Results of 24-hour ambulatory electrocardiography in dogs undergoing ovariohysterectomy following premedication with medetomidine or acepromazine

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Objective—To investigate heart rate characteristics in dogs undergoing ovariohysterectomy following premedication with medetomidine or acepromazine.

Design—Clinical trial.

Animals—43 client-owned dogs.

Procedure—24-hour ambulatory electrocardiography was performed beginning approximately 1 hour prior to administration of premedications. Dogs were premedicated with medetomidine and butorphanol (n = 21) or acepromazine and butorphanol (22) and, approximately 85 minutes later, were anesthetized with propofol and isoflurane. Electrocardiographic recordings were examined to determine heart rate, cardiac conduction disturbances (ventricular premature complexes and atrioventricular block), and indices of heart rate variability (HRV).

Results—Minimum heart rate during the 24-hour recording period was significantly lower among dogs given medetomidine than among dogs given acepromazine, but during the postoperative period, heart rate increased in all dogs as they became physically active. Intraoperative time domain HRV indices were lower and the low frequency-to-high frequency ratio was higher among dogs given acepromazine than among dogs given medetomidine; however, significant differences between groups were no longer seen by 6 hours after surgery. There was no significant difference between groups with regard to the number of ventricular premature complexes or to values of scaling exponent $\alpha 2$ (a nonlinear measure of HRV).

Conclusions and Clinical Relevance—Results suggest that there are greater enhancements in vagally related heart rate indices in medetomidine-treated dogs that may persist until 6 hours after surgery. Despite the low heart rates, dogs given medetomidine showed expected responses to surgery and positional stimuli, and the 2 preanesthetic protocols may not result in different prevalences of ventricular premature complexes. (*J Am Vet Med Assoc* 2005;226:738–745)

In surgical patients, the effects of perianesthetic medications and the physiologic perturbations induced by tissue trauma modulate various aspects of bodily function, particularly cardiac electrical and autonomic nervous system activities. In dogs, perioperative alterations in cardiac electrical activity have been documented through electrocardiography[1] but only intermittent monitoring and follow-up periods of only a few hours after surgery have traditionally been used. Alterations in autonomic nervous system activity have been examined mostly through measurement of plasma catecholamine concentrations.[2]

The use of intermittent electrocardiography can seriously impair the ability to detect arrhythmic events,[3] and in humans, heart rate behavior has been shown to be affected for hours or even days following surgery.[4,5] In addition, compared with measurement of circulating catecholamine concentrations, more detailed information on autonomic nervous system modulation of cardiac function can be obtained through the examination of beat-to-beat interval behavior, that is, **heart rate variability (HRV)**.[6,7] Short-term alterations in the beat-to-beat interval, as reflected in time domain HRV measures and high-frequency oscillations, mainly arise secondary to cardiac efferent vagal influences, whereas both sympathetic and parasympathetic activities can modulate lower frequency fluctuations.[6-8]

Little information is available on perioperative HRV in dogs,[a] but in humans, alterations in several measures have been documented.[4,5] These include alterations in newly described nonlinear HRV indices that probe the qualitative properties (fractal-like correlations) of heart rate behavior, revealing characteristics not detected by traditional analysis methods.[9-11] In humans, these nonlinear indices have shown promise as predictors of adverse cardiac events[11] and have even been associated with duration of the hospital stay in surgical patients.[5]

Medetomidine and acepromazine are frequently used for premedication of healthy dogs undergoing elective surgical procedures. Medetomidine, an α_2-adrenoceptor agonist, has dose-related sedative and analgesic properties[12] and affects various cardiovascular indices, commonly resulting in bradyarrhythmias.[12,13] Acepromazine is a

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phenothiazine tranquilizer with vasodilatory activity that can increase or decrease heart rate.[14] In experimental trials,[15] acepromazine has been shown to decrease the occurrence of ventricular dysrhythmias. Similar studies[16] with α_2-adrenoceptor agonists have not reached conclusive results.

When used for premedication, medetomidine and acepromazine have been reported to result in different degrees of neurohumoral arousal, as reflected in alterations in heart rate and plasma cortisol and catecholamine concentrations.[17] To our knowledge, however, no detailed examinations of alterations in perioperative heart rate behavior, including HRV, associated with preoperative administration of these 2 drugs have been published.

