RESEARCH PAPER

Physiological variables for the objective detection of nerve block failure in dogs

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Abstract

Objective To identify physiological variables for objectively detecting nociception indicative of intraoperative peripheral nerve block failure.

Study design A double-blinded randomized clinical study.

Animals A sample of 14 male (40.8 ± 12 kg; mean ± standard deviation) and 16 female (34.3 ± 11.4 kg) client-owned dogs.

Methods Dogs were randomly assigned to one of three groups for psoas compartment and proximal sciatic nerve blocks (0.2 mL kg^{-1} per site): guided bupivacaine (GBB), or saline (GSB) block or a blind bupivacaine block (BBB). Guided blocks were performed using an ultrasound-peripheral nerve locator combination. Premedication consisted of medetomidine 0.01 mg kg^{-1} and morphine 0.3 mg kg^{-1}. General anaesthesia was induced with propofol and maintained with isoflurane in oxygen. Receiver operator characteristic curve analysis was used to compare actual values and change in values of physiological variables between GSB and GBB. The Youden index and associated criterion for each physiological variable were used to determine an objective measure for nociception. Fisher's exact *t* test, McNemar's test and Cohen's kappa statistical analysis were used to determine association, differences and inter-score reliability between the objective and subjective scoring for BBB.

Results Cardiovascular variables had good discriminating ability to identify a nociceptive response ($p < 0.01$). The Youden indices for mean (MAP) and diastolic (DAP) arterial pressure were most reliable in detecting nociception. The highest sensitivity was that of ΔMAP (100%) with good agreement between the subjective and objective scores of Δheart rate or systolic arterial pressure (SAP). The use of ΔMAP, ΔSAP, ΔDAP had the best ability in indicating peripheral nerve block failure ($p < 0.001$).

Conclusions and clinical relevance Blood pressure values can detect a response to surgical stimulus in adequately anaesthetized dogs. The use of ΔMAP, ΔSAP or ΔDAP may be considered as objective measures to detect nerve block failure.

Keywords analgesia, failure, intraoperative nociception, nerve block, physiological variables.

Introduction

Nociception is the process by which the peripheral and central nervous system encodes a noxious stimulus (Merskey & Bogduk 1994). Post-anaesthetic pain because of the perception of these encoded signals plays an integral role in postoperative outcome. Concepts such as Enhanced Recovery After Surgery (ERAS) and fast-track surgery focus on abbreviating the time to full recovery. Peripheral nerve blocks play an important role in ERAS (Campoy 2022). There is a correlation between the intensity of the immediate postoperative pain and the development of persistent (maladaptive) pain (Kehlet et al. 2006). Therefore, the importance of detecting nerve block failure intraoperatively prior to the recovery period is apparent.

The change in physiological variables relating to the autonomic nervous system (ANS) forms the basis of several methods used for the assessment of nociception. Nociception results in an increased sympathetic tone (Miller & O'Callaghan 2002) which is mostly as a result of the intersection of the sympathetic branch of the ANS and nociceptive pathways (Benarroch 2006). Physiological variables [heart rate (HR), arterial blood pressure (BP), respiratory rate (f_R) and tidal volume (V_T)] are still used subjectively to detect nociception in humans (Stomberg et al. 2001). A 20% increase in mean arterial pressure (MAP) and HR has been used as criteria to determine peripheral nerve block failure in dogs (Papadopoulos et al. 2022). An increase in MAP is a sensitive indicator of nociception in isoflurane-anaesthetized pigs and horses (Haga et al. 2001; Haga & Dolvik 2005). Derivatives of physiological variables have been used to create objective measures for assessing the absence of nociception. The most common of these is heart rate variability (HRV) which has been assessed in dogs (Bergfeld et al. 2014). Algorithms that incorporate different combinations of HR, BP responses, HRV, pulse beat interval and pulse wave amplitude have also been developed. The cardiovascular depth of analgesic (CARDEAN) index makes use of pulse oximetry, electrocardiogram and oscillometric BP measurements (Rossi et al. 2012). The perfusion index uses the waveforms of the plethysmograph to analyse pulse interval and amplitude (Bonhomme et al. 2011; Bergmann et al. 2013). Perfusion index has been used to determine peripheral nerve block success in dogs (Gatson et al. 2016) Pupillometry assesses the ANS tone by means of an infrared pupillometer (Mills et al. 2022). Despite all these assessments, there is still no consensus on how to objectively confirm nociception, especially in anaesthetized veterinary patients (Ledowski 2019).

There is need for a practical, objective way to detect intraoperative nociception which is indicative of nerve block failure and thereby prompt the veterinarian to administer analgesics before the animal recovers.

The aim of this study was to identify routinely measured physiological variables that could be used to objectively detect a response to surgical stimulus and therefore indicate intraoperative nerve block failure. The null hypothesis was that physiological variables would be no different between ultrasound (US)-peripheral nerve locator (PNL)–guided blocks using saline compared with bupivacaine in anaesthetized dogs during arthrotomy.

