Original Article

jfms Journal of Feline Medicine and Surgery

Journal of Feline Medicine and Surgery
2018, Vol. 20(6) 554–562

DOI: 10.1177/1098612X17720327
journals.sagepub.com/home/jfm

This paper was handled and processed by the European Editorial Office (ISFM) for publication in *JFMS*

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Effects of sedation with dexmedetomidine and buprenorphine on echocardiographic variables, blood pressure and heart rate in healthy cats

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Abstract

Objectives Sedative agents are occasionally used to enable echocardiographic examination when screening cats for heart disease, such as hypertrophic cardiomyopathy (HCM). Owing to their haemodynamic effects, sedative agents may alter echocardiographic measurements. The aim of the study was to evaluate the effects of the sedative combination dexmedetomidine and buprenorphine on echocardiographic variables, blood pressure (BP) and heart rate (HR) in healthy cats.

Methods Fifty healthy, client-owned cats were prospectively recruited and included after physical examination. Cats were sedated intramuscularly with dexmedetomidine and buprenorphine, according to body weight. Blood pressure and HR measurements, echocardiographic and Doppler examinations were performed prior to sedation and repeated once cats had achieved acceptable sedation.

Results Left ventricular internal diameter at end-diastole and systole, right ventricular internal diameter at end-diastole, left atrium (LA), pulmonary artery (PA) deceleration time, and systolic, diastolic and mean arterial blood pressure increased after sedation ($P \leqslant 0.022$). Aortic and PA maximum velocity, fractional shortening, PA acceleration/deceleration time and HR decreased after sedation ($P < 0.0001$). Interventricular septum at end-diastole and systole, left ventricular posterior wall at end-diastole and systole, aortic diameter (Ao), left atrial/aortic diameter (LA/Ao) and pulmonic acceleration time did not change.

Conclusions and relevance Blood pressure increased and HR decreased post-sedation. While wall thickness and LA/Ao were not affected by sedation, indices of LA and left ventricular size increased. Further studies are needed using cats with HCM to assess the effect of this sedative combination on HCM screening results.

Accepted: 19 June 2017

Introduction

Alpha (α)$_2$-adrenoceptor agonists are commonly used for short-term sedation of cats. These agents may be used alone or in combination with different opioids, both as lone sedatives and as premedication before general anaesthesia. When α_2-adrenoceptor agonists are administered together with opioids, the sedative and analgesic effect might be enhanced.[1,2]

α_2-adrenoceptor agonists provide adequate sedation for most purposes,[3–5] and have the specific advantage of being completely reversible by a specific α_2-adrenoceptor antagonist, atipamezole.[6,7] However,

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adverse cardiovascular effects of various sedative drugs have previously been documented,[8–11] and for α_2-adrenoceptor agonists, decreased heart rate (HR), cardiac output and oxygen delivery, as well as altered pulmonary artery occlusion pressure, central venous pressure and systemic vascular resistance have been reported in dogs and cats.[1–3,8–10] Dexmedetomidine is the pharmacologically active D-isomer of the racemic compound medetomidine, which is a highly selective agonist at the α_2-adrenoceptor. Dexmedetomidine is not a pure α_2-adrenoceptor agonist, as it is also able to bind to noradrenergic imidazoline receptors.[7,12]

Buprenorphine is a potent semi-synthetic, highly lipophilic opioid derivative of thebaine. Buprenorphine is considered a partial agonist at mu opioid receptors, although some other classifications considered it to be a kappa antagonist.[13–15] Buprenorphine provides a moderate, long-acting analgesia and a lesser degree of sedation, with minimal respiratory depression and few adverse effects.[13,14,16,17]

The combination of dexmedetomidine and buprenorphine is sometimes used in veterinary medicine for sedation in cats, where buprenorphine is added to dexmedetomidine to facilitate chemical restraint and to enhance the analgesic effect of the α_2-adrenoceptor agonist alone.[4,5,11,18]

Screening for heart disease, such as hypertrophic cardiomyopathy (HCM), is performed by echocardiography in cats and screening programmes exist for various breeds.[19] HCM is the most common cardiomyopathy in cats. Most cats can be examined unsedated, but some cats (<5%) need to be sedated in order to perform the echocardiographic examination.[20] However, cardiovascular effects of sedative agents might affect the echocardiographic variables evaluated in the screening programmes.[9–11] We were interested in investigating if the combination of an α_2-adrenoceptor agonist and an opioid might be used in these cats to provide chemical restraint without affecting important echocardiographic variables. Cardiovascular effects of α_2-adrenoceptor agonists have previously been investigated in cats and dogs,[1,2,10,21,22] but echocardiographic and cardiovascular effects of the specific combination of dexmedetomidine and buprenorphine have, to our knowledge, not been evaluated in cats. This study therefore aims to evaluate effects of the combination dexmedetomidine and buprenorphine on echocardiographic variables, blood pressure (BP) and HR in healthy cats.

