

## Impact evaluation of two different general anesthesia protocols (TIVA with propofol vs isoflurane) on the total number of interventions to treat cardiovascular depression or arousal/movement episodes in dogs undergoing orthopedic surgery receiving an intrathecal anesthesia

Diego SAROTTI<sup>1)\*</sup>, Roberto RABOZZI<sup>2)</sup> and Paolo FRANCI<sup>3)</sup>

<sup>1)</sup>*Centro Veterinario Fossanese, Fossano, Italy*

<sup>2)</sup>*Clinica Veterinaria Roma Sud, Roma, Italy*

<sup>3)</sup>*Department of Animal Medicine, Production and Health –University of Padua, Legnaro, Italy*

(Received 21 November 2015/Accepted 3 June 2016/Published online in J-STAGE 23 June 2016)

**ABSTRACT.** The aim of this prospective, randomized clinical trial was to compare the total number of anesthetic interventions (TNAI) performed by the anesthetist to treat cardiovascular depression or arousal/movement episodes in dogs receiving intrathecal and general anesthesia (GA), maintained using propofol-based TIVA (group P) or isoflurane (group I). Mean arterial pressure (MAP) before ( $T_0$ ) and 12 min after intrathecal anesthesia ( $T_1$ ) and intraoperative vasoactive consumption were also compared. The TNAI to deepen the anesthetic plane or to treat hemodynamic depression in the pre-surgical and intra-surgical period was calculated in forty-two client-owned dogs randomly assigned to group P or I. Ten dogs for each group complied with the inclusion criteria and were analyzed. In pre-surgical period, the TNAI was higher in Group I [2 (0–5)] than Group P [0 (0–2)] ( $P=0.022$ ), and ephedrine consumption was also higher in Group I [75 (0–200)  $\mu\text{g}/\text{kg}$ ] than Group P [(0 (0–50)] ( $P=0.016$ ). MAP (mmHg) in Group P was 79 (66–95) at  $T_0$  and 65 (59–86) at  $T_1$  and 67.5 (50–73) and 57 (53–66) in Group I, respectively. At  $T_0$  and  $T_1$ , MAP was higher in Group P ( $P=0.005$  and  $P=0.006$ , respectively). No differences were found between the two groups in the intrasurgical period ( $P>0.05$ ). This study shows that the GA protocol can have a relevant impact on the TNAI performed by the anesthetist in the pre-surgical period of anesthesia, to treat cardiovascular depression or arousal/movement episodes in dogs receiving intrathecal anesthesia.

**KEY WORDS:** anesthetic intervention, dog, intrathecal anesthesia, isoflurane, TIVA

doi: 10.1292/jvms.15-0661; *J. Vet. Med. Sci.* 78(10): 1549–1555, 2016

The operating theater is a place where balancing productivity with patient safety and staff satisfaction is extremely difficult. The anesthetist must be able to find the best compromise between safety and smooth patient turnover, while guaranteeing excellent perioperative conditions for both the patient and the surgeon. When working in a busy veterinary hospital, anesthetists may take responsibility for more than one case at the same time; therefore, simple and efficacious anesthetic protocols that require less effort by the anesthetist are preferable.

For orthopedic patients, combining general and regional anesthesia techniques (combined anesthesia) can provide excellent perioperative conditions with a high degree of safety [3, 13, 21]. When combined anesthesia is employed, a protocol is required to guarantee optimum hemodynamic conditions, a stable anesthetic plane and immobility. Although there is a lack of evidence in the literature, presumably, some perioperative complications that affect subjects undergoing a regional block could be influenced by the anesthetic protocol used. The most frequent complication requiring anesthetist

attention during the perioperative period in healthy dogs undergoing neuraxial anesthesia is cardiovascular depression [22]. However, Bosmans *et al.* [1] also reported a remarkably high incidence of arousal/movement (A/M) episodes (4/23) when performing neuraxial anesthesia in isoflurane-anesthetized dogs. Even though the veterinary literature does not provide more information on this complication, the authors' clinical impression is that when anesthesia is maintained with a volatile agent in non or lightly premedicated dogs, the A/M incidence is close to or superior to that found by Bosmans *et al.* [1] in dogs undergoing a regional block. Both hypotension and A/M events in dogs receiving regional anesthesia can increase the anesthetist's workload, the procedural time, and the administration of vasoactive drugs or a bolus of propofol, thus making these techniques less attractive in clinical practice. Hypotension can increase the perioperative risk of morbidity and mortality [9, 26]. In contrast to humans, propofol-based total intravenous anesthesia (TIVA) seems to decrease the risk of hypotension in dogs. Iizuka *et al.* [11] reported the incidence of intraoperative hypotension (IOH) in dogs anesthetized with isoflurane-fentanyl or propofol-fentanyl as being 65.3% and 27.6%, respectively, suggesting that propofol-fentanyl is associated with a lower risk of IOH than isoflurane-fentanyl anesthesia. Moreover, the authors' clinical impression suggests that propofol-based TIVA decreases the incidence of A/M compared with isoflurane-induced anesthesia in lightly premedicated