Materials and methods

Animals and housing

A sample of 30 client-owned dogs of different breeds that were to undergo an arthrotomy and dynamic cranial cruciate ligament repair were included in the study after informed owner consent. Inclusion criteria were dogs weighing $\geq$ 20 kg with unilateral pathology of a stifle joint requiring an arthrotomy and deemed healthy based on clinical examination and routine haematology and serum biochemistry assessments (American Society Anesthesiologists classification score of I or II). Dogs that had radiographic evidence of concurrent osteoarthritic changes in any other joint of the pelvic limb or with concurrent neurological disease were not included. Dogs were excluded if peripheral nerve blocks were contraindicated such as coagulopathy or infection at the nerve block site. Hypotension or unsuccessful arterial cannulation were also used as exclusion criteria. The study was conducted at Valley Farm Animal Hospital, Pretoria, Gauteng, RSA. The dogs were housed in hospital cages and fed kibble twice a day and water was freely available except during the immediate perioperative period. The study was approved by the Animal Ethics Committee of the University of Pretoria (V035-17).

Study design

A prospective double-blinded randomized clinical trial was planned. The study complied with CONSORT guidelines. Population sampling was opportunistic, following informed client consent. Randomization was achieved by means of an online balanced block randomization technique (two investigators, three groups; Sealed Envelope Ltd., UK). Dogs were randomly assigned to one of two investigators and one of three groups: guided bupivacaine block (GBB), guided saline block (GSB) or blind bupivacaine block (BBB). The second block for randomization (group) was only known by the assigned investigator. The other investigator assigned to recording the variables was blinded to the allocated group. The study was divided into two parts (Fig. S1).

Part A: To evaluate commonly measured physiological variables to detect if the magnitude of response to surgical stimulation between GSB and GBB groups was different. These physiological variables were used to objectively score nerve block outcome.

Part B: To assess agreement of the objective score of nerve block outcome determined in part A with subjective and confidence scoring. A BBB was performed and objective and subjective scores were assigned and agreement between them were assessed.

Sample size

The sample size necessary for comparison of means was calculated at 10 dogs per group. MAP was used as the variable of interest for the calculation by applying these assumptions: type I error of 0.05, type II error of 0.20, difference of means of 4 mmHg and standard deviation of 3 mmHg.

Experimental procedures

The dogs were starved of food for 6 hours prior to premedication. The order and timing of procedures was standardized (Fig. S2). Premedication consisted of medetomidine 0.01 mg kg^{-1} (Domitor, 1 mg mL^{-1}; Zoetis; RSA) and morphine 0.3 mg kg^{-1} (Morphine, 10 mg mL^{-1}; Pharma-Q Holdings (Pty) Ltd., RSA) mixed in one syringe and injected intramuscularly (IM). Dogs were left undisturbed for 15 minutes. An intravenous (IV) cannula (Jelco 20 G; Smiths Medical, UK) was aseptically placed and secured in one of the cephalic veins. At 30 minutes after premedication, propofol 2–4 mg kg^{-1} [Fresenius Propoven 1%; Fresenius Kabi (Pty) Ltd., RSA] was administered IV until the trachea could be intubated with a cuffed 8.0–12 mm inner diameter polyvinyl endotracheal tube (ETT) (Ho-lee tube;

JC Medical, RSA). The ETT was connected to a circle circuit with a fresh gas (mixture of oxygen and medical air with an F_IO_2 of 0.5) flow rate of 2 L minute^{-1}. Anaesthesia was maintained using isoflurane in oxygen [Isofor; Safeline Pharmaceuticals (Pty) Ltd., RSA] with the vaporizer (Penlon Sigma Delta) initially set at 2% and titrated to an end-tidal isoflurane concentration (F_E'Iso) of 1.6%. Perioperative antibiotics using cefazolin [Zefkol, 100 mg mL^{-1}; Litha Pharma (Pty) Ltd., RSA] was administered IV at 20 mg kg^{-1} after induction of anaesthesia and repeated every 90 minutes during anaesthesia.

The dog was placed in lateral recumbency with the surgical pelvic limb in the non-dependent position. The block sites were clipped and aseptically prepared. The psoas compartment block (Fig. 1a; Mahler 2012; Portela et al. 2013) was performed before the lateral proximal sciatic nerve block (Fig. 1b; Costa-Farré et al. 2011). Injectate volume for all blocks was standardized at 0.2 mL kg^{-1}. Saline (Sodium Chloride 0.9%; Fresenius Kabi) was administered for GSB and bupivacaine (Macaine 5 mg mL^{-1}; Adcock Ingram, RSA) for GBB and BBB. Guided blocks were performed using US (Esaote MyLab-One; Lomaen Medical, RSA) with a 4–13 MHz linear transducer (Touch SL3323, Esaote MyLab-One; Lomaen Medical) in combination with a PNL (Stimpod NMS 450; Xavant Technology, RSA). On completion of the blocks, a timer was started to count down from 60 minutes. A confidence score of the block was recorded (Table 1) along with an assessment of the ease of landmark palpation. Then the surgical site was shaved and aseptically prepared. A cannula (Jelco 22 gauge; Smiths Medical) was aseptically introduced and secured in the dorsopedal artery contralateral to the operated limb being operated. Once the surgical preparation was complete, the dog was moved to the theatre table and placed in dorsal recumbency. The dog was connected to the anaesthetic machine, as described previously, and monitor sensors and leads were attached. The invasive BP transducer [Sembu TR transducers; SSEM Mthembu Medical (Pty) Ltd, RSA] was zeroed to atmospheric pressure at the level of the sternal manubrium. A fast-flush test was performed to subjectively ensure adequate

