso was initially set at 1.3% and decreased by 0.05% every 5 minutes. Isoflurane was reduced if HR and MAP remained within 20% of baseline (Mosing et al. 2010; Tayari et al. 2022), and the surgical anaesthetic plane was maintained (absence of palpebral reflex and voluntary movements, and mild jaw tone) (Grubb et al. 2020). Animals were positioned in dorsal recumbency, and a Trendelenburg position was applied. Pneumoperitoneum was obtained by mechanical insufflation between 8 and 10 mmHg. During surgery, dogs were laterally tilted to improve the visualisation of the ovaries. A 5-minute interval in the surgical procedure followed, to ensure an eventual haemodynamic stabilisation and not to interfere with the assessment of nociception. A 20% increase in HR and/or MAP from the previous value recorded 5 minutes before was considered to be a sign of nociception and a bolus of 3 µg kg<sup>-1</sup> of fentanyl was administered IV. In case the variables were not restored within 5 minutes, fentanyl infusion was started at an increasing rate between 2 and 10 µg kg<sup>-1</sup> hour<sup>-1</sup> until return to pre-nociception values. The time of administration of fentanyl, if necessary, and the surgical phase during which nociception was detected, were recorded. The following surgical phases of laparoscopic ovariectomy were considered: P<sub>1</sub>, skin incision and first port insertion; P<sub>2</sub>, insufflation of the abdomen; P<sub>3</sub>, second port insertion; P<sub>4</sub>, traction and cauterization of the first ovary; P<sub>5</sub>, traction and cauterization of the second ovary; P<sub>6</sub>, deflation of pneumoperitoneum and extraction of the trocars; P<sub>7</sub>, suturing of the skin. In case of hypotension (MAP < 60 mmHg), FE'Iso was



reduced by 0.1%, every minute. If hypotension persisted despite FE'Iso of 0.8%, a bolus of 10 mL kg<sup>-1</sup> of lactate Ringer's solution was administered over 10 minutes. If hypotension persisted, noradrenaline (Noradrenaline sulfate, 2 mg mL<sup>-1</sup>, Galenica Senese, Siena, Italy) infusion was started at 0.05 µg kg<sup>-1</sup> minute<sup>-1</sup> and increased by 0.05 µg kg<sup>-1</sup> minute<sup>-1</sup> every 5 minutes until MAP ≥ 60 mmHg. In presence of bradycardia (HR < 60 beats minute<sup>-1</sup>) causing concurrent hypotension, atropine 20 µg kg<sup>-1</sup> (Atropine sulfate 1 mg mL<sup>-1</sup>, ATI, Bologna, Italy) was administered IV. At the end of surgery, administration of isoflurane was interrupted, and mechanical ventilation was stopped once the dog returned to spontaneous breathing. Each animal was then moved to the recovery room and tracheal extubation was performed when the swallowing reflex was restored. Duration of anaesthesia and surgery were recorded. Meloxicam 0.2 mg kg<sup>-1</sup> (Meloxidolor 5 mg mL<sup>-1</sup>; Le Vet Beheer, Oldeholtspade, Netherlands) was administered IV during recovery to all dogs.

**Postoperative management:** An hour after extubation, pain assessment was started by a third investigator blinded to the group allocation (L.D.M), using the SF-GCMPS. Evaluations were performed every hour up to 8 hours starting from the QLB execution. In case of a score ≥ 6/24, methadone 0.2 mg kg<sup>-1</sup> was administered IV, and the postoperative pain monitoring for the purposes of this study was interrupted. Time from the block to the first postoperative methadone administration, if necessary, was recorded and compared between groups.

**Statistical Analysis:** The number of dogs enrolled in the study was based on the incidence of rescue analgesia administration, using an online sample size calculator (ClinCalc.com). Considering a mean incidence of rescue analgesia of 10% in group L<sub>QLB</sub> (Viscasillas et al. 2021b) and a clinically significant difference of 70% between the two groups, the minimum number of animals per group was seven. This calculation utilised an  $\alpha$  of 0.05 and a power of 80%. Data were analysed for distribution with a D'Agostino-Pearson test. Data were expressed as either mean and standard deviation, or median and range for BCS and SF-GCMPS. A Student's T-test was used to compare age, weight, duration of anaesthesia and surgery, and time from the block to starting of surgery between groups. An analysis of variance (ANOVA) test for repeated data was used to evaluate the trend within each group for HR,  $f_R$ , SAP, MAP, and FE'Iso. BCS was compared between groups using a Mann-Whitney test. A Chi-square test was used to compare the number of dogs requiring rescue fentanyl and vasoactive drugs between groups. A Friedman test with a Dunn's *post hoc* was used to evaluate the trend in postoperative pain scores within each group, while a Mann-Whitney test compared the scores between the two groups at each time point. Statistical difference was considered significant for  $p < 0.05$ . Prism Version 6.0 (GraphPad Software Inc., CA, USA) was used to analyse data.

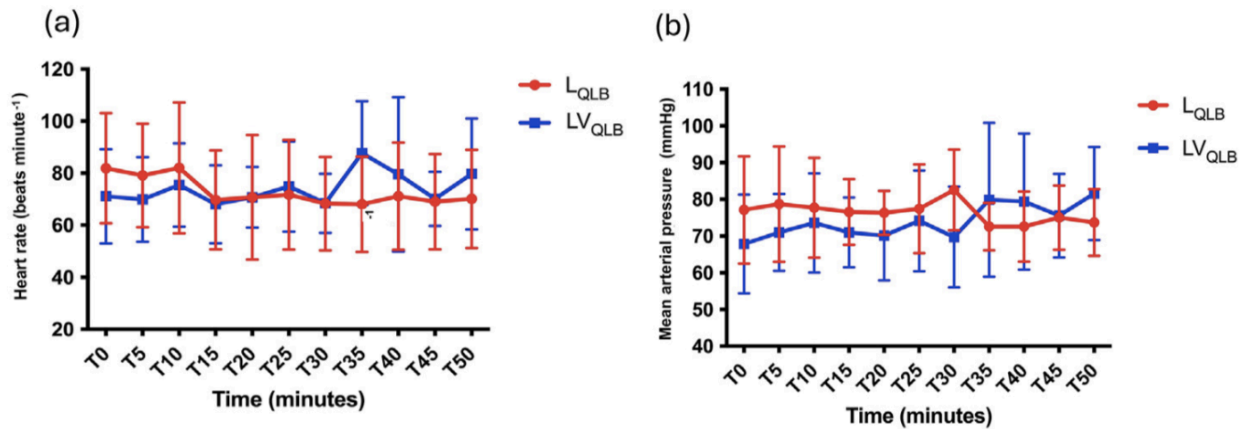
## Results

A total of 15 dogs were enrolled but 14 concluded the study uneventfully: one dog from group LV<sub>QLB</sub> was excluded because of conversion of the surgery into a laparotomic ovariectomy, due to intraoperative haemorrhage. No significant statistical differences were found regarding demographic data, duration of anaesthesia, and duration of surgery (Table 1).

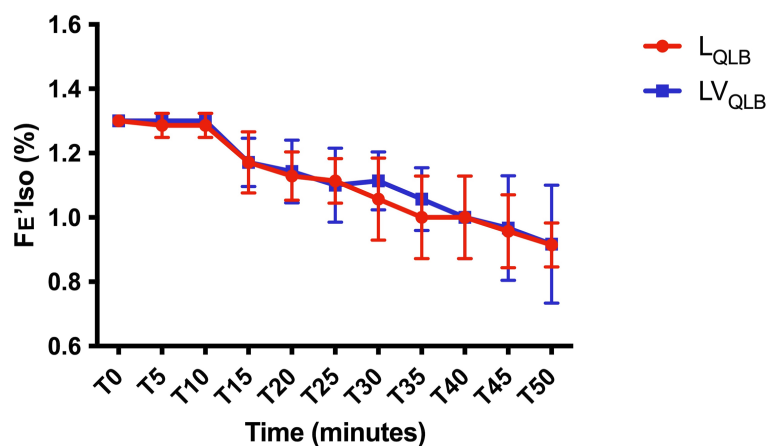
**Table 1** Demographic data, duration of anaesthesia and surgery (minutes) and time from the block to the starting of surgery (minutes) measured in the 14 dogs included in the study (n = 7 per group). L<sub>QLB</sub>, lateral quadratus lumborum block; LV<sub>QLB</sub>, latero-ventral quadratus lumborum block. Results are presented as mean and standard deviation.

Group	Age (months)	Weight (kg)	Duration anaesthesia (minutes)	Duration surgery (minutes)	Time from block to the starting of surgery (minutes)
L <sub>QLB</sub>	19 ± 5	23 ± 8	108 ± 29	59 ± 24	27 ± 8
LV <sub>QLB</sub>	21 ± 6	20 ± 7	112 ± 31	64 ± 24	27 ± 6

BCS was 5/9 (3–5) in group L<sub>QLB</sub> and 5.5/9 (4–8) in group LV<sub>QLB</sub>. Time to perform the block was 170 ± 39 seconds in group L<sub>QLB</sub> and 165 ± 44 seconds in group LV<sub>QLB</sub>, without statistically significant difference. The intraoperative values of HR, MAP [Figs. 1(a), (b)],  $f_R$ , FE'Iso (Fig. 2) did not differ significantly between the two groups. Bradycardia was recorded in 1/7 dogs in group LV<sub>QLB</sub> which was corrected with one bolus of 20 µg kg<sup>-1</sup> of atropine administered IV. No hypotension was recorded in dogs included in this study.



**Figure 1 (a)**, Intraoperative heart rate, beats per minute (beats minute<sup>-1</sup>); (b), intraoperative mean arterial blood pressure (mmHg) measured in the 14 dogs enrolled in the study. Dogs were randomly allocated to one of two groups: L<sub>QLB</sub>, receiving the lateral quadratus lumborum block (QLB); group LV<sub>QLB</sub>, receiving the latero-ventral QLB. Data are shown as mean and standard deviation.



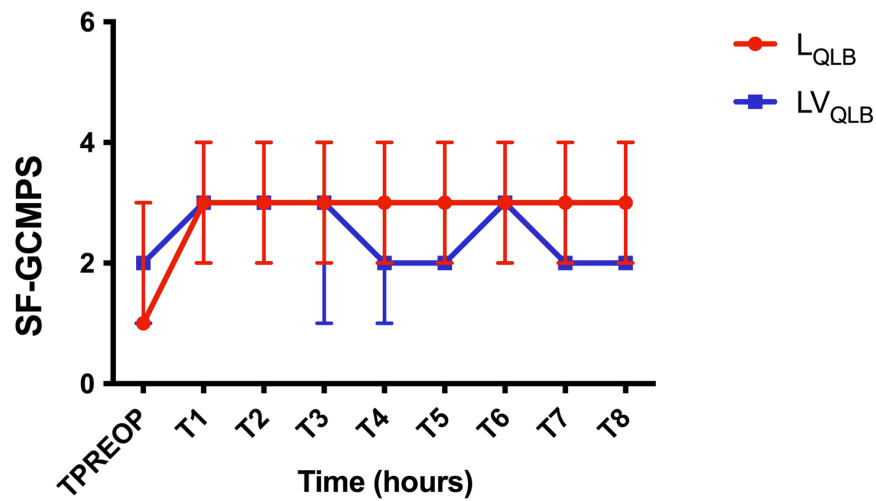
**Figure 2** Intraoperative end-tidal concentration of isoflurane (FE'Iso (%)) measured in the 14 dogs enrolled in the study. Dogs were randomly allocated to one of two groups: L<sub>QLB</sub>, receiving the lateral quadratus lumborum block (QLB); group LV<sub>QLB</sub>, receiving the latero-ventral QLB. Data are shown as mean and standard deviation.

A significant difference between groups ( $p = 0.02$ ) was detected regarding the number of dogs requiring at least one bolus of rescue fentanyl, during the intraoperative period. One bolus of fentanyl was administered in 2/7 dogs in group L<sub>QLB</sub> and in 7/7 dogs in group LV<sub>QLB</sub>. No dogs in group L<sub>QLB</sub> and LV<sub>QLB</sub> required fentanyl infusion. Data regarding the distribution of intraoperative rescue fentanyl administration in the two groups are summarised in the Table 2.

**Table 2:** Distribution of intraoperative rescue fentanyl boluses ( $3 \mu\text{g kg}^{-1}$ ), during specific surgery phases in the two groups of dogs ( $n = 7$  per group) receiving the quadratus lumborum block., either as a lateral quadratus lumborum block ( $L_{QLB}$ );, or a latero-ventral quadratus lumborum block ( $LV_{QLB}$ );  $P_1$ , skin incision and first port insertion ;  $P_2$ , insufflation of the abdomen;  $P_3$ , second port insertion;  $P_4$ , traction and cauterization of the first ovary;  $P_5$ , traction and cauterization of the second ovary;  $P_6$ , deflation of pneumoperitoneum and extraction of the trocars;  $P_7$ , suturing the skin.

Group	Dog	Distribution of intraoperative rescue fentanyl boluses						
$L_{QLB}$		$P_1$	$P_2$	$P_3$	$P_4$	$P_5$	$P_6$	$P_7$
	1		x					
	2							
	3		x					
	4							
	5							
	6							
	7							
$LV_{QLB}$								
	1							
	1				x	x		
	2					x		
	3				x	x		
	4					x		
	5					x		
	6				x			
	7					x		

No dogs required rescue methadone during the eight hours after the execution of the QLB and no differences were found regarding postoperative pain scores between the two groups (Fig. 3).



**Figure 3** Preoperative (Tpreop) and postoperative pain scores using the short-form Glasgow Composite Measure Pain Scale (SF-GCMPS) at 1, 2, 3, 4, 5, 6, 7, 8 hours after block execution in the 15 dogs enrolled in the study. Dogs were randomly allocated to one of two groups: L<sub>QLB</sub>, receiving the lateral quadratus lumborum block (QLB); group LV<sub>QLB</sub>, receiving the latero-ventral QLB. Data are shown as median and range.

## Discussion

In this study, a significantly smaller number of dogs receiving a QLB performed with the lateral approach (Garbin et al. 2020b) required rescue analgesia during surgery, compared with those receiving the latero-ventral approach (Marchina-Gonçalves et al. 2023). Therefore, our initial hypothesis was confirmed.

Surgical manipulation of the ovaries produced nociception in all dogs in group LV<sub>QLB</sub>, and in none of dogs in group L<sub>QLB</sub>. The QLB performed with latero-ventral approach did not produce a substantial spread of injectate to sympathetic trunk spread (Marchina-Gonçalves et al. 2023), responsible for the visceral innervation of the abdomen, while this occurred for the lateral approach (Garbin et al. 2020b). We hypothesized that this difference in outcome was caused by the thoracolumbar fascia surrounding the *quadratus lumborum* muscle, which might have prevented the spread of solution towards the sympathetic trunk. Positioning the needle tip latero-ventrally to the quadratus lumborum muscle, below the aponeurosis of the *transversus abdominis* muscle, does not mean that the thoracolumbar fascia has been perforated. The results of our study suggest that the direct blockade of nerves fibres from the sympathetic trunk could be involved in the abdominal visceral analgesic effect of the QLB in dogs. However, the mechanism of action of this IFP block is still unclear (Lönnqvist & Karkmar 2019, Chin et al. 2021).

In the present study, 2/14 dogs (14.2%) required intraoperative rescue analgesia during P<sub>1</sub>, P<sub>2</sub> and P<sub>3</sub>. In a previous RCT, 9/16 dogs (56.2%) receiving the same block experienced nociception during the same surgery phases (Degani et al. 2023). This discrepancy can be attributable to the different premedication protocol used in these studies (methadone 0.2 mg kg<sup>-1</sup> and dexmedetomidine 3 µg kg<sup>-1</sup> IM versus fentanyl 5 µg kg<sup>-1</sup> IV). The inclusion of an opioid and an α<sub>2</sub>-adrenoceptor agonist in this study aimed to replicate clinical practice. Combinations of analgesics and sedatives drugs are often administered in premedication, in clinical settings.

