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Surgery

Full paper

Epidural anesthesia in dogs undergoing hindlimb orthopedic surgery: effects of two injection sites.

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Running title: EFFECT OF 2 SITES OF EPIDURAL INJECTION

Abstract

This prospective clinical trial evaluated the effects of epidural anesthesia (EA) placed at the lumbosacral compared to the L5-L6 junction in dogs undergoing hindlimb orthopedic surgery. In all, 98 dogs were randomly assigned to receive injection at either L7-S1 (LS group) or L5-L6 (LL group) at the same local anesthetic regimen (1 mg/kg bupivacaine 0.5% and 0.1 mg/kg morphine 1%). Fentanyl (1 µg/kg) was the intraoperative rescue analgesia (iRA) administered if mean arterial pressure increased by 30% above pre-stimulation value. Procedural failure, iRA, hypotension, motor block resolution, and postoperative side effects were recorded. There were 7/47 (15%) epidural procedural failures in the LS group and 8/51 (16%) (P=1.00) in the LL group; iRA was administered in 21/40 (52%) LS group dogs and in 13/43 (30%) LL group dogs, respectively (P=0.047). The incidence of hypotension was 10/40 (25%) and 16/43 (37%) in the LS group and the LL group, respectively (P=0.25). Proprioceptive residual deficit at 8 hr after EA was recorded in 3/26 (12%) in group LS dogs and in 13/26 (50%) group LL dogs, respectively (P=0.01). The proprioceptive residual deficit at 24 hr in one dog (LL group) resolved within 36 hr. No episodes of postoperative urinary

retention, pruritus or neurological damage were recorded. The L5-L6 EA decreased significantly iRA but delays the proprioceptive recovery time. Further studies are needed to determine whether a lower bupivacaine dose reduces the duration of the residual block retaining the same incidence of iRA.

KEYWORDs: dog, epidural anesthesia, injection site, intraoperative rescue analgesia, orthopedic surgery.

Introduction

Epidural anesthesia (EA) has become less attractive in veterinary clinical research, whereas peripheral nerve block, which uses electrical impulses or echography to locate nerves, has gained wider acceptance with higher success rates and fewer side effects [9]. Despite the loss of research interest, EA retains unique clinical features: simplicity of execution, bilateral block, and long-lasting and effective postoperative analgesia, which can be extended with an epidural catheter. While EA placed in a midline approach at the lumbosacral junction has been extensively investigated in small animals, more cranial administration in a paramedian approach with cephalad angulation has been anecdotally reported [7]. In humans, the injection site is one of the factors affecting the spread of the solution through the epidural space [27], its concentration in the cerebrospinal fluid, and its accumulation in the epidural fat [4, 12]. In dogs undergoing combined general and EA with bupivacaine 0.5% (0.2 ml/kg) and morphine 1% (0.01 ml/kg) at the lumbosacral space for hindlimb surgery, 36% needed intraoperative rescue analgesia (iRA) within 60 min and 48% within 80 min, respectively, after epidural injection [24].

The lumbosacral plexus serves the entire pelvic limb; it is formed by the ventral branches of L3 to S3 intervertebral nerves. The main nerves of this plexus which need to be blocked to provide analgesia to the hind limb are (from cranial to caudal): lateral cutaneous femoral, femoral, obturator, sciatic, caudal cutaneous femoral [6]. The nerves that form the cranial part of the lumbosacral plexus can be blocked only with an optimal epidural cranial spread of local anesthetic

(LA), exiting the vertebral canal far cranial from the lumbosacral space, while the nerves caudal to the obturator nerve run in the lumbo-sacral epidural space before leaving the vertebral canal and for this reason they are more exposed to LA [6]. More cranial LA injection compared to lumbosacral junction may increase the probability to block the cranial part of the lumbosacral plexus.