\*CORRESPONDENCE TO: SAROTTI, D., c/o CVF, Via Cuneo 29/E, 12045 –Fossano (CN), Italy. e-mail: diego.sarotti@libero.it

©2016 The Japanese Society of Veterinary Science

This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial No Derivatives (by-nc-nd) License <<http://creativecommons.org/licenses/by-nc-nd/4.0/>>.

dogs, while a regional block is being performed.

The aim of this study was to compare the total number of anesthetic interventions (TNAI) performed by the anesthetist to treat cardiovascular depression or A/M episodes and to monitor arterial blood pressure (ABP), heart rate (HR) and the amount of ephedrine administered in dogs that had received an intrathecal injection of bupivacaine and morphine hyperbaric solution and who were being maintained in general anesthesia (GA) with isoflurane or propofol.

## MATERIALS AND METHODS

This study was approved by the Ethical Committee of the University of Padua (Prot. N. 242819), and all owners gave their informed consent. All anesthetic procedures were performed by the same experienced operator, who was aware of the assigned technique.

*Animals: Inclusion criteria:* Dogs older than 6 months presenting to the Clinic, from January 2014 to January 2015, for various scheduled surgical procedures involving the pelvic limbs, based on the American Society of Anesthesiologists (ASA) physical status classification I or II as determined following clinical examination.

*Anesthesia protocols:* Before induction of GA, catheterization of the cephalic vein was performed. General anesthesia was then induced by administering fentanyl 2.5 µg/kg intravenously (IV) and propofol to effect. After orotracheal intubation and inflation of the cuff, the dog was connected to the breathing system. All patients included in this study received intermittent positive pressure ventilation (Cato, Draeger, Germany), and their metatarsal artery was catheterized. The electrocardiogram, HR, invasive blood pressure, respiratory rate, arterial oxygen saturation, fraction of inspired oxygen (FiO<sub>2</sub>), end-tidal carbon dioxide concentration (FE'CO<sub>2</sub>), end-tidal isoflurane concentration (FE'Iso) and esophageal temperature were monitored continuously (GE Datex Ohmeda AS). Lactated Ringer's solution (Ringer Lattato; Fresenius Kabi, Isola della Scala (VR), Italy) was administered IV during anesthesia in all of the dogs. Once the plane of anesthesia was stable, the systolic pressure variation (SPV) was measured with the dog in left lateral recumbency in accordance with Gouvêa & Gouvêa [8]. In brief, the 'wedge pressure' function in the monitor's invasive pressures channel was applied to the systemic arterial curve: (Step 1) the arterial pressure curve was labeled 'pulmonary arterial pressure', and the scale was adjusted accordingly; (Step 2) the 'wedge pressure menu' was accessed; (Step 3) the ComWheel was pressed to confirm; the screen freezes at this point, and a blue horizontal line appears; and (Step 4) the operator is free to move this line to the uppermost point of the curve and then move it down to the lowest systolic pressure [8].

The SPV was calculated as the difference between the maximum and the minimum systolic pressure (SPmax and SPmin, respectively) over a single respiratory cycle and was expressed as a percentage:  $SPV\% = 100 \times (SPmax - SPmin) / (SPmax + SPmin) / 2$ . The median value over three consecutive SPV measurements was taken. If the dog was

not completely suited to mechanical ventilation, or there was a detectable HR variability, or the mean arterial pressure (MAP) was <50 mmHg, SPV measurement was suspended. Propofol (1 mg/kg) was given and SPV measurement was resumed 5 min later, if abnormalities in the ventilatory pattern were due to an inadequate depth of anesthesia. Dogs with an MAP <50 mmHg, compatible with a deep plane of anesthesia, had their FE'ISO decreased. Subjects were excluded from the study, if these abnormalities did not respond to the relevant interventions or if they required a vasopressor. Every dog with an SPV higher than 4.5% under a peak inspiratory pressure of 8 cmH<sub>2</sub>O received 3 ml/kg of lactated Ringer's solution intravenously at a rate of 999 ml/hr using an infusion pump [21]. Every dog with an SPV higher than 4.5% not responder to fluid administration were excluded. The body temperature was maintained above 35°C during the perioperative period using an active heating system (Bair Hugger Warmer Model 505, Augustine Biomedical Design, Eden Prairie, MN, U.S.A.). General anesthesia was maintained in dogs assigned to Group I with isoflurane and to Group P with a propofol-based TIVA. Median values of HR and ABP were recorded before (T<sub>0</sub>) and 12 min after intrathecal injection (T<sub>1</sub>). When hypotension and bradycardia were observed, according to the definition given below, the lowest value registered by the monitor was recorded in the results.