The reported injectate volume for the QLB ranges between 0.3–0.6 mL kg<sup>-1</sup> per side (Garbin et al. 2020a, b; Alaman et al. 2022; Viscasillas et al. 2021b; Marchina-Gonçalves et al. 2022; Marchina-Gonçalves et al. 2023). None of the approaches previously described produced a consistent cranial dispersion of injectate towards the VRSNs between T9 and T13, regardless of the volume used. Taking into account these findings, we decided to use 0.3 mL kg<sup>-1</sup> to avoid excessive dilution of the

ropivacaine concentration, which could have affected the quality and duration of the block (Tayari et al. 2017; Degani et al. 2023).

The QLB performed with the latero-ventral approach could be considered as a variation of the transversus abdominis plane (TAP) block, providing similar analgesic effect. Our results, compared with those from previous studies, where the TAP block was evaluated in dogs submitted to laparoscopic ovariectomy (Paolini et al. 2022; Espadas-González et al. 2022), seem to corroborate this hypothesis. Despite controversy in literature regarding the efficacy of the TAP block on visceral pain (Freitag et al. 2018; Paolini et al. 2022; Espadas-González et al. 2022), this technique has been demonstrated in cadaver studies to stain only the VRSNs and their branches, involved in the innervation of the abdominal wall (Castañeda-Herrera et al. 2017; Drozdzyńska et al. 2017; Romano et al. 2021). Further RCTs are necessary, to compare the analgesic effect of QL and TAP blocks in dogs undergoing abdominal surgery.

The results regarding the postoperative period in this study are consistent with those from previous research (Degani et al. 2023), in which the time to the first postoperative methadone administration in dogs receiving the QLB with ropivacaine 0.5% was  $10.2 \pm 2.5$  hours, even without any anti-inflammatory drug administration. In that study, both approaches resulted in an opioid-free postoperative period for at least 8 hours, despite differences were found in the intraoperative period in terms of rescue fentanyl administered (Degani et al. 2023). However, it is possible that the administration of meloxicam could have masked differences in postoperative analgesic effect between the two approaches used in this study.

Studies in human medicine assessed whether there is indeed a difference in postoperative analgesic effect related to the approach used to perform the QLB in humans. Kim et al. (2020) found that targeting a more superficial injection point would result in lower postoperative pain scores. On the other hand, evidence from Uppal et al. (2020) suggested that the transmuscular approach might be more effective compared with the posterior approach. However, Korgvee et al. (2021) found no differences in their systematic review. To our knowledge, this study is the first in comparing the analgesic effects of different QLB approaches in dogs undergoing abdominal surgery. Further studies are thus needed to determine and compare the analgesic effect of different approaches for the QLB in the canine species.

Although no statistically significant differences were found regarding intraoperative physiological variables monitored during anaesthesia, some data are worth to be discussed. Despite no

differences in HR between groups, MAP in dogs in group LV<sub>QLB</sub> was slightly lower than in those in group L<sub>QLB</sub> [Fig 1(b)]. In the authors' opinion, lower MAP was more likely to occur in group LV<sub>QLB</sub>, because a higher number of dogs required rescue fentanyl in this group (Table 2). Opioids can produce enhancement of the parasympathetic tone and cause changes in cardiac output, systemic vascular resistance, and blood pressure (Keating et al. 2013). However, it is important to highlight that this study was not sufficiently powered to detect differences in these variables.

The present study has several limitations. Firstly, a small sample of dogs was included in this RCT. Therefore, studies with larger numbers of animals are needed to confirm these results. Secondly, dogs included in this study received a premedication consisting of an opioid and an  $\alpha_2$ -adrenoceptor agonist, as well as a NSAID during recovery. It is quite likely that the administration of these drugs influenced the analgesic effect of the QLB and masked any postoperative difference between the two approaches evaluated in this study. Furthermore, the possibility to assess postoperative pain for 8 hours after the QLB execution did not allow us to measure the exact duration of the postoperative analgesic effect of the block and detect any difference between the two approaches. However, postoperative hospitalisation is not always considered essential after laparoscopic ovariectomy (Wormser & Runge, 2016). In our institutions, for instance, dogs are usually discharged between 8 and 12 hours after surgery. Finally, the same anaesthetist performed all blocks, possibly biasing the results. As US-guided locoregional anaesthesia techniques are considered operator-dependent, it is not possible to exclude that different results could have been obtained by involving multiple operators with different levels of experience.

In conclusion, the QLB performed with the lateral approach is a valuable adjunct to a multimodal analgesic protocol for dogs undergoing laparoscopic ovariectomy, as it reduces the need for intraoperative rescue analgesia. Further research is needed to confirm the results of this study.



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# Experimental Section

## Study 3:

**Description and outcomes of an ultrasound-guided technique for catheter placement in the canine quadratus lumborum plane: a cadaveric tomographic study and clinical case series**

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## Abstract

This study aimed to describe an ultrasound-guided technique for implanting catheters for local anaesthetic administration into the quadratus lumborum (QL) interfascial plane in canine cadavers and assessing the spread along the vertebral bodies (VBs) by computed tomography (CT). Phase 1: eight canine cadavers received one catheter per hemiabdomen, followed by injection of contrast media solution [low volume ( $L_v$ )  $0.3 \text{ mL kg}^{-1}$  or high volume ( $H_v$ )  $0.6 \text{ mL kg}^{-1}$ ]. Phase 2: postoperative pain of five dogs was managed by injecting  $0.3 \text{ mL kg}^{-1}$  of ropivacaine 0.5% through QL-catheters every eight hours, up to 72 hours after abdominal surgery. Pain was assessed using the Short Form of the Glasgow Composite Measure Pain Scale, and methadone  $0.2 \text{ mg kg}^{-1}$  was administered intravenously when pain score was  $\geq 6$ . Number of VBs stained by contrast between the QL and psoas minor muscles was significantly higher in group  $H_v$  than group  $L_v$ . Catheter tip was visualized in the retroperitoneal space in 1/16 hemiabdomen in phase 1 and 2/10 hemiabdomens in phase 2. Rescue analgesia was required in 3/5 dogs during the postoperative period. The QL catheter placement technique appears feasible and may be included in a multimodal analgesic approach for dogs undergoing abdominal surgeries.

**Keywords:** analgesia; dog; quadratus lumborum block; computed tomography; postoperative period; locoregional anaesthesia

## Introduction

The ultrasound (US)-guided quadratus lumborum (QL) block is a locoregional anaesthesia technique through which local anaesthetic (LA) is injected into the thoracolumbar fascia enveloping the QL muscle. The aim is to desensitize the ventral rami of the spinal nerves and the sympathetic trunk, which are responsible for the somatic and visceral innervation of the abdomen, respectively [Garbin 2024]. The QL block has been reported as an effective technique for abdominal perioperative analgesia in humans [Akrman et al. 2018, Uppal et al. 2020], dogs [Viscasillas et al. 2021a, Degani et al. 2023] and cats [Dos-Santos et al. 2024]. Recently, cadaveric and clinical studies proposed the inclusion of a caudal QL block in the pain management of dogs undergoing orthopedic hindlimb surgery and orchiectomy [Otero et al 2024a, Otero et al. 2024b, Paolini et al. 2024].

Garbin et al. evaluated the spread of 0.3 mL kg<sup>-1</sup> per side of dye-lidocaine solution injected in canine cadavers, performing the QL block with a lateral approach [Garbin et al. 2021a]. The injection was performed after positioning the tip of the needle between the lateral aspect of the QL muscle and the transverse process of the first lumbar vertebra (L1). The authors of that study reported a median spread (range) of 4 (3-5) ventral rami of spinal nerves, within the twelfth thoracic (T12) and third lumbar (L3) vertebrae. A consistent spread along the sympathetic trunk within T11 and L3 was also reported. According to the results of a clinical trial performed in female dogs undergoing laparoscopic ovariectomy, this approach resulted in a reduction of perioperative opioid consumption, compared to a systemic fentanyl-based protocol [Degani et al. 2023].

The duration of the postoperative analgesic effect of the QL block in dogs undergoing abdominal surgeries reported in veterinary literature varies between four and 10 hours, depending on the LA, volume and concentration used [Viscasillas et al. 2021a, Degani et al. 2023]. In the institutions of the authors of this study, the QL block is performed in dogs with severe abdominal pain, poorly responsive to traditional systemic analgesic therapy, both preoperatively and postoperatively. However, to perform this technique safely, dogs need to be deeply sedated or anaesthetized, which can be a contraindication. In human medicine, implantation of catheters in the QL interfascial plane (IFP) has been described to extend the duration of effect of a single-shot block in the postoperative period [Kadam et al. 2018, Zhu et al. 2019, Pooley et al. 2022]. Recently, the insertion of catheters into the transversus abdominis plane (TAP) and between the QL and psoas minor (Pm) muscles in dogs has been reported in two case series [Freitag et al. 2018, Camargo Fontanela et al. 2024]. In both reports, administration of bupivacaine 0.5% through the catheters every 6 or 12 hours resulted in a reduction in pain scores in dogs after different abdominal surgeries, or in presence of pancreatitis.

The aim of this study was to (1) describe an US-guided technique for placing catheters for LA administration in the QL IFP in canine cadavers, (2) to assess the spread of two different volumes (0.3 *versus* 0.6 mL kg<sup>-1</sup>) per side of contrast media solution injected through the catheters using computed tomography (CT), (3) to describe the outcomes of five dogs undergoing different abdominal surgeries, in which catheters bilaterally implanted in the QL IFP were included in a multimodal postoperative analgesic plan. We hypothesized that this technique is feasible in dogs and that using a higher volume of injectate would result in greater spread along the vertebral bodies (VBs).



## Materials and Methods

This study was divided into two phases. In the first phase, eight canine cadavers were used to describe the technique and assess the spread of the contrast media solution by computed tomography (CT). Ethical approval was obtained from the University of Liege, Belgium, approval for animal experimentation (Commission d'éthique animale; n. 2647). In the second phase, we report the use of bilateral QL-catheters in five client-owned dogs for ropivacaine intermittent administration for postoperative analgesia, after different open surgeries. Each owner signed an informed written consent and agreed that data from their animals could be used for the purpose of this study.

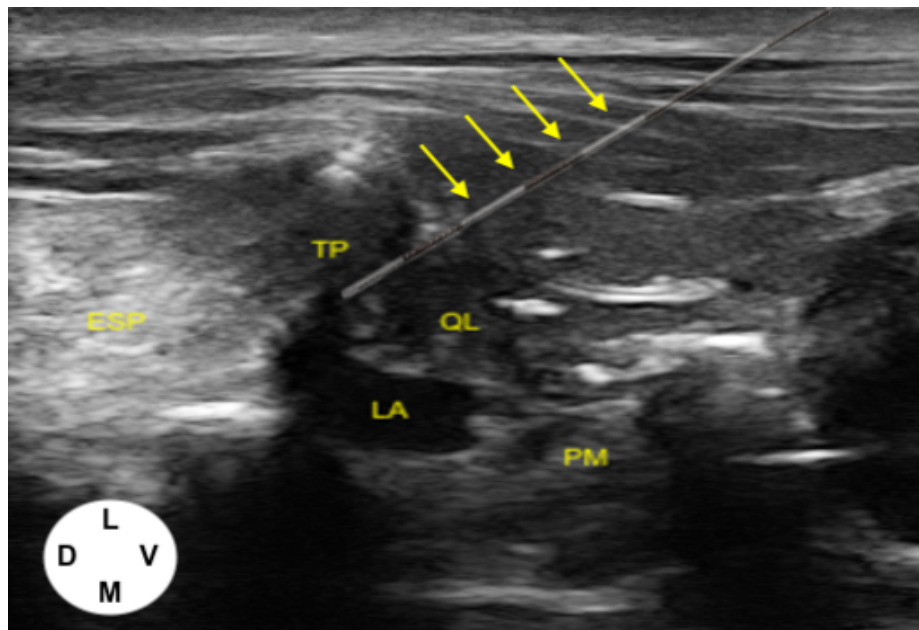
### First Phase

In the first phase of this study, we included eight canine cadavers intended for hands-on training in general surgery for students at the Faculty of Veterinary Medicine of the University of Liege. Dogs were euthanized for reasons unrelated to this study. Exclusion criteria comprised presence of lesions on skin or muscles of the thoracolumbar area, as well as alterations in the conformation and number of vertebrae between T8 and L7.

### US-Guided Catheter Placement Technique

Cadavers were positioned in either lateral recumbency and the hair on the dorso-lateral thoracolumbar area of both hemiabdomens was clipped. Complete sets for epidural anaesthesia (Perifix® Complete Set, B Braun, Melsungen, Germany) with a Tuohy needle (1.30 × 80 mm, 18G), catheter (0.85 × 0.45 × 1,000 mm, 20G), filter and a self-adhesive securement device, were used in this study. The lateral approach described for the US-guided QL block [Garbin et al. 2020a] was used to place all catheters, with a 14 MHz high-frequency linear transducer (L7HD3VET; Clarius Mobile Health, BC, Canada), connected to a touchscreen tablet (iPad Air, fifth generation; Apple, CA, USA). Implantations of catheters were performed by the same investigator (M.D.), assisted by a second one (C.T.). The transverse process of L1, the QL and the erector spinae (ESP) muscles were sonographically visualized (Figure 1). The needle was introduced with an in-plane technique in a ventrolateral-to-mediadorsal direction and advanced towards the ventral aspect of the transverse process of L1, with the bevel of the needle directed dorsally. Once the needle passed through the thoracolumbar fascia and came into contact with the transverse process, the bevel was rotated of 180° in a ventral direction and a bolus of 0.05 mL kg<sup>-1</sup> of saline solution (Mini-Plasco NaCl; B Braun, Germany) was injected. Confirmation of correct positioning of the needle was obtained by

visualization of the hydrodissection between the dorsal aspect of QL muscle and the ventral aspect of the transverse process of L1 (Figure 1). Then, the catheter was inserted through the needle and advanced 3-4 cm into the IFP. The needle was removed, and the catheter was fixed to the skin, using a 3-0 suture (Ethilon; Ethicon, NJ, USA), with a finger-trap pattern. The catheter was cut approximately 15 cm from the insertion point of the skin and secured with the self-adhesive device. Time to perform the technique, considered as the interval between the start of the US scanning and withdrawal of the Tuohy needle, was recorded. The same technique was performed on both sides.



**Figure 1.** Post-injection ultrasound image of the anatomical structures and needle trajectory (yellow arrows) to perform the lateral quadratus lumborum (QL) block: QL, quadratus lumborum muscle; Pm, psoas minor muscle; TP, transverse process of L1; ESP, erector spinae muscles; LA, local anaesthetic.

### Tomographic Study

After implantation of both catheters, CT scans of the region between T8 and L7 were performed, using 64 slice multidetector scanner (Somatom Confidence 64, Siemens, Erlangen, Germany). Cadavers were positioned in sternal recumbency, with their forearms and hindlimbs extended. Each cadaver received one injection per hemiabdomen, performed through the catheter, either with 0.3 (group L<sub>v</sub>) or 0.6 mL kg<sup>-1</sup> (group H<sub>v</sub>) of injectate. The solution for injection was prepared by adding 25 mL of ioexhol radiographic contrast media (Ultravist 300, Bayer, Berlin, Germany) to 500 mL of saline solution (Vetivex® 9 mg mL<sup>-1</sup>, Dechra Veterinary Products, Belgium). Right and left-sided injections

were randomized using a free software ([www.random.org](http://www.random.org)). A second investigator (C.T.) performed the injections by hand maintaining the speed as consistently as possible, but not specifically controlled. Acquisition parameters used depended on the size of the dog (ranges: 100 - 140 kV, 250 – 300 mAs, and pitch factor = 0.9). Scan tube current was modulated by automatic exposure control (Care Dose, Siemens Medical Solutions, International). Image data sets were reconstructed using parameters of 120 mm field of view, 512 × 512 matrix, 1 mm slice thickness and Br34 reconstruction algorithm (window level 45 and window width 410). A three-dimensional reconstruction of the CT images was performed using Syngo.via (VB60A\_HF06, MM Reading, Siemens Healthineers, Erlangen, Germany), and a board-certified radiologist (G.B.) blinded to group allocation, assessed the location and the distribution of the contrast medium, by counting the number of VBs. Visualization of radiographic contrast between the QL and Pm muscles (spinal nerves area), as well as ventromedially to Pm muscle (sympathetic trunk area), was recorded and compared between the groups. The location of the catheter insertion site into the skin was also recorded for each hemiabdomen.