In this view, injecting the LA at the L5-L6 interspinous space seems the best compromise, given its middle position along the lumbosacral plexus and vicinity to the lumbar intumescence that reducing the epidural space from L3 to L6 metamers, may facilitate LA cranial spread. Furthermore, the spinal process of L6 is higher than that of L7, so it can be easily palpated while positioning the Tuohy needle.

Our hypothesis was that an epidural injection placed at L5-L6 rather than at the lumbosacral joint would reduce the need for iRA in dogs undergoing hindlimb orthopedic surgery. The primary endpoint was to compare the incidence of iRA after epidural injection of bupivacaine and morphine at either the lumbosacral junction (LS group) or between the fifth and the sixth lumbar vertebra (LL group). The secondary endpoint was the occurrence of postoperative complications (prolonged neurological deficit, urinary retention, pruritus, neurological damage).

Materials and Methods

The study protocol was approved by University of Padua (Prot. no. 206437); informed written consent was obtained from all dog owners. Client-owned dogs presenting to the Centro veterinario fossanese between September 2018 and September 2019 for scheduled surgery of the hindlimb were evaluated. All dogs deemed healthy on physical examination, with complete blood count and serum biochemistry were enrolled. Exclusion criteria were: American Society of Anesthesiologists classification (ASA) >2, age <6 months, skin infection involving the lumbosacral area, history of bleeding disorders, uncorrected hypovolemia, central or peripheral nervous diseases, spinal anatomical abnormality, and history of intervertebral disc disease.

Study Design

For this prospective randomized clinical trial, the dogs were assigned to one of two treatment groups (LS or LL group) by simple randomization based on a computer-generated randomization sequence (www.randomizer.org). All anesthetic procedures were performed by the same experienced operator, and all surgical procedures were performed by the same surgeon who was unaware of the assigned anesthesia technique. All procedures were conducted preferably in a day-surgery regimen, and the dogs were discharged home as soon as they were able to walk. The manuscript conforms to the Consolidated Standards of Reporting Trials (CONSORT) Statement 2010 for reporting randomized clinical trials [16].

Anesthesia Protocol

All dogs were fasted for at least 6 hr before undergoing surgery; water was freely available. A cephalic vein was catheterized, and general anesthesia was induced with 2 μg/kg of fentanyl (50 μg/ml; Fentadon; Dechra Eurovet Animal Health BV, Bladel, Holland) and propofol (10 mg/kg; Proposure; Merial Corden Pharma, Milan, Italy) administered intravenously (IV) to effect. General anesthesia was maintained using a variable rate of propofol (Syringe-driver Graseby 3500; Smiths Medical, Saint Paul, MN, USA) titrated to keep a sluggish palpebral reflex. Patients received intermittent positive pressure ventilation (Cato; Draeger, Lübeck, Germany) to maintain normocapnia with an oxygen and medical air mixture to provide a fraction of inspired oxygen (FIO_2) of 0.4. A dorsal-pedal artery was catheterized to monitor arterial blood pressure invasively. Lactated Ringer's solution (Fresenius Kabi, Isola della Scala, Italy) was administered IV at a rate of 5 ml/kg/hr during anesthesia. A multiparametric monitor (AS/3; Datex Ohmeda, Salo, Finland) was used to assess cardiovascular (systolic [SAP], mean [MAP], and diastolic [DAP] arterial blood pressure, heart rate [HR]), and respiratory parameters ($PECO_2$, peak inspiratory pressure, respiratory rate, tidal volume, FIO_2), and esophageal temperature (T, °C). Data were manually recorded every 5 min until the end of anesthesia. During the perioperative period, body temperature was maintained above 36 °C with an active heating system (Bair Hugger Warmer Model 505; Augustine Biomedical Design, Eden Prairie, MN, USA). The propofol dose for anesthesia induction and maintenance after epidural

injection, the time from induction to epidural injection, from epidural injection to skin incision, from skin incision to end of the surgery, and the median anesthesia time were recorded.