Materials and methods

The study was approved by Stockholm Ethical Committee, Stockholm, Sweden, and the use of client-owned cats was approved by the Board of Agriculture, Jönköping, Sweden. Informed written owner consent was obtained.

Animals

Fifty clinically healthy client-owned cats scheduled for castration or spaying were consecutively included in the study at Anicura Albano Animal Hospital in Stockholm between February 2014 and October 2015.

As inclusion criteria for the study, the cats had to be healthy upon physical examination and free from echocardiographic evidence of heart disease. Cats with heart murmur or any sign of cardiovascular or other organ-related or systemic disease were excluded from the study, as were pregnant cats.

Overall study design

All examinations were performed in a quiet examination room. Each cat underwent a physical examination, BP was measured and the cat was weighed. A baseline echocardiographic examination was then performed without sedation. After baseline data were collected, the cat was given an intramuscular injection of dexmedetomidine (Dexdomitor; Zoetis) and buprenorphine (Temgesic; Indivior) according to body weight (dexmedetomidine at 0.04 mg/kg and buprenorphine at 0.01 mg/kg).[5,23] Drugs were drawn up separately and combined in one syringe before administration. At 10 mins post-injection, subjective sedative depth was assessed by presence of lateral recumbency, response to assessor contact, degree of muscle relaxation and whether or not manual restraint was needed in order to perform the post-sedation examinations. When adequate sedation depth had been assured, the BP measurement was repeated and thereafter a second echocardiographic examination was performed. The study part of the protocol was then finished and the cat was anaesthetised for castration or spaying. All echocardiographic examinations and BP measurements were performed by the same examiner (EJ).

BP

BP measurements were performed using an oscillometric device (petMAP Graphic; Cardiocommand). The cats were acclimatised to the room for approximately 5 mins. Cats were minimally restrained in a standing position, a forelimb was lifted to the level of the heart and a cuff with a width of approximately 40% of the forelimb circumference was applied to the antebrachium with the artery marker placed ventrally.[24,25] Once reliable consecutive readings were obtained, an average of five consecutive BP recordings were made before sedation. The same procedure was repeated after sedation but with the cat in lateral recumbency with the cuff placed on the upper front leg.[25] Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MAP) and BP device-obtained HR were noted. Mean values were calculated and used in the statistical analysis.

Echocardiographic examination

All examinations were performed by use of the same ultrasonographic unit equipped with a 12-4 MHz transducer (Philips IE33; Philips Ultrasound). Cats were gently restrained in right and left lateral recumbency on an ultrasound examination table. M-mode, two-dimensional, colour flow Doppler and spectral Doppler echocardiographic examinations were conducted using standard transthoracic techniques.[26–30] The right parasternal short-axis view was used to measure the right (RVIDd) and left (LVIDd) ventricular internal diameters at end-diastole and the left ventricular internal diameter at end-systole (LVIDs), as well as interventricular septum at end-diastole (IVSd) and end-systole (IVSs), left ventricular posterior wall at end-diastole (LVPWd) and end-systole (LVPWs) and fractional shortening (FS), in M-mode on five consecutive cycles. The left atrium (LA), aortic diameter (Ao) and left atrial to aortic root (LA/Ao) ratio was measured from the right parasternal short-axis view on three consecutive cycles.[31] The pulmonary artery outflow velocity (PA V_{max}), as well as pulmonary artery acceleration (PA AT) and deceleration (PA DT) times, was measured from the right short axis-view from a pulsed-wave Doppler signal on three consecutive cycles. The aortic outflow velocity (Ao V_{max}) was measured from the left apical parasternal long-axis view using a pulsed-wave Doppler signal on three consecutive cycles. Screening of potential regurgitation through the tricuspid, mitral, aortic and pulmonary valves was performed routinely by colour Doppler echocardiography from right short-axis and long-axis views and left long-axis apical view, with the Nyquist limit set at 61.6 cm/s. If evidence of heart disease, including valvular insufficiencies, was found during the presedation echocardiographic examination, the cat was excluded from the study.

