



Echocardiographic Effects of Tiletamine-zolazepam and Ketamine-diazepam in Dogs Undergoing Ovariohysterectomy

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ABSTRACT

Background: Echocardiography is ultrasound of heart. In order to promote reduction in mortality rates due to anaesthesia, it is essential to understand the potential depressant effects of anaesthetic drugs on the cardiovascular system, so that anaesthetic procedures are conducted in the best possible way. Cardiac monitoring during surgery offers rapid and safe information about the alterations that may appear during the surgical procedure that can affect cardiac functions.

Methods: The present study was undertaken to evaluate the echocardiographic effects of Tiletamine-zolazepam and Ketamine-diazepam anaesthetic combination in twelve healthy female dogs for ovariohysterectomy. These twelve dogs were randomly allotted to two equal groups irrespective of age, breed and body weight. Dogs were anaesthetized with Tiletamine-zolazepam (7.5 mg/kg, IV) in group I and Ketamine (5.0 mg/kg, IV)-Diazepam (0.5 mg/kg, IV) in group II. Atropine sulphate (0.04 mg/kg IM) followed by butorphanol (0.2 mg/kg IM) after 10 minutes was used as preanaesthetic drugs. Echocardiographic indices were recorded at different time intervals during the study period.

Result: Non-significant changes were found in both systolic and diastolic functions. Thus, present findings suggested that Tiletamine-Zolazepam and Ketamine-Diazepam anaesthetic combinations provided good cardiovascular stability in dogs undergoing ovariohysterectomy.

Key words: Diazepam, Dogs, Echocardiography, Ketamine, Tiletamine-zolazepam.

INTRODUCTION

Intravenous infusion of injectable anaesthetics, either alone or in combination with analgesic drugs is termed as total intravenous anaesthesia (TIVA) (Enouri *et al.*, 2008). Although anaesthesia achieved by injectable agents is safe, but may cause some potential side effects and complications particularly of cardiovascular system leading to mortality. In order to reduce mortality rates due to anaesthesia, it is essential to understand the potential depressant effects of anaesthetic drugs on cardiovascular system, so that anaesthetic procedures are conducted in the best possible way (Bille *et al.*, 2014). The patient administered with injectable anaesthesia should also be continuously monitored for vital parameters. Most anaesthetic agents cause a dose-dependent depression of the cardiovascular system and its monitoring allows not only an assessment of adequate circulatory function, but also provides information on depth of anaesthesia. Echocardiography is a non-invasive diagnostic tool for evaluating the structure and function of heart (Boon, 2011). It is useful in the assessment of heart valve, configuration and motion (Fox *et al.*, 1988). Dynamic images of the contracting heart are created with two-dimensional and motion mode (M-mode) while blood flow through the heart can be assessed with Doppler ultrasound (Boon, 2011). Standard echocardiography is commonly performed to non-invasively assess myocardial function and several two-dimensional (2D) and M-mode measurements such as systolic left ventricular diameter and index volume or fractional shortening (%FS) that are often used as indices of myocardial performance. Ultrasound can discriminate

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between blood filled cardiac chambers and soft tissue structures of heart. Evaluation of echocardiographic variables achieved over time after administration of anaesthetic agents provides an effective method for the evaluation of the safety of the anaesthetic protocol used. There was no studies on echocardiographic effect of tiletamine-zolazepam and comparative evaluation of echocardiographic effect of tiletamine-zolazepam and ketamine-diazepam in dogs. Hence, the objective of the study was to evaluate the echocardiographic effects following administration of the injectable anaesthetic combinations tiletamine-zolazepam and ketamine-diazepam in dogs undergoing ovariohysterectomy.

MATERIALS AND METHODS

The study was undertaken on twelve healthy female dogs to the Department of Veterinary Surgery and Radiology, College of Veterinary Sciences, Lala Lajpat Rai University of Veterinary and Animal Sciences, Hisar from October 2022 to March 2023. Atropine sulphate (0.04 mg/kg IM) followed by butorphanol (0.2 mg/kg IM) after 10 minutes was used as preanaesthetic drugs. Anaesthetic combinations Tiletamine-Zolazepam (7.5 mg/kg, IV) in group I and Ketamine (5.0 mg/kg, IV)-Diazepam (0.5 mg/kg, IV) in group II were used as induction as well as maintenance agents in dogs undergoing ovariohysterectomy. All the animals were subjected to thorough systemic investigation protocol for recording of parameters *viz.*, history, echocardiographic indices, doppler echocardiographic indices and statistical analysis. History included age, breed and body weight was recorded at the time of presentation in all the animals.