## Second Phase

### Cases Presentation

Five dogs of different breeds and American Society of Anaesthesiologists (ASA) statuses, undergoing open adrenalectomy or cholecystectomy, were recruited in the second phase of the study. Demographic and medical data are reported in Table 1. Procedures were performed at the Veterinary Teaching Hospital of the University of Liege between May 2024 and July 2024. Prior to anaesthesia, each dog underwent a complete physical examination, including body condition score (BCS) on a nine-point scale evaluation [LaFlamme et al. 1997], and blood tests screening (hematology, serum biochemistry, coagulation times). Physical examinations were unremarkable for all dogs, except for Case 3. A moderate-severe left apical systolic murmur was detected. An echocardiography was performed and revealed a stage B1 mitral valve endocardiosis. The anaesthetic protocol was at the discretion of the anaesthesiologist in charge of each case. However, all dogs received an intraoperative fluid-therapy with lactated Ringer's solution at 3-5 mL kg<sup>-1</sup> hour<sup>-1</sup> and a preoperative QL block performed with 0.3 mL kg<sup>-1</sup> of ropivacaine 0.5% per side [Garbin et al. 2020a].

**Table 1.** Demographic and medical data of the five dogs included in the study. ASA, American Society of Anaesthesiologists; BCS, body condition score (nine-point scale evaluation); F, female; M, male; MC, male castrated.

	<b>Case 1</b>	<b>Case 2</b>	<b>Case 3</b>	<b>Case 4</b>	<b>Case 5</b>
<b>Breed</b>	Siberian Husky	Beagle	Chihuahua	Brittany Spaniel	Mixed breed
<b>Sex</b>	F	M	M	MC	MC
<b>Age (years)</b>	6	8	11	9	11
<b>Weight (kg)</b>	23.5	29	4.6	18.3	13
<b>BCS</b>	5/9	6/9	5/9	5/9	4/9
<b>ASA status</b>	3	2	4	3	4
<b>Condition</b>	Right-sided cortisol-secreting adenocarcinoma	Left-sided non-secreting adrenal mass	Emphysematous cholecystitis, pancreatitis	Right-sided phaeochromocytoma	Gallbladder mucocele, pancreatitis

### Catheter Placement and Postoperative Management

Catheters were implanted bilaterally at the end of the surgery, following the technique described in the first phase of the study. The region was clipped and scrubbed, and the procedure was performed aseptically. Catheters were fixed to the skin as previously described and then anchored to the adhesive pad provided in the kit for epidural catheters. The anti-bacterial filters were connected and then sutured to the skin. A semi-occlusive dressing and a tubular bandage (TG, Lohmann & Rauscher, Neuwied, Germany) were used to protect the catheters. The dogs were then moved to the CT scan room. A volume of 0.1 mL kg<sup>-1</sup> of contrast media solution, divided in two aliquots, was injected through each catheter and a CT scan was performed after each injection. Once the catheter tip or the spread around the QL muscle was visualized, the second aliquot was injected, and a second CT scan was performed to confirm the spread in the same target areas evaluated in the first phase of the study. At the end of the procedure, anaesthesia was discontinued and tracheal extubation was performed once the swallowing reflex was restored. Dogs were then transferred to the Intensive Care Unit, and a standardized pain management protocol was applied, as follows. Pain was assessed every hour using the Short Form of the Glasgow Composite Measure Pain Scale (SF-GCMPS) [Reid et

al. 2007] starting one hour after extubation ( $T_E$ ) until the pain score was  $\geq 6$  ( $T_0$ ). A volume of 0.3 mL  $\text{kg}^{-1}$  of ropivacaine 0.5% was injected through the catheters at  $T_0$ , and then every eight hours up to 72 hours. Pain assessment was repeated every four hours as of  $T_0$ , or more frequently if the dogs were deemed uncomfortable or unsettled. The evaluations were carried out by the critical care clinician present in clinics at the time of assessment. In case of pain score  $\geq 6/24$ , methadone 0.2 mg  $\text{kg}^{-1}$  was administered intravenously (IV). Hospitalization time, pain scores, and number of rescue methadone administrations during the postoperative period were recorded.

### Statistical Analysis

The number of cadavers needed for the study was calculated based on the spread of contrast media solution. The alpha error was set at 0.05 and the power at 80%. Considering a mean  $\pm$  standard deviation (SD) of VBs involved in the spread to be  $4 \pm 1$  in group  $L_V$  and six in group  $H_V$  [10], the number of dogs required to assess a significant difference between the two groups was calculated to be four. This number was then increased to eight to ensure sufficient data to perform statistics and to account for any potential variability in procedural execution. The normality of data distribution was evaluated with a D'Agostino & Pearson test, and results are expressed as mean  $\pm$  SD or median (range). Prism Version 9.0 (GraphPad Software Inc., CA, USA) was used to analyse data. A Fisher's exact test was used to compare the number of VBs stained between sides (right and left), and a Mann-Whitney test was used to compare the number of VBs involved in the spread between  $H_V$  and  $L_V$ . A Student's T-test was used to compare the time to position the catheter for each side. Data are reported as numbers of cases (n/n) and percentage (%). A  $p$ -value  $< 0.05$  was considered statistically significant.

## Results

### First Phase

The mean  $\pm$  SD weight of the cadavers was  $19.1 \pm 6.7$  kg, and the median (range) body condition score (BCS) was 5 (4-6) out of 9. Breeds, sex, weight, and BCS are reported in Table 2.

**Table 2.** Breed, sex, weight and BCS (nine-point scale evaluation) of the canine cadavers used in the study.

Breed	Sex	Weight	BCS (out of 9)
English Setter	Neutered male	23	5
Border Collie	Female	17	4
Mixed breed	Neutered male	22	6
Mixed breed	Female	13	5
American Amstaff	Neutered male	22	5
Border Collie	Neutered male	25	6
Jack Russell	Neutered male	6	4
Siberian husky	Female	25	5

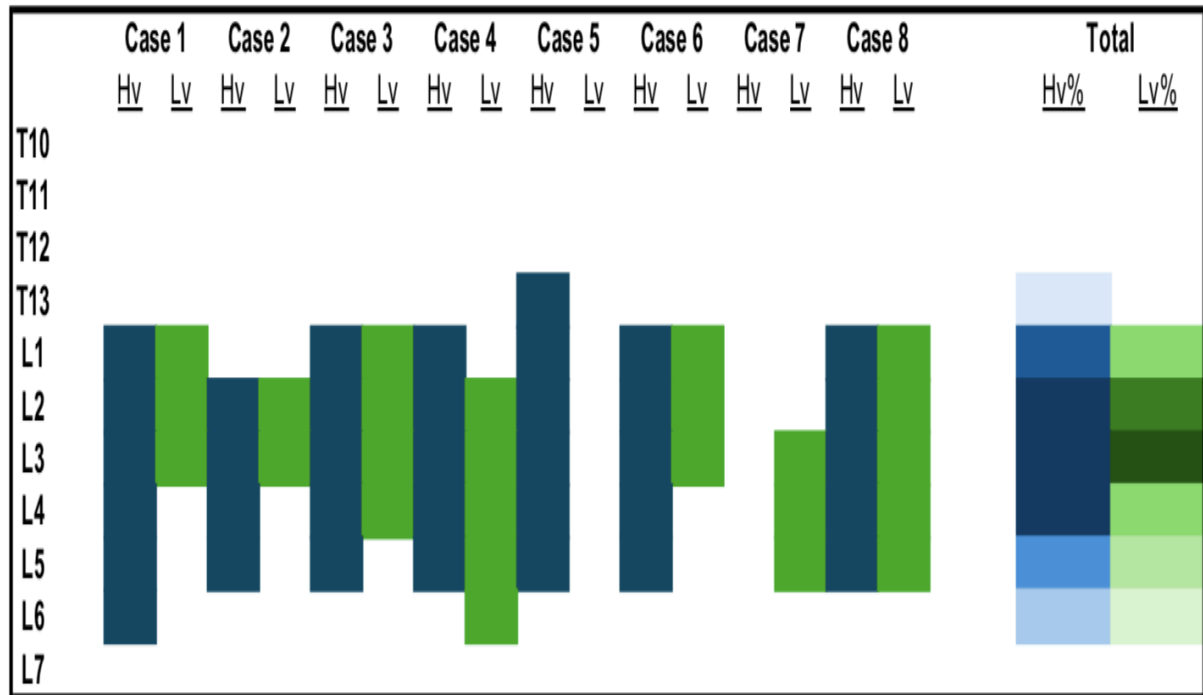
### US-Guided Catheter Placement

Catheter placement technique was completed in all 16 hemiabdomens. Time to perform the technique was  $255 \pm 65$  seconds on the right hemiabdomen and  $273 \pm 81$  seconds on the left hemiabdomen ( $p = 0.6$ ). The insertion point of the catheter into the skin was localized at the level of L2, L3, and L4 in 12.5%, 50%, and 37.5% of cases, respectively.

### Tomographic Study

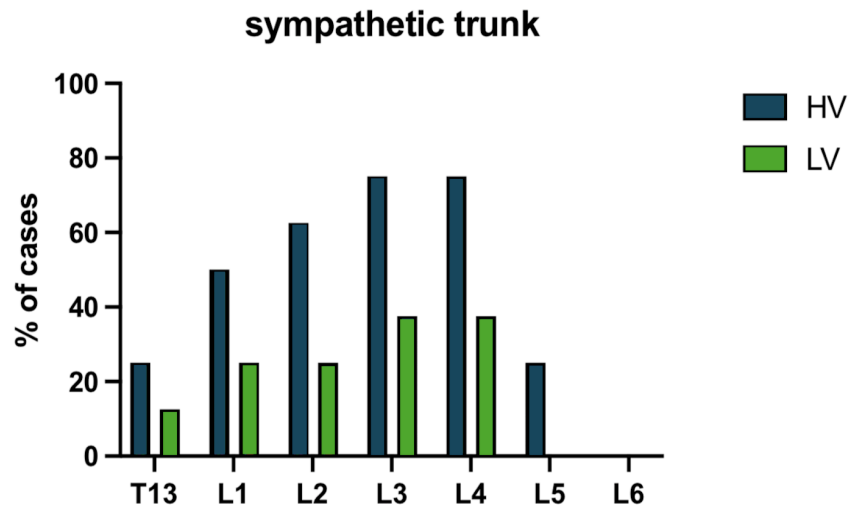
Contrast media solution was injected in all hemiabdomens, except one in group H<sub>v</sub>. In that particular case, unusually high resistance to injection was noted and the catheter tip was then tomographically visualized in the retroperitoneal space at the level of T13. In all other cases, it was not possible to clearly visualize the catheter tip location because of the presence of the contrast medium effacing the border of the catheter tip.

Contrast solution was visualized between the QL and Pm muscles in 7/8 hemiabdomens in group L<sub>v</sub> and 6/7 hemiabdomens in group H<sub>v</sub>. At this level, the number of VBs stained by the contrast was significantly higher ( $p = 0.01$ ) in group H<sub>v</sub>, 5 (4-6), compared to L<sub>v</sub>, 3.5 (0-5) (Figure 2). The sympathetic trunk area was involved by the spread in 3/8 and 6/7 hemiabdomens, in groups L<sub>v</sub> and H<sub>v</sub>, respectively. At this level, the number of VBs covered by the spread did not result significantly different between the two groups ( $p = 0.08$ ): 0 (0-5) for group L<sub>v</sub> and 4 (0-5) for group H<sub>v</sub>.



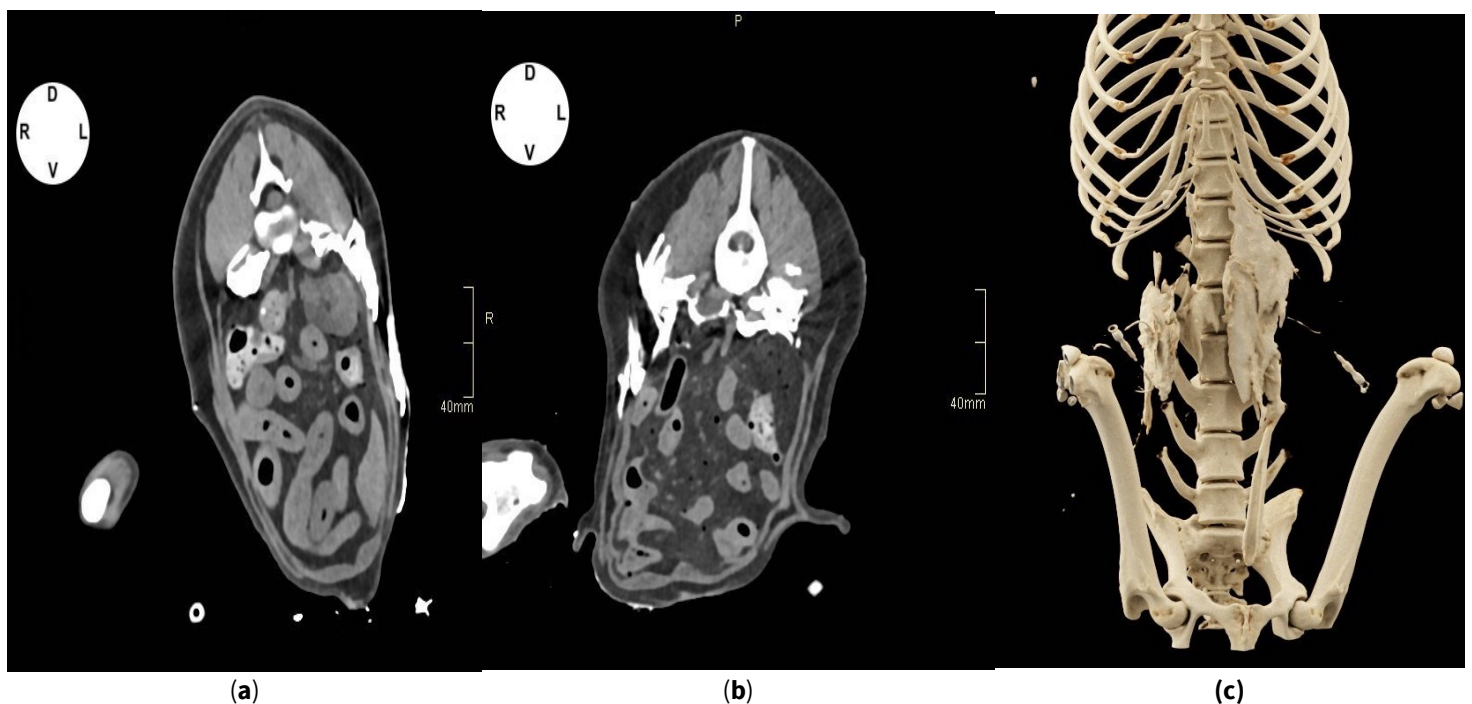
**Figure 2.** Stain of vertebral bodies (VBs) between the quadratus lumborum (QL) and psoas minor (Pm) muscles in the cadavers included in this study, after high volume (H<sub>v</sub>) or low volume (L<sub>v</sub>) of contrast media solution. For the total amount, the colour intensity is indicative of the success rate with darkening shading indicating a higher success rate.

Spread of contrast between the QL and Pm muscles in group L<sub>v</sub> was mostly found at the levels of L3 (87.5%), and L2 (75%), slightly less at L1 and L4 (50%), L5 (37.5%) and L6 (25%). In group H<sub>v</sub>, spread of contrast media solution was consistently detected between QL and Pm muscles at the level L2, L3 and L4 (87.5%), less frequently at L1 (75%) and L5 (62.5%), and finally at L6 (25%) and T13 (12.5%) (Figure 2). The spread of injectate was visualized in the sympathetic trunk area between T13 and L4 (37.5% of cases at L3 and L4, 25% at L1 and L2, and 12.5% of cases at T13) in group L<sub>v</sub>, and between T13 and L5 (75% at L3 and L4, 62.5% at L2, 50% at L1, 62.5% at L2, and 25% at L5 and T13) in group H<sub>v</sub> (Figure 3).



**Figure 3.** Distribution of contrast solution ventromedially to the psoas minor muscle (sympathetic trunk area), at the level of the different vertebral bodies. Data are expressed in percentage (%).