In order to perform the regional technique, anesthetized dogs were positioned in lateral recumbency, and the skin over the L<sub>3</sub>-S<sub>1</sub> vertebrae was aseptically prepared after clipping the hair. A lack of cerebral spinal fluid (CSF) outflow was considered a procedural failure in intrathecal anesthesia. The intrathecal injection was administered using a paramedian approach at the level of the intervertebral space between L<sub>5</sub> and L<sub>6</sub> using a 75-mm-long 25 G Quincke needle (Spinal needle; Pic, Grandate (CO), Italy). Once the CSF outflow became visible in the hub of the needle, the intrathecal solution was injected over 20 sec. The needle bevel always faced cranially during administration of the intrathecal solution. Once the injection was complete, dogs were maintained in lateral recumbency, with the pelvic limb to be operated on lowermost, for 12 min and were then placed in dorsal recumbency.

The bupivacaine (Bupisen iperbarica 0.5%; Galenica Senese, Monteroni d'Arbia (SI), Italy) dose calculations were based on body mass (BM) and spinal cord length (SCL) as suggested by Sarotti *et al.* [22].

Bupivacaine 0.5% (mg): 0.3 BM (kg) + 0.05 SCL (cm)

Spinal cord length (SCL) was recorded as the distance between the caudal part of the spinal process of L7 and the occipital bone.

The 1% morphine dose was 0.3 mg in dogs less than 10 kg, 0.5 mg in dogs between 11 and 20 kg, and 1 mg in dogs over 20 kg (Sarotti *et al.*) [23].

*Event definition and treatment:* Hypotension was defined as being when every MAP value was lower than 60 mmHg. When hypotension was noticed, the anesthesia plane was lightened and SPV was checked again. Every dog with an SPV higher than 4.5% under a peak inspiratory pressure of 8

cmH<sub>2</sub>O received 3 ml/kg of lactated Ringer's solution intravenously at a rate of 999 ml/hr using an infusion pump [21]. When these actions were not able to raise the MAP above 60 mmHg, a bolus of ephedrine was administered until a maximal total dose of 200 µg/kg was reached. If the hypotension did not respond to these treatments, a noradrenaline infusion at 0.1–1 µg/kg/min was administered.

Bradycardia was defined as being when every HR value was below 60 bpm. When bradycardia was observed, atropine at 20 µg/kg IV was administered. Bradycardia ranging between 55 and 59 bpm as a consequence of ephedrine administration was not treated.

An A/M episode was defined as any body movement or sign of lightening of the GA, such as spontaneous or rapid eye blinking, resistance towards the ventilator or muscular tremors. When lightening of anesthesia was observed, 1 mg/kg IV propofol was administered.

The TNAI was defined as being the total number of measures taken by the anesthetist either to deepen the anesthetic plane or to treat hemodynamic depression between stabilization of the anesthetic plane after induction of anesthesia and skin incision.

*Statistical analysis:* Dogs were assigned to one of the two treatment groups according to a computer-generated randomization sequence after the placement of a catheter in the metatarsal artery. The estimated sample size required to detect a difference in the primary endpoint (difference in MAP between groups) with a power of 80% and an alpha error of 5% using a two independent groups study design has been calculated. The effect size (d) of 1.42 was obtained assuming a MAP difference at T<sub>1</sub> of 10 mmHg, with a standard deviation of 7 mmHg. The minimum sample size calculated was nine subjects for each group. Categorical variables were reported as frequencies and percentages, and differences between groups were analyzed using the Fisher's exact test. Continuous variables were checked for normal distribution by visual inspection of bar graphs and histograms, and by using the Shapiro–Wilk test. Data not normally distributed were reported as the median and the range (minimum–maximum), and differences were analyzed using the Mann-Whitney U test. The significance level was set at 5% for all statistical methods (MedCalc Software for Windows version 12.5, Ostend, Belgium).

