



## Echocardiographic and Biochemical Assessments Following combinations of Acepromazine-Ketamine and Xylazine-Ketamine Anesthesia in Dogs

Mahmoud A Nawar<sup>1\*</sup>, Mohamed W El-Sherif<sup>2</sup>, Adel Sobhy<sup>3</sup>, Hazem Shaheen<sup>4</sup>, Mostafa M Kassem<sup>5</sup>

<sup>1</sup>Department of Surgery, Faculty of Veterinary Medicine, Damanhour University, 22511, Damanhour, Egypt

<sup>2</sup>Department of Surgery, Anesthesiology, and Radiology, Faculty of Veterinary Medicine, New Valley University, 72511, New Valley, Egypt

<sup>3</sup>Department of Surgery, Faculty of Veterinary Medicine, Damanhour University, 22511, Damanhour, Egypt

<sup>4</sup>Department of Pharmacology, Faculty of Veterinary Medicine, Damanhour University, 22511, Damanhour, Egypt

<sup>5</sup>Department of Surgery, Faculty of Veterinary Medicine, Alexandria University, 21544, Alexandria, Egypt

### ABSTRACT

The present study investigated echocardiographic and biochemical changes following ketamine anesthesia induction in dogs sedated with acepromazine (0.2 mg/kg) or xylazine (3 mg/kg). Seven dogs of both sexes were assigned to this experiment with a mean weight of  $20 \pm 4.8$  kg. Fifteen minutes after administering the acepromazine as pre-anesthetic medication, ketamine (3 mg/kg) was administered to 7 dogs in the group: Acepromazine-ketamine (AK). Systolic blood pressure (SBP) was measured, and echocardiography was performed immediately before application of the sedative protocol (M0), 15 minutes after the sedation (M1), and immediately after anesthesia induction (M2). The second anesthetic protocol was performed one month later with the same seven dogs; group: xylazine-ketamine (XK). Non-significant differences were observed in SBP and hemodynamic variables such as cardiac index, shortening fraction, and ejection fraction, between groups at all time points evaluated (M0, M1, and M2). The SBP was significantly reduced after anesthetic induction in dogs in the AK group. It can be concluded that; both AK and XK protocols similarly reduce the SBP in dogs subjected to anesthetic induction. All anesthetic induction protocols maintained a stable CI in all pre-medicated dogs. None of the two anesthetic protocols which were evaluated promoted significant echocardiographic changes. Furthermore, ketamine and xylazine combination hurt myocardial function. On the other hand, due to their cardiac depressant effects, acepromazine and xylazine anesthetic integration should be applied with attention in ill cases.

**Keywords:** Acepromazine, Xylazine, Ketamine, Echocardiography, Dogs.

\*Correspondence: Mahmoud A Nawar

Department of Surgery, Faculty of Veterinary Medicine, Damanhour University

Email: [mahmoudnawar1st@gmail.com](mailto:mahmoudnawar1st@gmail.com)

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### 1. Introduction

Chemical restraints are widely used in veterinary practice to increase the ease and safety of handling animals for diagnostic and therapeutic purposes. Acepromazine and xylazine are two drugs in this class that has been released for veterinary use. The basic mechanism of action of

acepromazine is through inhibition of dopaminergic-2 receptors in the brain (Garner, Kirby, and Rudloff 2004). The characteristics of acepromazine are that it can be anticonvulsant, antispasmodic, hypotensive, antiemetic, and hypothermic, and its administration produces muscle relaxation and no analgesic action (Achneck et al. 2007). Acepromazine has an elongated duration of action and is related to hypotension secondary to marked peripheral vasodilatation and response variability (Menzies-Gow, N.J. 2008). Xylazine sedative and analgesic actions are owing to stimulation of the pre- and post-synaptic  $\alpha_2$  adreno-receptors in the pontomedullary of the CNS, which decreases sympathetic outflow and causes sedation (Rand, Reynolds, and Priest 1996). Side impacts of  $\alpha_2$  adrenergic stimulation include initial hypertension followed by hypotension and bradycardia (Haapalinna et al. 1997).