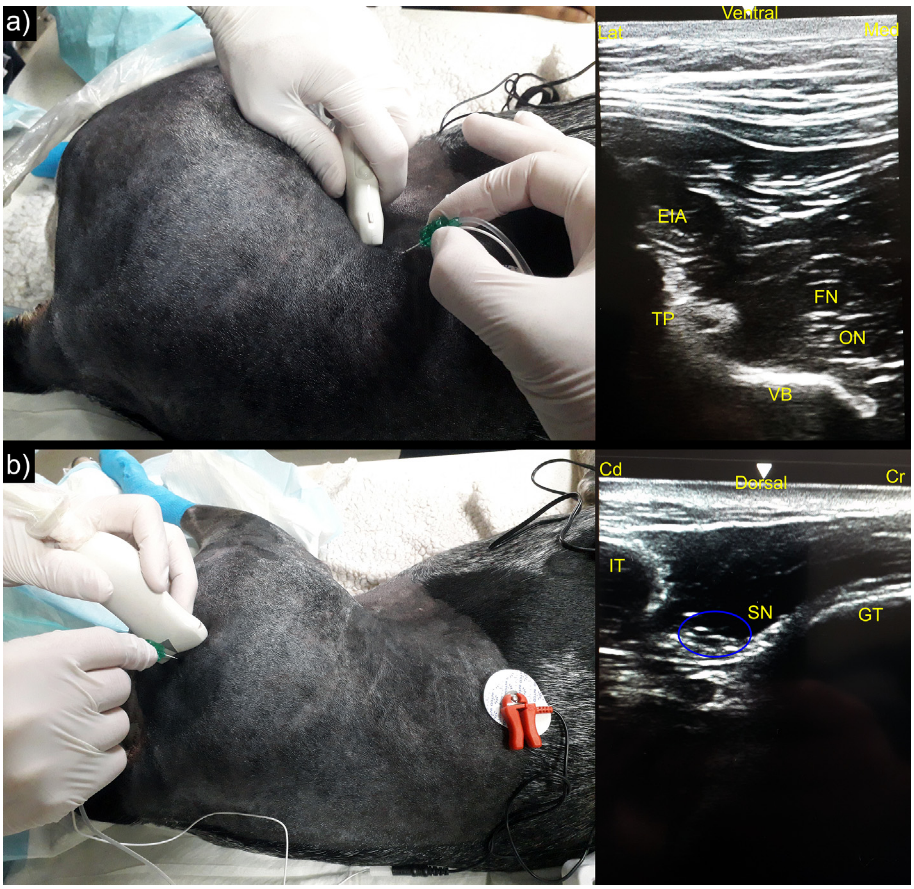

Figure 1 Ultrasound and peripheral nerve locator–guided psoas compartment (a) and lateral proximal sciatic (b) nerve block being performed on a dog. Ultrasound images obtained are shown on the right. External iliac artery (EIA), seventh lumbar vertebral body (VB) and its transverse process (TP), femoral nerve (FN) and obturator nerve (ON), ischiatic tuberosity (IT), greater trochanter of the femur (GT) and the sciatic nerve (SN) indicated.

Table 1 Block confidence score used for the guided saline (GSB; 10 dogs), guided bupivacaine (GBB; 10 dogs) and blind bupivacaine (GBB) groups. Scale of 1 (poor) to 4 (high) confidence scoring that the block will be successful for guided (ultrasound and peripheral nerve locator) and blind techniques, respectively. The score was performed immediately post block prior to surgery.

Subjective score	Description
Guided	
1	Not confident at all, no confidence of needle in correct position
2	Poor confidence, appropriate response with peripheral nerve locator (PNL), but not confirmed with ultrasound
3	Fairly confident, PNL response, correct anatomical location but no doughnut sign
4	Very confident, PNL response, visualization of doughnut sign
Blind	
1	Not confident at all, cannot properly identify anatomical landmarks
2	Poor confidence, unsure of facial plane
3	Fairly confident
4	Very confident, nerve response observed

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dampening of invasive BP system. An isotonic crystalloid (lactated Ringer's solution; Fresenius Kabi) was administered at 5 mL kg^{-1} $hour^{-1}$ for the duration of anaesthesia. The first surgical incision was planned for 60 minutes after the blocks were performed.

Intraoperative monitoring

Physiological variables were monitored with a Primus (Dräger, RSA) anaesthetic workstation and multiparameter physiologic monitor (Infinity Delta XL; Dräger) by an experienced anaesthetist (blinded investigator). During the surgical procedure, f_R, HR, invasive SAP, MAP and DAP, oesophageal temperature (T) and Fe′Iso were monitored continuously but recorded at standardized time points relevant to this study. The study time points were 1 minute before, at the time of (0 minutes) and 1, 2, 4, 5, 6, 8, 10, 15, 20 and 25 minutes after the skin incision (first surgical event). In addition, event notes were made on the datasheet when the joint was opened and distended (arthrotomy; second surgical event), using a stifle extractor for at least 2 minutes. A binomial subjective score was assigned by the anaesthetist who was unaware of the allocated group as 'Yes' if there was a response to surgical stimulation or 'No' if there was no discernible response at each time point. Criteria for a response to surgical stimulation (Yes) was movement, a lightened plane of anaesthesia or an increase (>25%) in the measured physiological variable values.