Epidural Anesthesia

Epidural anesthesia was administered after clipping the hair from the spinous process of L4 to S2; the skin was aseptically prepared with chlorhexidine (4%) and alcohol (70%). Epidural anesthesia was administered using a Tuohy needle (Perican 22, 20 or 18 gauge; B. Braun, Melsungen, Germany) with the dog in lateral recumbency and the pelvic limbs held forward. A radiograph of the body area was taken to check for correct needle positioning before epidural injection [15]. If the radiograph showed incorrect positioning, two further attempts to reach the epidural space could be undertaken. After the third attempt, the procedure was aborted, and the case was recorded as a procedural failure. An isobaric solution of bupivacaine (5 mg/ml; Bupisen, Galenica Senese, Monteroni d'Arbia (SI), Italy) at 1 mg/kg and morphine (10 mg/ml; morphine hydrochloride, Monico, Mestre (VE), Italy) at 0.1 mg/kg was slowly administered. The administered bupivacaine 0.5% dose was limited to 30 mg (6 ml) in dogs weighing over 30 kg [10].

LS Group

In a midline approach at the lumbosacral intervertebral space (L7-S1), the needle was advanced perpendicularly into the skin until an increase in resistance was felt, indicating that the ligamentum flavum had been reached. The stylet was removed, and an air-filled loss of resistance (LOR) syringe (Perifix; B. Braun) was connected to the needle. While the needle was advanced, the operator pressed the syringe plunger until a LOR to air injection and a sudden LOR to needle advancement were felt.

LL Group

In a paramedian approach, the needle was inserted on the dependent side, lateral to the caudal margin of the spinous process of the 6th lumbar vertebra. The needle was advanced in a slightly ventral, cranial, and medial direction while aiming for the vertebral lamina. When the needle reached the lamina, it was withdrawn and then advanced again in a more cephalad angulation until the hard-elastic consistency of the ligamentum flavum, positioned between the 5th and the 6th lumbar

intervertebral space (L5-L6), could be felt with the tip of the needle. The operator used the LOR technique to identify the epidural space as described above.

Intraoperative Evaluation and Treatment

A bolus of fentanyl (1 μg/kg IV) was used as iRA if the mean arterial pressure (MAP) rose by more than 30% of the pre-incisional value, defined as the mean value of the MAP measured during the 5 min before skin incision. The fentanyl bolus was repeated every 3 min until the MAP reached the pre-incisional value. The iRA incidence and the number of fentanyl boluses were recorded for each group.

In the event of intraoperative movement, a brisk palpebral reflex or spontaneous breathing against mechanical ventilation, propofol 1 mg/kg was administered IV. Such cases were recorded as arousal events. The occurrence of iRA in relation to body weight and age was recorded.

Events of bradycardia (HR <60 beats/min and hypotension [MAP <60 mmHg for at least 5 min or MAP <55 mmHg] were recorded. Hypotension was treated by reducing the propofol infusion rate by 20% and giving a 3 ml/kg bolus of Lactated Ringer's solution IV over 60 sec. An additional 2 ml/kg of fluid over 60 sec was administered if the MAP was increased after the first bolus. If hypotension persisted, a bolus of ephedrine (50–100 μg/kg) and/or a continuous rate infusion of norepinephrine (0.1–0.3 μg/kg/min) was given. At 30 min before the end of the operation, 0.2 mg/kg of meloxicam (5 mg/ml; Meloxidolor; Dechra, Raamsdonksveer, Holland) were administered subcutaneously (SC). At the end of the operation, the urinary bladder was voided manually. Intraoperative evaluation was performed by the same operator who administered the epidural anesthesia.

Postoperative Evaluation and Treatment

An experienced operator blinded to treatment evaluated postoperative pain at 4, 6, and 8 hr after epidural injection according to the Glasgow composite pain scale short form [21]. Methadone (10 mg/ml; Semfortan; Dechra Eurovet Animal Health BV) 0.1 mg/kg was administered IM if the pain score was ≥6/24. The dogs were re-evaluated 30 min later to check whether it was sufficient, or a further methadone IM dose (0.1 mg/kg) was needed.