In included cats, images and loops were collected during each pre- and post-sedation examination and measurements were made at a later occasion with the examiner blinded to cat identity and whether the cat was sedated or not. The mean value for each echocardiographic variable was used in the statistical analysis.

HR

HR measurements were obtained in both unsedated and sedated cats by two different methods: from the BP recordings (HR [BP device]) and from the five consecutive M-mode heart cycles obtained during the echocardiographic examination (HR [echo]). The mean value from each method was calculated and used in the statistical analysis.

Assessment of echocardiographic acquisition variability

Within-day variability of echocardiographic acquisition was assessed in five cats. Each cat was examined at three different time points before and after sedation on a given day, each time following the same standardised protocol. The cat was first examined three times before sedation, allowing the cat to stand up for approximately 1 min on the examination table between examinations. Thereafter, the cat was sedated using dexmedetomidine and buprenorphine, and starting 10 min post-injection another three examinations were performed, approximately 1 min apart.

Thirteen variables (Table 1) were measured on each of the six acquisitions for each cat. During measurements the examiner was blinded to cat identity and whether the cat was sedated or not. The resulting mean values and SDs for the pre- and post-sedation measurements were used to determine the coefficient of variation (CV).

Table 1 Within-day variability of echocardiographic variables in five healthy cats before and after an intramuscular injection with dexmedetomidine and buprenorphine

Variable	SD	CV (%) and range
Pre-sedation RVIDd	0.02	10.4 (4.9–15.8)
Pre-sedation LVIDd	0.09	4.0 (2.7–14.9)
Pre-sedation LVIDs	0.10	13.2 (4.3–23.0)
Pre-sedation FS	5.60	12.1 (6.2–16.6)
Pre-sedation LA	0.10	7.8 (4.0–14.0)
Pre-sedation Ao	0.07	7.1 (4.1–11.0)
Pre-sedation LA/Ao	0.06	5.7 (3.0–7.8)
Pre-sedation IVSd	0.02	4.9 (4.5–5.7)
Pre-sedation IVSs	0.09	11.0 (3.2–15.8)
Pre-sedation LVPWd	0.03	7.2 (4.7–9.5)
Pre-sedation LVPWs	0.07	10.7 (3.4–27.0)
Pre-sedation PA V_{max}	0.03	5.4 (2.0–8.0)
Pre-sedation Ao V_{max}	0.04	5.6 (3.9–7.7)
Post-sedation RVIDd	0.05	15.8 (9.0–21.0)
Post-sedation LVIDd	0.15	9.7 (6.9–13.4)
Post-sedation LVIDs	0.13	11.8 (7.2–19.4)
Post-sedation FS	4.50	12.3 (2.7–22.0)
Post-sedation LA	0.11	10.3 (7.0–12.5)
Post-sedation Ao	0.09	9.3 (5.3–12.7)
Post-sedation LA/Ao	0.08	7.3 (4.3–10.5)
Post-sedation IVSd	0.03	7.8 (4.0–18.9)
Post-sedation IVSs	0.06	8.8 (1.7–15.6)
Post-sedation LVPWd	0.07	5.4 (2.4–9.6)
Post-sedation LVPWs	0.06	10.1 (5.8–15.5)
Post-sedation PA V_{max}	0.06	13.8 (2.0–33.0)
Post-sedation Ao V_{max}	0.06	11.1 (3.1–37.7)

CV = coefficient of variation; RVIDd = right ventricular internal diameter at end-diastole; LVIDd = left ventricular internal diameter at end-diastole; LVIDs = left ventricular internal diameter at end-systole; FS = fractional shortening; LA = left atrial diameter; Ao = aortic diameter; IVSd = interventricular septum at end-diastole; IVSs = interventricular septum at end-systole; LVPWd = left ventricular posterior wall at end-diastole; LVPWs = left ventricular posterior wall at end-systole; PA V_{max} = maximum velocity in pulmonary artery; Ao V_{max} = maximum velocity in aorta

The following cut-off values were used: <5% excellent, <10% good, <15% acceptable variability.

Statistical analysis

Statistical analysis was performed using commercially available software (JMP version 11.0.0; SAS Institute). Data are presented as medians and interquartile ranges (IQRs). Changes in BP, HR and echocardiographic variables were calculated by subtracting the post-sedation value from the pre-sedation value of each variable and the difference was evaluated by Wilcoxon-signed rank test. To account for the size of the pre-sedation (baseline) value, the absolute and relative change in each variable was evaluated against the pre-sedation value by univariate regression analysis, for BP, HR and echocardiographic variables. Potential effects of dose of dexmedetomidine or buprenorphine on changes in BP, HR and echocardiographic variables were also evaluated by univariate regression analysis.