Intraoperative analgesia and rescue interventions

Morphine [0.3 mg kg^{-1}; Morphine, 10 mg mL^{-1}; Pharma-Q Holdings (Pty) Ltd.] was administered to all dogs intraoperatively every 2 hours and postoperatively every 4 hours for 24 hours. Meloxicam (5 mg mL^{-1}, Metacam; Boehringer Ingelheim, RSA) 0.2 mg kg^{-1} was administered subcutaneously 1 hour prior to induction followed by a daily oral dose of 0.1 mg kg^{-1} for 5 days. Furthermore, dogs assigned to the GSB group were administered US-guided nerve blocks (0.1 mL kg^{-1} bupivacaine 5 mg mL^{-1} per site) of the medial saphenous and lateral proximal sciatic nerves (Costa-Farré et al. 2011) at the end of surgery prior to recovery.

In dogs where the anaesthetist deemed the response to surgical stimulation as severe (tachycardia, tachypnoea, rapidly lightened plane of anaesthesia), rescue analgesic drugs were administered without delay. The rescue protocol consisted of transiently increasing the Fe′Iso to 1.8%–2.0%, administering a single intramuscular dose of ketamine 1 mg kg^{-1} and a constant rate infusion of fentanyl 0.005 mg kg^{-1} $hour^{-1}$ intraoperatively and postoperatively for 24 hours.

Data analysis

Physiological variables recorded at the time of the second event (arthrotomy) and up to two time points after were included. Data at these time points were examined and the highest values for the majority of variables within that time point were taken as a response to surgical stimulus. If there was no change in the variables, then the values at the time of the event were used. Data distribution was assessed by inspecting descriptive statistics, histograms plots and the Anderson–Darling test for normality.

Part A

A binomial classification was used where dogs were expected to either respond (Yes; GSB) or not respond (No; GBB) to surgical stimulation. This binomial classification was applied to receiver operator characteristic (ROC) curves comparing the actual value and the change in the physiological variables between GSB and GBB at the arthrotomy event. The change in value of a variable (Δ value) was calculated by subtracting the value at the event from the value recorded 1 minute before start of surgery. The prevalence of the response to surgery was set to 50%. The Youden index (J) and associated criterion for each variable was used as the objective cut-off point between response (indicating block failure) and no response to surgical stimulation. In addition, sensitivity, specificity, positive and negative likelihood ratios, and positive and negative predictive values for the detection of nerve block failure were calculated from criterion values.

Part B

The associated criterion for each variable (determined in part A) was used as an objective score to detect a response to surgical stimulation in the BBB group (10 dogs). The agreement between the objective score and the binomial subjective score for each variable in the BBB group was assessed by means of 2 × 2 contingency tables. Fisher's exact test (determine association), McNemar's test (determine differences) and Cohen's kappa (assess inter-score reliability) values were calculated. The Kendall tau-b rank correlation coefficient was used to assess the agreement between the binomial subjective and objective score for each of the assigned confidence scores.

Data were presented as mean ± standard deviation. Data analyses were performed using commercially available statistical software (Minitab version 18; Minitab Ltd. LLC; PA, USA and MedCalc Statistical Software version 20.211; MedCalc Software, Belgium). Fisher's exact, McNemar and Kendall tau-b p values of <0.05 were considered significant. Cohen's kappa values were assessed as: no (≤0), slight (0.01−0.20), fair (0.21−0.40), moderate (0.41−0.60), substantial (0.61−0.80) and perfect (0.81−1.00) agreement.

Results

A sample of 14 male (40.8 ± 12 kg body weight; 5 ± 1 out of 9 body condition; 4.4 ± 2.6 years old) and 16 female (34.3 ± 11.4 kg body weight; 6 ± 2 out of 9 body condition; 4.6 ± 2.5 years old) dogs were included in the study. All dogs completed the study, none of the responses to surgical stimulus were severe and therefore none of the dogs required rescue analgesic intervention. Anaesthetic times were 116.5 ± 37.4 minutes for premedication to arthrotomy and 71.3 ± 24.4 minutes for block to arthrotomy.

Part A

The results for the ROC analysis indicated that cardiovascular variables had a good and respiratory variables had a poor discriminating ability in distinguishing a response to surgical stimulus (Table 2).

Evaluation of J indicated that HR, ΔHR, f_R and Δf_R did not meet the empirical benchmark (i.e. J > 0.5) for diagnostic purposes. The J for MAP and DAP were the most effective for detecting a response to surgical stimulus. The highest specificity was that of SAP. However, the disproportion in sensitivity (60%) and specificity (95%) made SAP a poor indicator on its own. The highest sensitivity was that of ΔMAP. However, the disproportion in sensitivity (100%) and specificity (60%) made ΔMAP a poor indicator on its own.

Part B

There was an association between the subjective and objective scores with ΔHR or SAP only (Fig. 2). There was no difference between objective and subjective scores for ΔHR or SAP. There was no agreement for Δf_R, slight agreement for HR, ΔSAP, ΔMAP and f_R, fair agreement for MAP, DAP and ΔDAP, moderate agreement for ΔHR and substantial agreement for SAP with the subjective score. The strength and direction of the association (Kendall tau-b) of the objective score with each confidence score is shown in Fig. 3. BP variables and their effectiveness in objective detection of nerve block failure are presented in Table 3.