Erratic distribution of contrast medium was observed in both groups in the retroperitoneal space in 37.5% of cases in group H<sub>v</sub> and 50% in group L<sub>v</sub>, and in the ESP plane in 28.5% of cases in group H<sub>v</sub> and 25% in group L<sub>v</sub>. Contrast was found also in the TAP (37.5% of cases in group H<sub>v</sub> and 50% in group L<sub>v</sub>) and abdominal subcutaneous tissue (28.5% of cases in group H<sub>v</sub> and 37.5% in group L<sub>v</sub>), mostly between L2 and L4. No contrast medium was visualized in the epidural space, peritoneal, or intrathoracic cavity (Figure 4 a, b).



**Figure 4.** Computed tomographic images in transverse plane with **soft tissue** window of canine cadavers, after injection of different volumes of contrast media solution through catheters implanted in the quadratus



lumborum (QL) plane. (a) Transverse image at L3: contrast can be visualized in the transversus abdominis plane (TAP), between the QL and psoas minor (Pm) muscles, and subcutaneously. (b) Transverse image at L3: Contrast can be observed between the QL and Pm muscles, ventromedially to the Pm muscle, in the TAP and ESP plane. (c) Volume-rendered three-dimensional reconstruction image of the thoracolumbar area between T12 and L4 vertebrae showing distribution of the contrast and catheter positioning.

## Second Phase

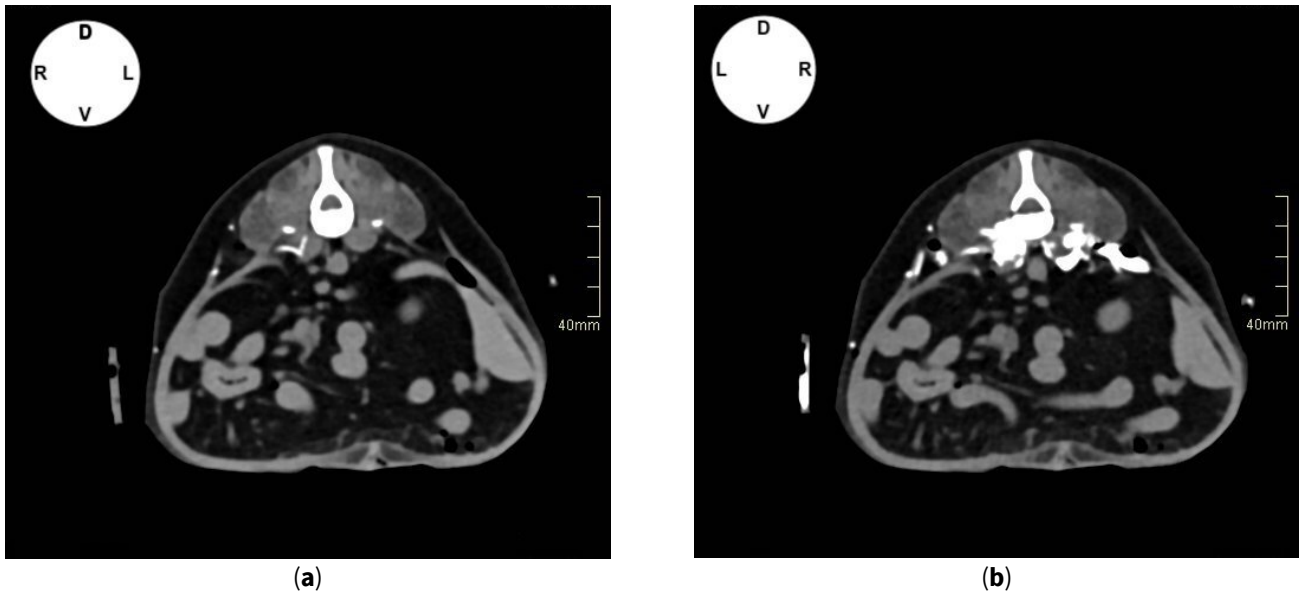
Five dogs were included in the second phase of the study. The median (range) age and weight of the study were 9 (6–11) years old and 18.3 (4.6–29) kg, respectively. Surgery and anaesthesia concluded uneventfully in all cases. Data regarding type of surgery, anaesthetic protocol, intra- and postoperative medications, duration of anaesthesia and surgery, and time between  $T_E$  and  $T_0$  are reported in Table 3.

**Table 3.** Data regarding type of surgery, anaesthetic protocol, intra- and postoperative medications, duration of anaesthesia and surgery and time between  $T_E$  and  $T_0$ .  $T_E$ , one hour after extubation;  $T_0$ , first administration of ropivacaine through catheters (pain score  $\geq 6$  out of 24).

	Case 1	Case 2	Case 3	Case 4	Case 5
<b>Surgery</b>	Right-sided adrenalectomy	Left-sided adrenalectomy	Cholecystectomy	Right-sided adrenalectomy	Cholecystectomy
<b>Premedication</b>	Dexmedetomidine $1 \mu\text{g kg}^{-1}$ , methadone $0.2 \text{ mg kg}^{-1}$ IV	Dexmedetomidine CRI $1 \mu\text{g kg}^{-1} \text{ hour}^{-1}$ , methadone $0.2 \text{ mg kg}^{-1}$ IV	Maropitant $1 \text{ mg kg}^{-1}$ , methadone $0.2 \text{ mg kg}^{-1}$ IV	Acepromazine $10 \mu\text{g kg}^{-1}$ IM, methadone $0.2 \text{ mg kg}^{-1}$ IV	Maropitant $1 \text{ mg kg}^{-1}$ , methadone $0.2 \text{ mg kg}^{-1}$ IV
<b>Induction</b>	Propofol $2 \text{ mg kg}^{-1}$ IV	Propofol $2 \text{ mg kg}^{-1}$ IV	Ketamine $1 \text{ mg kg}^{-1}$ , propofol $1 \text{ mg kg}^{-1}$ IV	Propofol $2 \text{ mg kg}^{-1}$ IV	Midazolam $0.2 \text{ mg kg}^{-1}$ Propofol $1.5 \text{ mg kg}^{-1}$ IV
<b>Maintenance</b>	Isoflurane in oxygen/air mixture	Isoflurane in oxygen/air mixture	Isoflurane in oxygen/air mixture	Isoflurane in oxygen/air mixture	Isoflurane in oxygen/air mixture
<b>Intraoperative medication</b>	Dexmedetomidine CRI $1 \mu\text{g kg}^{-1} \text{ hour}^{-1}$ IV	-	Fentanyl infusion $5\text{--}10 \mu\text{g kg}^{-1} \text{ hour}^{-1}$ IV	Fentanyl infusion $2\text{--}5 \mu\text{g kg}^{-1} \text{ hour}^{-1}$ IV	Ketamine $1 \text{ mg kg}^{-1}$ IV

<b>Postoperative medication</b>	Prednisolone 0.5 mg kg <sup>-1</sup> IV BID, cefazoline 20 mg kg <sup>-1</sup> IV TID trazodone 4 mg kg <sup>-1</sup> PO TID	Meloxicam 0.2 mg kg <sup>-1</sup> IV SID, cefazoline 20 mg kg <sup>-1</sup> IV TID	Meloxicam 0.2 mg kg <sup>-1</sup> IV SID, amoxicilline clavulanic acid 20 mg kg <sup>-1</sup> TID maropitant 1 mg kg <sup>-1</sup> SID, ondasetron 0.5 mg kg <sup>-1</sup> PO BID, pimobendan 0.5 mg kg <sup>-1</sup> PO BID	Meloxicam 0.2 mg kg <sup>-1</sup> IV SID, cefazoline 20 mg kg <sup>-1</sup> IV TID, trazodone 4 mg kg <sup>-1</sup> TID	Meloxicam 0.2 mg kg <sup>-1</sup> IV SID, amoxicilline clavulanic acid 20 mg kg <sup>-1</sup> TID, maropitant 1 mg kg <sup>-1</sup> SID
<b>Duration of anaesthesia (minutes)</b>	360	255	90	240	120
<b>Duration of surgery (minutes)</b>	300	210	60	180	65
<b>T<sub>E</sub> – T<sub>0</sub> (minutes)</b>	60	180	300	180	300
<b>Hospitalisation time (hours)</b>	48	48	72	72	72

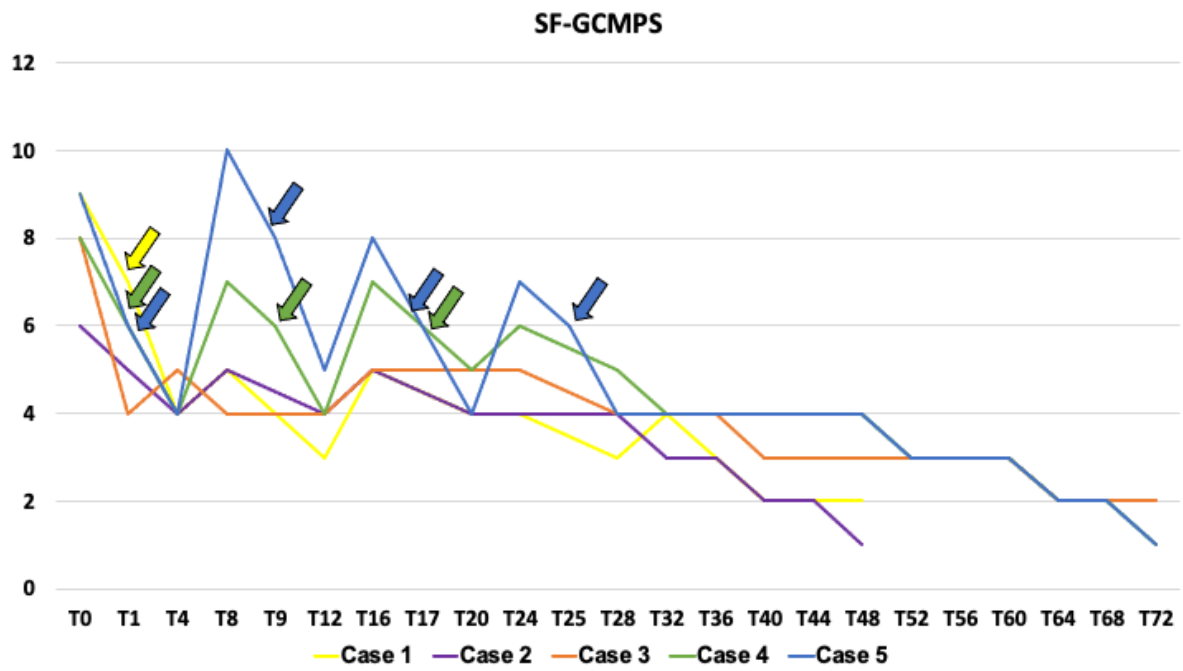
The QL-catheters placement technique was completed in all five dogs. After the first injection of contrast, the catheter's tip was visualized dorsally to the QL muscle or between the QL and Pm muscles in all cases (at the level of L1 in Case 1 and 5, L2 in case Case 2,3, L3 in Case 4) except for one catheter in Case 1 and one in Case 5, where the catheter tip was found, respectively, in the left- and right-side retroperitoneal space. In both cases, the mispositioned catheter was withdrawn, and injections of ropivacaine were performed only on the contralateral side. The CT scan images taken after injecting the second aliquot of contrast, showed spread of solution in the target areas in all remaining cases (Figure 5a, b).



**Figure 5.** (a) Computed tomographic (CT) images in transverse plane (L2) with soft tissue window of Case 3, after injection of contrast media solution through catheters implanted in the quadratus lumborum (QL) plane. (a) Catheter tip and contrast media can be visualized between the QL and psoas minor (Pm) muscles on the right side, after injection of 0.5 ml of solution. (b) Spread of 0.05 ml kg<sup>-1</sup> of contrast media between the QL and psoas minor (Pm) muscles, inside and ventromedially the Pm muscle, between the transversalis and thoracolumbar fasciae.

Methadone 0.2 mg kg<sup>-1</sup> was administered IV once in Case 1, three times in Case 4 and four times in Case 5, during the first 24 hours after surgery (Figure 6).

No rescue analgesia was required in the remaining postoperative period. An opioid-free pain management was achieved in Case 2 and Case 3 for 48 and 72 hours, respectively. No complications associated with the use of QL-catheters, such as infections, motor impairment, or systemic side effects to ropivacaine, were recorded during the study period. Catheters were removed 48 and 72 hours after surgery in Cases 1 and 2, and 3 to 5, respectively.



**Figure 6.** Postoperative pain scores at different time points, using the short-form Glasgow Composite Measure Pain Scale (SF-GCMPS) in the five dogs enrolled in the study. Arrow colors correspond to the cases receiving rescue analgesia, matching the line colors in the graph.

## Discussion

The first part of this study aimed to describe an US-guided technique to implant catheters for bilateral LA administration in the QL IFP in canine cadavers and to compare the spread of 0.3 *versus* 0.6 mL kg<sup>-1</sup> of contrast media solution along the VBs. The second part described the outcomes of five dogs, in which the injection of ropivacaine 0.5% through QL-catheters was implemented in a multimodal analgesic regimen for postoperative abdominal pain. The use of larger volume resulted in a significantly higher number of VBs affected by the spread only between the QL and Pm muscle, but not in the sympathetic trunk area. The case series demonstrated the clinical feasibility of the technique and the potential of an intermittent LA injection through QL-catheters for implementation in the management of post-laparotomy pain in dogs.

The first phase demonstrated the feasibility of the US-guided catheter placement technique described in this study. A previous case-series reported the use of the transmuscular approach [Garbin et al. 2020b] to implant catheters between the QL and Pm muscles [Camargo Fontanela et al. 2024]. We decided to opt for the lateral approach [10], directing the tip of the needle towards the latero-ventral aspect of the transverse process of L1, because the visualization of the plane between QL and Pm muscles is not always achievable in both small and large breed dogs [Garbin et al. 2020a, Garbin et al. 2020b]. The time required to perform the technique was acceptable, suggesting its potential for routine practice with adequate training. However, procedures were performed by two anaesthetists experienced in US-guided locoregional anaesthesia, which may limit generalization of the results.

Garbin et al. injected 0.3 mL kg<sup>-1</sup> of dye-lidocaine solution in canine cadavers, observing a median spread involving four (3-5) ventral rami of spinal nerves between T13 and L3, after dissection [Garbin et al. 2020a]. Results obtained in this study, using the same volume of contrast media solution, are similar. Increasing the volume to 0.6 mL kg<sup>-1</sup> resulted in a significantly higher number of VBs involved by the spread, but not in diffusion towards those between T9 and T13, as already reported in veterinary literature [Garbin et al. 2020a, Garbin et al. 2020b, Viscasillas et al. 2021b, Marchina-Goncalves et al 2022, Alaman et al. 2022, Marchina-Goncalves et al. 2023]. In addition, contrast media solution was observed in the sympathetic trunk area in a higher number of hemiabdomens in group H<sub>v</sub>, in comparison with group L<sub>v</sub>. These findings are in contrast with results obtained by Garbin et al., who reported a spread to the sympathetic trunk between T11 and L2, after injecting 0.3 mL kg<sup>-1</sup> of dye-lidocaine solution [Garbin et al. 2020a]. However, it is important to note that our study did not

involve anatomical dissection of cadavers. This limitation is significant because the distribution of contrast media often does not align with the staining of nerves [Viscasillas et al. 2021b]. Our results suggest that higher volumes of LA could result in more extensive desensitization of the abdomen. However, clinicians should be aware that increasing the volume of injectate would result in dilution of LA and therefore in decreased analgesic effect duration in the postoperative period [Degani et al. 2023].

The tomographic study revealed a caudally directed spread, aligning with previous findings [Viscasillas et al. 2021b, Marchina-Goncalves et al. 2022]. Viscasillas et al. hypothesized that this finding could be a consequence of the needle trajectory, which was inserted in a caudal direction, from dorsolateral to ventromedial [Marchina-Goncalves et al. 2022]. Despite advancing the needle in the opposite direction, the catheter tip might have turned caudally during advancement. Additionally, in the present study, the insertion point of the catheter into the skin was positioned caudally to L1 in all cases, likely due to anatomical differences in ribs conformation. Contrast media distribution was most consistently observed at the level of VBs between L2 and L4, suggesting a catheter tip position caudal to L1, though the exact location was not confirmed.

