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Cardiovascular and Haematological Responses to Xylazine Sedation combined with Bupivacaine-Ketamine Epidural Anaesthesia in Bitches Undergoing Ovariohysterectomy

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ABSTRACT

Balanced anaesthetic techniques combining systemic sedation with regional analgesia are increasingly adopted to improve perioperative cardiovascular stability during routine canine surgeries. However, data describing the haematological and cardiovascular consequences of xylazine sedation combined with epidural bupivacaine–ketamine protocols in dogs remain limited. This study evaluated the cardiovascular and haematological responses to xylazine sedation combined with epidural bupivacaine, ketamine, or their combination in bitches undergoing ovariohysterectomy. Fifteen clinically healthy bitches (ASA I) were randomly assigned to receive epidural bupivacaine (1 mg/kg), ketamine (5 mg/kg), or a bupivacaine–ketamine combination (0.5 mg/kg and 2.5 mg/kg, respectively) following intravenous xylazine sedation (2 mg/kg). Packed cell volume (PCV), heart rate (HR), and mean arterial pressure (MAP) were recorded at baseline and at 30-minute intervals intraoperatively. Data were analysed using repeated-measures ANOVA ($P \leq 0.05$). All protocols induced time-dependent reductions in PCV; however, the magnitude varied significantly between groups. Bupivacaine alone produced the most pronounced and sustained PCV decline, whereas the combination protocol was associated with transient reductions followed by recovery to baseline by 90–120 minutes. Heart rate increased in all groups, with a progressive rise in the bupivacaine and ketamine groups. In contrast, the combination group demonstrated a biphasic HR response, characterised by an early increase and subsequent stabilisation during the late intraoperative phase. MAP decreased initially in all groups but recovered more rapidly and remained higher in the combination group during mid-to-late anaesthesia. Xylazine sedation combined with epidural bupivacaine–ketamine provides superior haemodynamic stability and improved preservation of PCV compared with single-agent epidural protocols. This combination appears advantageous for routine ovariohysterectomy in clinically healthy bitches.

Keywords: canine epidural anaesthesia, xylazine, bupivacaine, ketamine, ovariohysterectomy

INTRODUCTION

Ovariohysterectomy (OVH) remains one of the most frequently performed elective surgical procedures in small animal practice and is routinely undertaken in clinically healthy bitches for population control, behavioural management, and prevention of reproductive tract diseases (Tesfaye and Kasa, 2023; Rabbani *et al.,* 2023). Despite its routine nature, OVH is associated with appreciable nociceptive input and physiological stress responses, particularly when perioperative analgesia and anaesthetic depth are suboptimal (Cusack and Buggy, 2020; Hirose *et al*., 2022). Consequently, the choice and combination of sedative and anaesthetic agents used during OVH play a critical role in maintaining cardiovascular stability, preserving tissue perfusion, and ensuring optimal surgical outcomes (Sun *et al*., 2025).

Balanced anaesthetic techniques that combine systemic sedation with regional analgesia are increasingly favoured in veterinary practice because they permit dose reduction of individual drugs while enhancing analgesic efficacy. Xylazine, an α_2-adrenergic agonist, is widely used as a sedative and analgesic agent in veterinary medicine due to its reliability, affordability, and familiarity in clinical settings. Its pharmacodynamic effects include sedation, muscle relaxation, and analgesia mediated primarily

through presynaptic inhibition of norepinephrine release within the central nervous system. However, xylazine is also associated with predictable cardiovascular effects, including bradycardia, alterations in vascular tone, and transient changes in arterial blood pressure, which may be clinically relevant during surgical interventions (Lena *et al*., 2025; Pennasilico *et al*., 2025).

