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Echocardiographic indices probe during dexmedetomidine/midazolam - ketamine anesthesia in dogs undergoing ovariohysterectomy

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Abstract

Cardiovascular and respiratory alterations during anesthesia are of major concern in canines. Thus, it is essential to understand the potential depressant effects of anesthetic drugs on cardiovascular system; so that, anesthetic procedures are conducted in the best possible way. The objective of the study was to assess and compare the echocardiographic indices during dexmedetomidine and midazolam anesthesia in dogs undergoing elective ovariohysterectomy. Twenty-eight female dogs brought to the department for elective ovariohysterectomy were randomly divided into two groups comprising of 14 each. Sedation was achieved with dexmedetomidine and G_{MID}. Physiological parameters and echocardiographic indices were evaluated before drug administration (T_0), after 10 min of sedation (T_1), after induction (T_2) and at the end of surgery (T_3) in both groups. Heart rate was significantly higher at T_1, T_2 and T_3; while, rectal temperature was significantly lower at T_3 in G_{MID} compared to the G_{DEX}. There was a significant decrease in stroke volume and cardiac output values at T_1 and then, a significant increase at T_2; whereas, there was a non-significant decrease at T_3 in both groups. Ejection fraction and fractional shortening values decreased significantly at T_1, increased significantly at T_2 and then, decreased significantly at the end of surgery (T_3). Dexmedetomidine-ketamine and midazolam-ketamine combinations provide better hemodynamic and respiratory stability in the dogs undergoing elective ovariohysterectomy. Systolic functions were minimally altered with G_{MID} compared to G_{DEX}. Thus, G_{MID} is more cardio stable compared to G_{DEX}.

Introduction

Anesthesia is a state of controlled and temporary loss of sensation manifested by analgesia, muscle relaxation and unconsciousness. The clinician selects one or more drugs to achieve the types and degrees of anesthesia being appropriate for the surgery and safe for the patient. Premedication is a crucial step of the anesthetic management as the choice of the sedative affects the subsequent anesthetic protocol.[1] In dogs, the most common sedative drugs are α_2-agonists, most often dexmedetomidine (dex) and medetomidine, and often used in conjunction with opioids or non-steroidal anti-inflammatory drugs for a synergistic effect.[2] The sedative action of dex is due to stimulation of α_2-adrenoceptors subtypes a, b and c in locus coeruleus of the brain.[3] Midazolam is an imidazobenzodiazepine acting as an agonist on the gamma-aminobutyric acid receptor. Similar to other benzodiazepine agonists, it induces anti-convulsant, anxiolytic, sedative/hypnotic, amnesic and centrally mediated muscle relaxant effects.[4] Ketamine is a dissociative anesthetic primarily used as an induction and maintenance agent. It induces dissociative anesthesia, a trance like state providing pain relief, sedation and amnesia.[5] Mortality due to cardiovascular and respiratory alterations during anesthesia is of major concern in canines.[6] In order to promote reduction in mortality rates due to anesthesia, it is essential to understand the potential depressant effects of anesthetic drugs on the cardiovascular system; so that, anesthetic procedures are conducted in the best possible way.[7] The reaction of the cardiovascular system to anesthetics can be different and thus, echocardiography should be applied for the scanning of direct vascular impacts of anesthetics.[8] It allows an evaluation of the space relationship between

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structures, cardiac movement and blood flow features and the precise and non-invasive diagnosis of cardiac alterations as well as follow-up therapy and to determine the prognosis through direct vision of cardiac chambers. Conventional echocardiographic modalities include real time B-mode, M-mode and Doppler modes. The M-mode recordings permit quantitative measurement of cardiac dimensions and detailed analysis of complex motion patterns depending on transducer angulation. It facilitates analysis of time relationships with other physiological variables such as heart sounds and pulse tracings, which can be recorded simultaneously.[9] However, to date, no study has been found addressing the effects of a dexmedetomidine-ketamine or midazolam-ketamine combinations on echocardiographic variables of dogs undergoing elective ovariohysterectomy. Therefore, the present study was designed to assess and compare the echocardiographic effects of G_{DEX} and G_{MID} in dogs undergoing elective ovariohysterectomy.