Echocardiography

Echocardiographic examination was carried out in a dark, quiet room, with dogs loosely restrained by their owner. The Siemens Acuson S2000 ultrasound machine (Siemens Healthcare Pvt. Ltd.) with multifrequency (4-9 MHz) cardiac probe was used for the present study. All the dogs were clipped on the right and left thoracic wall from 2nd to 7th intercostal spaces and placed in lateral recumbency on a specially designed table having "V"-shaped cut on the table top. Animals were kept quiet and comfortable to bring their heart rate to normal. After restraining the animal and application of the gel, the head of the transducer was placed over the palpated precordial beat over the chest. Then the proper echocardiography was done for individual dog in various modes *i.e.* right parasternal short axis view at chordae tendinae level (Fig 1). Echocardiography was performed before drug administration, after induction and at the end of surgery.

Two-dimensional echocardiography

Right parasternal long axis images

Left ventricular outflow view

The right parasternal location was obtained by placing the transducer from third to sixth intercostal spaces between the sternum and the costochondral junction. The transducer usually was placed within the 3rd to 5th intercostal space for small dogs and 4th to 6th intercostal space for large dogs. Reference mark was directed towards the animal's neck and face directed towards the animal's lumbar spine. Most animal have more than one echocardiography "windows", so the one with best resolution was chosen. Left ventricular outflow image include the aortic root, left ventricular outflow tract, left atrium, left ventricular chamber and mitral valve (Boon, 2011).

Four chamber view

Parasternal four-chamber images of the heart were obtained by rotating the reference mark of the transducer towards the spine past the shoulder after the left ventricular outflow plane though the heart was visualized (Boon, 2011).

Right parasternal short-axis images

Transverse or short-axis images of the heart were obtained by rotating the transducer towards the sternum with reference mark turned 90 degrees from its location for the long-axis plane. The transducer was held more perpendicular to the examination table. The fanning motion for scanning from apex to base followed the length of the heart along the imaginary line extending from the xiphoid to the shoulder (Boon, 2011).

Left ventricle with chordae tendinae

Transducer was rotated until images of the left ventricle show a circular shape with symmetrical papillary muscles and then slight fanning towards the base of the heart shows chordae tendinae at their attachment points to the papillary muscles (Boon, 2011) (Fig 1).

Mitral valve

The transducer was pivoted slightly towards the neck. At the level of the mitral valves, both sides of the valve should be attached to the lateral walls. The transducer was rotated back and forth until a symmetrical oval shaped valve was seen within the left ventricular chamber. Movement of the mitral valve in this imaging plane is referred to as the "fish mouth" (Boon, 2011).

Heart base-aorta

The transducer was pivoted more towards the neck and the aorta appeared in the middle of the image. Sometimes the transducer needed to be moved cranially to intercostal space and dorsally to improve the image. The image of the closed valve leaflets in this plane is often called the "Mercedes sign". The image in this plane includes the aorta, left atria, right atria, tricuspid valve, right ventricle, pulmonary valve and pulmonary artery. Echocardiography was performed before drug administration, after induction and at the end of surgery (Boon, 2011).