Discussion

In this study, dogs in the GSB group that were surgically stimulated during a surgical plane of anaesthesia demonstrated a detectable response to arthrotomy. The cardiovascular variables, unlike the respiratory variables, showed good diagnostic ability to detect nociception. We propose the use of ΔMAP (>6 mmHg), ΔSAP (>10 mmHg) or ΔDAP (>8 mmHg) as cut-off values for the objective detection of nerve block failure in dogs undergoing arthrotomy. There was a poor association between nerve block confidence scoring and the outcome of the block based on subjective and objective scores.

Nurse anaesthetists, practising in human medicine, speculated that a degree of overlap existed in physiological variables used for the intraoperative assessment of a response to surgical stimulation and anaesthetic depth (Stomberg et al. 2001). However, cardiovascular variables (HR and BP) and ventilatory variables (f_R and VT) had better association with a response to surgical stimulation (i.e. nociception) compared with the assessment of anaesthetic depth (Stomberg et al. 2001). However, an inadequate plane of anaesthesia can make the distinction between nociception and arousal difficult to determine. The minimum alveolar concentration (MAC) of isoflurane in the dog is 1.28% (Steffey & Howland 1977). A MAC multiple of 1.2−1.4 (Fe′Iso of 1.54%−79%) is required to inhibit movement in response to a noxious stimulus in 95% of anaesthetized humans (De Jong & Eger 1975; Aranake et al. 2013). The current study was not a MAC finding study and all dogs were maintained at a clinically relevant Fe′Iso of 1.6 ± 0.06%. In human medicine, isoflurane at a concentration of 1.5 times MAC did not prevent a haemodynamic response to noxious stimuli (Inada et al. 1997). Similarly, in our study,

Table 2 Summary of the receiver operator characteristic (ROC) analysis of guided saline block (GSB; 10 dogs; response to surgical stimulus) and guided bupivacaine block (GBB; 10 dogs; no response to surgical stimulus) indicating the maximum potential effectiveness of heart rate (HR), ΔHR, respiratory rate (f_R), Δf_R, systolic arterial pressure (SAP), ΔSAP, mean arterial pressure (MAP), ΔMAP, diastolic arterial pressure (DAP) and ΔDAP in detecting a response to surgical stimulus (stifle arthrotomy). All dogs were premedicated with medetomidine 0.01 mg kg^{-1} and morphine 0.3 mg kg^{-1} injected intramuscularly, anaesthesia was induced with propofol and maintained with isoflurane (Fe′Iso 1.6%) in oxygen.

	ROC AUC	ROC 95% CI	*p*	Z	J	J 95% CI	AC	AC 95% CI	SE (%)	SP (%)	PPV	NPV	PLR	NLR
HR	0.75	0.59–0.88	0.0023	3.05	0.5	0.22–0.65	>77	67–83	80	70	72.7	77.8	2.67	0.29
ΔHR	0.76	0.6–0.88	0.0007	3.39	0.45	0.2–0.65	>1	−2 to 10	55	90	84.6	66.7	5.5	0.5
f_R	0.57	0.4–0.72	0.46	0.73	0.2	0.1–0.35	>10	6–13	40	80	66.7	57.1	2	0.75
Δf_R	0.5	0.34–0.66	0.98	0.03	0.15	0.1–0.2	>−1	−4–3	65	20	44.8	36.4	0.81	1.75
SAP	0.82	0.66–0.92	<0.0001	4.77	0.55	0.25–0.65	>127	123–135	60	95	92.3	70.4	12	0.42
ΔSAP	0.8	0.64–0.91	0.0001	3.81	0.6	0.35–0.75	>10	2–19	95	65	73.1	92.9	2.71	0.08
MAP	0.89	0.76–0.97	<0.0001	7.77	0.7	0.45–0.85	>80	74–84	90	80	81.8	88.9	4.5	0.13
ΔMAP	0.8	0,69–0.94	<0.0001	4.90	0.6	0.3–0.75	>6	1–12	100	60	71.4	100	2.5	0.00
DAP	0.93	0.8–0.99	<0.0001	9.69	0.75	0.42–0.9	>73	68–78	85	90	89.5	85.7	8.5	0.17
ΔDAP	0.86	0.72–0.95	<0.0001	5.76	0.65	0.33–0.8	>8	2–21	95	70	76.0	93.3	3.17	0.07

AC, associated criterion; AUC, area under the curve; CI, confidence interval; J, Youden index; NLR, negative likelihood ratio; NPV, negative predictive value; *p*, significance level; PLR, positive likelihood ratio; positive predictive value; SE, sensitivity; SP, specificity; Z, Z-score.

where dogs were anaesthetized at 1.25 times MAC, there was a detectable haemodynamic response to surgical stimulation in the GSB group when compared with the GBB group.

Ward et al. (2018) suggested an overconfidence in the success of peripheral nerve block techniques leading to a biased subjective assessment of the response to a surgical stimulus. Furthermore, intraoperative subjective assessment of a response to surgical stimulation in humans is reliant on a change in cardiovascular and respiratory variables (Stomberg et al. 2001). This can explain why our subjective score was similar to the objective scores for ΔHR and SAP for the detection of nerve block failure. However, the clinical application of using the cut-off values for HR (>77 beats $minute^{-1}$ and ΔHR (>1 beat $minute^{-1}$) to define a response to surgical stimulation is impractical. HR of 77 beats $minute^{-1}$ or greater overlaps with the expected HR range for anaesthetized dogs and a change of 1 beat $minute^{-1}$ is too small a fluctuation to arouse any concern (Redondo et al. 2007). In some of the dogs in the GSB group, a decrease in HR was evident. The decrease in HR occurred concurrently with a substantial increase in DAP and was most likely as a result of an arterial baroreceptor reflex. The use of SAP to detect a response to surgical stimulus was inadequate.