Materials and Methods

The present study was conducted on twenty-eight female dogs irrespective of age, breed and body weights brought to the Department of Veterinary Surgery and Radiology, College of Veterinary Sciences, Lala Lajpat Rai University of Veterinary and Animal Sciences, Hisar, India, for elective ovariohysterectomy. These animals were randomly divided into two groups comprising of 14 animals in each group. In animals of both groups, 0.04 mg kg^{-1} atropine sulfate (Neon Laboratories Ltd., Mumbai, India) and 0.30 mg kg^{-1} meloxicam (Intas Pharmaceuticals Pvt. Ltd., Ahmedabad, India) were administered intramuscularly (IM) as pre-medication agents. For sedation in G_{DEX} and G_{MID} groups, intramuscular 15.00 µg kg^{-1} dexmedetomidine (Neon Laboratories Ltd.) and intravenous 0.50 mg kg^{-1} midazolam (Neon Laboratories Ltd.) were administered, respectively. Induction was achieved by administration of 5.00 mg kg^{-1} ketamine hydrochloride (Troikaa Pharmaceuticals Ltd., Dehradun, India) intramuscularly till effect. Anesthesia was maintained by administration of intramuscular dexmedetomidine + ketamine and intravenous midazolam + ketamine in G_{DEX} and G_{MID} groups, respectively.

Dogs having normal physiological and echocardiographic values were included in the study. Physiological parameters and echocardiographic indices were recorded before drug administration (T_0), after 10 min of dexmedetomidine/midazolam administration (T_1), after induction with ketamine (T_2) and at the end of surgery (T_3) in animals of both groups.

Echocardiographic examination was carried out in a dark, quiet room, with dogs loosely restrained by their owner. The Siemens Acuson S2000 ultra-sound machine (Siemens Healthcare Pvt. Ltd., Erlangen, Germany) with multi-frequency (4.00 – 9.00 MHz) cardiac probe was used for the present study. All the dogs were clipped on the right thoracic wall from 2nd to 7th inter-costal spaces and placed in lateral recumbency on a specially designed table having V- shaped cut on the table top. Transducer was placed over the inter-costal spaces of animal after applying coupling gel through the cut on the table. The M-mode echocardiographic measurements of the left ventricle were made from the right para-sternal short-axis view at the level of the papillary muscles (Fig. 1). Left ventricular internal diameter in systole and diastole (LVIDs and LVIDd, respectively), inter-ventricular septum in systole and diastole (IVSs and IVSd, respectively), left ventricular posterior wall in systole and diastole (LVPWs and LVPWd, respectively), end diastolic volume (EDV), end systolic volume (ESV), stroke volume (SV), cardiac output (CO), ejection fraction (EF), fractional shortening (FS), left ventricular ejection time (LVET) and left ventricular mass (LVM) were measured. The E point to septal separation (EPSS) and EF slope were measured from the right para-sternal short-axis view at mitral valve level (Fig. 2). Left atrial to aortic (LA/Ao) ratio was measured in real time B-mode echocardiography.

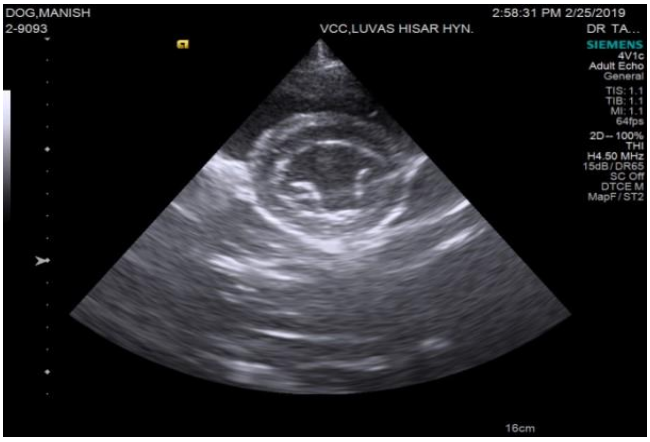

Fig. 1. Echocardiogram showing right para-sternal short-axis view at papillary muscle level (mushroom-shaped appearance).