Doppler echocardiography

The Doppler examination was performed to determine the velocity of moving blood or tissue with the animal positioned

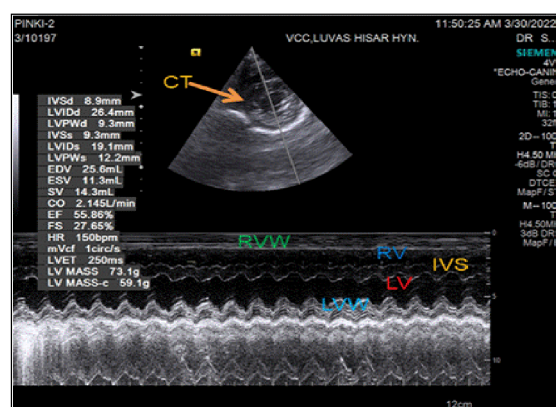


Fig 1: Echocardiogram showing right parasternal short axis view at chordae tendinae level.

in left lateral recumbency and examined from the cranial and caudal (apical) position. For optimal Doppler studies, the ultrasound beam was directed as parallel as possible to blood flow. From the cranial position, the base of the heart and the great vessels were examined while from the caudal (apical) position, the two, four and five-chamber views of the heart were examined.

The following parameters were evaluated in Doppler echocardiography (Fig 2 and 3).

- 1) Peak velocity of E- wave of mitral valve [MVEpt(m/sec.)].
- 2) Peak velocity of A-wave of mitral valve [MVApt(m/sec.)].
- 3) Ratio of E and A wave of mitral valve (E/A ratio).
- 4) Maximum aortic valve velocity [AVV_{max}(m/sec.)].
- 5) Maximum aortic valve pressure gradient [AVPG_{max} (mmHg)].

Statistical analysis

The statistical analysis was conducted via SPSS software. One-way ANOVA test was used to determine significant difference between different groups and between different time intervals. All the data values were expressed as Mean $\pm$ SE. P-values <0.05 was considered as statistically significant.

RESULTS AND DISCUSSION

The Mean value of age was 24.17 months and 27.33 months in groups I and II, respectively. The mean value of the body weight of dogs was 16.00 kg and 14.92 kg in groups

I and II, respectively. Out of twelve dogs, the breed of dogs in both groups was mongrel (n=6).

The effects of Tiletamine-Zolazepam and Ketamine-Diazepam combination on echocardiographic indices are shown in Table 1. Left Ventricular Internal Diameter at diastole (LVIDd) and Left Ventricular Internal Diameter at systole (LVIDs), Inter Ventricular Septum at diastole (IVSd) and Inter Ventricular Septum at systole (IVSs), Left Ventricular Posterior Wall Thickness at diastole (LVPWd) and Left Ventricular Posterior Wall Thickness at systole (LVPWs) showed non-significant changes in both the groups. The mean values of End Diastolic Volume (EDV) and End Systolic Volume (ESV) decreased non-significantly at induction and at the end of surgery as compared to before drug administration in both the groups whereas non-significant variations between the groups during entire observation period. Stroke Volume and Cardiac Output showed non-significant variation within groups and in between the groups. The mean values of Ejection Fraction and Fraction Shortening showed non-significant higher values when compared to before drug administration till the end of surgery in both the groups, whereas non-significant lower values when compared till before drug administration to the end of surgery in between the groups. Left Ventricular Ejection Time showed non-significant variation in both the groups. E-Point to Septal Separation and Left Atrium to Aortic Ratio changed non-significantly in both the groups in comparison to respective base values during entire observation period.

The effects of Tiletamine-Zolazepam and Ketamine-Diazepam combination on Doppler echocardiographic indices are shown in Table 2. Peak velocity of E-wave of mitral valve changed non-significantly between the groups during entire observation period. In group I, Peak velocity of E-wave of mitral valve decreased significantly ($p<0.05$) after induction and at the end of surgery as compared to before drug administration and non-significant difference was observed between induction and at the end of surgery, whereas in group II, the values decreased significantly ($p<0.05$) and non-significantly at the end of surgery as compared before drug administration and at induction, respectively. Peak velocity of A-wave of mitral valve changed non-significantly between the groups in comparison to respective base values during entire observation period. In both the groups, the Mean $\pm$ SE values for Peak velocity of A-wave of mitral valve significantly ($p<0.05$) decreased at induction and at the end of surgery. E and A wave ratio of mitral valve showed non-significant increase and decrease in groups I and II, respectively. However, non-significant variation was observed in between the groups. Maximum aortic velocity and maximum aortic pressure gradient showed non-significant decreased when compared to before drug administration till the end of surgery in group II and non significant variation in group I. No significant variation observed in between the groups.