Xylazine is often given in integration with ketamine along with anesthetic applications (Ritschl et al. 2015). Ketamine hydrochloride dissociates the cyclohexylamine group used for chemical restraint and the creation and maintenance of anesthesia in several species (Fleming 2001). Ketamine is seldomly used alone because of its association with poor muscle relaxation, tachycardia, and catalepsy or muscle rigidity. Consequently, we can give ketamine in integration with acepromazine, xylazine, and diazepam to decrease the adverse impacts. Hence, realizing the impacts of the ketamine in combination with other sedatives may help come out with the safest combination for surgical procedures in the native dog breed (Gross 2009). Ketamine is integrated with an alpha-2-agonist (e.g., xylazine) or a phenothiazine tranquilizer (e.g., acepromazine) to help relaxation and analgesia of muscles, prevent seizures and prolong the duration of the anesthetic effect (Sager and Norkus 2018). Ketamine is associated with an instant onset, good to excellent sedation of one to two hours' duration, excellent analgesia, and fine recovery. The analgesia and sedative effects are owing to central nervous system depression and the muscular relaxation is due to the central inhibition of intraneural transmission (Loots and Wiseman 2006). Unlike many anesthetics, ketamine usually stimulates cardiovascular function in normal animals, causing an increase in heart rate (HR) and mean arterial pressure (MAP). The use of ketamine as a single anesthetic has been restricted by muscle hypertonicity and myoclonus, a violent recovery, and the occasional occurrence of convulsions (Sumitra et al. 2004). Echocardiographic researches in animals tell that xylazine causes a marked reduction in myocardial contractility (Hanton et al. 2008). The present experimental study aimed to investigate both echocardiographic and biochemical changes following ketamine anesthesia induction in dogs, which were sedated with acepromazine (0.2 mg/kg) or xylazine (3 mg/kg).

## 2. Materials and Methods

### Study area

The present study was conducted from August 2021 to October 2021 at the Animal Panorama Clinic of the Faculty of Veterinary Medicine, Damanhour University, Damanhour, Egypt.

### Ethical approval

The present study was ethically approved by the Faculty of Veterinary Medicine, Damanhour University ethics and animal use committee with a reference number; 1-8/2021.

### Study population

The present study was conducted on mature and healthy native breeds of dogs with an average weight of  $(20 \pm 4.8 \text{ kg})$  aged between 6-12 months. Dogs were checked healthy according to physiologically normal parameters such as body temperature, heart rate, respiration rate, and oxygen sufficiency.

### Sample size

The present study was conducted on seven mature and healthy native breeds of dogs (four males and three females).

### Treatment design

The seven dogs were treated with two protocols as pre-medicated with two different sedatives one month apart, and the same anesthetic induction was used. The experimental procedures were conducted on the same group of dogs one month apart.

### Administration of Drugs

#### Protocol (A): Acepromazine with ketamine (AK)

All dogs were sedated with acepromazine (0.2 mg/kg) IM. (acepromal 10 mg, acepromazine maleate 10 mg, Brovafarma Co. Russia). After fifteen minutes of premedication, anesthetic induction ketamine HCl (3 mg/kg) IM (ketamine 50 mg as hydrochloride, Sigmatic Pharmaceutical Industries, Egypt) was administered.

#### Protocol (B): Xylazine with ketamine (XK)

All dogs were sedated with xylazine HCl (2 mg/kg) IM (XYLA-JECT 2%, Adwia pharmaceutical Co.10<sup>th</sup> of Ramadan city, Egypt). After fifteen minutes of premedication, anesthetic induction ketamine HCl (3 mg/kg) IM (Ketamine 50mg as hydrochloride, Sigmatic Pharmaceutical Industries, Egypt) was administered with a one-month interval between the two protocols.

### Echocardiographic and biochemical parameters

Place echocardiographic monitoring before sedation, fifteen minutes from sedation, then after induction of anesthesia to investigate end-diastolic volume, end-systolic volume, ejection fraction stroke volume, heart rate, and cardiac output by using My lab 30 gold estate with a micro convex transducer five MHz according to the procedures of **Cardoso et al (2018)**.

Three ml of blood samples were collected from the cephalic vein of each experimental dog before administration of the sedative and thirteen minutes after administration of the sedative and anesthetic agents. Twenty-four hours later, immediately after collection, the blood samples were transferred in a sterile plain test tube to apply centrifugation to obtain serum to investigate the effect of different protocols on cardiac enzymes cardiac troponin I and creatine kinase MB, total serum protein, creatinine, cholesterol, triacylglycerol, and the lipid profile using commercial kits (Biodignostic Co., Giza, Egypt).