Potential associations between BP or HR and changes in echocardiographic variables were assessed by regression analysis with change in each echocardiographic variable as the dependent variable and the same pre-sedation echocardiographic variable plus change in HR, SBP, DBP or MAP as explanatory variables. Potential associations between BP variables and HR were assessed by regression analysis with the change in HR obtained during BP recording as the dependent variable and pre-sedation HR obtained during BP recording value plus change in SBP, DBP or MAP as explanatory variables. The same analyses were also performed with change in BP variables as dependent variables and pre-sedation BP variables and change in HR as explanatory variables. A P value of <0.05 was considered significant for the analyses.

Results

The study group consisted of 16 males and 34 females. No cats were excluded from the study. The median body weight was 3.6 kg (IQR 2.8–4.1 kg) and the median age was 9.5 months (IQR 6.0–21.3 months). Ten breeds were represented in the study (31 domestic shorthairs, three Cornish Rex, one Bengal, one Burmese, one Maine Coon, one Norwegian Forest Cat, one Persian, six Ragdolls, one Siamese, four Siberians). The median dose of dexmedetomidine was 0.038 mg/kg (IQR 0.034–0.041 mg/kg) and the median dose of buprenorphine was 0.009 mg/kg (IQR 0.007–0.011 mg/kg).

The within-day echocardiographic acquisition variability, assessed in five cats, showed acceptable (CV <15 %) to good (CV <10 %) variability for most variables (Table 1). Generally, the results were similar pre- and post-sedation. The lowest CV was found for pre-sedation LVIDd (4.0%) and the highest for post-sedation RVIDd (15.8%).

Effect of sedation on echocardiographic variables, BP and HR

Ten mins post-injection, all cats were sedated and in lateral recumbency, showed profound muscle relaxation, minimal or no response to assessor contact, and did not require any manual restraint in order to perform the examinations. Post-sedation BP measurements were therefore initiated 10 mins post-sedation and lasted for approximately 3 mins, immediately followed by echocardiographic examination. No change in sedation depth was noted during the examinations. Pre- and post-sedation values for echocardiographic variables, BP and HR are given in Table 2. Comparing pre- to post-sedation values, indices of ventricular diameters (LVIDd, LVIDs, RVIDd) and LA, all BP variables (SBP, DBP and MAP) and PV DT increased; flow velocities (Ao V_{max} and PA V_{max}), FS, AT/DT and both HR variables (HR [BP device] and HR [echo]) decreased, while indices of wall thickness (IVSd, IVSs, LVPWd, LVPWs), Ao, LA/Ao and PA DT remained unchanged. Minimal mitral insufficiencies were seen in 11/50 cats post-sedation. Sedative dosage/kg had no significant effect on echocardiographic variables, BP or HR, within the relatively narrow dose range administered in this study. Associations between pre-sedation value and absolute, as well as relative change in the same variable post-sedation for each echocardiographic, BP and HR variable, are shown in Table 3. The absolute change was associated with the pre-sedation value for all variables, except PA deceleration time, and the relative change was associated with the pre-sedation value for all variables, except PA deceleration time and PA AT/DT.

Associations between changes in echocardiographic variables, BP and HR

According to the regression analysis, change in LVIDd was associated with change in SBP ($P = 0.036$) and pre-sedation LVIDd ($P = 0.0002$) with an adjusted model R^2 of 0.32. The change in LVIDs was associated with change in DBP ($P = 0.0012$) and pre-sedation LVIDs ($P = 0.0006$) with an adjusted model R^2 of 0.34. The change in LVIDs was also associated with change in MAP ($P = 0.0032$) and pre-sedation LVIDs ($P = 0.0016$) with an adjusted model R^2 of 0.31.

None of the BP variables were associated with any other echocardiographic variable. HR was not associated with any of the echocardiographic variables. No association was found between the HR variables (HR [BP device] or HR [echo]) and any of the BP variables (SBP, DBP or MAP).