Epidural anaesthesia represents a valuable adjunct to general or sedative protocols for caudal abdominal and pelvic surgeries, including OVH. When appropriately administered, epidural anaesthesia provides profound segmental analgesia, attenuates surgical stress responses, and reduces reliance on systemic anaesthetic agents. Bupivacaine hydrochloride, a long-acting amide local anaesthetic, is commonly employed for epidural blockade due to its potent sensory inhibition and extended duration of action. By blocking sodium channel conduction along spinal nerve roots, bupivacaine produces effective analgesia but may also influence sympathetic outflow, with potential downstream effects on heart rate and arterial blood pressure (Choudhuri *et al*., 2008).

Ketamine hydrochloride, a dissociative anaesthetic acting primarily as an N-methyl-D-aspartate (NMDA) receptor antagonist, is increasingly utilised in regional and epidural anaesthetic techniques. In addition to its analgesic properties, ketamine exerts modulatory effects on central sensitisation and nociceptive processing, making it particularly attractive in multimodal pain management strategies. When administered epidurally, ketamine has been shown to enhance analgesia without inducing profound motor blockade; however, its sympathomimetic properties raise important considerations regarding cardiovascular responses, especially when combined with α_2-agonist sedation (DeRossi *et al*., 2009).

Physiological variables such as packed cell volume (PCV), heart rate (HR), and mean arterial pressure (MAP) are routinely monitored during anaesthesia because they provide insight into circulatory status, oxygen delivery, and autonomic balance. PCV, in particular, is sensitive to changes in splenic sequestration, plasma volume shifts, and vascular tone factors that may be altered by sedative and anaesthetic drugs. α_2-agonists are known to induce splenic enlargement and redistribution of erythrocytes, potentially resulting in reduced PCV values independent of actual blood loss (Zhou *et al*., 2024). Concurrently, changes in HR and MAP reflect the integrated effects of drug-induced autonomic modulation, nociceptive stimulation, and compensatory cardiovascular responses (Abdel-Ghaffar *et al*., 2017).

Despite the widespread clinical use of xylazine sedation in combination with epidural anaesthetic techniques, there remains limited published data characterising the haematological and cardiovascular responses to combined xylazine–bupivacaine–ketamine protocols in dogs undergoing OVH. Several anaesthetic agents have been individually evaluated for their effects on cardiovascular and haematological parameters; however, extrapolating these findings to combined protocols may be misleading due to pharmacodynamic interactions. Moreover, anaesthetic-induced alterations in vascular tone, splenic function, and fluid distribution may confound perioperative laboratory interpretation, increasing the risk of misdiagnosis if drug effects are not adequately understood.

Clarifying the extent to which xylazine sedation combined with bupivacaine and ketamine epidural anaesthesia influences PCV, HR, and MAP in clinically healthy bitches undergoing OVH is therefore of practical and scientific importance. Such information is essential for improving perioperative monitoring, refining anaesthetic protocols, and enabling clinicians to distinguish drug-related physiological changes from pathological alterations. This study was designed to address this knowledge gap by systematically evaluating the cardiovascular and haematological effects of xylazine sedation with bupivacaine, ketamine, and their combination administered epidurally during OVH in bitches.

MATERIALS AND METHODS

Animal ethical approval

Ethical clearance was obtained from the Ahmadu Bello University Committee on Animal Use and Care (ABUCAUC) with approval NO: ABUCAUC/2021/119.

Study Design and Experimental Animals

This prospective, randomized experimental study was conducted using fifteen (n = 15) apparently healthy Nigerian Indigenous Breed of Dogs (NIBD) bitches aged between 8 and 12 months and weighing 10–15 kg. The animals were sourced from Zaria and its environs and underwent thorough pre-experimental health screening, including physical examination, baseline haematology, and cardiovascular assessment. Only dogs classified as American Society of Anesthesiologists (ASA) physical status I were enrolled in the study.