### Data collection

Data were collected on echocardiographic effects (end-diastolic volume, end-systolic volume, ejection fraction stroke volume, heart rate, cardiac output), biochemical effects (cardiac enzymes cardiac troponin I and creatine kinase MB, total serum protein, creatinine, cholesterol, triacylglycerol, and the lipid profile)

### Experimental procedures

All dogs fasted for 12 hours before anesthetic administration. Two anesthetic protocols were designed, protocol A (AK): premedication with acepromazine (0.2 mg/kg) IM followed by administration of ketamine HCl (3 mg/kg) IM for induction, and the other protocol B (XK): premedication with xylazine HCl (2mg/kg) IM followed by administration ketamine HCl (3 mg/kg) IM for induction. Both anesthetic protocols were applied in the same animal group one month apart between the two protocols. Venous blood samples were collected from each dog for biochemical analysis (M0), then each dog was laid in right lateral recumbency. An echo ready 5-7.5 MHz transducer (*Esaoe - My lab™ 30 gold, veterinary ultrasound scanner*) was used for B mode

echocardiography. Fingertip was used to guide the most pulsative area between the 3<sup>rd</sup> and the 6<sup>th</sup> ribs to locate the heart. When determined, the micro convex probe with the mark under the thumb was applied longitudinally in the intercostal space. The right parasternal long-axis four-chamber (RPLAX) view is defined (**Figure 1**). After that, the probe turned 90° anticlockwise to reach the parasternal short axis (RPSAX) view where recorded (**Figure 2**). Motion mode (m-mode) was used to measure the ejection fraction by getting the fractional shortening from the m-mode and the current equation;  $FS \% = \frac{LVEDd-LVEDs}{LVEDd}$   $EF \% = FS \times 2$  (**Bakirel et al. 2008**).

Before sedation, echocardiographic measurements (T0) were noted. Sedative premed: acepromazine (protocol A) was administered, then, after 15 minutes, the second round of echocardiographic measures (T1) (after sedation) was performed. After 15 minutes of administration of acepromazine, ketamine was administered. Five minutes after induction, another round of echocardiographic evaluation (T2). Three venous blood samples (in plain tubes to evaluate biochemical parameters through their serum) from each dog were collected throughout the experiment: M0, before sedation; M1, after sedative and induction administration, after 24 hours to evaluate the biochemical parameters.

In protocol B, the same steps were performed in the same animal group by the same surgeon in the same circumstances one month apart from the former protocol, while xylazine was used as the sedative.

## 3. Statistical analysis

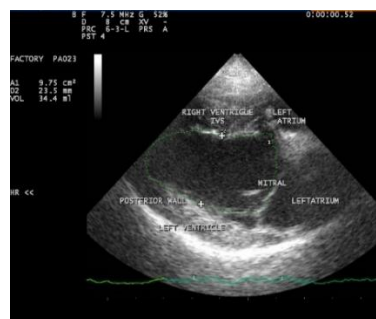
Data were applied to the computerized statistical program and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp) The Shapiro-Wilk test was used to verify the normality of distribution. Quantitative data were described using range (minimum and maximum), mean, standard deviation, and median. The significance level of the acquired results was judged at the 5% level.

The used tests were the student t-test for normally distributed quantitative variables, to compare two studied protocols and ANOVA with repeated measures for normally distributed quantitative variables, to compare between more than two periods, and the Post Hoc test (Bonferroni adjusted) for pairwise comparisons.

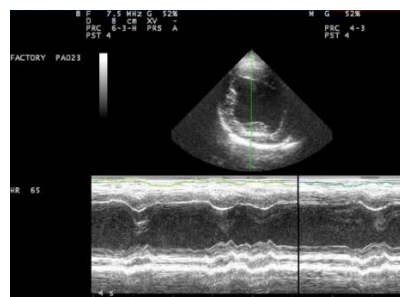
## 4. Results

### A. Echocardiographic findings

The outcome of end-diastolic volume ranged  $(55.8 \pm 2.4 \text{ ml})$ , and the end-systolic volume (ESV) ranged  $(25.4 \pm 2.8 \text{ ml})$  in all cases, while the range of stroke volume was  $(30.14 \pm 3.15 \text{ ml})$ . The average parameters in conscious, healthy dogs were ejection fraction (EF%)  $(54.71 \pm 5.8\%)$ , heart rate (HR)  $(91.7 \pm 9.7 \text{ bpm})$ , and cardiac output  $(2.68 \pm 0.3 \text{ lpm})$  (**Figure 3**). Other cardiac efficiency parameters of the conscious state were evaluated through echocardiography.



**Figure 1.** Locating the probe at the right long axis of the heart showing the four chambers, the so-called RPLAX view (End diastolic volume was:34.4 ml)



**Figure 2.** Shows the right parasternal short-axis view at the level of papillary muscles (mushroom shape), which appear in B-mode in the upper and M-mode (motion mode) in the lower of the image.