The use of the absolute associated criterion values of the cardiovascular variables in this study might not be directly translatable to every dog undergoing a surgical procedure and general anaesthesia. The cardiovascular effects of isoflurane and medetomidine and the antinociceptive effect of medetomidine and morphine most likely had an unquantifiable influence on the associated criterion values. It is important to consider the effect of the different anaesthetic drug combinations administered and the cardiovascular system function of the dog. Therefore, the authors speculate that using ΔBP values are better suited for detecting a response to surgical stimulation. Furthermore, based on negative predictive values, we speculate that the ΔBP variables would have fewer false negatives associated with their use. However, the ΔBP variables lack specificity (≤70%). Based on the positive predictive values, we speculate that ΔBP variables might have false positives associated with their use. Thought should be given to the relevance of false-positive nerve block failures in veterinary anaesthesia and its effect on ERAS (Campoy 2022). Unnecessary analgesic interventions (polypharmacy), owing to a high proportion of false positives, could result in longer periods of sedation, increased time to ambulation, increased time to intake of oral solids and fluids and therefore an increased duration of hospital stay.

There is a major limitation regarding the use of recommended BP variables. Consideration should be given to the availability and accuracy of BP monitoring equipment. We speculate that the use of oscillometric BP measurement is more conventional than invasive BP measurement for orthopaedic surgery in otherwise healthy animals. The degree of agreement required between invasive arterial BP and veterinary-specific oscillometric devices is wide. According to the American College of Veterinary Internal Medicine (ACVIM) consensus statement for dogs and cats (Brown et al. 2007), 50% of oscillometric measurements should be within 10 mmHg or 80% of their measurements within 20 mmHg of invasive pressure readings (SAP, DAP). These ranges are larger than those proposed for our ΔBP variables, and we therefore hesitate to recommend use of an oscillometric device in the detection of a response to surgical stimulus.

We anticipated that the BBB group would have a larger proportion of block failure associated with its use than the GBB group. Therefore, the BBB group was used to assess and