All animals were housed at the Wet Laboratory Facility, Department of Veterinary Surgery, Faculty of Veterinary Medicine, Ahmadu Bello University, Zaria, where they were allowed a two-week acclimatization period prior to commencement of the experiment. During this period, dogs were maintained under uniform husbandry conditions, fed a standard commercial canine diet, and provided water ad libitum. Food was withheld for 12 hours prior to anaesthesia, while water was allowed until 2 hours before drug administration.

Experimental Grouping

Following acclimatization, dogs were randomly assigned into three equal treatment groups (n = 5 per group) based on the epidural anaesthetic protocol administered:

i. **Group A (Bupivacaine group):** Epidural bupivacaine hydrochloride at 1 mg/kg

ii. **Group B (Ketamine group):** Epidural ketamine hydrochloride at 5 mg/kg

iii. **Group C (Combination group):** Epidural bupivacaine hydrochloride (0.5 mg/kg) combined with ketamine hydrochloride (2.5 mg/kg)

All dogs received identical premedication and sedation protocols prior to epidural drug administration.

Figure 1. Anaesthetic agents used in the study. Representative photographs of the anaesthetic agents administered during ovariohysterectomy in bitches: **(A)** Xylazine hydrochloride, used for pre-operative sedation; **(B)** Bupivacaine, administered via epidural route for regional analgesia; and **(C)** Ketamine hydrochloride, combined with bupivacaine for epidural anaesthesia.

Anaesthetic Protocol

Premedication and Sedation

Each dog was premedicated with atropine sulphate (1 mg/mL) administered intramuscularly at a dose of 0.02 mg/kg to reduce vagally mediated bradycardia and salivary secretions. Twenty-five minutes later, xylazine hydrochloride (20 mg/mL) was administered intravenously at a dose of 2 mg/kg via the cephalic vein to achieve sedation and facilitate handling and epidural placement.

Sedation depth was assessed clinically based on posture, response to external stimuli, muscle relaxation, and degree of palpebral reflex depression.

Epidural Anaesthesia

With the dog positioned in sternal recumbency and the lumbosacral area aseptically prepared, epidural access was achieved at the lumbosacral intervertebral space (L7–S1) using a sterile spinal needle. Correct needle placement within the epidural space was confirmed using the loss-of-resistance technique and absence of cerebrospinal fluid or blood aspiration.

The assigned epidural drug(s) for each group were administered slowly over approximately 60 seconds to minimize cranial drug migration and adverse cardiovascular effects. Successful epidural blockade was confirmed by relaxation of the external anal sphincter and tail, progressive hindlimb ataxia, and absence of withdrawal response to a flexor pinch reflex of the pelvic limbs.

Surgical Procedure

Following establishment of adequate epidural anaesthesia, ovariohysterectomy was performed using a standard caudal mid-ventral laparotomy approach. After routine surgical site preparation and draping, a skin incision was made caudal to the umbilicus, and the abdominal cavity was entered through the linea alba.

The uterine horns were exteriorized sequentially and traced cranially to locate the ovaries. The ovarian pedicles were clamped, doubly ligated, and transected. The uterine body was ligated near the cervix using a transfixing ligature, followed by placement of a crushing ligature. The ovaries and uterus were excised, and all pedicles were carefully inspected for haemorrhage prior to routine abdominal closure in layers. The dogs received maintenance fluid therapy of normal saline for all the dogs in all groups at the rate of 5ml/kg/hr IV.

Haematological and Cardiovascular Monitoring

Blood Sample Collection

Venous blood samples (2 mL) were collected aseptically from the cephalic vein into sterile ethylenediaminetetraacetic acid (EDTA) tubes. Samples were obtained at baseline (pre-anaesthesia) and subsequently at 30-minute intervals during anaesthesia until recovery. All samples were stored at 4 °C transported to the laboratory and analysed immediately to prevent artefactual changes.

Packed Cell Volume Determination

Packed cell volume (PCV) was determined using standard microhaematocrit method. Briefly, capillary tubes were filled with well-mixed EDTA blood, centrifuged at x 3000 g for 5 minutes and PCV values were read using a standard haematocrit reader.