The Mean $\pm$ SE value of age was 24.17 and 27.33 months in groups I and II, respectively. The Mean $\pm$ SE

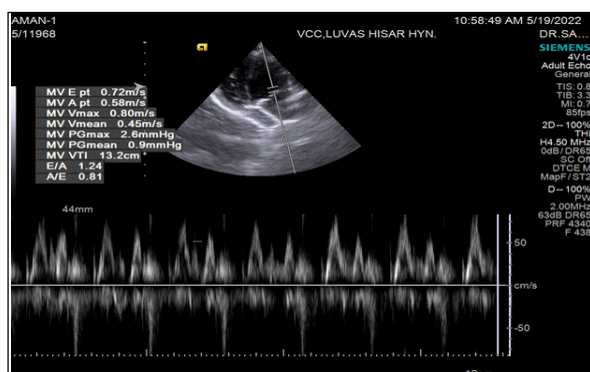


Fig 2: Doppler echocardiogram showing left parasternal apical view at mitral valve level.

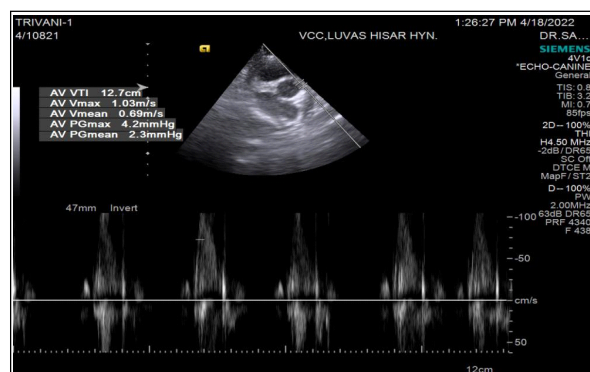


Fig 3: Doppler echocardiogram showing left parasternal apical view at aortic valve level.

Table 1: Echocardiographic indices recorded at different time intervals in both the groups (Mean $\pm$ SE).

Echocardiographic indices	Group	Before drug administration (T0)	After induction (T1)	At the end of surgery (TS)
LVIDd (mm)	I	37.77 $\pm$ 2.82	34.72 $\pm$ 1.13	41.33 $\pm$ 0.85
	II	35.35 $\pm$ 1.12	33.98 $\pm$ 1.35	36.17 $\pm$ 2.73
LVIDs (mm)	I	20.85 $\pm$ 1.70	17.95 $\pm$ 1.95	21.12 $\pm$ 1.28
	II	26.05 $\pm$ 0.41	22.17 $\pm$ 1.72	22.62 $\pm$ 2.58
IVSd (mm)	I	8.03 $\pm$ 0.22	6.42 $\pm$ 1.09	7.48 $\pm$ 0.80
	II	7.65 $\pm$ 0.82	6.70 $\pm$ 0.46	7.58 $\pm$ 0.81
IVSs (mm)	I	10.28 $\pm$ 0.51	7.48 $\pm$ 1.35	8.38 $\pm$ 0.27
	II	9.87 $\pm$ 0.64	8.87 $\pm$ 0.38	8.48 $\pm$ 1.27
LVPWd (mm)	I	8.98 $\pm$ 0.55	8.73 $\pm$ 1.47	7.62 $\pm$ 0.46
	II	8.13 $\pm$ 0.88	8.87 $\pm$ 0.24	8.13 $\pm$ 0.70
LVPWs (mm)	I	8.55 $\pm$ 0.98	8.50 $\pm$ 1.37	10.45 $\pm$ 0.62
	II	10.00 $\pm$ 0.74	11.72 $\pm$ 0.82	10.13 $\pm$ 1.25
EDV (ml)	I	40.47 $\pm$ 4.77	38.48 $\pm$ 1.72	39.95 $\pm$ 1.90
	II	42.47 $\pm$ 3.51	41.73 $\pm$ 3.67	42.33 $\pm$ 6.90
ESV (ml)	I	24.75 $\pm$ 2.38	20.65 $\pm$ 2.54	18.43 $\pm$ 2.35
	II	24.80 $\pm$ 0.97	17.40 $\pm$ 3.39	19.38 $\pm$ 5.36
SV (ml)	I	16.75 $\pm$ 3.55	19.82 $\pm$ 0.82	21.83 $\pm$ 3.38
	II	17.68 $\pm$ 2.87	15.33 $\pm$ 1.85	12.95 $\pm$ 3.57
CO (L/min)	I	1.53 $\pm$ 0.30	1.78 $\pm$ 0.14	2.53 $\pm$ 0.57
	II	1.92 $\pm$ 0.35	2.03 $\pm$ 0.27	1.62 $\pm$ 0.46
EF (%)	I	52.85 $\pm$ 11.66	56.60 $\pm$ 8.47	57.98 $\pm$ 6.73
	II	50.30 $\pm$ 3.60	54.76 $\pm$ 5.50	56.78 $\pm$ 10.45
FS (%)	I	25.87 $\pm$ 6.51	27.12 $\pm$ 5.50	30.62 $\pm$ 4.73
	II	25.16 $\pm$ 2.01	26.95 $\pm$ 2.96	29.46 $\pm$ 5.69
LVET (ms)	I	255.83 $\pm$ 40.12	251.67 $\pm$ 10.75	297.83 $\pm$ 20.33
	II	229.33 $\pm$ 37.04	259.67 $\pm$ 36.51	240.33 $\pm$ 17.87
EPSS (mm)	I	2.82 $\pm$ 0.72	2.70 $\pm$ 0.64	4.05 $\pm$ 0.90
	II	3.79 $\pm$ 0.75	4.02 $\pm$ 0.45	4.48 $\pm$ 0.80
LA/Ao	I	0.98 $\pm$ 0.02	1.02 $\pm$ 0.04	1.03 $\pm$ 0.04
	II	0.91 $\pm$ 0.02	0.97 $\pm$ 0.04	0.95 $\pm$ 0.05