The ability to walk was tested at 3, 4, 5, 8, and 12 hr after the neuraxial technique. The dogs were assisted to stand up, if necessary, but they had to walk on their own. The ability to walk was not evaluated in the dogs unable to walk before surgery or had postoperative leg bandaging. In the dogs without postoperative bandaging of the operated leg, the proprioceptive residual deficit was assessed by supporting the dog's weight and placing the dorsum of the paw on the ground. A delayed response was defined as a greater than 2-sec lag between paw placement and correction.

Urinary retention was defined as the inability to spontaneously void in the presence of bladder overdistension. Bladder overdistention was evaluated by abdominal palpation and ultrasonography in the dogs that did not spontaneously urinate within 12 hr after discharge from the veterinary clinic. The owners were instructed to monitor their dog's micturition and to report episodes of prolonged sedation and marked lameness. If the owner noted that the dog had not urinated for at least 12 hr, the dog was to be returned to the veterinarian hospital.

Statistical Analysis

The estimated sample size to detect a difference in the primary endpoint (power of 80% and alpha error of 5%) assuming an iRA incidence (derived from a pilot study) of 50% in the LS group and 25% in the LL group, respectively, [28] was 55 dogs per group. Accounting for possible dropouts, we enrolled 60 dogs per group, with interim statistics planned after at least 80 or 100 dogs met the inclusion criteria to interrupt the study if the data indicated superiority of one of the two groups. Categorical variables are reported as frequency and percentage; Fisher's exact test was used to determine frequency distribution independence between the two groups. The Lilliefors test was performed on continuous variables to check for normal distribution. Not normally distributed data are reported as the median and the range (minimum-maximum) and were analyzed by using the Mann–Whitney *U* test. The intraoperative time-to-event probability of iRA was analyzed using Kaplan–Meier survival analysis. The curves were analyzed using the log-rank test, and the hazard ratio statistic was computed. Potential confounding factors between groups were investigated with a univariate logistic regression model.

Statistical analysis was performed using MedCalc Software for Windows version 12.5 (MedCalcSoftware, Ltd., Belgium). Significance was set at 5% for all statistical methods. The odds ratio (OR) and confidence intervals (CI) were calculated using the odds ratio function of the epitools library in R version 4.1.2.

Results

Demographics (breed, age, weight, ASA class, type of surgery) are presented in Appendix A1. There was no difference between the two groups for median weight, age, or area of surgery (Appendix A1). Procedural data for median interval time in the LS and the LL group from induction to epidural injection (min), from epidural injection to skin incision (min), from skin incision to end of surgery (min), and the median anesthesia time (min) are presented in Table 1. The CONSORT diagram shows the number of dogs entered in intraoperative and postoperative analysis (Fig 1).

The study sample was 98 dogs: 47 in the LS group and 51 in the LL group. Epidural injection failed in 7/47 (15%) group LS dogs and 8/51 (16%) group LL dogs (P = 1.00), respectively. No cases of accidental dural puncture with outflow of cerebrospinal fluid were recorded.

The overall iRA percentage in the LL group (13/43; 30%) was lower than that in the LS group (21/40; 52%) (OR 0.40 with P= 0.047, 95% CI 0.16 to 0.97).

The probability of iRA over time described by a Kaplan-Meier survival curve is shown in Fig. 2. The median fentanyl (µg/kg) consumption during surgery was 1 (0-3) µg/kg in the LS group and 0 (0-2) µg/kg in the LL group, respectively (P = 0.15). The median time to the first fentanyl bolus was 45 min (range, 35-110) in the LS group and 48 min (range, 35-80) in the LL group, respectively (P = 0.76).

Body weight was checked as a confounding factor and a logistic regression was made with body weight as predictor of iRA as dependent variable. In neither group (LL and LS) body weight was shown to be a significant predictor of iRA (OR in LS group: 1.03 with P = 0.25; 95% CI 0.97 to

1.09; OR in LL group: 1.05 with $P = 0.24$; 95% CI 0.97 to 1.13). The median body weight was 14 kg (range, 2-46) in the dogs that needed iRA and 8 kg (range, 3-34) in those that didn't ($P = 0.12$).