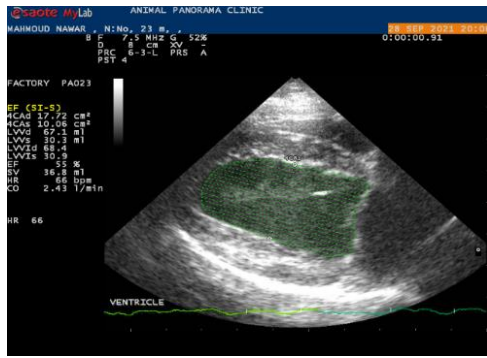


Figure 3. Shows the left ventricle in a conscious state as the ejection fraction was [55%], stroke volume [36.8 ml], and cardiac output [2.43 l/min].



Figure 4. Shows the right parasternal short-axis view at the level of the heart base showing the normal ratio between LA: AO as (1.5:1) in diameter

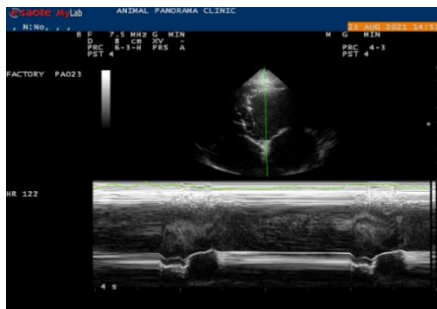


Figure 5. Shows the left apical 4 chamber view showing the heart upside down as the atriums in the lower of the image, the left atrium at the right side and the right atrium at the left side, the two ventricles at the upper and the interventricular septum isolate between them

The average echocardiographic parameters after administration of acepromazine as a sedative agent were, EDV (59.46 ± 3.75 ml), ESV (31.91 ± 2.05), EF% (54.2 ± 3.4 %), Stroke volume (27.7 ± 3.3), cardiac output (2.51 liter/min), HR (90.2 ± 6.2 bpm). All these parameters were tabulated in **Table 2**. The ratio evaluated between the left atrium and aorta didn't exceed 1.5:1 in the two protocols (Figure 4). After ketamine induction (AK protocol), the end-diastolic volume ranged (54.4 ± 1.3 mL), end-systolic volume ranged (25.9 ± 1.7), ejection fraction % ranged (54.2 ± 3.4 %), Stroke volume (28.45 ± 2.9 mL), heart rate (81.2 ± 6.5 bpm), cardiac output (2.2 ± 0.3 liter/min). All echocardiographic parameters were presented in **Table 3** and **Figure 5**.

In the second protocol (XK), the parameters after xylazine injection as a sedative agent the end-diastolic volume (EDV) ranged as (59.2 ± 3.2 mL), end-systolic volume ranged as (28.26 ± 2.4), stroke volume (31.01 ± 3.05), Ejection fraction% ranged as (59.2 ± 6.2), cardiac output (2.44 ± 0.5 l/min), Heart rate (80.1 ± 6.8 bpm). Cardiac parameters are presented in **Table 4**. After anesthesia induction by ketamine (XK protocol), the mean end-diastolic volume was (56.31 ± 4.3), the mean end-systolic volume (23.01 ± 2.7 ml), the mean ejection fraction% was (59.28 ± 6.2%), mean stroke volume was (33.28 ± 3.2), mean heart rate (83.28 ± 6.7), cardiac output (2.7 ± 0.4). **Figures 6-13** show the cardiac efficiency parameters variations following the two anesthetic protocols.

**B. Biochemical findings**

Cardiac troponin I was ranged in the conscious state as (0.039 ng/ml), and there was a slight elevation in the acepromazine ketamine protocol as (0.072 ng/mL) after recovery, a frequent increase in cardiac troponin I and creatine kinase MB after anesthesia in the different protocols. The total serum protein level in a conscious state before giving any anesthetics was ranged as (5.8 g/dL). Its range during anesthesia with acepromazine and ketamine was (6.3 g/dL) and after recovery was (5.6 g/dL), but after anesthesia with xylazine and ketamine, it was (6.2 g/dL), and after recovery, it became (5.9 g/dL). The creatinine level in a conscious state was (0.7 mg/dL) and during anesthesia with acepromazine and ketamine was (1.1 mg/dL). After recovery, it was (0.77 mg/dL), but during anesthesia with xylazine and ketamine was (1.13mg/dl), and after recovery, it was (0.8mg/dL). The biochemical analysis resulted in a range of (216.4 mg/dL) for the level of serum cholesterol in conscious state dogs, level of triacylglycerol was ranged as (97.2 mg/dL), high-density lipoprotein HDL was ranged as (123.2 mg/dL), low-density lipoprotein was (98.5 mg/dL), and very-low-density lipoprotein was ranged as (20.2 mg/dL). The result of using Acepromazine and ketamine during anesthesia (M1) the serum cholesterol level was (182.14 mg/dL), the level of triacylglycerol was (103.14 mg/dL), High-density lipoprotein was ranged to (103.2 mg/dL), Low-density lipoprotein level was (98.5 mg/dL), and very-low-density lipoprotein was ranged as (20.14 mg/dL). After recovery, the level of serum cholesterol was ranged as (163.2 mg/dL), the level of triacylglycerol was (95.7 mg/dL), high-density lipoprotein was ranged to 116.2 mg/dL, low-density lipoprotein was (96.4 mg/dl), and very-low-density lipoprotein was ranged after recovery as (20.7 mg/dL). Biochemical parameters were analyzed and presented in **Tables 1, 2, 3, and 4**.