## RESULTS

Forty-two dogs were enrolled in this study. Intrathecal injection in 5/42 (12%) and the placement of a catheter into the dorsal metatarsal artery in 15/42 (36%) dogs failed, and two cases were excluded because their SPV was higher than 4.5% despite the administration of a bolus of fluid. The remaining 20 dogs, which had complied with the inclusion criteria, were divided evenly into two groups and analyzed. Two dogs in Group I and one in Group P received a bolus of fluid before the intrathecal injection, because their SPV was higher than 4.5% under a peak inspiratory pressure constantly maintained at 8 cmH<sub>2</sub>O. The demographic data (Breed, Age, BM, SCL and ASA category) of both groups can be

found in Appendix Table A1. Procedural data concerning the median local anesthetic dose used for neuraxial blockade, the median dose of morphine, the median dose of propofol used for induction of anesthesia, the median dose of propofol per kilogram of body weight per hour and the median value of FE'iso in the first hour are reported in Table 1. The MAP at T<sub>0</sub> and at T<sub>1</sub> was higher in Group P, as is shown in Fig. 1 ( $P=0.0005$  and  $P=0.006$ ). Complete hemodynamic data at T<sub>0</sub> and T<sub>1</sub> are reported in Table 2. Hypotension, vasoactive consumption, A/M, propofol consumption due to A/M, bradycardia, atropine consumption and TNAI in Groups P and I in pre-surgery and intra-surgical periods are reported, respectively, in Tables 3 and 4. In pre-surgery period, TNAI was higher in Group I, as shown in Fig. 2 ( $P=0.022$ ), while in intraoperative period, TNAI was not different between groups ( $P>0.05$ ). In pre-surgery period, ephedrine consumption was higher in Group I ( $P=0.016$ ), while in intraoperative period, ephedrine consumption was not different between groups ( $P>0.05$ ).

## DISCUSSION

This study shows that the GA protocol can have a relevant impact on the total number of interventions performed by the anesthetist in the pre-surgical period of anesthesia, to treat cardiovascular depression or arousal/movement episodes in dogs receiving intrathecal anesthesia.

This aspect of combined anesthesia has not been investigated in the veterinary literature, even though such anesthesia is very frequently used in veterinary practice. According to this study, dogs, undergoing neuraxial anesthesia, which was maintained under anesthesia using a propofol-based TIVA, required less interventions to control cardiovascular depression or involuntary movements compared with dogs maintained under isoflurane-induced anesthesia. This can be an important feature when deciding on an anesthetic protocol in a busy veterinary practice, where maintaining an elevated surgical patient flow is important. There is no published work examining the relationship between workload and anesthetic safety in veterinary care. In a survey of the medical sector [6], 63% of the respondents suggested that they had made workload-related errors. Regional anesthesia techniques can only contribute significantly to the quality and efficiency of the perioperative care of veterinary patients when complications, possibly arising from these procedures, are minimized. In fact, in the authors' experience, when performing a regional anesthesia technique using a volatile anesthetic, it is more difficult to resolve the conflicting requirements of having an adequate and stable hypnotic level while limiting hypotension and cardiovascular depression in dogs. In particular, subjects undergoing neuraxial anesthesia are exposed to a high risk of hypotension [6], which is mainly due to sympathetic nerve supply blockade and bradycardia. The degree to which this occurs depends on the balance between sympathetic and parasympathetic activities, the extent of the sympathetic block, the degree of cardiac filling and the adequacy of cardiac function [28]. Additionally, the concurrent administration of systemic anesthetic drugs, such as iso-

Table 1. Procedural data [median (range)] for Groups I and P

	Group P (n=10)	Group I (n=10)	P-value
Bupivacaine dose (mg)	8.7 (4–14.9)	13.5 (2.31–16)	0.21
Bupivacaine dose related to BM (mg/kg)	0.42 (0.40–0.59)	0.45 (0.4–0.85)	0.32
Bupivacaine dose related to SCL (mg/cm)	0.15 (0.1–0.19)	0.18 (0.07–0.18)	0.32
Morphine dose (mg)	1 (0.3–1)	1 (0.3–1)	0.81
Morphine dose related to BM (mg/kg)	0.03 (0.027–0.07)	0.03 (0.025–0.11)	0.28
Propofol induction bolus (mg/kg)	5 (4–6)	5 (4–7)	0.56
Mean propofol rate infusion in the first hours (mg/kg/h) versus mean ET isoflurane (%) in the first hour	25 (20–35)	1 (0.8–1.2)	Not evaluated

BM: body mass; SCL: spinal cord length; ET: end-tidal.