Also, the age was not a predictor of iRA in both groups (OR in LS group: 0.93 with $P = 0.48$; 95% CI 0.79 to 1.12; OR in LL group: 1.046 with $P = 0.08$; 95% CI 0.64 to 1.03). The median age was 4.5 years (range, 0.58-12) in the dogs that received iRA and 5 years (range, 0.5-12.5) in those that didn't. ($P = 0.11$)

Hypotension developed in 10/40 (25%) LS group dogs and in 16/43 (37%) LL group dogs, respectively ($P = 0.25$) and bradycardia in 3/40 (7%) LS group dogs and in 5/43 (11%) LL group dogs, respectively ($P = 0.71$). No arousal events during surgery were recorded.

Postoperative ability to walk was evaluated in 52 dogs; no differences between the two groups were noted (Table 2).

The odds ratio to have a proprioceptive residual deficit at 8 hr in Group LL compared to group LS was 7.14 ($P = 0.01$; 95% CI 33.33 to 1.85). Proprioceptive residual deficit at 8 hr was recorded in 3/26 (12%) group LS dogs and in 13/26 (50%) group LL dogs ($P = 0.01$).

Median body weight is 8 (2-33) kg and 20 (3-34) kg in group LS and LL respectively and differs for body weight ($P = 0.01$). Body weight was checked as a confounding factor and a logistic regression was made with body weight as predictor of proprioceptive residual block as dependent variable. In neither group (LL and LS) body weight was shown to be a significant predictor of residual blockage (OR in LL group: 1.07 with $P = 0.23$; 95% CI 0.98 to 1.17; OR in LL group: 1.05 with $P = 0.55$; 95% CI 0.94 to 1.17).

A proprioceptive residual deficit at 24 hr after epidural injection was recorded in 1 LL group dog, which resolved completely within 36 hr.

All dogs were evaluated according to the Glasgow pain scale at 4 hr after epidural injection, 35/43 (81%) and 30/40 (75%) at 6 hr, and 17/43 (39%), and 15/40 (37%) at 8 hr in the LS group and the LL group, respectively. None required postoperative rescue analgesia during the observation period.

No episodes of postoperative urinary retention, pruritus, or neurological damage were recorded.

Discussion

To our best knowledge, this is the first clinical experimental study in dogs to show that the space of epidural injection affects EA efficacy and to report a consistent number of epidural punctures performed via the paramedian approach. Less need for iRA was recorded for the dogs that received a more cranial injection of LA in the epidural space (LL group) than those that received lumbosacral administration (LG group). A possible explanation for the difference is the better matching between the spinal metamers innerving the body area operated and the local anesthetic block in the LL group [5, 19]. The more cranial LA injection into the epidural space may have allowed for a more cranial spread of the LA throughout the epidural canal, thus providing a more profound nerve block of the L4-L6 spinal metamers from which the femoral nerve derives [18, 22]. In addition, the abundant fat surrounding the cauda equina, which works as a reservoir of LA, may limit the cranial spread of LA when an epidural injection is given at the lumbosacral intervertebral space. Furthermore, the lumbar intumescence reduces the epidural space from the L3 to the L6 intervertebral space and this may have facilitated the spread of the LA in the LL group [14, 26].

The need for iRA was significantly lower in the LL group, though its incidence remained relatively high (30%). The success rate of epidural analgesia is a frequent clinical problem in human medicine, where epidural block fails to provide adequate surgical analgesia in up to 50% of cases [4, 11]. At any rate, we may speculate that epidural anesthesia is subjected to a certain degree of failure no matter a failure in the technical execution of the block and the dosing regimen, which could stem from the difficulty to achieve an even distribution of the LA within the epidural space [8]. There is some evidence that the use of air for identifying the epidural space with the LOR technique [13] can affect epidural spread and reduce block quality [23]. We cannot rule out that the use of air in the LOR technique may have contributed to increasing the incidence of iRA.