Table 1. Shows cardiac troponin I and creatine kinase- MB before, after injection of sedative and anesthetic agent, and after recovery in the two protocols

Parameter	Time range	AK Protocol (n= 7)	XK Protocol (n= 7)	p
cTn I (ng/ml)	Before sedation	0.039 <sup>b</sup> ± 0.021	0.037 <sup>c</sup> ± 0.021	1.000
	Mean ± SD.			
	After sedation	0.072 <sup>a</sup> ± 0.019	0.078 <sup>b</sup> ± 0.042	0.723
	Mean ± SD.			
	After anesthetic induction ketamine	0.113 <sup>a</sup> ± 0.048	0.117 <sup>a</sup> ± 0.062	0.885
	Mean ± SD.			
	(p <sub>0</sub> )	(0.008 <sup>*</sup> )	(0.003 <sup>*</sup> )	
CK MB (U/L)	Before sedation	5.40 <sup>b</sup> ± 0.84	5.38 <sup>a</sup> ± 0.84	1.000
	Mean ± SD.			
	After sedation	5.99 <sup>a</sup> ± 0.38	5.56 <sup>b</sup> ± 0.77	0.213
	Mean ± SD.			
	After anesthetic induction ketamine	6.13 <sup>a</sup> ± 0.27	6.0 <sup>a</sup> ± 0.47	0.541
	Mean ± SD.			
	(p <sub>0</sub> )	(0.046 <sup>*</sup> )	(0.048 <sup>*</sup> )	

**Table 2.** Shows total Serum protein and Creatinine before, after injection of sedative and anesthetic agent, and after recovery in the two protocols

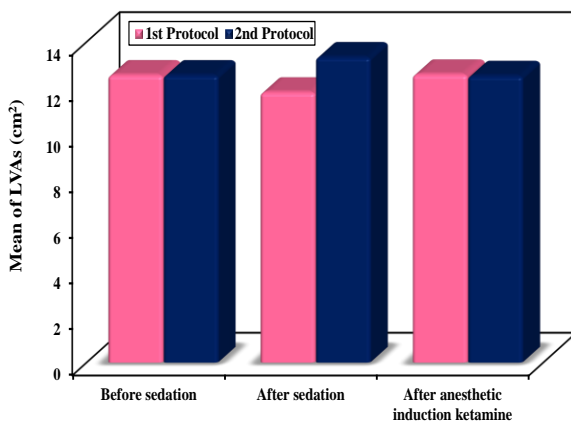
Parameter	Time range	AK Protocol (n= 7)	XK Protocol (n= 7)	p
Total protein (g/dl)	Before sedation Mean ± SD.	5.76 <sup>b</sup> ± 0.42	5.86 <sup>a</sup> ± 0.42	-
	After administration of sedation and anesthesia	6.33 <sup>a</sup> ± 0.54	6.20 <sup>a</sup> ± 0.62	0.686
	After recovery (p <sub>0</sub> )	5.60 <sup>b</sup> ± 0.40 (<0.001 <sup>*</sup> )	5.91 <sup>a</sup> ± 0.49 (0.203)	0.212
Creatinine mg/dl	Before sedation Mean ± SD.	0.76 <sup>b</sup> ± 0.13	0.79 <sup>b</sup> ± 0.13	-
	After administration of sedation and anesthesia	1.10 <sup>a</sup> ± 0.14	1.14 <sup>a</sup> ± 0.15	0.642
	After recovery Mean ± SD. (p <sub>0</sub> )	0.77 <sup>b</sup> ± 0.11 (<0.001 <sup>*</sup> )	0.87 <sup>b</sup> ± 0.08 (<0.001 <sup>*</sup> )	0.077