Discussion

In our study, echocardiographic and cardiovascular variables post-sedation with dexmedetomidine and buprenorphine were compared with pre-sedation values in healthy cats. Atrial and ventricular diameters and all BP variables

Table 2 Median (interquartile range) pre- and post-sedation values of echocardiographic variables, blood pressure and heart rate in 50 healthy cats sedated with dexmedetomidine and buprenorphine

	Pre-sedation	Post-sedation	Change	*P* value
LVIDd (cm)	1.62 (1.49–1.74)	1.67 (1.53–1.77)	–0.08 (–0.17 to 0.05)	0.015
LVIDs (cm)	0.87 (0.81–1.06)	1.15 (0.98–1.24)	–0.25 (–0.38 to –0.08)	<0.0001
IVSd (cm)	0.36 (0.32–0.41)	0.37 (0.33–0.39)	0.00 (–0.04 to 0.04)	0.75
IVSs (cm)	0.50 (0.45–0.58)	0.49 (0.44–0.55)	0.01 (–0.03 to 0.10)	0.089
Ao V_{max} (m/s)	0.90 (0.85–0.98)	0.42 (0.36–0.55)	0.48 (0.37–0.57)	<0.0001
PA V_{max} (m/s)	0.86 (0.76–0.96)	0.41 (0.37–0.56)	0.43 (0.31–0.5)	<0.0001
PA AT (ms)	0.53 (0.41–0.58)	0.48 (0.41–0.52)	0.02 (–0.05 to 0.1)	0.088
PA DT (ms)	0.54 (0.44–0.64)	0.9 (0.69–1.21)	–0.38 (–0.54 to –0.22)	<0.0001
PA AT/DT	0.99 (0.86–1.06)	0.54 (0.42–0.68)	0.43 (0.31–0.56)	<0.0001
Left atrium (cm)	1.05 (1.00–1.10)	1.10 (1.00–1.13)	0.00 (–0.10 to 0.00)	0.022
Aorta (cm)	0.90 (0.90–1.00)	0.90 (0.90–1.00)	0.00 (–0.10 to 0.00)	0.52
LA/Ao	1.11 (1.00–1.22)	1.11 (1.10–1.22)	0.00 (–0.11 to 0.00)	0.37
FS (%)	44.0 (37.4–49.9)	30.4 (26.1–33.1)	12.6 (7.1–19.9)	<0.0001
RVIDd (cm)	0.20 (0.19–0.27)	0.25 (0.20–0.35)	–0.04 (–0.12 to 0.01)	0.002
LVPWd (cm)	0.39 (0.34–0.42)	0.38 (0.35–0.42)	0 (–0.03 to 0.04)	0.58
LVPWs (cm)	0.56 (0.49–0.65)	0.57 (0.49–0.61)	0.01 (–0.04 to 0.06)	0.82
HR (BP device) (bpm)	164 (144–186)	90 (80–100)	72 (56–91)	<0.0001
HR (echo) (bpm)	189 (161–220)	93 (80–100)	90 (70–122)	<0.0001
SBP (mmHg)	156 (141–171)	174 (158–185)	–15.5 (–31.5 to –0.25)	0.0006
DBP (mmHg)	101 (87–109)	120 (105–131)	–14.5 (–35 to –2.75)	<0.0001
MAP (mmHg)	118 (111–130)	137 (121–148)	–15 (–30.5 to –5.75)	<0.0001

Median change is displayed as the post-sedation value subtracted from the pre-sedation value
LVIDd = left ventricular internal diameter at end-diastole; LVIDs = left ventricular internal diameter at end-systole; IVSd = interventricular septum at end-diastole; IVSs = interventricular septum at end-systole; Ao V_{max} = maximum velocity in aorta; PA V_{max} = pulmonary artery maximum velocity; PA AT = pulmonary artery acceleration time; PA DT = pulmonary artery deceleration time; PA AT/DT = pulmonary artery acceleration time/deceleration time; LA/Ao = left atrial to aortic root ratio; FS = fractional shortening; RVIDd = right ventricular dimension at end-diastole; LVPWd = left ventricular posterior wall at end-diastole; LVPWs = left ventricular posterior wall at end-systole; HR (BP device) = blood pressure device-obtained heart rate; HR (echo) = echocardiographically obtained heart rate; SBP = systolic blood pressure; DBP = diastolic blood pressure; MAP = mean arterial pressure

increased, while flow velocities in the aorta and the pulmonary artery, FS and HR all decreased post-sedation. Ventricular and septal wall thicknesses and LA/Ao, which are important variables in HCM screening programmes,[19] were unchanged but showed significant positive absolute, as well as relative, changes compared with pre-sedation values, meaning that cats with the highest pre-sedation value could show the largest decrease. Results should therefore be interpreted cautiously and further studies on cats with HCM are warranted.