We noted, however, that immediate postoperative analgesia was sufficient in all dogs in which postoperative pain was evaluated. Nevertheless, the brevity of postoperative pain monitoring precludes a comparison of the overall duration of postoperative analgesia between the two techniques. Nearly 90% of the dogs in both groups were able to walk at 8 hr postoperative; however, a proprioceptive residual deficit at 8 hr was recorded in 50% of the LL group dogs and in 13% of the LS group dogs. It is reasonable to assume that a longer residual block ensued after the more profound block in the LL group (lower iRA incidence).

Body weight didn't reach a statistical significance as predictor of proprioceptive residual deficit.

For this study we limited the LA dosage to 6 ml in dogs weighing >30 kg [10]. Though this cut-off lacks scientific evidence, it has been suggested [2] to shorten motor recovery in big sized dog. The dose regimen used in our study did not seem to increase the incidence of prolonged motor block and the need for iRA in the large dogs. Previous studies have suggested dose regimens according to length of the spine [2, 17] based on the hypothesis that there is no linear relationship between body weight and LA dose requirement. This notion is largely supported by anatomical studies performed with methylene blue in dogs [25]. However, correlating the level of an effective nerve block with the spread of a marker solution can be misleading. Studies using contrast medium in humans failed to find a strong correlation between the epidural spread of a solution and the level of the sensitive block [26].

Ours is the first clinical study to report a consistent number of epidural punctures performed via the paramedian technique and to show that it is not burdened by a higher incidence of procedural failure than the median approach to L7-S1 although the intervertebral spaces cranial to L7-S1 are much smaller. The paramedian approach offers bony landmarks (e.g., the spinal process and the vertebral lamina) that help direct the needle toward the interspinous space. Differently, in the median technique, if the bone instead of the ligamentous flavum is reached at the first attempt, the operator does not know where to redirect the needle. One concern with using a more cranial epidural approach is the potentially higher risk of damaging the spinal cord than at the L7-S1 level. In humans, however,

when thoracic epidural catheterization is performed by a trained operator, the incidence of permanent neurological complications can be as low as <0.02% [1]. Monitoring needle insertion into the epidural space remains a criticality that impacts on the success of the block and reduces the risk of iatrogenic nerve damage. In our study, we used the LOR technique coupled with radiography to increase the accuracy of the epidural technique, which can be achieved only with LOR. Nonetheless, the risk of intrathecal puncture or nerve damage cannot be completely ruled out. Future studies are required to prove the safety profile of the paramedian epidural anesthesia technique in dogs.

A proprioceptive residual block at 24 hr was recorded in one LL group dog. The transient neurological syndrome following epidural anesthesia is a well-known complication in humans [3, 20]. The syndrome is unlikely related to mechanical problems. A more plausible explanation is the profound effect of the nerve response spectrum to the LA, since neuronal reaction to LA is variable in nature [20].

Our study has several limitations. The lack of standardization of the type of surgery may have introduced a bias in the evaluation of iRA, though the type of surgery did not differ between the two groups. The anesthesiologists involved in the study were not blinded to group treatment, and they were free to manage anesthetic depth without a pre-set protocol. This limitation may have been an additional source of bias. Finally, the postoperative observation period was too short to evaluate postoperative rescue analgesia needs thoroughly. Further studies are needed to define this aspect better.

In this sample of dogs undergoing hindlimb orthopedic surgery, the occurrence of iRA was lower in the group that received an epidural injection of LA at the L5-L6 level than in the group that received an epidural injection at the lumbosacral level, but the recovery of nerve function was slower. Further studies are needed to determine whether injection at L5-L6 with a lower LA dosage can reduce the duration of postoperative residual block without increasing the need for iRA.