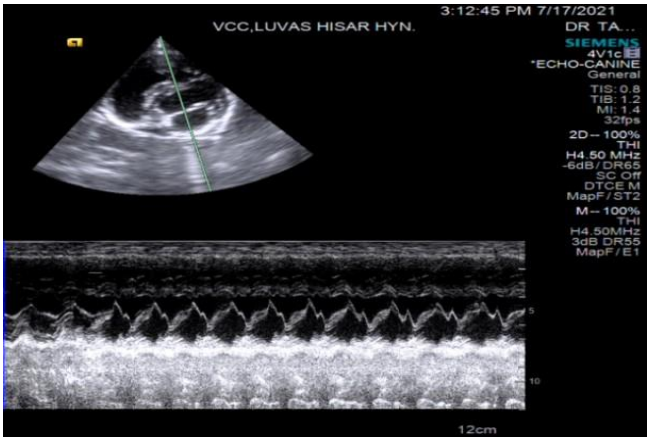

Fig. 2. Echocardiogram showing right para-sternal short-axis view at mitral valve level (Fish mouth appearance).

Statistical analysis. Statistical analysis was conducted *via* SPSS Software (version 23.0; IBM Corp., Armonk, USA). Two-way ANOVA test was used to determine a significant difference between different groups and different time intervals. All the data were expressed as Mean ± SE and pair wise comparison was done using Duncan Test. The *p*-values ≤ 0.05 were considered as statistically significant.

Results

The mean age of animals was 2.82 ± 0.55 and 2.34 ± 0.38 years, and body weight was 18.93 ± 2.14 and 18.36 ± 1.95 kg in G_{DEX} and G_{MID}, respectively. All the animals were female. The breeds included in the present study were Mongrel, Labrador, Pomeranian, Pug, Rottweiler and Pakistani Bully.

The values of heart rate (beats *per* min), respiratory rate (breaths *per* min) and rectal temperature (˚C) at different time intervals are shown in Table 1. Heart rate and rectal temperature were significantly ($p \leq 0.05$) higher (T_1, T_2 and T_3 intervals) and lower (T_3 interval) in G_{MID} compared to the G_{DEX}, respectively. Respiratory rate showed non-significant changes at different time intervals. Within the group comparison, the mean values of heart rate in G_{DEX} decreased significantly ($p \leq 0.05$); while, they increased significantly ($p \leq 0.05$) in G_{MID} at T_1 and then, increased significantly ($p \leq 0.05$) at T_2 in both groups. However, the values decreased non-significantly (G_{DEX}) and significantly (G_{MID}) at T_3 compared to the T_2. Rectal temperature and respiratory rate showed significantly lower values at T_1, T_2 and T_3 compared to the base values (T_0) in both groups.

The values of echocardiographic indices at different time intervals are shown in Table 2. The mean values of LVIDd, EDV and EF slope were significantly ($p \leq 0.05$) higher at T_0, T_1 and T_2 intervals in G_{DEX} compared to the G_{MID}. Significant ($p \leq 0.05$) higher values (LVIDs, ESV, LVET and LVM) and lower values (FS) were observed at T_1, T_2 and T_3 intervals in G_{DEX} compared to the G_{MID}. The mean values of LVPWd and SV were significantly ($p \leq 0.05$) higher at T_2 interval; whereas; LVPWs showed significantly ($p \leq 0.05$) higher values before drug administration in G_{DEX} compared to the G_{MID}. A non-significant variation was observed in the values of IVSd, ISVs and LA/Ao ratio at different time intervals.

Comparison within the group revealed significant differences in the values of SV, CO, EF, FS, LVET and EPSS at different time intervals in both groups. The mean values of LVIDs were increased significantly ($p \leq 0.05$) from T_2 to T_3 in G_{DEX}. A significant decrease was observed in the values of ESV at T_1 and T_2 interval compared to T_0; whereas, the mean values of EDV decreased and increased significantly ($p \leq 0.05$) at T_1 and T_3 time interval, respectively, in G_{MID}. A non-significant variation was observed in the mean values of LVIDd, IVSd, ISVs, LVPWd, LVPWs, LVM, EF Slope and LA/Ao ratio in both groups at different time intervals in the present study.