In cats, combining an α_2-agonist with an opioid has been shown to result in more adequate sedation than using an α_2-agonist alone.[2,4,5] In our study, the α_2-agonist dexmedetomidine was combined with the opioid-derivative buprenorphine. The post-sedation BP measurement, approximately 10 mins post-injection, when all cats had reached adequate sedation depth, showed increased BP vs pre-sedation values. Various studies using dexmedetomidine alone or in combination with other drugs have shown divergent results concerning the effect on BP in cats.[1,4,32–34] Several studies show an increase in BP,[32–34] whereas in some studies using low doses of dexmedetomidine or medetomidine, BP remained unchanged compared with baseline.[1,4] Dosage of the α_2-agonist, time to measurement, as well as drug combinations, differ between studies, which might explain the discrepancies in effects on BP. Furthermore, differences between BP measurement methods and stress levels of the cats between studies might also affect the results.[24,25]

In our study, the α_2-agonist was given at the per label sedation dose of approximately 0.04 mg/kg.[5,23] It was combined with buprenorphine at a median dose of 0.01 mg/kg, a dose that has previously been shown to provide good sedation in cats when combined with dexmedetomidine.[5] In an experimental study on cats, rats and dogs, buprenorphine alone at the same dose had no significant effect on BP.[13] The contribution of each drug on BP in our study can only be speculated, but based on previous results, the rise in BP post-sedation is most likely attributed to haemodynamic effects of the α_2-agonist with a time-dependent increase in systemic vascular resistance,[1] and less so to an effect of buprenorphine.

The decrease in HR post-sedation was pronounced. Bradycardia has been shown in several studies using α_2-agonists in cats,[1,4,32,34] and is likely caused by decreased central sympathetic nervous tone and a baroreceptor-mediated

Table 3 Association between pre-sedation value and absolute and relative change in the same variable post-sedation for each echocardiographic, blood pressure and heart rate variable in 50 healthy cats sedated with dexmedetomidine and buprenorphine

	Absolute change		Relative change	
	R^2 value	*P* value	R^{2-} value	*P* value
LVIDd	0.28	<0.0001	0.33	<0.0001
LVIDs	0.20	0.001	0.31	<0.0001
IVSd	0.16	0.004	0.18	0.002
IVSs	0.49	<0.0001	0.39	<0.0001
Ao V_{max}	0.33	<0.0001	0.09	0.035
PA V_{max}	0.31	<0.0001	–	0.22
PA AT	0.30	<0.0001	0.33	<0.0001
PA DT	–	0.28	–	0.28
PA AT/DT	0.26	0.0002	–	0.07
Left atrial diameter	0.36	<0.001	0.37	<0.0001
Aortic diameter	0.35	<0.0001	0.34	<0.0001
LA/Ao	0.39	<0.0001	0.40	<0.0001
FS	0.50	<0.0001	0.30	<0.0001
RVIDd	0.22	0.0005	0.27	<0.0001
LVPWd	0.19	0.002	0.17	0.003
LVPWs	0.55	<0.0001	0.50	<0.0001
HR (BP device)	0.44	<0.0001	0.11	0.02
HR (echo)	0.76	<0.0001	0.37	<0.0001
SBP	0.50	<0.0001	0.53	<0.0001
DBP	0.35	<0.0001	0.40	<0.0001
MAP	0.24	0.0003	0.29	<0.0001

LVIDd = left ventricular internal diameter at end-diastole; LVIDs = left ventricular internal diameter at end-systole; IVSd = interventricular septum at end-diastole; IVSs = interventricular septum at end-systole; Ao V_{max} = maximum velocity in aorta; PA V_{max} = pulmonary artery maximum velocity; PA AT = pulmonary artery acceleration time; PA DT = pulmonary artery deceleration time; PA AT/DT = pulmonary artery acceleration time/deceleration time; LA/Ao = left atrial to aortic root ratio; FS = fractional shortening; RVIDd = right ventricular dimension at end-diastole; LVPWd = left ventricular posterior wall at end-diastole; LVPWs = left ventricular posterior wall at end-systole; HR (BP device) = blood pressure device-obtained heart rate; HR (echo) = echocardiographically obtained heart rate; SBP = systolic blood pressure; DBP = diastolic blood pressure; MAP = mean arterial pressure

response to the increased systemic vascular resistance.[1,14,18] In addition, buprenorphine can reduce HR,[13] which might have contributed to the pronounced bradycardia post-sedation in the present study. In one study, combining dexmedetomidine with atropine prevented bradycardia, but instead led to transient hypertension.[34]

Several echocardiographic variables were affected by sedation. Both atrial and ventricular dimensions increased, while FS decreased, as previously shown in dogs sedated with dexmedetomidine.[22,35] In the regression analysis, change in LVIDd showed a weak association with change in SBP, while change in LVIDs was weakly associated with change in DBP, as well as MAP. These findings might be explained by the increase in systemic vascular resistance combined with a decrease in stroke volume and an increase in central venous pressure shown in cats in response to an α_2-agonist,[1] leading to larger ventricular volumes. Furthermore, the pronounced post-sedation bradycardia leads to longer diastole, which allows longer filling times and thereby larger end-diastolic volumes.