Table 2. Hemodynamic data [median (range)] for Groups I and P before intrathecal injection (T<sub>0</sub>) and 12 min later (T<sub>1</sub>)

	Group P (n=10)	Group I (n=10)	P-value
SAP T <sub>0</sub> (mmHg)	115 (94–143)	94 (75–134)	0.0005
MAP T <sub>0</sub> (mmHg)	79 (66–95)	67.5 (50–73)	0.0005
DAP T <sub>0</sub> (mmHg)	63.5 (59–76)	55 (33–60)	0.0007
HR T <sub>0</sub> (bt/min)	87 (76–150)	92 (74–135)	0.56
SAP T <sub>1</sub> (mmHg)	102.5 (86–129)	87 (74–104)	0.041
MAP T <sub>1</sub> (mmHg)	65 (59–86)	57 (53–66)	0.006
DAP T <sub>1</sub> (mmHg)	51.5 (45–69)	47 (41–53)	0.034
HR T <sub>1</sub> (bt/min)	76.5 (60–100)	75 (54–130)	0.61

HR: heart rate; SAP: systolic arterial pressure; MAP: mean arterial pressure; DAP: diastolic arterial pressure.

flurane or propofol anesthetics, can impair the compensatory hemodynamic response (vasoconstriction in unblocked areas of the body) to neuraxial administration of local anesthetics [16, 25]. An experimental study in vagotomized cats found that the baroreceptor reflex is significantly better maintained with propofol than with isoflurane at equipotent doses [24]. Isoflurane and propofol administration causes hypotension mainly through a combination of three mechanisms: myocardial contractility impairment, a decrease in systemic vascular resistance and an increase in venous capacitance [14, 18, 24, 29]. However, a lower risk of hypotension has been found when propofol was compared with isoflurane to maintain anesthesia in dogs undergoing various surgical and diagnostic procedures [13]. A similar finding has been reported in cats when general anesthesia was maintained with propofol [14], but it differs from humans in that propofol

Table 3. Pre-surgical period: hypotension, vasoactive consumption, arousal/movement (A/M), propofol consumption due to A/M, bradycardia, atropine consumption and the total number of anesthetic interventions (TNAI) in Groups P and I

	Group P (n=10)	Group I (n=10)	P-value
Hypotension (%)	3/10 (30%)	6/10 (60%)	0.37
Total ephedrine consumption ( $\mu$ g/kg) [median (range)]	0 (0–50)	75 (0–200)	0.016
Total noradrenalin consumption ( $\mu$ g/kg) [median (range)]	0	0	>0.05
A/M (%)	1/10 (10%)	5/10 (50%)	0.07
Total propofol consumption due to A/M (mg/kg) [median (range)]	0 (0–1)	1.5 (0–3)	0.019
Bradycardia (%)	0/10 (0%)	2/10 (20%)	0.47
Total Atropine consumption ( $\mu$ g/kg) [median (range)]	0	0 (0–20)	>0.05
TNAI (n) [median (range)]	0 (0–2)	2 (0–5)	0.022

Table 4. Intra-surgical period: hypotension, vasoactive consumption, arousal/movement (A/M), propofol consumption due to A/M, bradycardia, atropine consumption and the total number of anesthetic interventions (TNAI) in Groups P and I

	Group P (n=10)	Group I (n=10)	P-value
Hypotension (%)	1/10 (10%)	0/10 (0%)	>0.05
Total ephedrine consumption ( $\mu$ g/kg) [median (range)]	0 (0–25)	0	>0.05
Total noradrenaline consumption ( $\mu$ g/kg) [median (range)]	0	0	>0.05
A/M (%)	0	1/10 (10%)	>0.05
Total propofol consumption due to A/M (mg/kg) [median (range)]	0	0 (0–1)	>0.05
Bradycardia (%)	0/10 (0%)	1/10 (10%)	>0.05
Total Atropine consumption ( $\mu$ g/kg) [median (range)]	0	0 (0–20)	>0.05
TNAI (n) [median (range)]	0 (0–1)	0 (0–1)	>0.05

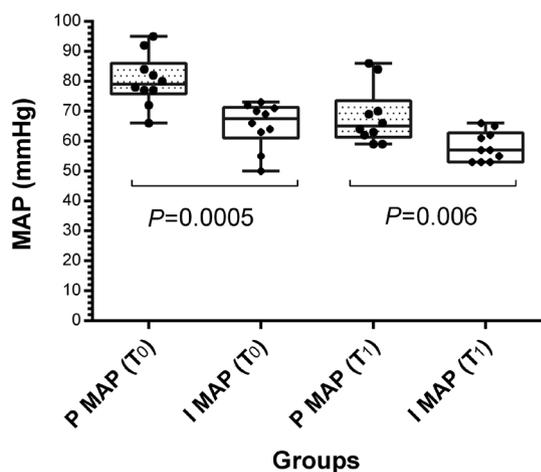


Fig. 1. Box plots of the mean arterial pressure (MAP) before (T<sub>0</sub>) and 12 min after intrathecal injection (T<sub>1</sub>) in Groups P and I. MAP is higher in dogs in the Group P compared with those in Group I at T<sub>0</sub> ( $P=0.0005$ ) and T<sub>1</sub> ( $P=0.006$ ). Dots refer to the value of individual cases. The whiskers show the range values, the width of the box shows the interquartile range, and the bar in the box is the median value.