Conflict of Interest Statement: The authors declare no conflict of interest

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Appendix A: Demographic data of dogs [median (range)] that met the inclusion criteria for allocation to the LS group or the LL group in which EA was successful performed. ASA class (American Society of Anaesthesiologists); TPLO (tibial plate levelling osteotomy); FHNO (femoral head and neck ostectomy).

	Group LS (n=40)	Group LL (n=43)	*P*
Breed (no.)	13 Mixed breed 3 Labrador 3 Yorkshire 2 Pincher 2 Dachshund 2 Beagle 2 Jack Russel 13 Other breeds	17 Mixed breed 4 Labrador 4 AMSTAF 3 Beagle 2 Pincher 2 Setter 2 Yorkshire 9 Other breeds	
Age (years)	5.5 (range, 0.5-12)	4 (range, 0.6-13)	0.24
Weight (kg)	8 (range, 2-46)	15 (range, 3-34)	0.15
Type of surgery	1 Achilles tendon repair 1 Osteosynthesis of a tibial fracture 11 FHNO 3 Medial patellar luxation repair 5 Extracapsular repair of anterior cruciate ligament 18 TPLO 1 Osteosynthesis of femoral fracture	1 Achilles tendon repair 3 Osteosynthesis of a tibial fracture 4 FHNO 3 Medial patellar luxation repair 4 Extracapsular repair of anterior cruciate ligament 24 TPLO 4 Osteosynthesis of femoral fracture	

ASA Class (no.)	ASA I 37/40	ASA I 35/43	0.20
	ASA II 3/40	ASA II 8/43	0.20

Table 1 Procedural data for the Group LS (epidural anesthesia placed at the lumbosacral junction) and the Group LL (epidural anesthesia placed to the L5-L6 junction).

	Group LS (n=40)	Group LL (n=43)	*P*
Median propofol induction bolus (mg/kg)	5.5 (range, 4.0-8.0)	5.0 (range, 4.0-7.0)	0.43
Median propofol rate infusion (mg/kg/hr) after epidural injection	24 (range, 15-30)	23 (range, 15-35)	1.00
Median time between induction and epidural injection (min)	16 (range, 15-35)	17 (range, 15-28)	0.70
Median time between epidural injection and skin incision (min)	25 (range, 21-28)	28 (range, 22-35)	0.42
Median time between epidural injection and end of surgery (min)	90 (range, 60-120)	95 (range, 60-110)	0.65
Median time of entire anaesthesia duration (min)	115 (range, 90-160)	110 (range, 85-140)	0.51

Table 2. Percentage of dogs able to walk (%) at 3, 4, 5, 8, and 12 hr after local anaesthetic injection and proprioceptive residual deficit at 8 hr in 52 dogs. No differences between the two groups concerning the ability to walk were recorded. Proprioceptive residual deficit at 8 hr results higher in Group LL (epidural anesthesia placed at the lumbosacral junction), (*P* = 0.01). Group LL (epidural anesthesia placed to the L5-L6 junction).

	Group LS n=26 (%)	Group LL n=26 (%)	*P*
Ability to walk			
At 3 hr	1/26 (4)	3/26 (12)	0.35
At 4 hr	5/26 (19)	5/26 (19)	1.00
At 5 hr	18/26 (70)	11/26 (42)	0.09
At 8 hr	24/26 (92)	23/26 (88)	1.00
At 12 hr	26/26 (100)	25/26 (96)	1.00
Proprioceptive residual deficit			
At 8 hr	3/26 (12)	13/26 (50)	0.01