In addition to the bradycardia, decrease in stroke volume leads to decrease in cardiac output and a myocardial depressant effect of α_2-agonists has been speculated,[36] which might also explain the decrease in FS. Furthermore, the lower FS post-sedation might be due to decreased central sympathetic nervous tone compared with the awake cat, in which stress from the manual restraint in a clinical environment might lead to higher FS.[37] Cardiac output might also decrease as a result of the increased afterload due to increased systemic vascular resistance induced by α_2-agonists, which might explain the decrease in both aortic and pulmonary artery flow velocities post-sedation in the present study. Again, in comparison with previous studies, different times to measurement might affect results.[1,32]

No valvular regurgitations pre-sedation were noted in the present study. Post-sedation, minimal trace insufficiencies across the mitral valve were present in approximately 20% of the cats. In a previous report, using the same dose of dexmedetomidine, minimal insufficiencies over the mitral or aortic valves were seen post-sedation in most cats.[37] The different results might be related to different times to post-sedation echocardiography (10–13 mins in the present study vs 15–38 mins in the other

study). Other possible reasons may be differences in study populations and in the Nyquist limit in the Doppler settings between studies. In our study of 50 apparently healthy cats, none was excluded owing to discovery of heart disease, suggesting a relatively low prevalence of heart disease compared with previous studies.[20,38,39] One possible explanation for this is the relatively low median age of the cats in our study (9.5 months).

Hypothetically, wall thicknesses might be expected to decrease post-sedation if the left ventricular dimension increases and wall thicknesses might increase if the dimension decreases, as a function of left ventricular volume. In a previous study, a mildly decreased left ventricular end-diastolic dimension and mildly increased left ventricular end-diastolic wall thickness was found when sedating cats with a combination of acepromazine, butorphanol and ketamine.[40] In the present study, the left ventricular dimension showed a mild increase post-sedation. None of the indices of wall thickness (IVSd, LVPWd, IVSs and LVPWs) changed significantly post-sedation. However, looking at associations between pre-sedation values and change in the same variables post-sedation, there were significant positive associations in both absolute and relative change for all indices of wall thickness. This means that the largest reductions in wall thickness could be seen in the cats with the largest pre-sedation values. Similar associations were found for indices of left heart size (LA, LA/Ao, LVIDd and LVIDs), again meaning that the larger the pre-sedation value, the greater the potential change in the same variable.

Another possible explanation is that some changes could be attributable to regression to the mean; that is, if the first measurement over-estimated the variable that was being measured it tended to be smaller when measured a second time, and vice versa. When screening for feline heart disease, including HCM, IVSd, LVPWd and LA/Ao are important variables.[20] In the majority of cats in the worldwide PawPeds HCM screening programme, echocardiographic examinations were reported to be performed in unsedated cats, but in a number of cats (<5%) sedation was used.[20] The present study only included healthy cats with normal wall thicknesses. Owing to the positive associations between pre-sedation wall thicknesses and change in the same variables described above, there could be a risk of underestimating wall thickness during sedation, especially in cats with thick walls; that is, cats with HCM. Similarly, LA/Ao might be underestimated. Further studies on cats with HCM are therefore warranted.

Also, one must be aware of potential effects on diastolic function of an α_2-agonist. It has previously been shown in dogs that transmitral E velocity, A velocity and A′ velocities decrease, whereas E/A increases with dexmedetomidine.[22,35] Diastolic dysfunction is an important factor in feline cardiomyopathy,[41,42] but assessment of diastolic function by transmitral flow measurements or tissue Doppler is not included in most HCM screening programmes,[19] and was therefore not included in the present study protocol. It has also been reported that medetomidine may mask the presence of a dynamic left ventricular outflow tract obstruction by increasing systemic vascular resistance and thus decreasing the pressure gradient between the left ventricle and aorta.[1] Therefore, presence of hypertrophic obstructive cardiomyopathy could theoretically be missed during a screening examination if the cat is sedated with dexmedetomidine.