Discussion

The mean age and body weight of animals showed non-significant variations in both groups. However, Howe has suggested that spaying at an early age increases longevity and reduces the chances of life-threatening affections such as mammary neoplasia and pyometra.[10] Heart rate and rectal temperature were significantly higher (T_1, T_2 and T_3 intervals) and lower (T_3 interval) in G_{MID} compared to the G_{DEX}, respectively. Respiratory rate showed a non-significant variation at different time intervals. Comparison within the group revealed that the mean values of heart rate in G_{DEX} decreased significantly; while, they increased significantly in G_{MID} at T_1, then significantly increased at T_2 in both groups. However, the values decreased non-significantly in G_{DEX} and significantly in G_{MID} at T_3 compared to T_2 interval. Rectal temperature and respiratory rate showed significantly lower values at T_1, T_2 and T_3 compared to T_0 in both groups. Administration of atropine sulfate caused increase in the heart rate which remained significantly higher for five min in spite of systemic administration of dexmedetomidine, however, heart rate was progressively declined after treatment with dexmedetomidine which may be attributed to activation of parasympathetic tone.[11] Albeit, Yoo *et al.* reported an increase in heart rate after pre-medication with atropine and midazolam in dogs.[12] Muir *et al.* stated that atropine can compromise the depressant effect of dexmedetomidine or midazolam or dexmedetomidine-midazolam in propofol-induced anesthesia.[13] Reportedly, heart rate was significantly elevated in alfaxalone-butorphanol-midazolam group than alfaxalone-

Table 1. Physiological parameters recorded at different time intervals.

Parameters	Groups	Before administration	After 10 min of sedation	After induction	At the end of surgery
Heart rate (bpm)*	**G_{DEX}**	116.43 ± 5.86 ^{B}	65.36 ± 5.84 ^{aA}	97.79 ± 7.37 ^{aB}	77.64 ± 4.84 ^{aAB}
	G_{MID}	119.86 ± 7.68 ^{B}	125.79 ± 6.00 ^{bA}	151.29 ± 14.04 ^{bC}	96.43 ± 5.50 ^{bA}
Rectal temperature (˚C)	**G_{DEX}**	39.12 ± 0.05 ^{C}	38.98 ± 0.08 ^{B}	38.99 ± 0.05 ^{B}	38.55 ± 0.11 ^{aA}
	G_{MID}	39.20 ± 0.08 ^{C}	38.96 ± 0.17 ^{B}	38.97 ± 0.14 ^{B}	38.33 ± 0.15 ^{bA}
Respiratory rate (bpm)†	**G_{DEX}**	22.14 ± 1.19 ^{B}	17.29 ± 1.05 ^{A}	17.14 ± 1.24 ^{A}	19.14 ± 1.18 ^{A}
	G_{MID}	23.07 ± 1.17 ^{B}	19.14 ± 0.93 ^{A}	19.57 ± 0.64 ^{A}	18.21 ± 1.12 ^{A}

* bpm: beats *per* min; † bpm: breaths *per* min; G_{DEX}: Dexmedetomidine group; and G_{MID}: Midazolam group.
Means with different superscripts (^{ab} within a row, and ^{ABC} within a column) vary significantly at $p < 0.05$.

Table 2. Echocardiographic indices recorded at different time intervals.