The purpose of the study reported here was to investigate heart rate behavior in dogs undergoing ovariohysterectomy following premedication with medetomidine or acepromazine. Twenty-four–hour ambulatory electrocardiography was performed, and data were analyzed to determine minimum and maximum heart rates, cardiac conduction disturbances, and indices of HRV. Animals used in the present study were part of a larger investigation, and intermittent heart rates and perioperative epinephrine, norepinephrine, cortisol, and β-endorphin concentrations have been reported previously.[17]

Materials and Methods

Animals—Details of the dogs used in the present study have been published previously.[17] Briefly, 43 client-owned adult (median age, 5 years; range, 2 to 7 years) sexually intact dogs scheduled to undergo ovariohysterectomy at the Helsinki University Small Animal Hospital between January and August 2000 were enrolled in the study. Dogs represented various breeds. Six were German Shepherd Dogs, 4 were Doberman Pinschers, 3 were Dalmatians, 3 were Golden Retrievers, and 8 were mixed-breed dogs. The remaining 19 dogs represented 15 other breeds. Dogs were determined to be in good health on the basis of history and results of a complete physical examination, CBC, and serum biochemical profile. The study protocol was approved by the local Ethical Committee, and informed owner consent was obtained.

Study protocol and patient management—All dogs arrived at the hospital at or before noon and remained in the hospital for 24 hours. After a physical examination was performed, a Holter monitor[b] was fitted to the dog and recording was started. The dog was then placed in a cage. Cages used in the present study were a modified version of a hospital cage, with one wall made of clear acrylic plastic to allow video recording[c] of the dog's behavior. The cage was situated in quiet surroundings to avoid unnecessary disturbance.

Twenty-one dogs were randomly assigned to be premedicated with medetomidine (0.02 mg/kg [0.009 mg/lb], IM) and butorphanol tartrate (0.2 mg/kg [0.09 mg/lb], IM), and 22 were randomly assigned to be premedicated with acepromazine maleate (0.05 mg/kg [0.023 mg/lb], IM) and butorphanol (0.2 mg/kg, IM). Premedications were administered approximately 1 hour after dogs were placed in their cages. Approximately 15 minutes after premedications were administered, femoral and jugular catheters were placed and carprofen (4 mg/kg [1.8 mg/lb], IV) was administered. During these procedures, dogs were placed in lateral or dorsal recumbency with minimal or no restraint used. Approximately 85 minutes after administration of premedications, anesthesia was induced with propofol. Mean ± SD dosage of propofol was 1.3 ± 0.2 mg/kg (0.59 ± 0.09 mg/lb), IV, for dogs premedicated with medetomidine and 3.6 ± 0.7 mg/kg (1.64 ± 0.32 mg/lb), IV, for dogs premedicated with acepromazine. Anesthesia was maintained with isoflurane in oxygen. Mean ± SD end-tidal isoflurane concentration during anesthesia was 1.4 ± 0.3% for dogs premedicated with medetomidine and 1.6 ± 0.2% for dogs premedicated with acepromazine.

Ovariohysterectomy was performed by 1 of 3 experienced surgeons in a standard manner through a ventral approach. During anesthesia, end-tidal partial pressure of CO_2 was maintained at < 60 mm Hg by use of intermittent manual ventilation. Oxygen saturation as measured by pulse oximetry remained between 99% and 100%, and mean arterial blood pressure remained > 60 mm Hg throughout surgery in all dogs. Rectal temperature was maintained at ≥ 37°C (98.6°F) by use of heating blankets. At the completion of surgery, 15 minutes before administration of isoflurane was discontinued, buprenorphine (0.01 mg/kg [0.0045 mg/lb]) was administered IV. Mean ± SD durations of anesthesia and surgery were 73.6 ± 10.8 minutes and 38.9 ± 8.6 minutes, respectively, with no significant differences between dogs receiving medetomidine and those receiving acepromazine.

Dogs were allowed to recover from anesthesia in their cages. Mean ± SD time from the end of anesthesia until extubation was 12.5 ± 5.1 minutes, with no significant differences between groups. One dog (acepromazine group) became excited during recovery and was administered propofol (3.5 mg/kg [1.59 mg/lb], IV) and buprenorphine (0.005 mg/kg [0.0023 mg/lb], IV). In 7 dogs (2 in the acepromazine group and 5 in the medetomidine group), an additional dose of buprenorphine (0.01 mg/kg, IV) was administered 6 hours after surgery. Six hours after surgery, dogs were taken for a walk and water and food were offered. Dogs were taken for walks and physical examinations were performed at predetermined intervals thereafter. Approximately 24 hours after dogs were admitted to the hospital, ambulatory electrocardiography was discontinued and dogs were discharged.