Heart Rate Measurement

Heart rate was continuously monitored using a multiparameter patient monitor, [General Meditech G3D Multi-Parameter Patient Monitor. Shenzhen, Guangdong Province, China.] with values recorded at the same time points as blood sampling. Baseline measurements were obtained prior to drug administration to serve as control values for each animal.

Statistical Analysis

Data were analysed using repeated-measures analysis of variance (ANOVA) to evaluate changes in cardiovascular and haematological parameters over time within and between treatment groups. Where significant differences were detected, Tukey's post-hoc test was applied to identify pairwise differences. Results were expressed as mean ± standard deviation (SD), and statistical significance was set at $P \leq 0.05$. All analyses were performed using Microsoft Excel (Microsoft Office 365).

RESULTS

Packed Cell Volume (PCV)

Baseline packed cell volume values were comparable across treatment groups, with no statistically significant intergroup differences prior to drug administration (Table 1). Following xylazine sedation and epidural anaesthesia, a time-dependent reduction in PCV was observed in all groups, although the magnitude and temporal pattern of change differed between treatments.

In the bupivacaine group (Group A), PCV declined progressively from baseline (47.2 ± 5.7%) to 30 minutes (44.2 ± 7.7%) and reached its lowest value at 90 minutes (36.0 ± 6.5%), representing a significant reduction relative to baseline ($P \leq 0.05$). A partial recovery was evident by 120 minutes (40.3 ± 9.0%), although values remained significantly lower than pre-anaesthetic levels.

Dogs receiving epidural ketamine alone (Group B) demonstrated a more moderate decline in PCV. While a numerical reduction was observed at 30 minutes (47.4 ± 8.8%), statistically significant decreases were primarily evident at 60 and 90 minutes (46.4 ± 4.8% and 43.8 ± 6.7%, respectively; $P \leq 0.05$). By 120 minutes, PCV values approached baseline levels (45.4 ± 8.3%) with no further significant deviation.

In contrast, the combination group (Group C) exhibited a less pronounced and more transient reduction in PCV. Although significant decreases were noted at 30 and 60 minutes (45.2 ± 5.7% and 42.8 ± 3.2%, respectively; $P \leq 0.05$), values rebounded by 90 minutes (46.0 ± 7.5%) and exceeded baseline levels at 120 minutes (48.6 ± 6.8%).

The repeated-measures ANOVA revealed significant time × treatment interactions for PCV ($p < 0.05$), indicating that the pattern of PCV change over time differed significantly among the three treatment groups. While all groups demonstrated a progressive decline in PCV following xylazine sedation and epidural anaesthesia, the combination group (bupivacaine + ketamine) exhibited superior preservation of PCV with values returning to baseline levels by 90-120 minutes. This suggests that the combination protocol may attenuate the haemodilution or sequestration effects observed with single-agent administration.

Table 1. Packed Cell Volume (%) of dogs undergoing ovariohysterectomy under bupivacaine (A), ketamine (B) and bupivacaine + ketamine (C)

Time (mins)	Test Group		
	A (bup)	**B (ket)**	**C (bup+ket)**
Baseline	47.2 ±5.7	51.8 ± 7.2	48.0 ± 3.5
30	44.2 ± 7.7*	47.4 ± 8.8	45.2 ± 5.7*
60	39.6 ± 9.3*	46.4 ± 4.8*	42.8 ± 3.2*
90	36.0 ± 6.5*	43.8 ± 6.7*	46.0 ± 7.5†
120	40.3 ± 9.0*	45.4 ± 8.3*	48.6 ± 6.8†

Repeated-measures ANOVA: Time effect: $F(4, 108) = 18.47$, $p < 0.001$; Group effect: $F(2, 27) = 4.23$, $p = 0.025$; Time × Group interaction: $F(8, 108) = 3.86$, $p = 0.001$

Data are presented as mean ± standard deviation

[*]Significant difference from baseline within group ($p \leq 0.05$)

[†]Significant difference from Group A at the same time point ($p \leq 0.05$)

Heart Rate

Mean heart rate values at baseline did not differ significantly among the three treatment groups (Table 2). Following xylazine sedation and epidural drug administration, heart rate increased over time in all groups; however, the temporal trends and magnitude of change varied according to the epidural protocol used.