Echocardiographic indices	Groups	Before drug administration	After 10 min of sedation	After induction	At the end of surgery
LVIDd (mm)	G_{DEX}	36.70 ± 1.15 ^{a}	37.30 ± 1.79 ^{a}	36.28 ± 1.54 ^{a}	34.64 ± 1.65
	G_{MID}	32.33 ± 1.43 ^{b}	26.99 ± 1.13 ^{b}	28.93 ± 1.35 ^{b}	30.42 ± 1.46
LVIDs (mm)	G_{DEX}	25.71 ± 1.55 ^{AB}	27.81 ± 2.12 ^{aAB}	26.19 ± 1.36 ^{aA}	28.23 ± 1.65 ^{aB}
	G_{MID}	22.75 ± 1.55	20.35 ± 1.37 ^{b}	19.55 ± 1.53 ^{b}	22.89 ± 1.39 ^{b}
IVSd (mm)	G_{DEX}	7.91 ± 0.57	7.56 ± 0.60	7.86 ± 0.42	8.84 ± 0.76
	G_{MID}	8.69 ± 0.83	9.00 ± 0.64	8.09 ± 0.69	8.12 ± 0.61
IVSs (mm)	G_{DEX}	13.16 ± 0.74	10.29 ± 0.52	11.08 ± 0.58	11.45 ± 0.96
	G_{MID}	12.21 ± 1.34	10.07 ± 1.00	11.03 ± 0.73	10.00 ± 0.65
LVPWd (mm)	G_{DEX}	10.90 ± 0.83	10.64 ± 0.79	12.44 ± 1.16 ^{a}	11.14 ± 0.79
	G_{MID}	9.07 ± 0.47	9.15 ± 0.58	9.12 ± 0.62 ^{b}	9.15 ± 0.78
LVPWs (mm)	G_{DEX}	14.96 ± 1.28 ^{a}	13.26 ± 1.17	15.26 ± 1.25	14.56 ± 1.25
	G_{MID}	11.74± 0.61 ^{b}	11.69 ± 0.61	12.81 ± 0.79	12.49 ± 1.01
EDV (mL)	G_{DEX}	59.86 ± 5.40 ^{a}	60.14 ± 6.33 ^{a}	55.38 ± 5.39 ^{a}	58.99 ± 10.79
	G_{MID}	44.21 ± 4.77 ^{b,C}	28.03 ± 2.97 ^{bAB}	33.53 ± 3.83 ^{bABC}	37.21 ± 3.67 ^{C}
ESV (mL)	G_{DEX}	25.33 ± 3.57	32.75 ± 5.95 ^{a}	25.94 ± 3.30 ^{a}	34.86 ± 7.19 ^{a}
	G_{MID}	19.59 ± 4.35 ^{C}	14.74 ± 2.60 ^{bAB}	13.76 ± 2.67 ^{bA}	19.64 ± 2.87 ^{bC}
SV (mL)	G_{DEX}	33.78 ± 3.65 ^{C}	18.39 ± 2.62 ^{A}	29.37 ± 3.20 ^{aBC}	22.94 ± 4.32 ^{AB}
	G_{MID}	24.64 ± 2.64 ^{C}	13.29 ± 1.79 ^{A}	19.76 ± 2.29 ^{bBC}	17.79 ± 2.60 ^{AB}
CO (L *per* min)	G_{DEX}	3.80 ± 0.31 ^{D}	1.13 ± 0.16 ^{AB}	2.74 ± 0.30 ^{C}	1.73 ± 0.29 ^{B}
	G_{MID}	3.01 ± 0.39 ^{C}	1.30 ± 0.23 ^{A}	2.92 ± 0.39 ^{C}	1.80 ± 0.33 ^{B}
EF (%)	G_{DEX}	58.36 ± 4.29 ^{C}	39.77 ± 5.22 ^{A}	53.97 ± 3.52 ^{C}	41.30 ± 3.83 ^{B}
	G_{MID}	58.10 ± 4.08 ^{BC}	49.04 ± 5.19 ^{AB}	61.24 ± 4.51 ^{C}	48.11 ± 4.37 ^{A}
FS (%)	G_{DEX}	30.36 ± 2.87 ^{C}	19.70 ± 2.99 ^{aAB}	27.70 ± 2.54 ^{a,C}	18.44 ± 2.43 ^{aA}
	G_{MID}	30.47 ± 2.49 ^{BC}	25.00 ± 3.41 ^{bAB}	33.10 ± 3.42 ^{b,C}	23.96 ± 2.50 ^{bA}
LVET (ms)	G_{DEX}	298.93 ± 24.66 ^{A}	629.71 ± 55.91 ^{aBC}	409.50 ± 52.18 ^{aAB}	550.21 ± 50.17 ^{aB}
	G_{MID}	284.50 ± 23.02 ^{B}	329.64 ± 40.68 ^{b,B}	192.79 ± 21.87 ^{bA}	321.71 ± 30.71 ^{bB}
LVM (g)	G_{DEX}	126.64 ± 15.09	128.26 ± 15.05 ^{a}	143.03 ± 20.99 ^{a}	150.86 ± 29.47 ^{a}
	G_{MID}	98.11 ± 15.84	82.71 ± 11.39 ^{b}	66.73 ± 11.95 ^{b}	78.75 ± 11.82 ^{b}
EPSS (mm)	G_{DEX}	4.25 ± 0.67 ^{A}	7.13 ± 0.50 ^{BCD}	7.83 ± 0.69 ^{BCD}	7.39 ± 1.06 ^{BCD}
	G_{MID}	9.32 ± 6.15 ^{A}	10.98 ± 6.20 ^{BC}	8.67 ± 4.18 ^{AB}	11.04 ± 5.83 ^{AC}
EF Slope (mm *per* sec)	G_{DEX}	124.87 ± 8.92 ^{a}	141.41 ± 9.03 ^{a}	134.29 ± 9.11 ^{a}	117.02 ± 9.68
	G_{MID}	92.34 ± 7.20 ^{b}	99.61 ± 12.47 ^{b}	85.61 ± 8.01 ^{b}	91.99 ± 8.92
LA/Ao	G_{DEX}	0.95 ± 0.04	0.97 ± 0.03	0.98 ± 0.03	0.99 ± 0.03
	G_{MID}	0.94 ± 0.04	0.97 ± 0.04	0.97 ± 0.04	0.98 ± 0.04