**Table 3.** Shows high, low, and very low-density lipoprotein before and after injection of sedative and anesthetic agents in the two protocols

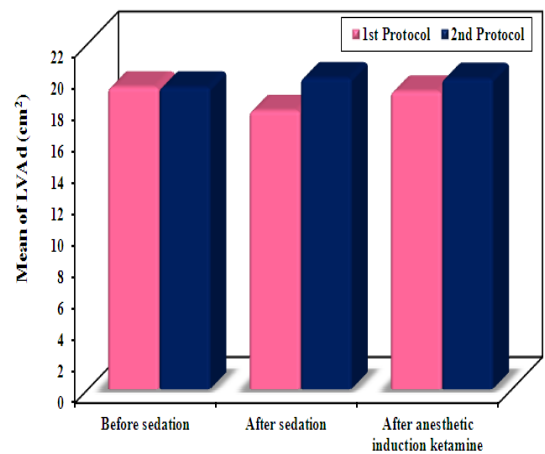
Parameter	Time range	AK Protocol (n= 7)	XK Protocol (n= 7)	p
HDL mg/dl	Before sedation	125.3 <sup>a</sup> ± 6.78	123.3 <sup>a</sup> ± 6.78	-
	After administration of sedation and anesthesia	103.3 <sup>c</sup> ± 9.45	102.7 <sup>c</sup> ± 4.39	0.887
	After recovery (p <sub>0</sub> )	116.3 <sup>b</sup> ± 6.85 (<0.001 <sup>*</sup> )	115.7 <sup>b</sup> ± 6.55 (<0.001 <sup>*</sup> )	0.876
LDL mg/dl	Before sedation	96.57 <sup>a</sup> ± 8.68	98.57 <sup>a</sup> ± 8.68	-
	After administration of sedative and anesthetic agent	97.86 <sup>a</sup> ± 5.55	99.57 <sup>a</sup> ± 9.88	0.696
	After recovery (p <sub>0</sub> )	96.43 <sup>a</sup> ± 7.21 (0.174)	94.14 <sup>b</sup> ± 6.52 (0.001 <sup>*</sup> )	0.545
VLDL mg/dl	Before sedation	23.29 <sup>a</sup> ± 2.56	20.29 <sup>ab</sup> ± 2.56	-
	After administration of sedative and anesthetic agent	20.14 <sup>a</sup> ± 1.57	21.57 <sup>a</sup> ± 1.72	0.131
	After recovery (p <sub>0</sub> )	20.71 <sup>a</sup> ± 2.43 (0.797)	18.86 <sup>b</sup> ± 2.41 (0.002 <sup>*</sup> )	0.177

**Table 4.** Showing cholesterol and Triacylglycerol before and after injection of sedative and anesthetic agents in the two protocols

Parameter	Time range	AK Protocol (n= 7)	XK Protocol (n= 7)	p
Cholesterol (mg/dl)	Before sedation	213.4 <sup>a</sup> ± 29.39	216.4 <sup>a</sup> ± 29.39	-
	After administration of sedative and anesthetic agent	182.1 <sup>b</sup> ± 27.13	192.7 <sup>b</sup> ± 29.65	0.500
	After recovery (p <sub>0</sub> )	163.3 <sup>c</sup> ± 31.04 (<0.001 <sup>*</sup> )	173.7 <sup>c</sup> ± 34.17 (<0.001 <sup>*</sup> )	0.561
Triacylglycerol (mg/dl)	Before sedation	94.29 <sup>b</sup> ± 7.16	97.29 <sup>a</sup> ± 7.16	-
	After administration of sedation and anesthesia	103.1 <sup>a</sup> ± 5.52	99.14 <sup>a</sup> ± 7.47	0.277
	After recovery (p <sub>0</sub> )	95.71 <sup>b</sup> ± 6.95 (<0.001 <sup>*</sup> )	94.29 <sup>b</sup> ± 6.26 (0.010 <sup>*</sup> )	0.693



**Figure 6.** Shows a comparison between the two studied protocols according to LVAs.



**Figure 7.** Showing comparison between the two studied protocols according to LVAd

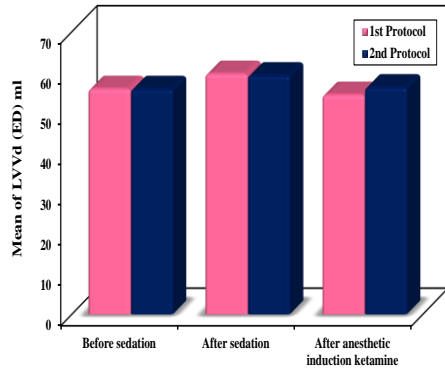


Figure 8. Shows a comparison between the two studied protocols according to LVVd. (EDV)