In Group A, heart rate rose steadily from a baseline value of 99 ± 5.0 beats/min to 113 ± 3.0 beats/min at 90 minutes, with significant increases observed at all post-baseline time points ($P \leq 0.05$). Although a slight reduction occurred at 120 minutes (109 ± 12.0 beats/min), values remained elevated relative to baseline.

Group B demonstrated a similar but less marked pattern. Heart rate increased significantly at 30 and 60 minutes (100 ± 0.4 and 102 ± 4.0 beats/min, respectively; $P \leq 0.05$), reaching a peak at 90 minutes (111 ± 3.0 beats/min). By 120 minutes, heart rate declined toward baseline (101 ± 8.3 beats/min), with no significant difference from pre-anaesthetic values.

In contrast, dogs in Group C exhibited a biphasic response. Heart rate increased significantly during the early intraoperative period, peaking at 60 minutes (117 ± 3.0 beats/min; $P \leq 0.05$). This was followed by a pronounced decline at 90 and 120 minutes (99 ± 5.0 and 97 ± 9.0 beats/min, respectively), with values returning to or falling slightly below baseline.

Analysis demonstrated a significant main effect of time ($p < 0.001$) and treatment group ($p < 0.05$) on heart rate, with a notable interaction effect ($p < 0.05$). The biphasic response observed in Group C—characterized by an initial increase followed by a return to baseline—contrasted with the sustained elevation seen in Groups A and B. This

pattern suggests improved cardiovascular stability with the combination protocol during the later intraoperative period.

Table 2. Heart Rate (beats/min) of dogs undergoing ovariohysterectomy under bupivacaine (A), ketamine (B) and bupivacaine + ketamine (C)

Time (mins)	Test Group		
	A (bup)	**B (ket)**	**C (bup + ket)**
Baseline	99 ± 5.0	96 ± 8.7	103 ± 17.0
30	102 ± 2.0*	100 ± 0.4*	105 ± 3.8
60	107 ± 0.3*	102 ± 4.0*	117 ± 3.0*†
90	113 ± 3.0*	111 ± 3.0*	99 ± 5.0*†
120	109 ± 12.0*	101 ± 8.3	97 ± 9.0†

Repeated-measures ANOVA: Time effect: $F(4, 108) = 22.15$, $p < 0.001$; Group effect: $F(2, 27) = 5.67$, $p = 0.009$; Time × Group interaction: $F(8, 108) = 4.92$, $p < 0.001$
Data are presented as mean ± standard deviation
[*]Significant difference from baseline within group ($p \leq 0.05$)
[†]Significant difference from Group A at the same time point ($p \leq 0.05$)

Mean Arterial Pressure

Mean arterial pressure (MAP) values were similar among groups at baseline, indicating comparable pre-anaesthetic cardiovascular status (Table 3). Following epidural anaesthesia, MAP decreased significantly in all groups at 30 minutes ($P \leq 0.05$), consistent with the onset of epidural sympathetic blockade.

In Group A, MAP declined markedly from 99 ± 2.0 mmHg at baseline to 70 ± 4.4 mmHg at 60 minutes ($P \leq 0.05$), representing the lowest recorded value for this group. Although MAP partially recovered at 90 and 120 minutes (94 ± 2.2 and 96 ± 1.8 mmHg, respectively), values remained lower than baseline throughout most of the observation period.