LVIDd: Left ventricular internal diameter in diastole; LVIDs: Left ventricular internal diameter in systole; IVSd: Inter-ventricular septum in diastole; IVSs: Inter-ventricular septum in systole; LVPWd: Left ventricular posterior wall in diastole; LVPWs: Left ventricular posterior wall in systole; EDV: End diastolic volume; ESV: End systolic volume; SV: Stroke volume; CO: Cardiac output; EF: Ejection fraction; FS: Fractional shortening; LVET: Left ventricular ejection time; LVM: Left ventricular mass; EPSS: E point to septal separation; LA/Ao: Left atrial to aortic ratio; G_{DEX}: Dexmedetomidine group; and G_{MID}: Midazolam group.
Means with different superscripts (^{ab} within a row and ^{ABC} within a column) vary significantly at $p < 0.05$.

butorphanol-dexmedetomidine group at 90 min after treatment;[14] whereas, it has been found that ketamine increases heart rate which may be due to increase in central release of catecholamine.[15] A non-significant increase in rectal temperature at 20 min and a significant decrease at 40 min after dexmedetomidine-butorphanol administration were also reported.[16] Further, decrease in body temperature was observed after butorphanol-midazolam administration in rabbits[17] and canines,[18] which may be due to decreased muscular activity and also direct action on the hypothalamus.[19]

Similar to the findings of the present study, Butola and Singh also recorded a non-significant decrease in rectal temperature along with a significant decrease in respiratory rate after administration of midazolam alone in dogs.[20] In this study, the rectal temperature decreased; but, the values were within the normal physiological range. Rafee *et al.* observed a non-significant decrease in respiratory rate with dexmedetomidine (IM) alone and/or in combination with butorphanol which may be due to activation of the α_2-adrenergic pathways, leading to locus coeruleus neurons inhibition.[21] The α_2-adrenergic agonists mainly attributed to the reduction of nor-adrenergic neurons of locus coeruleus activity on the pons. Nerve fibres extending from the locus coeruleus to other parts of the brainstem, including the respiratory centers, are generally considered excitatory in nature. Activation of α_2-adrenoreceptors found in the locus coeruleus is believed to be responsible for depressing nerve activity. Inhibition of excitatory stimuli to the respiratory centers could explain the decreased ventilatory drive. Moreover, it has been shown that midazolam causes more respiratory depression compared to dexmedetomidine in the rabbits.[22]