does not seem to provide clear advantages over inhalation anesthetics in terms of reducing IOH [5, 15]. In our study, the incidence of hypotension in the group I was double than in the group P, however, the sample size of the study was not adequate to reach a statistically significant difference on this aspect. Nevertheless, the amount of ephedrine consumed in the group I was significantly higher than in the group P in the pre-surgery period ( $P=0.016$ ). Compared with isoflurane, propofol better preserves aortic pressure and increases aortic compliance and thus improves the energy transmission from the left ventricle to the arterial system [4]. Goodchild & Serrao [7], in an experimental study, proved that cardiac output and arterial pressure are well preserved at propofol blood concentrations commonly used during maintenance in dogs if the preload is maintained. These authors also found that the preload reduction by a veno-dilator effect is the main mechanism that causes a decrease in cardiac output when using propofol in this species.

Bradycardia plays an important role in neuraxial anesthesia, causing hypotension. Cephalad spread of local anesthetic increases the likelihood of bradycardia via two postulated mechanisms: the blockade of sympathetic cardiac accelerator fibers that arise at T1-T4 [10] and decreased venous return [17]. Even though in this study, a low incidence of bradycardia was found, post-intrathecal injection lowering of blood pressure was not apparently compensated by a rise in HR. This may have been determined by the above-described mechanisms related to intrathecal anesthesia. In the current study, the decrease in HR due to intrathecal injection did not differ between the two groups. This finding is in agreement with the study of Deryck *et al.* [4], which concludes that HR did not differ between isoflurane and propofol anesthesia,

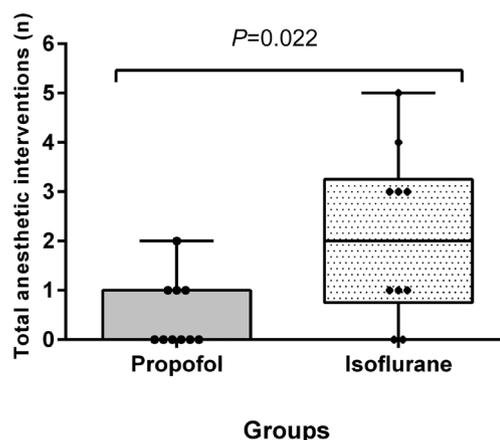


Fig. 2. Box plots of the total number of anesthetic interventions to deepen the anesthetic plane or to treat hemodynamic depression in the pre-surgical period is higher in Group I than in Group P ( $P=0.022$ ). Dots refer to the value of individual cases. The whiskers show the range values, the width of the box shows the interquartile range, and the bar in the box is the median value.

whereas aortic pressure was higher in dogs anesthetized with propofol.

Group I subjects received a significantly higher amount of propofol to treat A/M episodes ( $P=0.019$ ). Immobility is a fundamental requirement when a neuraxial block is carried out, as movement can increase risks ranging from nerve block failure to causing spinal cord damage. Many subjects in Group I had a mean blood pressure close to 60 mmHg in the pre-block period, and the dogs may have been kept at a lighter anesthesia plane in an attempt to avoid hypotension, which thus favored A/M episodes. However, an increased risk of awareness has been reported in pediatric patients maintained under anesthesia with volatile anesthetic agents compared with using TIVA (awareness rate 5% Vs 0.2%) [12].

Dogs enrolled in the current study underwent volemic assessment by measuring SPV after having reached a stable plane of anesthesia. SPV is a dynamic index of volemia validated in dogs undergoing graded exsanguination [19] and was recently characterized as a predictor of fluid responsiveness in the same species [20]. Fluids were administered when SPV (calculated as a percentage) was equal to or higher than 4.5% in an anesthetized dog under a peak inspiratory pressure constantly maintained at 8 cmH<sub>2</sub>O. There is a high probability that the subject would have hemodynamically benefited from a bolus of fluid. In the authors' opinion, volemic assessment can be particularly important when comparing hemodynamic events after neuraxial anesthesia in order to avoid jeopardizing results, because hypovolemia is well known to worsen post-puncture hypotension in subjects undergoing neuraxial anesthesia [2]. Even though, the importance of the volemic assessment in clinical practice, as well as during hemodynamic experimental studies, cannot

be underestimated, some limitations in this study on SPV use should be considered. Anesthesia was maintained with isoflurane, in the original study on the clinical use of SPV [21], and 4.5% has not been confirmed by any study as being the best threshold for fluid responsiveness when propofol is used to maintain anesthesia. This study compares isoflurane with propofol in the maintenance of anesthesia in the intraoperative period. No data were collected on duration and quality of recovery. This can be considered a limitation, because recovery can be a period when complications can call for anesthetist involvement, and therefore, can contribute to the anesthetist's workload. Tsai *et al.* [27], when comparing dogs' recovery from anesthesia maintained with isoflurane or propofol, found that the isoflurane-maintained group stood more quickly than the propofol-maintained group (mean time 27.7 vs. 34.5 min), even though the incidence of adverse effects was not different.