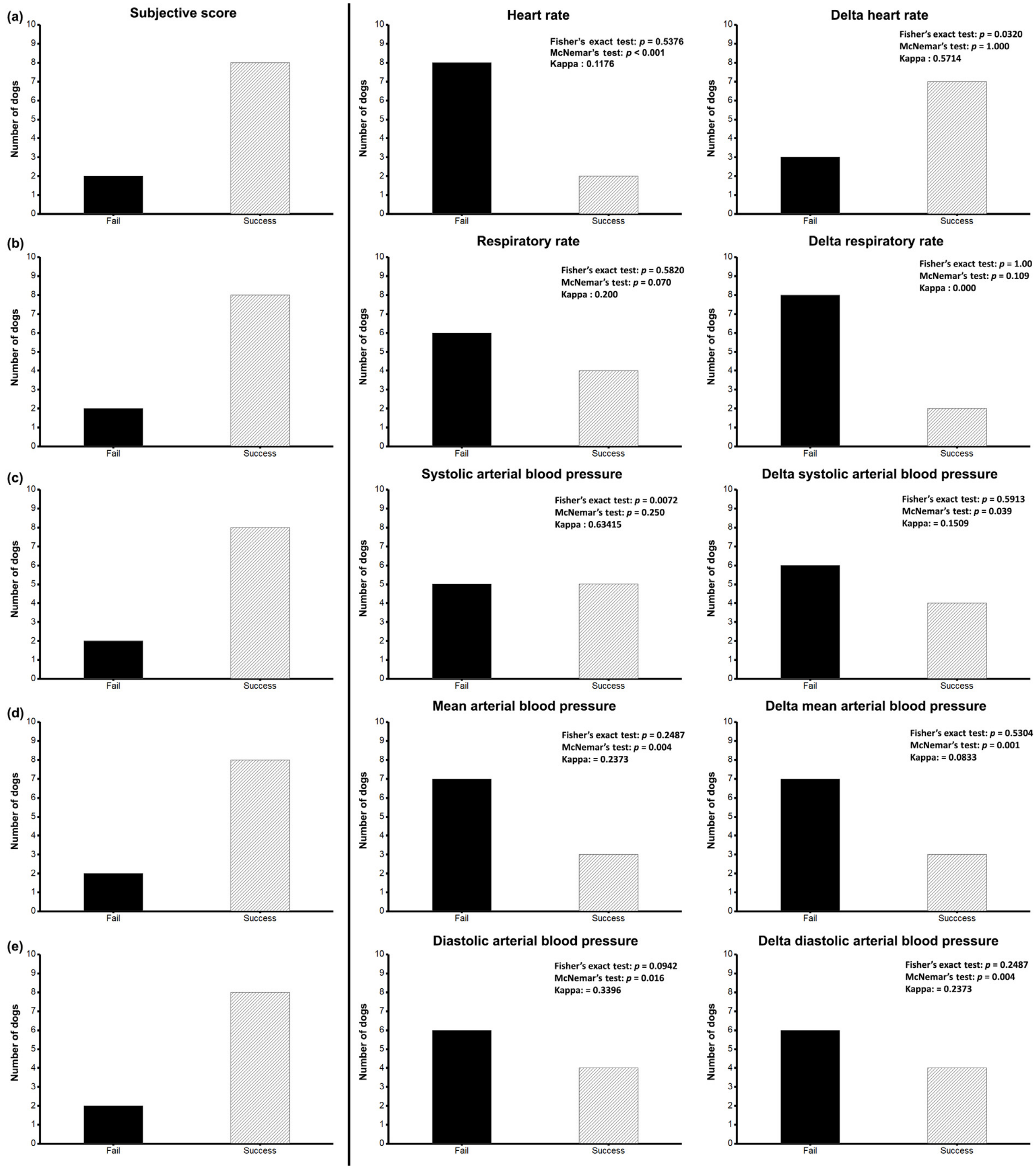

Figure 2 Summary of comparison of subjective (left column) and objective (middle and right columns) assessment of nerve block outcome for blind bupivacaine block (BBB; 10 dogs). Criteria for objective assessment indicated in Table 2. Criteria for subjective assessment was movement, a lightened plane of anaesthesia or an increase (>25%) in the measured physiological variable values. Number of dogs (count) indicated. Proportions of block failure (black histogram) and block success (shaded histogram) shown. Values for Fisher's exact *t* test, McNemar's test and Cohen's kappa coefficient indicated.

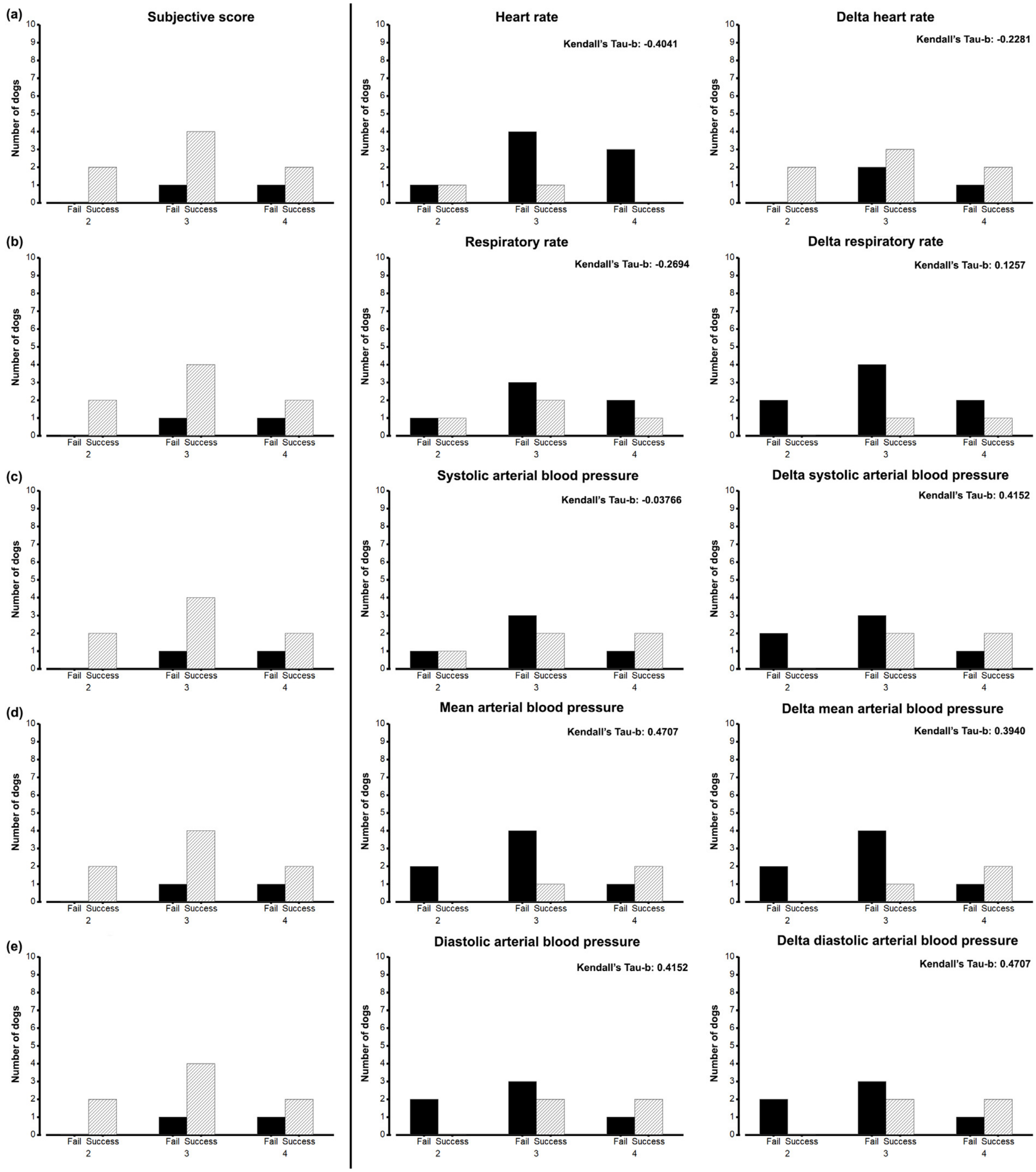

Figure 3 Summary of nerve block outcome (fail or success) for blind bupivacaine block (BBB; 10 dogs). Subjective score (left column) compared with objective scores (middle and right columns) after being stratified into the assigned confidence scores (2, 3 and 4) compared using Kendall tau-b rank correlation coefficient. Proportions of block failure (black histogram) and block success (shaded histogram) shown. Number of dogs (count) indicated. Criteria for objective assessment indicated in Table 2. Criteria for subjective assessment was movement, a lightened plane of anaesthesia or an increase (>25%) in the measured physiological variable values. Criteria for the confidence score is indicated in Table 1.