Ambulatory electrocardiography—Equipment used for 24-hour ambulatory electrocardiography has been described in detail elsewhere.[18] Briefly, 5 adhesive electrodes[d] were used to obtain 2 transthoracic leads. The recorder[b] was carried on the back of the dog with a specially designed jacket. To allow an assessment of the relationship between cardiac activities and perioperative events, the clock of the Holter monitor was synchronized with one worn by one of the members of the investigative team and with the clock on the video recorder used to record the dogs' behavior when in their cages.

Analysis of ambulatory ECGs—A standard Holter analysis system[e] was used to analyze ambulatory ECGs and determine hourly minimum, maximum, and average heart rates; number of episodes of second- and third-degree atrioventricular block; number of **ventricular premature complexes (VPCs)**; and number of sinus pauses > 2.0 seconds long. To more closely evaluate heart rate behavior, printouts of heart rate recorded every 2 minutes were also obtained. Analyses were conducted by a physician accustomed to reading canine ECGs. During analyses, data were manually inspected to detect possible artifacts and mislabeled beats. Full disclosure printouts were checked by a veterinarian and verified by a veterinary cardiologist to ascertain correct labeling of arrhythmic events.

To characterize perioperative HRV, the 24-hour recordings were analyzed in 30-minute segments and HRV indices were determined as mean values for each 30-minute period. The R-R interval data were digitally sampled and transferred from a scanner[f] to a computer for analysis.[g] Data were edited manually as described.[19] The R-R interval series was passed

through a filter that eliminated premature beats and noise and deleted filling gaps, as described.[19] All questionable portions containing artifacts or ectopic beats were then excluded manually by visual inspection of the R-R intervals. Only segments with at least 85% qualified sinus beats were included in the final analysis.

For frequency domain analysis of HRV, the ratio between **low-frequency (LF)** and **high-frequency (HF)** oscillatory components of HRV was calculated. Power spectrum densities of HRV were estimated by use of a fast Fourier transformation method. Power spectra were documented by measuring areas under 2 frequency bands: 0.04 to 0.15 Hz and 0.15 to 0.40 Hz (for LF and HF power spectra, respectively). Analyses were performed with time windows of 512 R-R intervals, and mean values were calculated for each of the 30-minute segments. The LF:HF ratio was documented as the ratio of LF power in milliseconds to HF power in milliseconds. High-frequency HRV represents mainly vagal influences on the heart, whereas the LF oscillatory component can be affected by both sympathetic and parasympathetic activities.[6,20] The LF:HF ratio has been implicated as a measure of the balance between the 2 autonomic nervous system influences at the sinoatrial node.[6,8]

For time domain analysis of HRV, the following indices were determined: SD of all normal-to-normal R-R intervals, square root of the mean squared differences of successive normal-to-normal R-R intervals, and proportion of interval differences for successive normal-to-normal R-R intervals > 50 milliseconds.[6] Mean heart rates were also documented for each of the 30-minute segments.

A **detrended fluctuation analysis (DFA)** technique was used to quantify the fractal-like scaling properties of the R-R interval data.[9,10] Root mean square fluctuations of integrated and detrended data were measured in observation windows of various sizes and then plotted against size of the window on a log-log scale. The scaling exponent α represents the slope of the line that relates the logarithm of the fluctuation to the logarithm of the window size. Low exponent values (near 0.5) correspond to random dynamics, and high values (near 1.5) correspond to highly correlated interbeat interval dynamics. An α value of 1 corresponds to 1/f noise and indicates the existence of long-range correlations in the R-R interval data, that is, partial dependence of the values at every time point on the values at all previous time points.[10] In humans, a scaling exponent of 1 has been documented for normal heart rate dynamics.[5,9,10] The correlation properties were measured for short-term (window size ≤ 11 beats, α1, DFA1) and intermediate-term (window size > 11 beats, α2, DFA2) fluctuations in the R-R interval data.[5]

Additional observations—Behavior of the dogs while in their cages was continuously recorded[c] to allow for comparisons between behavioral condition and cardiac data. The behavioral status of the dog (ie, whether lying down or in an upright position [sitting or standing]) was compared with cardiac characteristics (ie, minimum and maximum heart rates and cardiac conduction disturbances). In addition, for the first 6 hours after surgery, times when the dogs were seen to be physically active (ie, sitting or standing up) were specifically noted.