In order to maximize the advantages in performing a regional anesthetic technique, the anesthesia protocol should be carefully planned. The use of different protocols can affect the number of complications arising during the anesthetic period when a regional anesthetic block is performed. When intrathecal anesthesia is planned, maintaining anesthesia with propofol-based TIVA in dogs can guarantee better cardiovascular parameters, less A/M episodes and fewer interventions by the anesthetist than using volatile anesthetics in the pre-surgical period. These differences may be relevant to the safety of anesthetic procedures.

## REFERENCES

- Bosmans, T., Schauvliege, S., Gasthuys, F., Duchateau, L., Marcilla, M. G., Gadeyne, C. and Polis, I. 2011. Cardiovascular effects of epidural administration of methadone, ropivacaine 0.75% and their combination in isoflurane anaesthetized dogs. *Vet. Anaesth. Analg.* **38**: 146–157. [Medline] [CrossRef]
- Caplan, R. A., Ward, R. J., Posner, K. and Cheney, F. W. 1988. Unexpected cardiac arrest during spinal anesthesia: a closed claims analysis of predisposing factors. *Anesthesiology* **68**: 5–11. [Medline] [CrossRef]
- Carpenter, R. L., Caplan, R. A., Brown, D. L., Stephenson, C. and Wu, R. 1992. Incidence and risk factors for side effects of spinal anesthesia. *Anesthesiology* **76**: 906–916. [Medline] [CrossRef]
- Deryck, Y. L., Brimiouille, S., Maggiorini, M., de Canniere, D. and Naeije, R. 1996. Systemic vascular effects of isoflurane versus propofol anesthesia in dogs. *Anesth. Analg.* **83**: 958–964. [Medline] [CrossRef]
- Fanelli, G., Casati, A., Berti, M., Rossignoli L., Italian Study Group on Integrated Anaesthesia 1998. Incidence of hypotension and bradycardia during integrated epidural/general anaesthesia. An epidemiologic observational study on 1200 consecutive patients. *Minerva Anesthesiol.* **64**: 313–319. [Medline]
- Gaba, D. M., Howard, S. K. and Jump, B. 1994. Production pressure in the work environment. California anesthesiologists' attitudes and experiences. *Anesthesiology* **81**: 488–500. [Medline] [CrossRef]
- Goodchild, C. S. and Serrao, J. M. 1989. Cardiovascular effects of propofol in the anaesthetized dog. *Br. J. Anaesth.* **63**: 87–92. [Medline] [CrossRef]
- Gouvêa, G. and Gouvêa, F. G. 2005. Measurement of systolic pressure variation on a Datex AS/3 monitor. *Anesth. Analg.* **100**: 1864. [Medline] [CrossRef]
- Guyton, A. C. and Hall, J. E. 2006. Textbook of Medical Physiology. 10th ed. WB Saunders, Philadelphia.
- Hwang, J., Min, S., Kim, C., Gil, N., Kim, E. and Huh, J. 2014. Prophylactic glycopyrrolate reduces hypotensive responses in elderly patients during spinal anesthesia: a randomized controlled trial. *Can. J. Anaesth.* **61**: 32–38. [Medline] [CrossRef]
- Iizuka, T., Kamata, M., Yanagawa, M. and Nishimura, R. 2013. Incidence of intraoperative hypotension during isoflurane-fentanyl and propofol-fentanyl anaesthesia in dogs. *Vet. J.* **198**: 289–291. [Medline] [CrossRef]
- Jöhr, M. 2006. [Awareness: a problem in paediatric anaesthesia?]. *Anaesthesist* **55**: 1041–1049. [Medline]
- Kona-Boun, J. J., Cuvelliez, S. and Troncy, E. 2006. Evaluation of epidural administration of morphine or morphine and bupivacaine for postoperative analgesia after premedication with an opioid analgesic and orthopedic surgery in dogs. *J. Am. Vet. Med. Assoc.* **229**: 1103–1112. [Medline] [CrossRef]
- Liehmann, L., Mosing, M. and Auer, U. 2006. A comparison of cardiorespiratory variables during isoflurane-fentanyl and propofol-fentanyl anaesthesia for surgery in injured cats. *Vet. Anaesth. Analg.* **33**: 158–168. [Medline] [CrossRef]
- Modesti, C., Sacco, T., Morelli, G., Bocci, M. G., Ciocchetti, P., Vitale, F., Perilli, V. and Sollazzi, L. 2006. Balanced anesthesia versus total intravenous anesthesia for kidney transplantation. *Minerva Anesthesiol.* **72**: 627–635. [Medline]
- Mutoh, T., Nishimura, R., Kim, H. Y., Matsunaga, S. and Sasaki, N. 1997. Cardiopulmonary effects of sevoflurane, compared with halothane, enflurane, and isoflurane, in dogs. *Am. J. Vet. Res.* **58**: 885–890. [Medline]
- Otton, P. E. and Wilson, E. J. 1966. The cardiocirculatory effects of upper thoracic epidural analgesia. *Can. Anaesth. Soc. J.* **13**: 541–549. [Medline] [CrossRef]
- Pagel, P. S. and Wartier, D. C. 1993. Negative inotropic effects of propofol as evaluated by the regional preload recruitable stroke work relationship in chronically instrumented dogs. *Anesthesiology* **78**: 100–108. [Medline] [CrossRef]
- Perel, A., Pizov, R. and Cotev, S. 1987. Systolic blood pressure variation is a sensitive indicator of hypovolemia in ventilated dogs subjected to graded hemorrhage. *Anesthesiology* **67**: 498–502. [Medline] [CrossRef]
- Rabozzi, R. and Franci, P. 2014. Use of systolic pressure variation to predict the cardiovascular response to mini-fluid challenge in anaesthetised dogs. *Vet. J.* **202**: 367–371. [Medline] [CrossRef]
- Sarotti, D., Rabozzi, R. and Corletto, F. 2011. Efficacy and side effects of intraoperative analgesia with intrathecal bupivacaine and levobupivacaine: a retrospective study in 82 dogs. *Vet. Anaesth. Analg.* **38**: 240–251. [Medline] [CrossRef]
- Sarotti, D., Rabozzi, R. and Franci, P. 2013. A retrospective study of efficacy and side effects of intrathecal administration of hyperbaric bupivacaine and morphine solution in 39 dogs undergoing hind limb orthopaedic surgery. *Vet. Anaesth. Analg.* **40**: 220–224. [Medline] [CrossRef]
- Sarotti, D., Rabozzi, R. and Franci, P. 2015. Comparison of epidural versus intrathecal anaesthesia in dogs undergoing pelvic limb orthopaedic surgery. *Vet. Anaesth. Analg.* **42**: 405–413. [Medline] [CrossRef]
- Sellgren, J., Biber, B., Henriksson, B. A., Martner, J. and Pontén, J. 1992. The effects of propofol, methohexitone and isoflurane on the baroreceptor reflex in the cat. *Acta Anaesthesiol. Scand.*