Group I: Tiletamine-zolazepam; Group II: Ketamine-diazepam.

Table 2: Doppler echocardiographic indices recorded at different time intervals in both the groups (Mean $\pm$ SE).

Echocardiographic doppler indices	Groups	Before drug administration (T0)	After induction(TI)	At the end of surgery (TS)
MVEpt (mm)	I	0.83 ^B $\pm$ 0.05	0.75 ^A $\pm$ 0.07	0.74 ^A $\pm$ 0.04
	II	0.79 ^B $\pm$ 0.05	0.62 ^{AB} $\pm$ 0.06	0.55 ^A $\pm$ 0.04
MVApt (mm)	I	0.58 ^C $\pm$ 0.02	0.49 ^B $\pm$ 0.01	0.46 ^A $\pm$ 0.02
	II	0.46 ^C $\pm$ 0.04	0.42 ^B $\pm$ 0.05	0.41 ^A $\pm$ 0.05
E/A	I	1.45 $\pm$ 0.10	1.51 $\pm$ 0.12	1.64 $\pm$ 0.03
	II	1.72 $\pm$ 0.14	1.63 $\pm$ 0.12	1.35 $\pm$ 0.09
AW _{max}	I	1.00 $\pm$ 0.07	0.83 $\pm$ 0.13	0.89 $\pm$ 0.03
	II	0.98 $\pm$ 0.01	0.89 $\pm$ 0.07	0.84 $\pm$ 0.06
AVPg _{max}	I	4.00 $\pm$ 0.30	2.76 $\pm$ 0.32	3.18 $\pm$ 0.21
	II	3.84 $\pm$ 0.12	3.17 $\pm$ 0.46	2.90 $\pm$ 0.36

Means with different superscripts in a row differ significantly ($p < 0.05$).

Group I: Tiletamine-Zolazepam; Group II: Ketamine-Diazepam.

value of the body weight of dogs was 16.00 and 14.92 Kgs in groups I and II, respectively. Similar findings were also observed by Poonia (2021).