CT scans showed contrast media spread reaching L5 and L6 in both groups. Otero et al. (2024) described a caudal approach to the QL block, reporting spread towards the lumbar plexus with a  $0.3 \text{ mL kg}^{-1}$  dye solution injected at L6 [Otero et al. 2024a, Otero et al. 2024b]. In clinical trials, tonic muscle function was maintained with lidocaine 2% and ropivacaine 0.5%, without any postoperative motor deficits [Otero et al. 2024a, Otero et al. 2024b, Paolini et al. 2024]. Similarly, in our clinical case series, no dogs experienced hindlimb weakness secondary to possible motor impairment. However, in the second phase of the study, CT scan was used only to confirm catheter positioning and not to assess the spread of the solution along the VBs.

Contrast media was frequently observed in the retroperitoneal space, possibly due to the catheter tip perforating the transversalis fascia. Catheters were advanced 3-4 cm into the QL IFP, similarly to Camargo Fontanela et al., who confirmed final positioning under US guidance, by injecting 1 mL of bupivacaine and observing diffusion into the IFP. However, despite recording an analgesic effect, the authors of that study could not rule out catheter displacement [Camargo Fontanela et al. 2024]. In this study, contrast injection was performed after repositioning dogs from lateral to sternal recumbency, simulating a likely natural movement of a dog during the postoperative period. It cannot be ruled out that changes in recumbency and abdominal muscle tension might lead to

catheter tip dislodgment during the postoperative period. Further research is necessary to investigate and refine this technique, as well as to assess accurate catheter positioning in the QL IFP.

Diffusion of contrast in the TAP and subcutaneous tissues may be produced by leakage of solution from the insertion site, potentially caused by the difference in size between the Tuohy needle (18G) and the catheter (20G). In human medicine, LA leakage from catheters is a common complication that can result in block failure and inadequate analgesia [Dadure et al. 2009, Hattammaru et al. 2022]. In our study, the erratic spread of contrast to the TAP and subcutaneous tissue could explain the reduced diffusion to the sympathetic trunk area, recorded in group L<sub>v</sub>. This information could be crucial when selecting the appropriate needle and catheter sizes, especially in small breed dogs. However, dislodgement of the catheter tip from the QL plane due to the change in recumbency of the cadavers during the procedure, cannot be ruled out. Catheter dislodgment and secondary block failure are well documented complications in humans [Suksompong et al. 2020]. Further research assessing catheter displacement or dislodgement rates are warranted in veterinary medicine [Romano 2024].

Erratic spread of contrast in the epaxial compartment could be attributed to perforation of the thoracolumbar fascia, as previously hypothesized by Alaman et al. [Alaman et al 2022]. According to the technique described in this study, the needle was initially advanced with the bevel dorsally directed, to improve its sonographic visualization, and then rotated to allow the catheter to advance ventrally to the transverse process of L1. It is possible that the 180° rotation of the Tuohy needle bevel could have resulted in inadvertent perforation or laceration of the thoracolumbar fascia.

In the second phase of this study, catheters implanted in the QL IFP were used in five dogs undergoing open cholecystectomy or adrenalectomy. Dogs were included in the study based on the expected pain levels caused by the surgery. Cholecystectomy is known to cause significant postoperative pain, warranting effective analgesic management, such as the use of an epidural catheter, or a QL block [Garbin 2024, Samburgaro et al. 2022, Campoy et al. 2022]. Based on the authors' clinical experience, open adrenalectomy can result in moderate-severe postoperative abdominal pain, requiring administration of different systemic analgesics in IV infusion, such as opioids, ketamine, and lidocaine [Merlin et al. 2019].

Based on the pain scores, ropivacaine 0.5% administered via QL block and through catheters three times daily could be a valid integration into a multimodal analgesic regimen for postoperative abdominal pain in dogs. According to the design of this study, pain assessments were performed at

four hours intervals, to ensure a pain evaluation exactly halfway between two administrations of LA. Injections of ropivacaine 0.5% reduced pain scores at the four-hour post-administration assessment. However, in cases where pain scores remained  $\geq 6$  on the SF-GCMPS, rescue analgesia consisting of methadone  $0.2 \text{ mg kg}^{-1}$  IV was administered. This occurred in Case 1 (once), Case 4 (three times), and Case 5 (four times). Cases 2 and 3 did not require additional methadone within the initial 48-72 hours postoperatively. It cannot be ruled out that the need for rescue analgesia was due to potential dislodgment of the catheter, resulting in inadequate spread of LA to the target areas of the QL block. Moreover, cadaveric studies have shown that QLB, regardless of the approach used, often fails to produce adequate spread to the last thoracic ventral rami of the spinal nerves [Garbin et al. 2020a, Garbin et al. 2020b, Viscasillas et al. 2021b, Marchina-Goncalves et al. 2022, Alaman et al. 2022, Marchina-Goncalves et al. 2023]. As a result, desensitization of the cranial portion of the abdomen may be incomplete, potentially contributing to the need for rescue analgesia.

Ropivacaine was administered unilaterally due to catheter misplacement in the retroperitoneal space, in Case 1 and 5, where rescue analgesia was required once and four times, respectively. The variation in outcomes between these two cases may be attributed to the fact that the catheter that remained in place in Case 1 was on the same side as the adrenalectomy, where most visceral manipulation occurred during surgery.

Our findings align with reports in human medicine regarding the effectiveness of QL-catheters in reducing postoperative opioid use and improving pain management [Kadam et al. 2018, Zhu et al. 2019, Pooley et al. 2022]. In the case series by Camargo Fontanela et al., three dogs with severe abdominal pain were effectively managed with intermittent administration of  $0.3 \text{ mL kg}^{-1}$  per side of bupivacaine 0.5% twice daily [Camargo Fontanela et al. 2024]. The authors chose to use the same volume of ropivacaine 0.5%. This decision was taken, based on their clinical preference in using low volume-high concentration solutions of LA when performing IFP blocks [Degani et al. 2023, Martínez et al. 2024], to avoid excessive dilution and secondary reduction of analgesic effect duration. According to previous research, the analgesic duration of ropivacaine 0.5% administered via QL block after canine laparoscopic ovariectomy was approximately 10 hours [Degani et al. 2023]. In this case series, we chose to administer ropivacaine 0.5% every eight hours to ensure analgesic effect before the LA began to wear off.

There are some limitations to be considered, when interpreting these results. In the first phase of the study, injections of contrast media solution were performed in thawed canine cadavers. Density and viscosity of the contrast solution used in this study may be different from those of LA. In addition,



the spread of solution observed in cadavers does not necessarily reflect the one from live animals, due to different biophysical properties of tissues, such as fasciae integrity, and membranes permeability. Anatomical dissections were not performed, because the canine cadavers were meant to be utilized for practical teaching purposes, after the end of our experiment. CT scans images provide information on the diffusion pattern of the injectate and not on which structures are effectively stained [Viscasillas et al. 2021b], therefore comparisons with previous studies where cadavers were dissected, might be complicated. Additionally, dissections could have been helpful to assess the position of the catheter tip. The small sample size, lack of a control group, and influence of different analgesic drugs used in the perioperative period may pose difficulties in drawing solid conclusions on the analgesic efficacy of the technique presented in this study. Additionally, the dogs underwent different types of surgery, which introduces further variability. Finally, clinicians in charge of postoperative pain assessment were not blinded to the treatment, which could have biased the results.

In conclusion, US-guided catheter placement in the QL IFP appears feasible and may enhance postoperative analgesic management in dogs undergoing abdominal surgeries. This technique could reduce the systemic opioids consumption and improve pain management protocols. Further research is warranted to optimize the technique for clinical use, and larger sample sizes and standardized protocols are necessary to validate these findings. Clinicians should be aware of potential catheter misplacement, dislodgement, or leakage of LA from the insertion site, which could reduce the analgesic effect or lead to block failure.

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# Experimental Section

## Study 4:

**Perioperative analgesic efficacy of lumbar erector spinae plane block in dogs undergoing hemilaminectomy: a randomized blinded clinical trial**

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## Abstract

**Objective** To evaluate the perioperative analgesic effect of the unilateral lumbar erector spinae plane block (ESPB<sub>L</sub>) in dogs undergoing hemilaminectomy.

**Study design** Randomized, blinded clinical study.

**Animals** A total of 30 client-owned dogs undergoing thoracolumbar or lumbar hemilaminectomy for intervertebral disc extrusion (IVDE).

**Methods** Dogs were randomly assigned to receive a unilateral ESPB<sub>L</sub>, performed either with 0.4 mL kg<sup>-1</sup> ropivacaine 0.5% [group ROPI (*n* = 15)] or with saline solution [CNT group (*n* = 15)]. Dogs were premedicated intravenously (IV) with acepromazine 5 µg kg<sup>-1</sup> and methadone 0.2 mg kg<sup>-1</sup>, general anaesthesia was induced by administering IV midazolam 0.2 mg kg<sup>-1</sup> and propofol to effect and maintained with isoflurane. Fentanyl was administered as rescue analgesia. Bradycardia (heart rate (HR) < 60 beats minute<sup>-1</sup>) with hypotension was treated with atropine IV. The Short-Form of the Glasgow Composite Pain Scale was used pre- and postoperatively at 1, 2, 4, 8, 12, 16, 20 and 24 hours after extubation, and methadone 0.2 mg kg<sup>-1</sup> was administered IV when pain score was ≥ 5/20. HR and end-tidal concentration of isoflurane (FE'Iso) were compared between groups with ANOVA combined with a Dunnet's *post hoc* test. Time to the first rescue methadone and total dose of fentanyl (FEN<sub>tot</sub>, µg kg<sup>-1</sup> hour<sup>-1</sup>) and methadone (MET<sub>tot</sub>, mg kg<sup>-1</sup>) in the first 24 postoperative hours were compared using unpaired Student's T-test. Postoperative pain scores were compared with Mann-Whitney test and atropine administration with a Fisher's exact test; *p* < 0.05.

**Results** HR, FE'Iso, FEN<sub>tot</sub>, MET<sub>tot</sub> and atropine administration were significantly lower in group ROPI compared to CNT. Postoperative analgesic effect was significantly longer, and pain scores were significantly lower in group ROPI for all time points.

**Conclusions and clinical relevance** Unilateral ESPB<sub>L</sub> with ropivacaine reduced perioperative opioid consumption and the occurrence of bradycardia in dogs undergoing hemilaminectomy.



## Introduction

Hansen type I intervertebral disc extrusion (IVDE) is the most prevalent cause of spinal cord injury in dogs (Rossi et al. 2020). This condition results from degeneration of the intervertebral disc and displacement of the *nucleus pulposus* into the vertebral canal, producing contusion and compression of the spinal cord and nerve roots (Fenn & Olby 2020). Surgery is considered the elective treatment to achieve spinal decompression and avoid irreversible damages (Moore et al. 2020). Hemilaminectomy is currently the most frequently described surgical approach in veterinary medicine (Fenn & Olby 2020).

Pain management can be challenging in dogs with IVDE. Severe pain is produced by compression of the spinal cord, nerve roots and meninges (Platt 2004). Furthermore, to perform a hemilaminectomy the dorsal approach to the thoracolumbar spine causes inherent soft tissue and bone trauma at the level of IVDE, eliciting pain recently described as severe to excruciating (Monteiro et al. 2021).

Different analgesic techniques have been reported in dogs, such as systemic administration of combinations of opioids,  $\alpha_2$ -adrenoceptor agonists, ketamine, and lidocaine (Pascal et al. 2020, Skelding et al. 2021), postoperative epidural administration of morphine (Aprea et al. 2012) and blind injection of local anaesthetic (LA) into the epaxial muscles (McFadzean et al. 2021). However, the locoregional anaesthetic technique, which has stimulated the greatest interest in the last few years, in both human and veterinary medicine, is the erector spinae plane block (ESPB). It consists of the injection of LA, under ultrasound (US-) guidance, into the interfascial plane between the transverse processes of the thoracic or lumbar vertebrae and the erector spinae muscles. The aim is to desensitise the medial and lateral branches of the dorsal rami of the spinal nerves (DRSN). Cadaver studies conducted in dogs evaluated two approaches performed at different levels of the spine: a longitudinal approach for the thoracic portion (ESPB<sub>T</sub>) (Ferreira et al. 2019, Portela et al. 2020) and a transversal approach for the lumbar spine (ESPB<sub>L</sub>) (Medina-Serra et al. 2021). Cavalcanti et al. (2022) compared the two techniques in the thoracolumbar portion of the spine, from the eleventh thoracic (T11) to the second lumbar vertebra (L2), where an anatomical transition of the epaxial muscles occurs (Cavalcanti et al. 2022). The authors concluded that the transversal approach was more appropriate for injections caudal to T11. The main application of the ESPB reported in veterinary species is the provision of perioperative analgesia during spinal surgeries, such as hemilaminectomy (Portela et al. 2021). Benefits of including the ESPB<sub>T</sub> in a multimodal analgesic approach were described in retrospective studies (Portela et al. 2021, Viilmann et al. 2022). ESPB<sub>T</sub>

has proven to effectively reduce perioperative opioid consumption and intra- and postoperative complications, when compared to a standard opioid-based analgesic protocol (Portela et al. 2021, Viilmann et al. 2022). Nevertheless, only one case report describes the implementation of the ESPB<sub>L</sub> in the anaesthetic management of a dog undergoing lumbar hemilaminectomy (Rodriguez Mulet et al. 2021). Randomized clinical trials (RCTs) investigating the analgesic efficacy of the ESPB are lacking.

Therefore, this study investigated the perioperative analgesic effect of the unilateral ESPB<sub>L</sub> performed with ropivacaine in dogs undergoing hemilaminectomy for Hansen type I IVDE. We hypothesized that unilateral ESPB<sub>L</sub> with ropivacaine would (1) decrease the consumption of intra- and postoperative systemic analgesics and (2) reduce the occurrence of intraoperative cardiovascular complications.

## Materials and Methods

This blinded RCT was conducted at the Veterinary Teaching Hospital of the University of Liege. The Consolidated Standards of Reporting Trials (CONSORT) guidelines were applied (Schulz et al. 2010). Ethical approval was obtained from the competent Belgian authorities (Nr. 2531). By signing the informed consent, the owner agreed to enrol the dog in the study.

A total of 30 dogs of different breeds, ages, and weights, undergoing thoracolumbar or lumbar hemilaminectomy for Hansen type I IVDE, with a modified Frankel score (MFS) between 3 and 5, were recruited for this study (Sharp & Wheeler, 2005).

Prior to anaesthesia, each dog underwent a clinical examination, including body condition score (BCS) on a nine-point scale evaluation (Laflamme 1997). Based on the preoperative evaluation, only dogs with an American Society of Anaesthesiologists (ASA) status II, with a BCS ranging between 3 and 6 out of 9, were included in the study. Exclusion criteria comprised intractable behaviour, skin infection at the site of the ESPB<sub>L</sub>, history of previous hemilaminectomy, or administration of corticosteroids or non-steroidal anti-inflammatory drugs (NSAIDs) within 24 hours prior to surgery. Pain was assessed using the Short Form of the Glasgow Composite Pain Scale (SF-GCPS) (Reid et al. 2007) on admission, to obtain basal values.