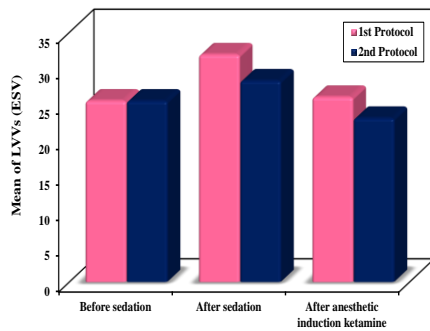


Figure 9. Shows a comparison between the two studied protocols according to LVVs (ESV)

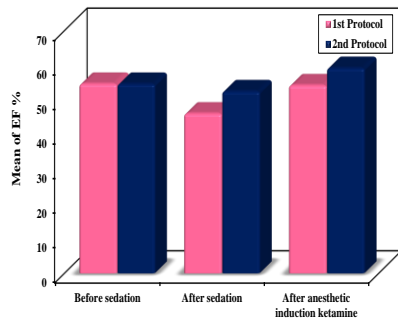


Figure 10. Shows a comparison between the two studied protocols according to EF%

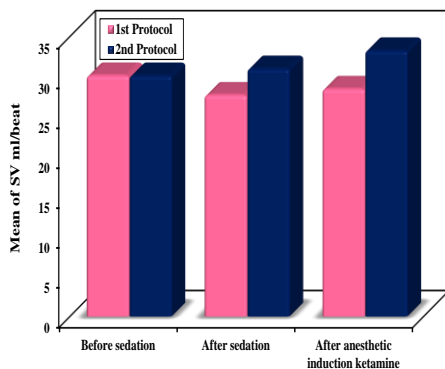


Figure 11. Shows a comparison between the two studied protocols according to SV

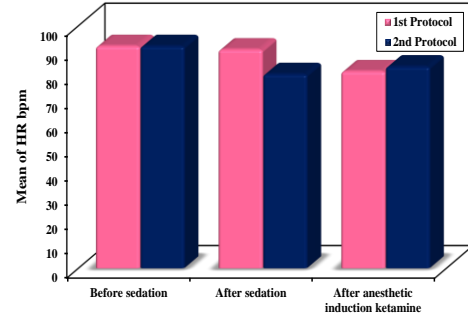


Figure 12. Shows a comparison between the two studied protocols according to HR

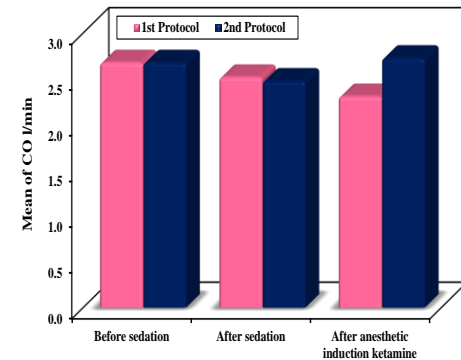


Figure 13. Shows a comparison between the two studied protocols according to CO

### 5. Discussion

The present research used two pre-anesthetics, acepromazine and xylazine, with a ketamine anesthetic induction agent. There was a non-significant difference between them in echocardiographic parameters except a significant decrease in heart rate after sedation by Xylazine and a significant increase in heart rate after induction by ketamine in xylazine ketamine protocol also, there was a non-significant difference in biochemical parameters except a significant increase in cardiac troponin I (cTnI) and creatine kinase MB after anesthesia relative to pre-anesthesia levels was observed in dogs after anesthesia with either acepromazine or xylazine ketamine and a significant increase in total serum proteins in xylazine ketamine after recovery than acepromazine ketamine. According to **Martinez and Papich (2009)**, when more than a single drug is given at the same time to an individual or during a time frame when a previously administered drug is still having its impact on the body, drug interactions may occur which may be beneficial or harmful. Acepromazine is often given as a pre-anesthetic agent as, in addition to resting the animal, it also decreases the dose of the anesthetic agent given to anesthetize animals (**Hazra et al. 2008**). Furthermore, it also decreases myocardial sensitization to catecholamines, thus reducing the risk of ventricular arrhythmias (**Monteiro et al. 2007**). However, despite these valuable effects, acepromazine induces vasodilatation due to an  $\alpha$ -adrenergic receptor blockade, which may lead to the establishment of hypotension through and after the induction of anesthesia (**Chen, Sinclair, and Dyson 2007**). After injection of acepromazine, there was a non-significant difference as an increase in end-systolic volume, which was at the conscious state ranging as  $55.8 \pm 2.4$  mL and became  $59.46 \pm 3.75$  mL followed by an increase in end-diastolic volume, which was in the conscious state of  $25.4 \pm 2.4$  mL and became  $31.91 \pm 2.05$  mL, the stroke volume also affected as occur reduction from  $30.14 \pm 3.15$  mL/beat to  $27.7 \pm 3.3$  mL/beat. The effect of acepromazine administration on heart rate is controversial, with some authors reporting an increase (**Driessen et al. 2011**) and others reporting no change (**Marroum et al. 1994; Walker and Geiser 1986**). However, the elevated left ventricular ESV leads to a secondary rise in left ventricular EDV because more blood stays inside the ventricle following the ejection. This extra blood is compiled to the venous return, thereby elevating ventricular filling, stretching the muscle fibers and increasing