The effects of Tiletamine-Zolazepam and Ketamine-Diazepam combination on echocardiographic indices are shown in Table 1. Cardoso *et al.*, (2018) studied the effect

of drugs acepromazine (0.05mg/kg) and butorphanol (0.3 mg/kg), which were administered intramuscularly and 15 minutes after this, echocardiography was evaluated. Thereafter, induction was done by diazepam (0.5 mg/kg) and ketamine (3 mg/kg) and observed that there was no significant difference between groups and between different time points. Poonia (2021) observed that left ventricular internal diameter at diastole decreased non-significantly after pre medication from the base value and then there was non-significant increase after induction and at the end of the surgery whereas non-significant variation in Left ventricular internal diameter at systole, inter ventricular septum at diastole (IVSd) and inter ventricular septum at systole (IVSs), end diastolic value and end systolic value, E-point to septal separation, left atrium to aortic ratio and left ventricular ejection time in dogs administered midazolam for sedation and ketamine for induction. Kumar (2021) recorded that left ventricular posterior wall thickness at diastole increased non-significantly after midazolam administration at various intervals during observation period in comparison to the respective base values.

In contrast to the present study, Suh *et al.* (2015) studied echocardiographic left ventricle indices for myocardial contractility after administration of the combination of medetomidine and tiletamine/zolazepam (DZ) in beagle dogs and found that it directly depress myocardial contractility evidenced by the increased Left ventricular internal diameter at systole during anaesthesia, although it was unclear which drug was more attributable for this myocardial depression, because many contributing factors were involved in myocardial contractility and stroke volume, cardiac output were decreased after the initiation of anaesthesia. The reduction of cardiac output in this study might be due to the decrease in heart rate, increase in vascular resistance or a direct depression of myocardial contractility. However, echocardiographic left ventricle indices gradually returned to baseline levels, since the tiletamine might improve cardiac performance as suggested by another study by Ko *et al.* (2007). Poonia (2021) observed that there was significant decrease in stroke volume and cardiac output after sedation and then increased significantly at induction, whereas decreased non-significantly at the end of the surgery and ejection fraction and fractional shortening declined significantly after premedication, increased significantly at induction and then decreased significantly at the end of surgery in the dogs administered midazolam for sedation and ketamine for induction.

The effects of tiletamine-zolazepam and ketamine-diazepam combination on Doppler echocardiographic indices are shown in Table 2. Cardoso *et al.* (2018) studied the effect of drugs acepromazine (0.05mg/kg) and butorphanol (0.3mg/kg), which were administered intramuscularly and 15 minutes after this, echocardiography was evaluated. Then, induction was done by diazepam 0.5mg/kg and ketamine 3 mg/kg and observed that there was no significant difference between the groups and between different time points for values of peak velocity of the E and A wave of the mitral valve, and peak velocity of the E and A

wave of the mitral valve ratio (E/A ratio) and also observed that there was no significant difference between the groups and between different time points for values of maximum velocity of the aorta and maximum aortic pressure gradient.

Singh *et al.* (2019) studied in Crossbred Holstein Friesian Cows on short axis M-mode echocardiography and found that echocardiography can be conducted in non-sedated crossbred cow in standing. Significant negative correlation for the parameters Relative wall thickness at end systole (RWTs) was observed in Crossbred Holstein Friesian cow.

Bodh Deepti *et al.* (2022) studied on Pulsed-wave Doppler Echocardiographic Parameters of Blood Flow through Mitral, Tricuspid and Aortic Valves in Healthy Indian Spitz Dogs and found that Mitral, tricuspid and aortic valve flow variables were unaffected by gender whereas isovolumic relaxation correlated positively with body weight.

Yadav *et al.* (2023) studied Characterization of Cardiac Diseases in Dogs Prevalent in Indian Conditions and concluded that Dilated cardiomyopathy (DCM) as the most prevalent cardiac affection. Left ventricular dilation, interventricular septum thinning, increased E point septal separation and left atrial enlargement were characteristic echocardiographic indices in DCM. Echocardiographic indices in hypertrophic cardiomyopathy were increased interventricular septum, left ventricular posterior wall and reduced left ventricular lumen. Labrador retriever found to be most predisposed breed for DCM while Rottweiler reported to be most affected with pericardial effusion.