Table 3 Recommended variables for the detection of nerve block failure in dogs undergoing stifle arthrotomy. All dogs were premedicated with medetomidine 0.01 mg kg^{-1} and morphine 0.3 mg kg^{-1} injected intramuscularly, anaesthesia was induced with propofol and maintained with isoflurane (FE′Iso 1.6%) in oxygen.

	Indicator	Value (mmHg)	SE (%)	SP (%)	PLR	NLR	
SAP	Weak	>127	60	95	12	0.42	
ΔSAP	Strong	>10	95	65	2.71	0.08	*
MAP	Strong	>80	90	80	4.5	0.13	*
ΔMAP	Strong	>6	100	60	2.5	0.00	*
DAP	Moderate	>73	85	90	8.5	0.17	
ΔDAP	Strong	>8	95	70	3.17	0.07	*

Diastolic (DAP), mean (MAP) and systolic (SAP) arterial pressure.
*Suggested for use in the detection of nerve block failure. NLR, negative likelihood ratio; PLR, positive likelihood ratio; SE, sensitivity; SP, specificity.

compare the performance of subjective and objective measures for detecting nerve block failure. The failure rate of blind nerve block techniques is highly variable with a range of 42.9% to 85% (Thomson et al. 2021; Van der Laan et al. 2021; Podsiedlik et al. 2022). The high variability is probably because of the interplay of factors such as the complexity of the block, body condition score of the animal (ease of structural palpation) and the operator (skill, familiarity and anatomical knowledge). Therefore, the expected BBB failure rate was in better agreement with the ΔBP variables (60% to 70%) than with the subjective scoring (20%). The success rate of PNL-guided femoral and sciatic nerve blocks in dogs is between 76% and 86 % (Vettorato et al. 2012; Portela et al. 2013). Vettorato et al. (2012) used intraoperative fentanyl requirement to qualify nerve block success. Portela et al. (2013) used the downward titration of FE′Iso and the concurrent cardiovascular response (>25% increase of HR or MAP) to determine success rate. The possibility of nerve block failure within the GBB group cannot be excluded. Therefore, criterion values should be interpreted with caution.

Serious complications (nerve injury, systemic toxicity) with peripheral nerve blocks are extremely rare. A prospective study of 7000 nerve blocks performed in humans indicated the prevalence of nerve injury and systemic toxicity as 0.0004% and 0.0001%, respectively (Barrington et al. 2009). There was an inherent degree of risk associated with the techniques used in all three groups. According to the proposed serious harm and morbidity (SHAM) score by McGuirk et al. (2011), the score for the use of a placebo and blind group in the current study was 3 (moderate risk). McGuirk et al. (2011) questioned the use of placebo treatments in peripheral nerve block studies. However, placebo groups still play an important role in peripheral nerve block studies (Papadopoulos et al. 2022). The BBB group had a higher degree of risk associated for nerve injury and block failure. To reduce the incidence of serious complication, a good standard of practice was maintained in all three groups. Excessive tissue probing was avoided during needle tip positioning, aspirations were performed prior to injecting and the needle tip was repositioned if there was resistance to injection. Upon critical evaluation of this study based on the Declaration of Helsinki (DOH), we feel that the inclusion of the saline block did not adversely affect any of our dogs. The shortfall of this study with regards to the DOH was that the saline block did not provide any direct health benefits (Ashall et al. 2023). Although the study will benefit future canine patients, and we feel that it was ethical best practice, it is debatable and open for criticism based on the shortfall.

The study had some notable limitations, especially because the recommended variables were derived from an otherwise healthy dog population undergoing surgery using a standardized anaesthetic protocol. The effect of different pain states, MAC multiples, anaesthetic drug combinations (antinociceptive and cardiovascular effects) and physiological states (especially cardiovascular function) on the associated criterion values for the cardiovascular variables remains to be determined. An opportunity exists for further improvement of this study, especially with regards to the values of the associated criterion in larger canine populations. This study will hopefully enable other clinicians to develop an objective tool with pertinent criterion values for the detection of peripheral nerve block failure.

Conclusion

The use of ΔBP variables should be considered as an objective score to detect a response to surgical stimulation and therefore nerve block failure. The determination of criterion values in different canine populations may help to evaluate the success of nerve block techniques, thereby improving ERAS.

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Authors' contributions

EPB and GEZ: study design, data collection, data management, data interpretation and preparation of the manuscript. AK: study design, data collection, data interpretation and preparation of the manuscript. CB: study design, data collection, data management and preparation of the manuscript.

Conflict of interest statement

The authors declare no conflicts of interest.

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Appendix A. Supplementary data

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