- 36: 784–790. [Medline] [CrossRef]
25. Stanton-Hicks, M. A. 1975. Cardiovascular effects of extradural anaesthesia. *Br. J. Anaesth.* **47** suppl: 253–261. [Medline]
26. Stoelting, R. K. and Hillier, S. C. 2006. *Pharmacology and Physiology in Anesthetic Practice*. 4th ed. Lippincott Williams & Wilkins, Philadelphia.
27. Tsai, Y. C., Wang, L. Y. and Yeh, L. S. 2007. Clinical comparison of recovery from total intravenous anesthesia with propofol and inhalation anesthesia with isoflurane in dogs. *J. Vet. Med. Sci.* **69**: 1179–1182. [Medline] [CrossRef]
28. Veering, B. T. and Cousins, M. J. 2000. Cardiovascular and pulmonary effects of epidural anaesthesia. *Anaesth. Intensive Care* **28**: 620–635. [Medline]
29. Wouters, P. F., Van de Velde, M. A., Marcus, M. A., Deruyter, H. A. and Van Aken, H. 1995. Hemodynamic changes during induction of anesthesia with etanalone and propofol in dogs. *Anesth. Analg.* **81**: 125–131. [Medline]

## Appendix

Table A1. Demographic data of dogs [median (range)] that met the inclusion criteria for Groups I and P

	Group P (n=10)	Group I (n=10)	P-value
Breed (n)	7 Mongrels 1 Labrador 1 Golden Retriever 1 German Shepherd	5 Mongrels 4 Labrador 1 Pointer	Not evaluated
Age (years)	5.5 (1.5–14)	7.5 (0.9–12.5)	0.8
BM (kg)	19.5 (7–35)	31.5 (2.7–40)	0.24
SCL (cm)	57.5 (44–75)	72.5 (30–80)	0.16
ASA Category (n)	ASA I (8) ASA II (2)	ASA I (9) ASA II (1)	1

BM: body mass; SCL: spine cord length; ASA, American Society of Anesthesiologists.