their preload. The increased secondary preload facilitates the ventricle to contract with greater force, which partially offsets the reduction in SV caused by the initial increase in afterload. Similarly, acepromazine has been recorded as either increasing or decreasing cardiac output (Steffey et al. 1985). A similar result was seen by Muir and Mason, where acepromazine caused a decrease in blood pressure and vascular resistance due to vasodilation (Muir and Mason 1993). Xylazine decreases the heart rate (Wagner, Muir, and Hinchcliff 1991), increases the incidence of cardiac arrhythmia (McCashin and Gabel 1975), and raises blood pressure (Muir and Mason 1993). Ketamine can profoundly alter heart rate and thereby obscure any intrinsic relationship between echocardiographic parameters and heart rate (Çetin, Çetin, and Toker 2005; McCashin and Gabel 1975). The EF, which can be evaluated from the left ventricular dimensions via M-mode echocardiography, is another cardiac function parameter. In this study, an echocardiograph evaluated the EF automatically using the Teichholz formula. The accuracy of the Teichholz formula has not been evaluated in small rodents. Still, it has been shown to predict EF in human beings more accurately than other proposed formulas that use M-mode measurements (Kronik, Slany, and Mossbacher 1979; Martin 1978). In this study, there was a frequent increase in cTnI after anesthesia in the different protocols used for healthy dogs presenting for routine procedures, suggesting minor myocardial cell damage occurred in these dogs during or soon after anesthesia. Elevation of heart rate and arterial blood pressure and these disturbances may have contributed to the cTnI increases detected. Cardiac Troponin I have been documented previously as a sensitive and specific marker of cardiac ischemia in humans and animals (Adams et al. 1993; Babuin and Jaffe 2005; Hagman et al. 2007; Sleeper, Clifford, and Laster 2001). Further, other work using the same assay has also documented low cTnI concentrations in normal dogs with ranges reported between < 0.2 and 0.3 ng mL and < 0.05–0.24 ng mL suggesting the majority of elevated and increasing cTnI concentrations detected were associated with myocardial cell damage (Hagman et al. 2007; O'Brien et al. 2006). Pre-anesthetic myocardial damage was hypothesized for dogs with a decrease of postoperative cTnI. After anesthesia, the measured cTnI concentrations may have decreased if the myocardium was recovering. Persistent or continued muscle injury will maintain high CK activity. In normal dogs, the CK-MB reference range is 4.9-6.3U/I, according to Aktas et al (1993). The increasing level of total serum protein might be due to transient anesthetic stress leading to rise in glucocorticoids, which might have led to a slight rise in total protein levels (Goel et al. 2018). This also occurred with Suttil et al (2017) following xylazine-propofol anesthesia in dogs, and with Munif, Alam, and Alam (2021) after injection of xylazine ketamine in dogs. This study shows that using acepromazine and xylazine as pre-anesthetic with ketamine leads to a significant decrease in serum total cholesterol and LDL levels after administration and recovery.

## 6. Conclusion

It can be concluded that; both AK and XK protocols reduce the like SBP in dogs subjected to anesthetic induction. All anesthetic induction protocols maintained a stable CI in all pre-medicated dogs. None of the two anesthetic protocols which were evaluated promoted significant echocardiographic changes. Furthermore, ketamine and xylazine combination hurt myocardial function. On the other hand, due to their cardiac depressant effects, acepromazine and xylazine combination anesthetic protocol should be used with care in sick dogs.

## Conflict of interests

There are no conflicts of interest stated by the authors.

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