**Preoperative management.** The following anaesthetic protocol was used in all animals: after intravenous (IV) catheter insertion into one of the cephalic veins, maropitant 1 mg kg<sup>-1</sup> (Cerenia; Zoetis, Netherlands), acepromazine 5 µg kg<sup>-1</sup> (Tranquinervin; Dechra Veterinary Products, Netherlands) and methadone 0.2 mg kg<sup>-1</sup> (Comfortan; Dechra Veterinary Products, Netherlands) were administered IV and lactated Ringer's (RL) solution (Vetivex; Dechra Veterinary Products, Belgium) was infused at 5 mL kg<sup>-1</sup> hour<sup>-1</sup>. Approximately 20 minutes later, anaesthesia was induced with midazolam 0.2 mg kg<sup>-1</sup> (Dormazolam; Produlab Pharma BV, Netherlands) and propofol (Diprivan; Aspen Pharma Trading Limited, Ireland) IV titrated to effect. The trachea was intubated with a suitably sized endotracheal tube, and anaesthesia was maintained with isoflurane (Isoflutek; Alivira Animal Health, Spain) in oxygen/air mixture, with a fraction of inspired oxygen (FIO<sub>2</sub>) of 60%. The vaporizer was adjusted to maintain end-tidal isoflurane concentration (FE<sub>1</sub>iso) at 1.2%. Prior to surgery, a computed tomography was performed under general anaesthesia to localize the IVDE. Subsequently, dogs were moved to the pre-surgery room, where the ESPB<sub>L</sub> was performed, after clipping and aseptic preparation of the skin. Dogs were divided into two groups using block randomization (<https://www.random.org>): dogs allocated in group ROPI received a unilateral US-

guided ESPB<sub>L</sub> with 0.4 mL kg<sup>-1</sup> of ropivacaine 0.5% (Ropivacaine hydrochloride; Fresenius Kabi, Belgium) while dogs in the control group (CNT) received 0.4 mL kg<sup>-1</sup> of saline solution 0.9% (Mini-Plasco NaCl; Braun, Germany). ESPB<sub>L</sub> was performed on the ipsilateral side of the planned hemilaminectomy by the same anaesthetist (M.D.), using an along visual axis technique (Di Franco et al. 2021). A 14 MHz high-frequency linear transducer (L7HD3VET; Clarius Mobile Health, BC, Canada), connected to a touchscreen tablet (iPad Air, fifth generation; Apple, CA, USA) was positioned at the level of the spinous process of the vertebra immediately caudal to the IVDE, in a transversal plane. The ESPB<sub>L</sub> was performed as described by Medina-Serra et al. (2021), with a 22-gauge spinal needle (Becton Dickinson; Spain) of adequate length, targeting the lateral aspect of the mammillary process of the vertebra one segment caudal to the IVDE (Cavalcanti et al. 2022). Correct positioning was confirmed by the visualization of hydro-dissection between the mammillary process of the vertebra and the *longissimus lumborum* muscle. The anaesthetist in charge of the block and intraoperative monitoring, as well as the surgeon were blinded to group allocation.

**Intraoperative management.** Dogs were then moved to the operating room and connected to a rebreathing system (Universal F; Kingsystem, IN, USA). Volume-controlled ventilation (Prima 320; Penlon, UK) was applied during the whole procedure to maintain end-expiratory CO<sub>2</sub> concentration (PE'CO<sub>2</sub>) between 35 and 45 mmHg (4.6–5.9 kPa). Heart rate (HR), peripheral arterial haemoglobin saturation (SpO<sub>2</sub>), systolic, mean, and diastolic arterial blood pressures measured by oscillometry (SAP, MAP, DAP), respiratory rate ( $f_R$ ), P<sub>E</sub>'CO<sub>2</sub>, FE<sub>1</sub>so and FIO<sub>2</sub> were continuously monitored using a multiparameter monitor (VT9000 Multimonitor; Veterinary Technics, Netherlands) and recorded every 5 minutes, starting from T0 (placement of the surgical drapes).

A 20% increase in HR or MAP from the corresponding values at T0 for more than 1 minute was considered to be a sign of nociception (Wenger et al. 2005) and a bolus of 2 µg kg<sup>-1</sup> of fentanyl (Fentadon, Dechra Veterinary Products, Netherlands) was administered IV. In case the cardiovascular values did not return to baseline values (T0) within 5 minutes, a continuous infusion of fentanyl was started at 0.5 µg kg<sup>-1</sup> hour<sup>-1</sup> and increased by 0.5 µg kg<sup>-1</sup> hour<sup>-1</sup> every 5 minutes, until the variables returned to the pre-stimulation values (Tayari et al. 2019). Timing and total dose of rescue fentanyl (bolus or infusion) (FEN<sub>tot</sub>, µg kg<sup>-1</sup> hour<sup>-1</sup>) were recorded. FEN<sub>tot</sub> was obtained by dividing the total dose of fentanyl administered by the duration of surgery and the weight of the dog. The following surgical steps of hemilaminectomy were considered to identify a specific time for rescue analgesia: S<sub>1</sub>, skin, subcutaneous, and fascial tissue incision; S<sub>2</sub>, elevation of musculature from the vertebral lamina(e); S<sub>3</sub>, removal of the articular process(es); S<sub>4</sub>, drilling of the vertebral

lamina and pedicle(s); S<sub>5</sub>, decompression of the spinal cord; S<sub>6</sub>, fascial plane suturing; S<sub>7</sub>, subcutaneous tissue and skin suturing.

In case of hypotension (MAP < 60 mmHg), FE Iso was reduced by 0.1% every 5 minutes. If hypotension persisted despite FE Iso of 0.8%, 10 mL kg<sup>-1</sup> of RL was administered over 10 minutes. If hypotension persisted, noradrenaline (Noradrenaline; Aguettant, Belgium) infusion was started at 0.05 µg kg<sup>-1</sup> minute<sup>-1</sup> and increased by 0.05 µg kg<sup>-1</sup> minute<sup>-1</sup> every 5 minutes until MAP ≥ 60 mmHg. In the presence of bradycardia (HR < 60 beats minute<sup>-1</sup>) causing concurrent hypotension, atropine (Atropine sulfate; Oterop, Belgium) (20 µg kg<sup>-1</sup> IV) was administered.

Duration of anaesthesia (from induction to extubation), duration of surgery, incidence of hypotension and bradycardia and any further perioperative complications were recorded. At the end of surgery, isoflurane was turned off and, once the animal returned to breathing spontaneously, mechanical ventilation was stopped. Each dog was then moved to the recovery room and tracheal extubation was performed once swallowing reflex was restored. Duration of anaesthesia (from induction to extubation), duration of surgery, incidence of hypotension and bradycardia and any further perioperative complications were recorded. All dogs received meloxicam (Meloxidolor; Dechra Veterinary Products, the Netherlands) 0.2 mg kg<sup>-1</sup> IV during recovery and gabapentin (Gabapentin; Sandoz, Belgium) 10 mg kg<sup>-1</sup> *per os* eight hourly during the postoperative period.

**Surgery.** All surgeries (thoracolumbar or lumbar hemilaminectomies) were performed by three residents of the European College of Veterinary Surgeons (ECVS) with different levels of experience, following a standard technique (Kerwin et al. 2018). All surgeries were performed under direct supervision of a board-certified (Dip. ECVS) surgeon (P.P.).

**Postoperative data assessment.** SF-GCPS was used to assess pain during the postoperative period. Pain was evaluated at 1 hour (T1), 2 hours (T2) and then every 4 hours (T4, T8, T12, T16, T20, T24) for 24 hours after extubation. When the pain score was ≥ 5/20, 0.2 mg kg<sup>-1</sup> of methadone was administered IV and pain was reassessed approximately 1 hour after administration. In case of a pain score ≥ 5/20, the dog received an additional dose of 0.2 mg kg<sup>-1</sup> IV of methadone. The total dose of rescue methadone (MET<sub>tot</sub>, mg kg<sup>-1</sup>) administered in the first 24 postoperative hours, as well the time from the block to the first rescue methadone was recorded and compared between groups. Pain was assessed by final year veterinary students or interns who were previously trained by M.D. and A.T. in the use of the SF-GCPS and were unaware of the treatment.

**Statistical Analysis.** The number of animals to be enrolled in the study was calculated based on the primary aim: decrease in the requirement of intraoperative fentanyl and postoperative methadone. With  $\alpha$  of 0.05, and  $\beta$  error of 0.2, a decrease of 70% in the fentanyl requirement in the ESPB<sub>L</sub> group and a mean fentanyl infusion of  $1.25 \pm 0.75 \mu\text{g kg}^{-1} \text{ hour}^{-1}$  - indicative of a successful peripheral nerve block (Vettorato et al. 2013) - a minimum of 12 dogs were required in each group. For methadone a decrease of 60% from a total mean dose of  $1.2 \pm 0.6 \text{ mg kg}^{-1}$  over the first 24 postoperative hours was calculated and the number of dogs required in each group was 11. The minimum number of dogs to be enrolled was increased to 15 to address potential losses of dogs or higher standard deviations. The normality of data distribution was evaluated with the D'Agostino-Pearson test. Skewed data were expressed as median and range while those normally distributed as mean and standard deviation. An unpaired Student's T-test was used to compare body weight, duration of the block, anaesthesia, and surgery,  $\text{FEN}_{\text{tot}}$ ,  $\text{MET}_{\text{tot}}$ , and postoperative analgesic effect duration between groups. For HR,  $f_R$ , SAP, MAP, and  $\text{FE}_{\text{Iso}}$  values, an analysis of variance (ANOVA) test for repeated data was used to evaluate the trend within each group. A Dunnet's *post hoc* test was used to compare values at T0 with all the subsequent times. A Mann-Whitney test was used to compare age, BCS, and the preoperative and the different postoperative pain scores (T1, T2, T4, T8, T12, T16, T20, T24). A Chi-square test was performed to evaluate the number of fentanyl boluses and the use of noradrenaline in both groups. Data regarding atropine administration were compared with a Fisher's exact test. Statistical difference was considered significant for  $p < 0.05$ . Prism Version 6.0 (GraphPad Software Inc., CA, USA) was used to analyse data.

## Results

A total of 30 dogs, classified as ASA II, undergoing thoracolumbar or lumbar hemilaminectomy for Hansen type I IVDE were enrolled in this study. The age was 48 (36–156) months in group ROPI and 60 (10–152) months in group CNT; the weight was  $9.8 \pm 4.7$  kg and  $11.9 \pm 3.7$  kg in group ROPI and in group CNT, respectively. BCS was 5 (4–6) in both groups. No statistically significant differences were detected between groups regarding age, weight or BCS. Breeds, MFSs, and IVDE localization are reported in Table 1. No differences were found regarding the preoperative pain score between groups.

**Table 1:** Group, breed, modified Frankel score (MFS) and localization of intervertebral disc extrusion (IVDE) of the dogs enrolled in the study. ROPI, lumbar erector spinae block (ESPB<sub>L</sub>) with ropivacaine 0.5%; CNT, ESPB<sub>L</sub> with saline solution. T (thoracic vertebrae); L (lumbar vertebrae).

Group	Breed	MFS	Localization IVDE
ROPI	Chihuahua	4	L2 – L3 left
	Mix breed	3	L1 – L2 right
	French Bulldog	3	L4 – L5 left
	Dachshund	4	T12 – T13 right
	French Bulldog	4	T13 – L1 right
	Poodle	4	L1 – L2 left
	French Bulldog	4	L1 – L2 right
	Poodle	3	L2 – L3 right
	French Bulldog	4	L4 – L5 left
	Dachshund	4	L2 -L3 left
	Dachshund	3	T13 – L1 right
	French Bulldog	3	L5 – L6 right
	French Bulldog	4	L1 – L2 right
	Dachshund	5	T12 – T13 right
	Dachshund	3	T12 – T13 right

<b>CNT</b>	Dachshund	5	T11 – T12 right
	Cocker spaniel	3	L5 – L6 left
	French Bulldog	4	L4 – L5 left
	French Bulldog	3	T11 – T12 right
	Dachshund	4	L2 -L3 left
	French Bulldog	4	L1 – L2 left
	French Bulldog	3	L3 – L4 right
	Cocker spaniel	3	L1 – L2 right
	Shitzu	4	T11 – T12 right
	Jack Russell Terrier	3	L2 – L3 right
	French Bulldog	4	L4 -L5 left
	French Bulldog	3	L5 – L6 left
	French Bulldog	4	L4 – L5 right
	Dachshund	4	T11 – T12 left

No statistically significant differences were detected among groups regarding duration of anaesthesia and surgery (Table 2).

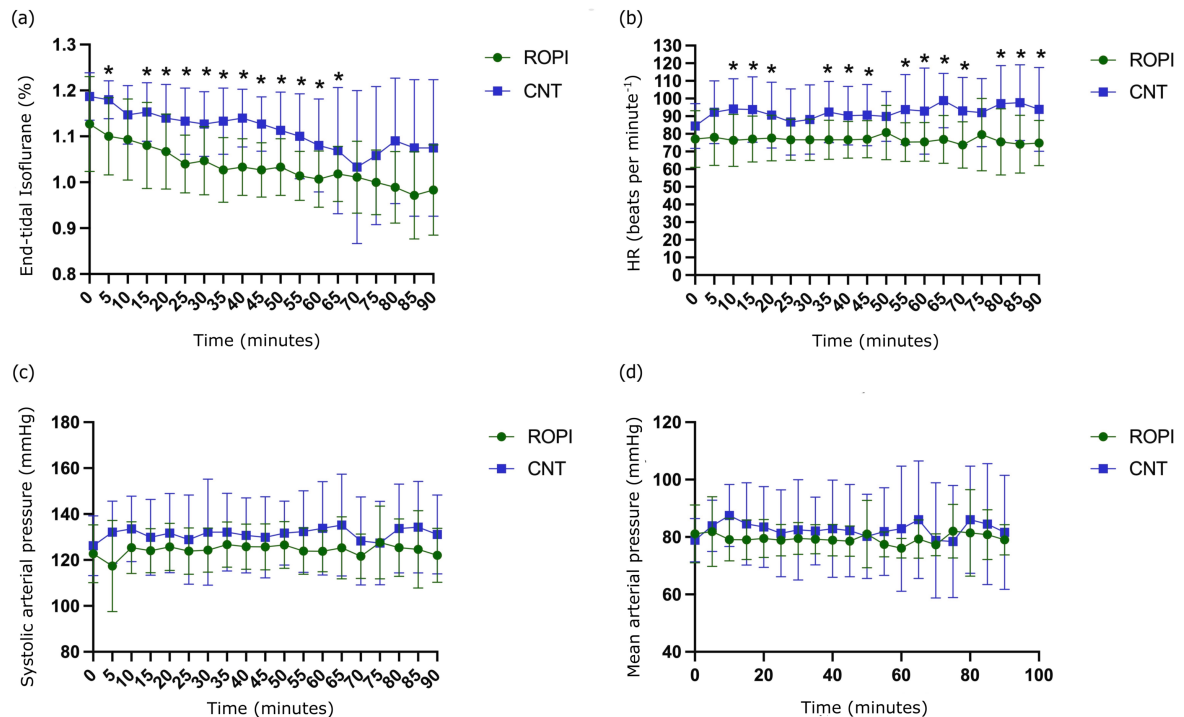
**Table 2:** Duration of anaesthesia and surgery (minutes) in the two groups. Group CNT, receiving the lumbar erector spinae block (ESPB<sub>L</sub>) with saline solution; group ROPI, receiving ESPB<sub>L</sub> with ropivacaine 0.5%. Results are presented as mean  $\pm$  standard deviation.

<b>Group</b>	<b>Duration anaesthesia (minutes)</b>	<b>Duration surgery (minutes)</b>
<b>ROPI</b>	144 $\pm$ 21.7	82.6 $\pm$ 22.2
<b>CNT</b>	158.3 $\pm$ 30.1	94.6 $\pm$ 27.4

HR and FE<sub>1so</sub> were significantly lower in group ROPI at several time points [Figs 1(a), 1(b)]. No statistically significant differences were found between the surgical time points within each group



for these variables. No statistically significant differences were found in SAP and MAP between the surgical time points within each group and between the two groups [Figs 1(c), 1(d)].



**Figure 1** (a), Intraoperative end-tidal concentration of isoflurane (FE Iso); (b), intraoperative heart rate (HR) (c) intraoperative systolic blood pressure and (d) intraoperative mean arterial blood pressure measured in the dogs enrolled in the study. Dogs were allocated to one of two groups: group CNT, receiving the lumbar erector spinae block (ESPB<sub>L</sub>) with saline solution; group ROPI, receiving ESPB<sub>L</sub> with ropivacaine 0.5%. CNT (control), ROPI (ropivacaine). \* Significant difference between the two groups ( $p < 0.05$ ). Data are shown as mean and standard deviation.

A significant difference between groups ( $p < 0.005$ ) was detected regarding the rescue fentanyl administered during surgery: at least one rescue fentanyl bolus was administered in 7/15 dogs in group ROPI. None of dogs in group ROPI needed a fentanyl infusion. In group CNT, at least one rescue fentanyl bolus was administered in all dogs. A total of 8/15 dogs in group CNT received a fentanyl infusion. FEN<sub>tot</sub> was significantly lower ( $p < 0.0001$ ) in group ROPI than in group CNT ( $0.7 \pm 0.9 \mu\text{g kg}^{-1} \text{ hour}^{-1}$  versus  $4.3 \pm 1.3 \mu\text{g kg}^{-1} \text{ hour}^{-1}$ ). Data and distribution of the use of rescue fentanyl are summarised in Tables 3 and 4.