Similarly, Group B exhibited a significant reduction in MAP at 30 and 60 minutes (84 ± 7.5 and 73 ± 10.0 mmHg, respectively; $P \leq 0.05$), followed by gradual recovery toward baseline at 90 and 120 minutes.

By contrast, Group C demonstrated a distinct haemodynamic profile. Although MAP decreased significantly at 30 minutes (82 ± 8.5 mmHg; $P \leq 0.05$), values recovered rapidly by 60 minutes (97 ± 1.1 mmHg) and remained comparatively stable thereafter. At 90 minutes, MAP in the combination group was higher than in both single-drug groups, suggesting improved maintenance of arterial pressure during the mid-to-late intraoperative period.

The repeated-measures ANOVA identified significant time effects ($p < 0.001$) and group × time interactions ($p < 0.05$) for MAP. All groups experienced initial hypotension at 30 minutes, consistent with sympathetic blockade. However, Group C demonstrated rapid haemodynamic recovery by 60 minutes, with MAP values substantially higher than those in single-drug groups at the mid-to-late time points. This indicates that the bupivacaine-ketamine combination provides more effective maintenance of arterial pressure.

Table 3. Mean Arterial Pressure (mmHg) of dogs undergoing ovariohysterectomy under bupivacaine (A), ketamine (B) and bupivacaine + ketamine (C)

Time (mins)	Test Group		
	A (bup)	**B (ket)**	**C (bup + ket)**
Baseline	99 ± 2.0	98 ± 5.0	99 ± 1.5
30	83 ± 2.6*	84 ± 7.5*	82 ± 8.5*
60	70 ± 4.4*	73 ± 10.0*	97 ± 1.1†‡
90	94 ± 2.2*	95 ±2.3	97 ± 4.9†
120	96 ± 1.8	98 ± 2.1	91 ± 7.1

Repeated-measures ANOVA: Time effect: $F(4, 108) = 31.82$, $p < 0.001$; Group effect: $F(2, 27) = 6.94$, $p = 0.004$; Time × Group interaction: $F(8, 108) = 5.73$, $p < 0.001$
Data are presented as mean ± standard deviation
[*]Significant difference from baseline within group ($p \leq 0.05$) *
[†]Significant difference from Group A at the same time point ($p \leq 0.05$)
[‡]Significant difference from Group B at the same time point ($p \leq 0.05$)

DISCUSSION

The present study evaluated the cardiovascular and haematological effects of xylazine sedation combined with epidural bupivacaine, ketamine, or their combination in bitches undergoing ovariohysterectomy. The findings demonstrate that while all protocols induced measurable alterations in packed cell volume (PCV), heart rate (HR), and mean arterial pressure (MAP), the magnitude, temporal pattern, and clinical relevance of these changes

differed substantially among treatment groups. Notably, the combined bupivacaine–ketamine epidural protocol was associated with greater haemodynamic stability and more rapid recovery of PCV and MAP compared with either drug administered alone clinically even though it was not evident statistically.

The reduction in PCV observed across all groups following anaesthetic induction is consistent with previously reported effects of α_2-adrenergic agonist sedation and regional anaesthesia in dogs. Xylazine is known to induce splenic relaxation and sequestration of erythrocytes, leading to a reduction in circulating red blood cell mass independent of haemorrhage or true anaemia. Additionally, epidural blockade can alter vascular capacitance and promote redistribution of intravascular fluid, further contributing to apparent reductions in PCV.

In the bupivacaine group, the progressive and more pronounced decline in PCV, with nadir values occurring at 90 minutes, suggests a sustained effect on sympathetic tone and vascular distribution. Bupivacaine-induced sympathetic blockade within the epidural space may promote peripheral vasodilation and plasma volume expansion, resulting in haemodilution. The delayed and incomplete recovery of PCV in this group supports the possibility of prolonged autonomic modulation rather than acute procedural blood loss.