The mean values of LVIDd, EDV and EF slope were significantly higher at T_0, T_1 and T_2 intervals in G_{DEX} compared to G_{MID}. Significant higher (LVIDs, ESV, LVET and LVM) and lower (FS) values were observed at T_1, T_2 and T_3 intervals in G_{DEX} compared to G_{MID}. It was observed that LVIDd and LVIDs significantly increased after pre-medication with intravenous G_{DEX} administration in healthy dogs in comparison with respective base values and these changes can indicate the enlargement of left ventricle, increase in afterload or decrease in cardiac contractility.[23] The mean values of LVPWd and SV were significantly higher at T_2 interval; whereas, LVPWs showed significant higher values before drug administration in G_{DEX} compared to G_{MID}. A non-significant variation was observed in the values of IVSd, ISVs and LA/Ao ratio at different time intervals. A significant difference in end diastolic left ventricular posterior wall thickness after sedation with dexmedetomidine in healthy dogs was also found that may be associated with reduced CO.[16] Congdon *et al.* observed a significant decline in CO after dex-medetomidine or dexmedetomidine-atropine.[24] The mechanisms responsible for decrease in CO include reduced metabolic demands by dexmedetomidine, myocardial depressant effect, increase afterload myocardial hypoxia, decrease in heart rate, cardiac dysfunction due to vasoconstriction and reduction of catecholamines concentration in the circulation. It was considered that some of these mechanisms are involved together being responsible for decrease in CO after administration of G_{DEX}.[25] Saponaro *et al.* reported that EF, FS and CO values significantly decrease;[26] whereas, EDV and ESV significantly increase after intravenous G_{DEX} administration in healthy dogs. G_{DEX} causes an afterload increase and subsequent profound bradycardia, a heart rate-dependent decrease in CO and vagal-induced arrhythmia.[27] Wang *et al.* reported increases in ESV and EDV with the dexmedetomidine administration that might be due to mitral regurgitation.[23] The results of G_{MID} are in accordance with the findings of Seo *et al.* who reported non-significant changes in LVIDd, LVIDs, FS, EF, SV and CO after treatment with midazolam-butorphanol and alfaxalone combinations in dogs.[18] The LVPWd was reported to increase non-significantly after midazolam-butorphanol adminstration.[14] The decline in ESV and EDV after midazolam-butorphanol combination could be related to SV reduction and a decline in CO. Midazolam maintains CO and SV despite a reduction in blood pressure. This non-significant effect might be related to anti-convulsant, anxiolytic, hypnotic and sedative effects of G_{MID}; but it is more or less free from cardiovascular effects in healthy and conscious animals and causes only slight decreases in cardiac performance in anesthetized rabbits.[28] Ketamine administration increases CO and heart rate and causes a significant elevation in blood pressure which may be due to increase in central release of catecholamine.[15]

A significant reduction in EF and FS values after sedation with dexmedetomidine and butorphanol combination in dogs was reported by other researchers.[16,23] However FS acts as an indicator to assess left ventricular systolic function, it decreased significantly after dexmedetomidine administration. This significant decrease in FS might be directly related to the increase in LVIDs and decrease in EF directly related to the increased ESV. The primary factors being responsible for the change in these parameters mostly include after-load, pre-load and cardiac contractility.[29] It has been reported that when FS decreases, it may be secondary to increase after-load, decreased pre-load or reduced cardiac contraction. Possidonio *et al.* found decreases in EF and FS after sedation with midazolam-morphine in healthy dogs; but the changes were within physiological range.[30] It has been revealed that mice anesthetized with combination of G_{MID} and ketamine show a significant increase in heart rate and FS over the 25-min study period.[31] Wang *et al.* found that EPSS increases after G_{DEX} administration.[23] This could be due to decline in systolic function and left ventricle dilatation. The EPSS is an index of ventricular dilation which may change when ventricular function is impaired. The increase in left atrial size after xylazine and medetomidine administration is presumably due to decreased left ventricular emptying being associated with depressed myocardial function.

It was concluded that both anesthetic combinations, dexmedetomidine-ketamine and midazolam-ketamine, provide better hemodynamic and respiratory stability in the dogs undergoing ovariohysterectomy. Systolic functions were minimally altered with G_{MID} and G_{DEX} produced undesirable alterations; but changes were within the normal clinical range. Therefore, G_{MID} is more cardio stable compared to G_{DEX}.

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Conflict of interests

The authors declare no conflict of interest.

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