**Table 3:** Number of dogs receiving fentanyl bolus at relevant time points during surgery. Dogs were allocated to one of two groups: group CNT, receiving the lumbar erector spinae block (ESPB<sub>L</sub>) with saline solution; group ROPI, receiving ESPB<sub>L</sub> with ropivacaine 0.5%. S<sub>1</sub>, skin, subcutaneous, and fascial tissue incision; S<sub>2</sub>, elevation of musculature from the vertebral laminae; S<sub>3</sub>, removal of the

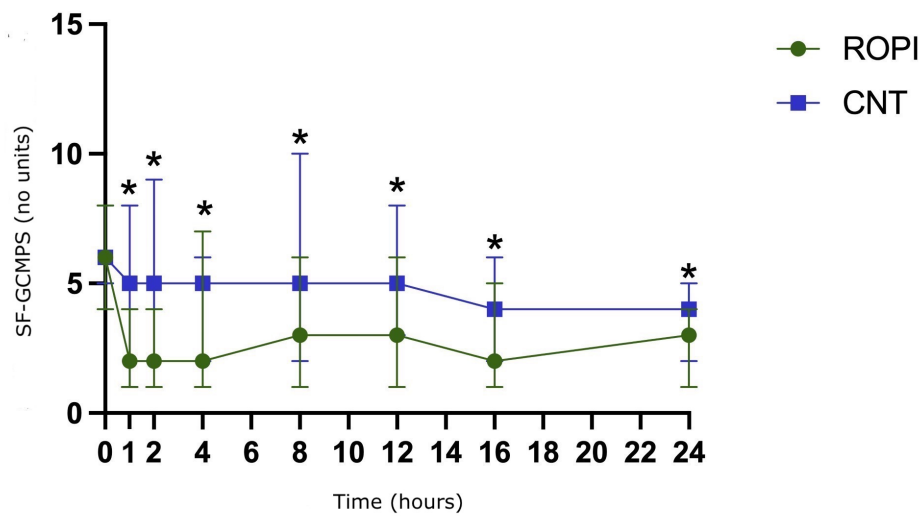
articular process; S<sub>4</sub>, drill of the vertebral laminae and pedicle; S<sub>5</sub>, decompression of the spinal cord; S<sub>6</sub>, fascial plane suturing; S<sub>7</sub>, subcutaneous tissue and skin suturing. CNT (control), ROPI (ropivacaine).

Group	Number of dogs that received fentanyl boluses during surgery						
Surgery times	S <sub>1</sub>	S <sub>2</sub>	S <sub>3</sub>	S <sub>4</sub>	S <sub>5</sub>	S <sub>6</sub>	S <sub>7</sub>
ROPI	2	-	-	-	4	2	1
CNT	5	7	7	5	8	1	7

**Table 4:** Number of dogs receiving fentanyl infusion at relevant time points during surgery. Dogs were allocated to one of two groups: group CNT, receiving the lumbar erector spinae block (ESPB<sub>L</sub>) with saline solution; group ROPI, receiving ESPB<sub>L</sub> with ropivacaine 0.5%. S<sub>1</sub>, skin, subcutaneous, and fascial tissue incision; S<sub>2</sub>, elevation of musculature from the vertebral laminae; S<sub>3</sub>, removal of the articular process; S<sub>4</sub>, drill of the vertebral laminae and pedicle; S<sub>5</sub>, decompression of the spinal cord; S<sub>6</sub>, fascial plane suturing; S<sub>7</sub>, subcutaneous tissue and skin suturing. CNT (control), ROPI (ropivacaine).

Group	Number of dogs that received fentanyl infusion during surgery						
Surgery times	S <sub>1</sub>	S <sub>2</sub>	S <sub>3</sub>	S <sub>4</sub>	S <sub>5</sub>	S <sub>6</sub>	S <sub>7</sub>
ROPI	-	-	-	-	-	-	-
CNT	3	2	2	5	5	4	3

Time elapsed between the EPSB<sub>L</sub> and the first rescue methadone was significantly longer ( $p < 0.0005$ ) in group ROPI than in group CNT ( $17.2 \pm 8.7$  hours *versus*  $5.6 \pm 7.4$  hours). Pain scores in group ROPI were significantly lower than in group CNT at each time point ( $p < 0.0005$ ) (Fig. 2).



**Figure 2** Preoperative (0 hour) and postoperative pain scores using the short-form Glasgow Composite Measure Pain Scale (SF-GCMPS) at 1, 2, 4, 8, 12, 16, 20 and 24 hours after extubation in the dogs enrolled in the study. Dogs were allocated to one of two groups: group CNT, receiving the lumbar erector spinae block (ESPB<sub>L</sub>) with saline solution; group ROPI, receiving ESPB<sub>L</sub> with ropivacaine 0.5%. CNT (control), ROPI (ropivacaine). \* Significant difference between the two groups ( $p < 0.05$ ). Data are shown as median and range.

MET<sub>tot</sub> administered in the first 24 postoperative hours in group ROPI was significantly lower ( $p < 0.001$ ) compared to group CNT ( $0.1 \pm 0.2 \text{ mg kg}^{-1}$  versus  $0.9 \pm 0.05 \text{ mg kg}^{-1}$ ). A total of 9/15 dogs in group ROPI and 2/15 dogs in group CNT did not receive any rescue analgesia during the first 24 postoperative hours. Hypotension was recorded only in group CNT (3/15 dogs): normotension was restored with one fluid bolus in two dogs, while the third dog also needed a noradrenaline infusion ( $0.05\text{-}0.15 \text{ } \mu\text{g kg}^{-1} \text{ minute}^{-1}$ ). The occurrence of bradycardia was significantly different between groups ( $p < 0.0169$ ): one bolus of  $20 \text{ } \mu\text{g kg}^{-1}$  of atropine was administered in 6/15 dogs only in group CNT. No further perioperative complications were recorded.

## Discussion

Results of the present study suggest that the addition of a unilateral ESPB<sub>L</sub> with a volume of 0.4 mL kg<sup>-1</sup> of ropivacaine 0.5% provided better intraoperative analgesia in these dogs than in those receiving the same block with saline solution. The use of the ESPB<sub>L</sub> block thus reduced the FEN<sub>tot</sub> and the occurrence of intraoperative bradycardia, in comparison with dogs which received methadone alone for premedication. Unilateral ESPB<sub>L</sub> ensured a long-lasting postoperative analgesic effect, reducing postoperative methadone requirement and pain scores.

The intraoperative analgesic efficacy of a unilateral ESPB<sub>L</sub> in our study was supported by the significantly lower FEN<sub>tot</sub> administered in group ROPI in comparison with group CNT. All dogs in group CNT required at least one rescue fentanyl bolus followed by an infusion in 8/15, while only 7/15 dogs in group ROPI needed rescue boluses. These findings are in line with previous studies (Portela et al. 2021, Viilmann et al. 2022) in which the ESPB<sub>T</sub> was associated with a reduction of the requirements of intraoperative rescue opioids. In addition, in this study, both HR and FE<sub>1</sub>so were significantly lower in group ROPI than in group CNT. These data are well reported in veterinary literature and confirm the advantages of locoregional anaesthesia, such as the sparing effect on inhalant anaesthetic drugs and a more stable anaesthetic plane during surgery, in comparison with a group receiving systemic analgesia (Grubb et al. 2020, Tayari et al. 2022).

Innervation of epaxial muscles, vertebral laminae and facet joints in dogs is provided by the medial branches of the DRSN (Forsythe & Ghoshal 1984, Evans & de Lahunta 2013). Rescue fentanyl was not required in group ROPI during S<sub>2</sub>, S<sub>3</sub> and S<sub>4</sub>. In group CNT instead fentanyl boluses and/or an infusion were administered in a greater number of dogs (Tables 3 and 4). Therefore, unilateral ESPB<sub>L</sub> performed with ropivacaine provided satisfactory analgesia during the most invasive and painful parts of the surgery (Cavalcanti et al. 2022). These results agree with previous cadaver studies, in which ESPB<sub>L</sub> was found effective in staining the medial branches of the DRSN (Medina-Serra et al 2021, Cavalcanti et al. 2022).

Innervation of intervertebral disc, dorsal longitudinal ligament and meninges in humans is provided by the meningeal branches of the spinal nerves (MBSN) (Bridge 1959, Groen et al. 1988). Cadaver and immunohistochemical studies conducted in dogs have demonstrated the presence of innervation to these structures (Waber-Wenger et al. 2014). However, there is controversy regarding the factual existence of the MBSN and the exact branching pattern of these nerve fibres remains unclear in dogs (Forsythe & Ghoshal 1984). Notably, only 4/15 dogs needed rescue fentanyl in group ROPI during S<sub>5</sub>,

while 8/15 required boluses and 5/15 dogs required an infusion in group CNT. Our results agree with a previous study (Viilmann et al. 2022), in which 64/93 (68.8 %) of dogs receiving ESPB<sub>T</sub> did not require rescue analgesia during the removal of herniated disc material. This effect could be due to the migration of LA into the epidural space, even if this finding was only rarely described in a cadaver study (Medina-Serra et al. 2021). The discrepancy between these findings and the clinical effect reported in our study could be due to the different biophysical properties of cadaver tissues in comparison with living ones. These differences include alterations in permeability and intra-compartmental pressures, as described in human medicine (Chin & El-Boghdady 2021).

Innervation of the skin and fascial planes of the dorsolateral aspect of the trunk is mainly supplied by the lateral branches of the DRSN (Forsythe & Ghoshal 1984, Evans & de Lahunta 2013). S<sub>1</sub>, S<sub>6</sub> and S<sub>7</sub> elicited nociception in 5/15 dogs in group ROPI. Notably, IVDE in these dogs was localized between T13 and L2, where, according to Cavalcanti et al. (2022), the ESPB<sub>L</sub> resulted in less effective staining of the lateral branches of the DRSN. In the authors' opinion, this finding could explain the poor analgesic effect during surgical manipulation of the skin and superficial tissue planes. However, skin can also be innervated by fibres from the contralateral side (Capek et al. 2015). Therefore, nociception could have been prevented by performing bilateral ESPB<sub>L</sub>.

Unilateral ESPB<sub>L</sub> in group ROPI provided a long-lasting postoperative analgesia, reducing pain scores and MET<sub>tot</sub> during the first 24 postoperative hours. Furthermore, 9/15 dogs in group ROPI did not receive any rescue methadone. Even though different local anaesthetic, volumes and approaches were used in our study, the results support the findings previously reported by Portela et al. (2021) and Viilmann et al. (2022). In our study, 2/7 French Bulldogs in group CNT did not require any rescue methadone in the postoperative period. Although individual variability and influence of other postoperative treatment cannot be excluded, pain assessment might be influenced by the breed. Despite the lack of scientific evidence regarding breed differences in pain sensitivity, results from a recent survey demonstrated that Bulldogs are ranked as a low pain sensitivity breed by veterinarians and owners (Gruen et al. 2020).

Although no statistically significant differences were found regarding intraoperative values of SAP and MAP between groups, hypotension was only apparent in group CNT. This finding agrees with the study of Portela et al. (2021), in which this complication occurred more frequently in dogs receiving systemic analgesia. Hypotension is one of the most described perioperative complications in dogs admitted for hemilaminectomy (Bruniges & Rioja 2019). In our study, higher FE<sub>1so</sub> was recorded in group CNT. Isoflurane causes dose-dependent reductions in systemic vascular resistance, and

myocardial contractility (Steffey et al. 2017), thus we speculate that the sparing effect of unilateral ESPB<sub>L</sub> on isoflurane prevented the occurrence of hypotension in group ROPI.

Bradycardia was only recorded in group CNT, where 6/15 dogs required atropine. This complication is well documented in dogs undergoing hemilaminectomy (Posner et al. 2014, Bruniges & Rioja 2019, Portela et al. 2021) and could be partially due to the high parasympathetic tone in breeds predisposed to IVDE (Harrison et al. 2012). In the authors' opinion, bradycardia was more likely to occur in group CNT because of higher FENT<sub>tot</sub> administered in this group. These results support the hypothesis that unilateral ESPB<sub>L</sub> guarantees a more stable anaesthetic and analgesic plane, reducing cardiovascular complications (Portela et al. 2021).

Even though efforts were made to standardize the study design, there are some limitations which should be mentioned. First, based on ethical grounds, all dogs in our study received methadone for premedication. Therefore, we cannot exclude the impact methadone had on the analgesic effect of the unilateral ESPB<sub>L</sub> seen in this study. Second, the hemilaminectomy procedure was performed by different ECVS residents and this may have produced some variation in our results. Nevertheless, all surgeries were performed following a standardized technique, under direct supervision of the same board-certified surgeon. Third, the hemilaminectomies were performed between T11 and L2 in 15/30 dogs and caudal to L2 in 15/30 dogs. However, the ESPB<sub>L</sub> was performed using the same approach (Medina-Serra et al. 2021) in both thoracolumbar and lumbar hemilaminectomies, as suggested by previous studies (Cavalcanti et al. 2022). Fourth, the MFS score was 5/5 in 2/30 dogs included in this study, one per group. Absence of deep pain perception could affect the overall evaluation of pain, according to other authors (Portela et al. 2021, Viilmann et al. 2022). However, in our clinical experience these dogs still experience pain in the anatomical area around the IVDE, while the absence of pain perception is usually evaluated by application of a noxious stimulus to the pelvic limbs and tail (Lewis et al. 2020). For that reason, we decided not to exclude these dogs from the study. Finally, final year students and interns assessed pain in the postoperative period. Even though they had received previous training and the SF-GCPS is routinely used in our hospital, lack of experience could have altered results regarding the postoperative analgesic effect of unilateral ESPB<sub>L</sub>.

The unilateral ESPB<sub>L</sub> performed with ropivacaine in dogs undergoing thoracolumbar or lumbar hemilaminectomy provided superior intraoperative, prolonged postoperative analgesia, and reduced total opioid consumption in the perioperative period, in comparison with dogs which received only methadone in premedication. Our results also showed that the unilateral ESPB<sub>L</sub>

provided a more stable anaesthetic plane and decreased the occurrence of intraoperative bradycardia.

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# Discussion

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## Discussion

The practice of evidence-based medicine in veterinary science, much like in human medicine, relies on a hierarchical structure of evidence to guide clinical decision-making. This hierarchy, often represented as a pyramid, ranges from high-level evidence at the apex, such as systematic reviews and RCTs, to lower-level evidence at the base, including expert opinion and case reports. A RCT is a prospective experimental study designed to assess the efficacy of an intervention by randomly allocating subjects into different groups, typically an intervention group and a control group. Randomization minimizes bias and provides a rigorous method for evaluating cause-effect relationships, ensuring that observed differences in outcomes can be attributed to the intervention rather than confounding variables. By balancing both known and unknown participant characteristics between groups, RCTs enhance the reliability of clinical research and are considered the gold standard for assessing treatment efficacy.

In the field of veterinary locoregional anaesthesia, particularly concerning US-guided IFP blocks, the current literature predominantly comprises cadaveric studies (Ferreira et al. 2019; Portela et al. 2020; Medina-Serra et al. 2020; Cavalcanti et al. 2022; Garbin et al. 2020a, b; Viscasillas et al. 2021a; Alaman et al. 2022a, Marchina-Gonçalves et al. 2022; Marchina-Gonçalves et al. 2023, Otero et al. 2024). These studies provide valuable anatomical insights and confirm the feasibility of delivering LA to the intended IFP. While cadaveric research is crucial for understanding the anatomical features and guiding the development of new techniques, it does not provide direct evidence of clinical efficacy or analgesic outcomes in live animals.

Another portion of the literature consists of case reports and case series (Zannin et al. 2020; Rodriguez Mulet et al. 2021; Viscasillas et al. 2021b, Herrera-Linares & Martinez, 2022; Chiavaccini et al. 2023). These reports document the application of IFP blocks in individual or small groups of clinical cases, offering preliminary observations on their analgesic effectiveness and safety. Although case reports and case series can highlight potential benefits and adverse effects, they lack the methodological rigour to establish causality or generalise findings to a wider population.