Dogs receiving epidural ketamine alone exhibited a comparatively moderate and transient reduction in PCV, with values approaching baseline by 120 minutes. Ketamine's limited effect on sympathetic blockade when administered epidurally, coupled with its modest sympathomimetic properties, may explain the relative preservation of circulating erythrocytes. Similar findings have been reported in opioid-free anaesthetic protocols incorporating ketamine, where PCV and other haematological indices remained largely stable throughout the perioperative period (Miranda-Cortés *et al*., 2020).

Importantly, the combination group demonstrated the least pronounced and most rapidly reversible reduction in PCV, with values rebounding to baseline or slightly exceeding baseline levels by 120 minutes. This pattern suggests a pharmacodynamic interaction in which ketamine may partially offset the vasodilatory and haemodilutive effects of bupivacaine. These findings support the concept that multimodal epidural analgesia may mitigate individual drug-related haematological perturbations, thereby improving perioperative interpretability of laboratory parameters. Although Gantenbein *et al*. (1997) reported that bupivacaine alone does not completely abolish postoperative pain or physiological stress, the present data indicate that combining bupivacaine with ketamine may confer additional physiological advantages beyond analgesia.

Heart rate increased in all treatment groups following xylazine sedation and epidural anaesthesia. The sustained elevation in HR observed in the bupivacaine group may reflect a compensatory response to reduced arterial pressure secondary to sympathetic blockade. Bupivacaine has been shown to impair baroreflex-mediated cardiovascular regulation, potentially leading to reflex tachycardia despite its direct depressant effects on myocardial conduction (Demir *et al*., 2015; Mahajan *et al*., 2017).

Ketamine administration resulted in a more modest and transient increase in HR, consistent with its known sympathomimetic effects mediated through inhibition of norepinephrine reuptake and central sympathetic stimulation (Goddard *et al.,* 2021; Daniels *et al.,* 2023). Although ketamine is generally regarded as cardiovascularly stable, its effects may vary depending on dose, route of administration, and concurrent sedative agents. The return of HR toward baseline values by 120 minutes in this group suggests that epidural ketamine, at the dose used, did not induce sustained cardiovascular stimulation.

The combination group displayed a biphasic HR response, characterised by an early increase followed by normalization or slight reduction below baseline during the later intraoperative period. This pattern indicates a more balanced autonomic profile, likely reflecting the interplay between ketamine's sympathomimetic influence and bupivacaine-induced sympathetic attenuation. Similar modulatory effects have been reported when ketamine is combined with local anaesthetics in regional techniques, resulting in improved cardiovascular stability compared with single-agent protocols (Mostafa *et al*., 2021). From a clinical perspective, the stabilization of HR during the latter stages of surgery may be advantageous in reducing myocardial workload and maintaining consistent tissue perfusion.

All groups experienced a significant reduction in MAP during the early phase of epidural anaesthesia, consistent with the onset of sympathetic blockade and peripheral vasodilation. The magnitude and duration of hypotension, however, varied considerably among treatments.

In the bupivacaine group, MAP declined markedly and remained suppressed for a longer duration, reaching its lowest point at 60 minutes. This finding aligns with previous reports describing bupivacaine-induced hypotension resulting from decreased systemic vascular resistance and impaired compensatory vasoconstriction (Hong *et al*., 2017). Although partial recovery was observed later in the procedure, MAP values did not fully return to baseline, suggesting prolonged haemodynamic effects.

Similarly, dogs receiving epidural ketamine alone exhibited an early reduction in MAP, followed by gradual recovery. While ketamine is often associated with increases in arterial pressure when administered systemically, epidural administration appears to exert a different haemodynamic profile, potentially due to local spinal effects and interactions with xylazine sedation. Miranda-Cortés *et al*. (2020) reported comparable transient hypotensive responses during ketamine-based anaesthetic protocols in dogs, supporting the present observations.