Another finding was the increase in PA deceleration time, and decrease in AT/DT. The PA acceleration time was numerically lower post-sedation but not significantly. Combined, these findings give the PA Doppler profile an appearance similar to the aortic profile. In healthy individuals, aortic and PA Doppler flow profiles differ in peak velocity and AT/DT because of differences in pressure, with higher velocity and lower AT/DT in the aorta compared with the PA.[43,44] In a previous study in healthy cats sedated with medetomidine, an increased pulmonary vascular resistance was found 15 mins post-sedation,[1] which is in accordance with the altered PA Doppler flow characteristics in the present study. Transient increase in pulmonary arterial pressure might explain these findings.

In total, 21 different echocardiographic variables were included in the study. The larger the number of included variables, the larger is the risk for a type 1 statistical error, that is, false-positive results, but the significance level can be adjusted for multiple comparisons by correcting the *P* value. In the present study, a main aim was to investigate potential effects of sedation on echocardiographic variables. Because we used the Wilcoxon signed rank test, which is a relatively robust test, we decided not to adjust the significance level in order not to risk missing potential differences induced by the sedation. Most variables showed either highly significant changes or were not significant (Table 2). Thus, the decision not to adjust the *P* value was based on the risk of potentially masking the effect of sedation.

Our study has several limitations. Because the study included privately owned cats, and because measurements were made both in awake and sedated cats, it was not possible to use an invasive BP method. Instead, indirect BP measurements were made by use of a standard non-validated oscillometric device, which might have led to lower accuracy and systematic differences in numerical results. However, the same device was used in all cats and the cat was used as its own control when comparing pre- with post-sedation values.[45] Another potential study limitation is the difference in positioning of the cat between measurements. The pre-sedation measurement was made with the cat in a standing position with an elevated forelimb, while for the post-sedation measurement the cat was positioned in lateral

recumbency with the cuff placed on the upper front leg. In both positions, attempts were made to keep the cuff at the level of the heart.[25] The cats were allowed to acclimatise for 5 mins before initiating BP measurements, which is on the lower end of the range of the recommended acclimatisation time of 5–10 mins.[25] The stress level of the cat and the so-called white coat effect could lead to elevation of BP, as well as HR, in a clinical environment in awake animals.[24] Therefore the true difference in BP between unsedated and sedated cats in this study might actually be larger than reported here, while the true difference in HR might be lower. Reliable consecutive readings were assured before BP recording began. Thereafter, five recordings were obtained, averaged and used in the statistical analysis; that is, no outliers were excluded.

As a consequence of the set up of the present study, with BP measurement performed once the cat had obtained sufficient sedation depth (at approximately 10 mins post-injection), followed by the echocardiographic examination (starting approximately 13 mins post-injection), there was a slight difference in time between investigations, during which sedation depth may have changed. However, HR, which was the only variable measured both during BP measurement and during echocardiographic examination, showed similar values post-sedation for both measurements and subjectively sedation depth did not change. Another limitation of the study is the lack of assessment of left ventricular diastolic function by transmitral flow measurements or tissue Doppler. Furthermore, post-sedation echocardiographic acquisitions for assessment of within-day variability were started 10 mins post-sedation, while again the post-sedation echocardiographic examination during the study was started approximately 13 mins post-sedation. Although all echocardiographic measurements were made with the observer blinded to cat identity, as well as whether the cat was sedated or not, the pronounced decrease in HR made post-sedation status rather obvious in echocardiographic images and loops containing more than one heart beat, such as in M-mode and spectral Doppler recordings. Finally, a limitation of the study is that only normal cats were examined.

Conclusions

BP increased and HR decreased post-sedation in this study on healthy cats. Several echocardiographic variables changed post-sedation, whereas septal and left ventricular wall thicknesses and LA/Ao, important variables in HCM screening programmes, did not change. They did, however, show significant positive absolute, as well as relative, changes compared with pre-sedation values, meaning that cats with the highest pre-sedation value could potentially show the largest decrease. These results therefore need to be interpreted cautiously and further studies using cats with HCM are warranted before sedation with the combination of dexmedetomidine and buprenorphine can be recommended for HCM screening.

Author note This article was presented, in part, at the 26th ECVIM-CA Congress, Gothenburg, Sweden, 2016, and at the Swedish Annual Veterinary Congress, Uppsala, Sweden, 2016.

Conflict of interest The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding The authors received no financial support for the research, authorship, and/or publication of this article.

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