In a few instances, retrospective studies have been conducted (Portela et al. 2021; Viilman et al. 2022, Martinez I Ferré et al. 2024; Alza Salvatierra et al. 2024). These studies analyse pre-existing data to assess outcomes in dogs that have undergone US-guided IFP blocks. While retrospective studies can provide more comprehensive data than individual case reports, they are limited by their

observational nature and potential biases in data collection and analysis. Retrospective studies also cannot control for confounding variables as effectively as prospective research.

At the start of this PhD research project, there was a substantial absence of RCTs in this area of veterinary anaesthesia. The scarcity of this type of studies in veterinary anaesthesia, especially in fields such as US-guided IFP blocks in dogs, can be attributed to several significant challenges. For instance, ethical considerations play a crucial role: enrolling animals in clinical trials requires owner consent, and the use of placebo controls can be ethically contentious, particularly in studies involving pain management. The studies conducted in this PhD thesis provide significant advancements in terms of evidence-based medicine in the field of veterinary anaesthesia, particularly in the application of QL and ES plane blocks for perioperative analgesia in dogs.

The QL block has been widely studied in human medicine, where it has been shown to provide effective analgesia for a variety of surgical procedures (Akerman et al. 2018; Kim et al. 2020; Uppal et al. 2020; Korgvee et al. 2021). However, its application in veterinary medicine is relatively novel, with only a handful of clinical studies available. Currently, evidence regarding the analgesic efficacy of this technique in dogs rely on the case-series from Viscasillas et al. (2021) and on the studies contained in this PhD thesis. Our findings align with those reported in human studies, particularly in terms of the block's ability to provide both somatic and visceral analgesia (Akerman et al. 2018; Kim et al. 2020; Uppal et al. 2020; Korgvee et al. 2021). The results of the first study demonstrated that the concentration of ropivacaine significantly influences the duration of postoperative analgesia provided by the QL block, in dogs undergoing laparoscopic ovariectomy. The use of 0.5% ropivacaine significantly prolonged the time to the first rescue analgesia compared to both 0.33% ropivacaine and a fentanyl-based protocol. These findings confirm that higher concentrations of LA provide superior postoperative analgesia, extending the duration before additional analgesic intervention is required (Portela et al. 2010; Fenten et al. 2015; Tayari et al. 2017). The clinical relevance of this study lies in its potential to improve perioperative pain management protocols for canine patients undergoing minimally invasive surgeries, offering a prolonged and stable analgesic effect without additional systemic analgesic administration.

The comparative study between the lateral and latero-ventral approaches to the QL block revealed that the first one is more effective in reducing the need for perioperative rescue analgesics. This finding is particularly important as it suggests that the anatomical approach to the block can significantly influence its effectiveness. Similar observations have been reported in human medicine, where different approaches to QL block have been shown to result in varying degrees of



analgesia (Akerman et al. 2018; Kim et al. 2020; Uppal et al. 2020; Korgvee et al. 2021). In addition, results of the second study provide information on the mechanism of action of the QL block. According to findings from cadaveric studies (Garbin et al. 2021b; Marchina-Gonçalves et al. 2023), only the lateral approach is able to provide spread of LA to both the ventral rami of the SN and the sympathetic trunk, which likely accounts for the more effective analgesia observed. The latero-ventral approach, while easier to perform, may not provide as extensive a spread, resulting in less effective pain control during abdominal surgeries, especially in case of visceral manipulation. This highlights the importance of understanding the anatomical and physiological principles underlying these blocks to optimize their application in clinical practice.

Notably, we did not record any collateral effect related to the QL block in our studies. In human medicine, and more recently in veterinary practice, the QL block has been associated with certain complications, including hypotension (Almeida & Assuncao, 2018; Sá et al. 2018), respiratory arrest (Herrera-Linares & Martinez, 2022), and development of retroperitoneal hematomas (Visoiu & Pan, 2019; Chiavaccini et al. 2023). These complications are probably related to the use of the dorsal approach to the QL block (Alaman et al. 2022a, Marchina-Gonçalves et al. 2022), where inadvertent injury to the lumbar arteries during needle insertion can occur, leading to significant bleeding. However, in our studies, neither the lateral nor the latero-ventral approaches resulted in such adverse effects. This absence of complications may be attributed to the use of more superficial approaches, which might avoid high-risk anatomical zones. Our findings suggest that the QL block can provide effective perioperative analgesia in dogs without the associated risks of serious complications. This reinforces the clinical applicability and safety of this technique in routine veterinary practice, particularly when more superficial approaches are chosen, such as the lateral approach described by Garbin et al. (2021b) or the latero-ventral, proposed by Marchina-Gonçalves et al. (2023). However, the relatively small sample size may have influenced the interpretation of our findings, particularly regarding the reduction in mean arterial pressure observed after the QL block in study 1. While the decrease in blood pressure was statistically significant, after injecting ropivacaine 0.33%, the limited number of animals included prevents us from drawing definitive conclusions about the clinical relevance of this effect or its potential impact on patient safety. A larger sample size would be necessary to better characterize the incidence of hypotension associated with this block. Additionally, the small sample size may have limited our ability to detect less frequent complications or side effects. Future studies with a greater number of cases are warranted to further evaluate the safety profile of this technique and to determine whether specific patient populations may be more susceptible to hemodynamic changes following this technique.

In the third study, the feasibility and outcomes of an US-guided catheter placement technique for continuous LA administration in the QL IFP were evaluated. This study was motivated by our clinical experience with the QL block in dogs undergoing abdominal surgeries at our Institution. The QL block is frequently performed for postoperative analgesic management, particularly in dogs that do not respond adequately to traditional systemic analgesic regimens. However, deep sedation or general anaesthesia are necessary to perform safely the QL block, which is not always feasible, especially in critically ill patients. This limitation prompted us to explore the possibility of implanting catheters in the QL IFP for postoperative LA administration. By developing the technique for catheter placement, we aimed to provide a method that could deliver continuous analgesia without the need for repeated sedation or anaesthesia, thereby enhancing patient comfort and safety during the critical postoperative period. The cadaveric phase demonstrated that a higher volume of injectate resulted in more extensive spread along the VBs, which could potentially enhance analgesic coverage. Clinically, the technique appeared feasible, with ropivacaine administered via catheters providing effective postoperative analgesia in most cases. The incorporation of a cadaveric study and a small series of clinical cases within the thesis is justified by the need to validate the anatomical and practical feasibility of the QL catheters implantation technique. Although the primary focus of the thesis is on providing clinical evidence through RCTs, the cadaveric study serves as a fundamental investigation to support clinical applications. By confirming the anatomical distribution of the injectate and the feasibility of technique, this study provides a basis for future RCTs that could definitively assess the analgesic efficacy of this novel approach in a larger cohort of dogs. The reported clinical cases, despite limited in number, offer preliminary insights into application of the technique, highlighting both its potential benefits and areas for further refinement. This study's results are significant as they suggest that LA administration through catheters implanted in the QL IFP could be a viable option for prolonged postoperative pain management in canine patients.

The fourth study assessed the analgesic efficacy of a unilateral lumbar ES plane block in dogs undergoing hemilaminectomy. The results showed that the ES plane block with ropivacaine significantly reduced perioperative opioid consumption and the incidence of bradycardia compared to a saline control group. Additionally, postoperative pain scores were significantly lower, and the duration of analgesia was longer in the group receiving the ES plane block. These findings underscore the effectiveness of ES plane block in providing robust perioperative analgesia for more invasive surgical procedures. The reduction in opioid consumption is particularly noteworthy as it

aligns with the goals of enhanced recovery protocols, which aim to minimize opioid use and improve postoperative outcomes. The study supports the inclusion of ES plane block in multimodal analgesia strategies for managing perioperative pain in canine patients undergoing spinal surgeries. Two recent RCTs have investigated the analgesic efficacy of the longitudinal ES plane block, comparing it with systemic opioid-based protocols in dogs undergoing thoracolumbar or lumbar hemilaminectomy, either with LAs alone or in combination with dexmedetomidine (Bendinelli et al. 2024; Pérez et al. 2024). Bendinelli et al. (2024) found a reduction in intraoperative fentanyl consumption in dogs receiving the block, with no significant differences in terms of intraoperative cardiovascular complications or postoperative methadone consumption. Similarly, Pérez et al. (2024) reported comparable findings, recording no additional benefit when dexmedetomidine was added to the LA solution. The differences in results between our study and these two RCTs may be attributed to the different approaches used. We opted for a lumbar ES plane block, guided by the evidence provided from previous cadaveric studies (Cavalcanti et al. 2022), while Bendinelli et al. (2024) and Pérez et al. (2024) employed a thoracic approach for both thoracic and lumbar hemilaminectomy. As noted by the authors of those studies, this could have influenced the overall analgesic efficacy of the ES plane block, particularly in cases of thoracolumbar and lumbar hemilaminectomy, where a transversal approach should be preferred, according to Cavalcanti et al. (2022). However, a recent cadaveric study documented no significant differences in spread along the vertebral column and dorsal rami of the SNs staining, after injection  $0.6 \text{ mL kg}^{-1}$  of dye solution at the level of T12, using either the longitudinal or transversal approach (Herrera-Linares et al. 2024). Further RCTs, comparing the analgesic efficacy of the approaches for the ES plane block at different portion of the spine, are warranted to establish which approach would guarantee better outcomes in dogs undergoing hemilaminectomy.

Sinus arrest secondary following ES plane block in dogs has been reported in a case-series and in a retrospective study (Sambugaro et al. 2022; Viilmann et al. 2022). In those cases, blocks were administered at L1, T13, and T13 using a longitudinal approach, with the dose of levobupivacaine ranging between 2.37 and 2.62 mg/kg. The authors of those studies hypothesized that those events might have been caused by LA systemic toxicity or potential epidural spread (Sambugaro et al. 2022; Viilmann et al. 2022). In human medicine, epidural spread following ES plane block has been reported in both cadavers and living patients (Chin & El-Boghdadly 2021). In dogs, it has been documented only in cadaveric studies, using either the longitudinal or transversal approach (Medina-Serra et al. 2021; Herrera-Linares et al. 2024). Several theories regarding this type of spread have been proposed (Chin et al. 2019). The dorsal rami of the SNs and vessels traverse the

thoracolumbar fascia and the intertransverse connective tissue (Evans and de Lahunta, 2013; Portela et al., 2020). These perforations, along with the costotransverse foramen, joints, and ligaments, might create a pathway for epidural diffusion (Chin et al. 2019). While this abnormal LA spread may contribute to analgesia (Adhikary et al. 2018; Schwartzmann et al. 2018), the large volume/dose of LA could result in extensive motor blockade (Selvi & Tulgar 2018) and hemodynamic instability from sympathetic blockade (Coviello et al. 2021; Sambugaro et al. 2022). Though all the dogs survived, aggressive intervention including the use of atropine, adrenaline, ephedrine, and intralipid was required (Sambugaro et al. 2022; Viilmann et al. 2022). In our study, such complications were not recorded. However, dogs with history of previous hemilaminectomies were excluded from our RCT. According to Sambugaro et al. (2022), this could be considered a relative contraindication, as the spread of LA to the epidural space may be favoured in such cases. ES plane block involves the use of large volumes/doses of LAs, so veterinary clinicians should always be careful about signs of LA systemic toxicity, following performance of this technique. Since veterinary patients are often anaesthetized when the blocks are performed, many of the early signs of systemic toxicity may be missed or misidentified as “normal/expected” general anaesthesia complications. Calculating the dose of LA for an ES plane block using lean body weight, keeping the total dose selected within the maximum recommended range (3 mg kg<sup>-1</sup> for ropivacaine, bupivacaine and levobupivacaine), and diluting the LA as needed to obtain the desired volume, is advisable.

While findings of this thesis are promising, several limitations must be acknowledged. Firstly, the studies were conducted in specific clinical settings with relatively small sample sizes, which may limit the generalization of results. Another limitation is the potential for operator-dependent variability in the success of the blocks. The accuracy of US-guided techniques can vary depending on the skill and experience of the clinician performing the block. While the studies were conducted by anaesthetists experienced in US-guided locoregional anaesthesia, outcomes may differ in less experienced hands. This highlights the need for standardized protocols to ensure consistent and safe application of these techniques in clinical practice. Additionally, the studies focused primarily on the immediate perioperative period, and long-term outcomes were not assessed. While the blocks were effective in reducing pain and opioid consumption in the short term, their impact on long-term recovery and overall patient outcomes remains unclear. Future studies should include longer follow-up periods to evaluate the sustained effects of IFP blocks and their influence on the quality of postoperative recovery.

The findings of this thesis suggest several directions for future research. In human medicine, the QL and ES plane blocks are currently used as analgesic techniques for a wide range of surgical procedures (Kim et al. 2020; Uppal et al. 2020; Korgvee et al. 2021, Viderman et al. 2022; Dost et al. 2022; Gao et al. 2022). In the two RCTs we conducted to assess the analgesic efficacy of the QL block in dogs, we selected laparoscopic ovariectomy as the model procedure. This choice was made because it is one of the most reproducible abdominal surgeries performed in our Institutions, eliciting both somatic and visceral nociceptive stimuli. Further studies are warranted to evaluate the impact of the QL block on opioid consumption in dogs undergoing various abdominal surgeries. As previously mentioned, the ES plane block has been incorporated into the perioperative analgesic management of human patients undergoing not only spinal surgeries but also procedures involving anatomical regions not innervated by the dorsal branches of the SNs, such as the thoracic and abdominal cavities (Viderman et al. 2022; Dost et al. 2022; Gao et al. 2022). Although the precise mechanism of action of the ES plane block remains to be fully elucidated, the diffusion of LA into the epidural and paravertebral spaces, thus affecting the ventral rami of the SNs, is currently considered to play a key role in producing analgesic effect of the ES plane block (Chin et al. 2020; Otero et al. 2020). In veterinary medicine, the primary indication for this IFP block remains spinal surgery, as most of the available evidence is derived from studies performed on dogs undergoing hemilaminectomy, with the dorsal rami of the SNs being the main target. Although epidural and paravertebral spread of injectate has only been observed in a few cases across two canine cadaveric studies (Medina-Serra et al. 2021; Herrera-Linares et al. 2024), the ES plane block has also been reported as part of multimodal analgesic approaches in dogs undergoing thoracotomy (Gómez Fernández et al. 2021) and sternotomy (Ferré et al. 2022), as well as in the management of visceral abdominal pain due to acute pancreatitis (Bartholomew & Ferreira, 2021). However, these case reports lack robust evidence, due to their inherent limitations. Therefore, RCTs are needed to assess the analgesic efficacy of the ES plane block in dogs undergoing thoracic and abdominal surgeries, to validate its use in analgesic protocols for such procedures, considering the availability of other effective US-guided locoregional anaesthesia techniques, such as paravertebral or QL blocks.

Further research is necessary also to refine the techniques employed for these blocks, particularly in optimising the volume and concentration of LA required for effective analgesia. For instance, in our studies, we utilised volumes of  $0.3 \text{ mL kg}^{-1}$  for the QL block and  $0.4 \text{ mL kg}^{-1}$  for the ES plane block, respectively. Although higher volumes are generally recommended in cadaveric studies to achieve a wider spread of the injectate, we chose to use lower volumes to maintain a high concentration of ropivacaine, aiming to ensure prolonged postoperative analgesia. However, it is

important to consider that a greater desensitisation of the area, and consequently better intraoperative nociception management, might have been achieved with higher volumes of LA. Further studies are required to validate our findings and to compare the effects of IFP blocks performed with different volumes and concentrations of LA.

Finally, as the use of the IFP blocks becomes more widespread, it will be important to conduct large-scale, multi-centre studies to validate their efficacy and safety. Such studies could also help establish standardized protocols and guidelines for the use of IFP blocks in veterinary anaesthesia, ensuring that these techniques are applied consistently and effectively across the profession.

In conclusion, this PhD thesis has provided valuable insights to our understanding and application of US-guided IFP blocks in veterinary medicine. The research not only validates the efficacy of these blocks in providing effective perioperative analgesia but also highlights the importance of technique, LA concentration, and anatomical considerations in achieving optimal outcomes. As the field continues to evolve, the findings of this thesis will serve as a foundation for further exploration and innovation, ultimately improving the standard of care for veterinary patients undergoing surgery.

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