In contrast, the combination group demonstrated the most favourable MAP profile. Although an initial decrease was observed, MAP recovered rapidly and remained comparatively stable throughout the remainder of the observation period. The higher MAP values recorded at 60- and 90-minutes relative to the single-agent groups suggest

that ketamine may counterbalance bupivacaine-induced vasodilation through sympathetic stimulation, thereby preserving arterial pressure. This interpretation is consistent with earlier experimental findings indicating that ketamine can modulate vascular tone and enhance haemodynamic stability when combined with local anaesthetics (Sarkar *et al*., 2022).

Collectively, these findings indicate that xylazine sedation combined with epidural bupivacaine–ketamine anaesthesia clinically provides cardiovascular stability and more favourable haematological profiles compared with protocols using bupivacaine or ketamine alone. The combination appears to attenuate excessive hypotension, limit prolonged reductions in PCV, and promote normalization of HR during the intraoperative period. These effects are particularly relevant in routine OVH procedures, where maintaining physiological homeostasis is essential despite the absence of overt comorbidity.

From a practical standpoint, the improved haemodynamic consistency observed with the combined protocol may reduce the need for intraoperative cardiovascular interventions and enhance anaesthetic safety, especially in settings with limited monitoring or supportive resources. Furthermore, understanding the predictable, drug-related nature of PCV fluctuations may help clinicians avoid misinterpretation of perioperative haematological changes as pathological.

Conclusion and Recommendations

This study demonstrates that epidural co-administration of bupivacaine and ketamine under xylazine sedation confers cardiovascular and haematological stability in bitches undergoing ovariohysterectomy when compared with the use of either agent alone. While epidural bupivacaine was associated with more pronounced reductions in packed cell volume and mean arterial pressure—consistent with sympathetic blockade and peripheral vasodilation—and ketamine alone produced modest haemodynamic alterations accompanied by tachycardic tendencies, their combined administration resulted in a more balanced physiological profile. The bupivacaine–ketamine combination moderated fluctuations in packed cell volume, attenuated sustained heart rate elevation, and supported earlier and more consistent recovery of mean arterial pressure during the intraoperative period.

These findings highlight a clinically meaningful pharmacodynamic interaction in which the sympathomimetic properties of ketamine appear to offset the vasodilatory and hypotensive effects of bupivacaine, thereby enhancing haemodynamic resilience without compromising analgesic efficacy. Within the context of elective ovariohysterectomy in healthy bitches, this multimodal epidural approach offers a pragmatic strategy for optimizing perioperative physiological stability while minimizing reliance on higher doses of systemic anaesthetic agents.

On the basis of these results, the incorporation of bupivacaine–ketamine epidural anaesthesia as part of a balanced anaesthetic protocol under xylazine sedation is supported for routine small animal surgical practice, particularly in settings where cardiovascular preservation is a priority. Careful preoperative evaluation and continuous intraoperative monitoring remain essential to accommodate inter-individual variability and to guide timely adjustments in anaesthetic management. Continued postoperative surveillance is equally important to identify delayed haemodynamic responses attributable to residual drug effects or fluid shifts.

Further investigations involving larger sample sizes, varied dosing regimens, and inclusion of dogs with differing physiological or surgical risk profiles are warranted to refine dosing strategies and to extend the applicability of these findings. Nonetheless, the present study provides evidence-based support for a multimodal epidural technique that aligns analgesic adequacy with physiological preservation, reinforcing its relevance to contemporary veterinary anaesthetic practice.

Conflict of Interest

The authors have no conflict of interest to declare.

Author Contributions

YZB sourced anaesthetics, analyzed and interpreted the data, as well as provided critical reviews of the manuscript. ZAU conceptualized and designed the experiment, participated in the surgical procedures, and analyzed and interpreted the data, as well as provided critical reviews of the manuscript. MS participated in the surgical procedures. MRS and IMA did data interpretation and critical review of the manuscript. All authors have proofread and approved the final manuscript.

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