FIG. 1 CONSORT 2010 Fw Diagram

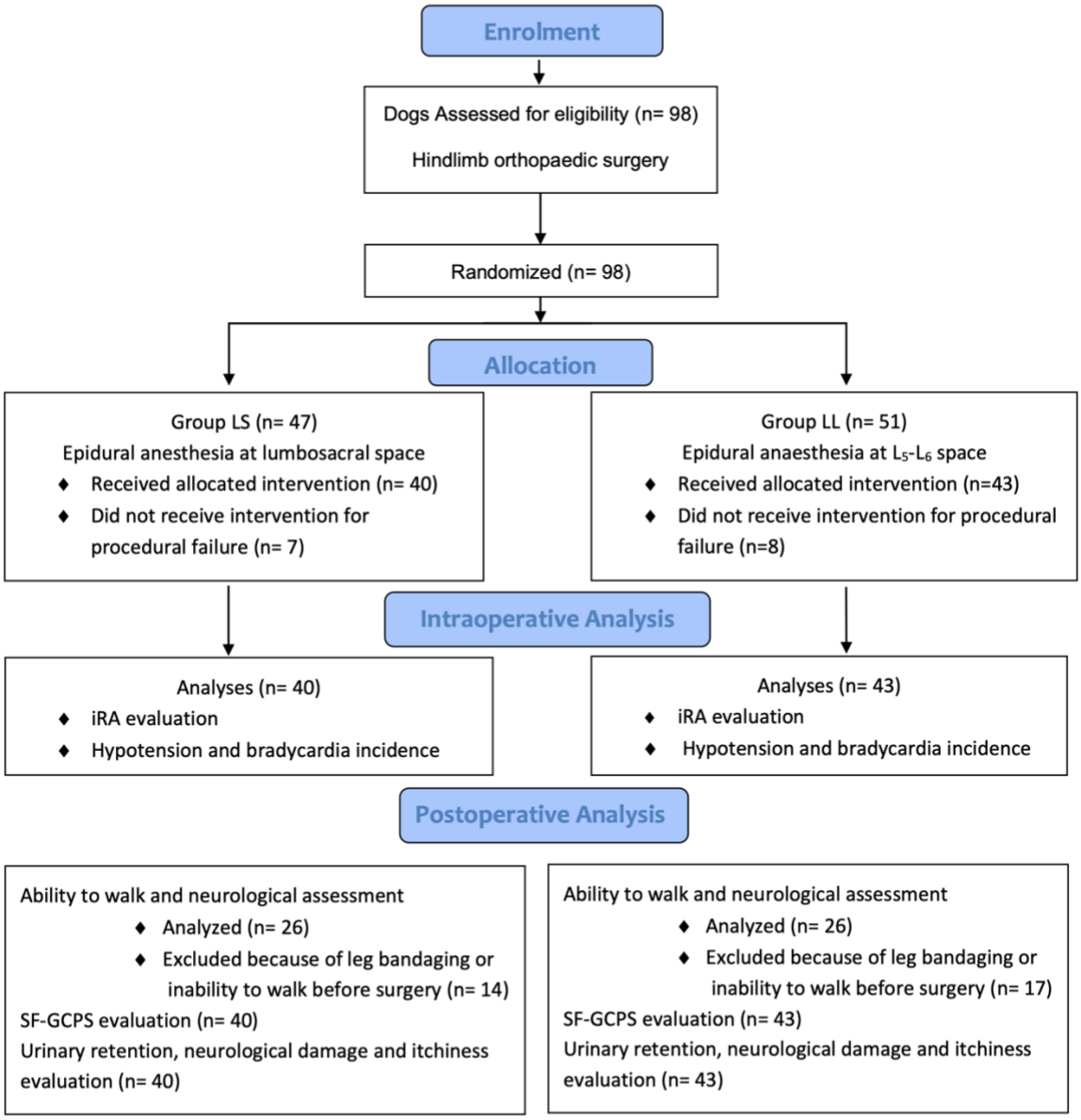

Figure 2 The time-to-event probability of intraoperative rescue analgesia (iRA) was analyzed using a Kaplan–Meier survival analysis for the two groups. The iRA percentage (100-iRa survival probability) at 80 min after epidural injection was 45% in the LS group and 30% in the LL group, respectively. The iRA survival curves differed significantly for the observation period (P = 0.046 log-rank test). Hazard ratios for the LL group with 95% CI were 0.50 (0.25 to 0.99). Censored' refers to subjects for which no events (iRA) were observed during surgery. A small vertical line denoted censored data in the graph.