CONCLUSION

There was non-significant variation in echocardiographic indices *i.e.* the systolic functions were normal, but significantly altered Doppler echocardiographic indices in both the groups, however the statistically significant values were within normal range *i.e.* diastolic functions were also normal. Both anaesthetic combinations were safe for cardiovascular system. On the basis of echocardiographic and Doppler echocardiographic indices, it was concluded that tiletamine-zolazepam and ketamine-diazepam anaesthetic combinations provided good cardiovascular stability in dogs undergoing ovariohysterectomy.

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Conflict of interest

The authors have no conflict of interest.

REFERENCES

- Bille, C., Auvigne, V., Bomassi, E., Durieux, P., Libermann, S. and Rattez, E. (2014). An evidence-based medicine approach to small animal anaesthetic mortality in a referral practice: The influence of initiating three recommendations on subsequent anaesthetic deaths. *Journal of Veterinary Anaesthesia and Analgesia*. 41: 249-258.

- Bodh, D., Mozammel, H., Saxena, A.C. (2022). Studies on pulsed-wave doppler echocardiographic parameters of blood flow through mitral, tricuspid and aortic valves in healthy Indian spitz dogs. *Indian Journal of Animal Research*. 56(10): 1246-1251. doi: 10.18805/IJAR.B-4256.
- Boon, J. A. (2011). *Veterinary Echocardiography*. 2nd Edn. Williams and Wilkins, Baltimore, USA.
- Cardoso, M.H., Tochetto, R., Padilha, V.S., Silva, G., Comassetto, F., Andrade, J.N.B.M. and Nilson, O. (2018). Echocardiographic evaluation of dogs subjected to different protocols of anaesthetic induction. *Ciencia Rural*. 48(8): 1-5.
- Enouri, S.S., Kerr, C. L., McDonell, W.N. and Dyson, D.H. (2008). Cardiopulmonary effects of anaesthetic induction with thiopental, propofol or a combination of ketamine hydrochloride and diazepam in dogs sedated with a combination of medetomidine and hydromorphone. *American Journal of Veterinary Research*. 69(5): 586-595.
- Fox, P.R., Sisson, S. and Moise, N.S. (1988). In: *Text Book of Canine and Feline Myocardial Diseases of Dogs*. W.B. Saunders Company, Philadelphia. p. 230.
- Ko, J.C., Payton, M., Weil, A.B., Kitao, T. and Haydon, T. (2007). Comparison of anesthetic and cardiorespiratory effects of tiletamine-zolazepam-butorphanol and tiletamine-zolazepam-butorphanol-medetomidine in dogs. *Veterinary Therapeutics*. 8: 113-126.
- Kumar, R. (2021). Evaluation of propofol and isoflurane anaesthesia in acepromazine/midazolam/Dexmedetomidine premedicated dogs with Special reference to echocardiography. Ph.D. thesis submitted to ICAR-Indian Veterinary Research Institute, Izatnagar (U.P.), India.
- Poonia, A. (2021). Echocardiographic Evaluation in Dogs undergoing Elective Surgery Under Dexmedetomidine/Midazolam-Ketamine Anaesthesia. M.V.Sc. thesis submitted to Lala Lajpat Rai University of Veterinary and Animal Sciences, Hisar.
- Singh C.K., Singh N., Singh T., Singh P., Mohindroo J., Mahajan S.K. (2019). Clinical study on short axis M-mode echocardiography in Crossbred Holstein Friesian Cows. *Indian Journal of Animal Research*. 54(2): 249-253. doi:10.18805/ijar.B-3762.
- Suh, S., Kim, T. J., Lee, E. C. and Hyun, C. (2015). Effect of Medetomidine and Combination of Medetomidine/ Tiletamine/ Zolazepam and Medetomidine/ Tiletamine/ Zolazepam/ Tramadol on echocardiographic cardiac contractility in dogs. *Journal of Veterinary Clinics*. 32(5): 422-425.
- Yadav, A., Kumar, T., Sindhu, N., Agnihotri, D., Jajoria, C. and Sharma, M. (2023). Characterization of Cardiac Diseases in Dogs Prevalent in Indian Conditions. *Indian Journal of Animal Research*. 57(5): 644-649. doi: 10.18805/IJAR.B-4544.