Statistical analyses—The Student *t* test was used to compare minimum and maximum heart rates during the 24-hour perioperative period between groups. Prevalence of conduction disturbances was analyzed by use of the Fisher exact test and Wilcoxon rank sum test. Hourly heart rates and HRV indices were analyzed by use of repeated-measures ANOVA. Values obtained during and after surgery were compared with initial values and values obtained after premedications had been administered. Values of the LF:HF ratio were analyzed as logarithmic interventions because of the skewed distribution of the original data. For all analyses, values of $P < 0.05$ were considered significant. **Confidence intervals (CI)** were calculated on the basis of data for each time point in question.

Results

Because of technical errors, ambulatory ECG recordings were not obtained for 2 dogs premedicated with acepromazine and behavioral data were unavailable for 1 dog premedicated with medetomidine. For 1 dog premedicated with medetomidine, the quality of the ECG recorded during the night was not suitable for analysis; median duration of the remaining ECG recordings was 23.8 hours (range, 23.3 to 24.2 hours). Scaling exponents α1 and α2 could not be calculated for 8 dogs, including 7 dogs premedicated with medetomidine and 1 dog premedicated with acepromazine.

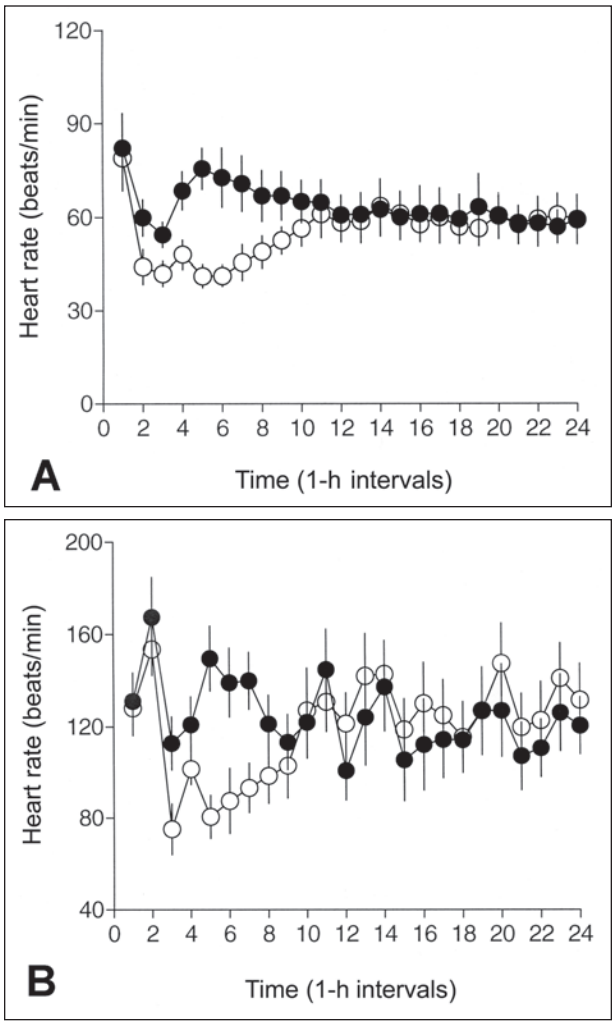

Figure 1—Mean minimum (A) and maximum (B) hourly heart rates in dogs undergoing ovariohysterectomy following premedication with medetomidine (n = 21; open circles) or acepromazine (20; solid circles) and anesthesia with isoflurane. Data were obtained by means of 24-hour ambulatory electrocardiography. Premedications were administered during the second time interval, and dogs were anesthetized during the fourth time interval. Surgery was completed and isoflurane administration was discontinued by the end of the fifth time interval. Error bars represent 95% confidence interval. Note, in this figure, the first time interval is < 1 hour, approximately 20 minutes.

The dogs seemed to tolerate monitoring well, in that none of the dogs were seen trying to remove the device.

Heart rate—Minimum heart rate during the 24-hour recording period was significantly lower among dogs given medetomidine (mean, 38 beats/min; 95% CI, 35 to 40 beats/min) than among dogs given acepromazine (mean, 48 beats/min; 95% CI, 45 to 51 beats/min). This was mainly attributed to low heart rates during the preoperative sedation phase and within the first few hours after surgery in dogs given medetomidine (**Figure 1**). In approximately half the dogs given acepromazine, minimum heart rate was observed during the night when the dogs were seen lying down with their heads rested. For all dogs, the lowest heart rate measured was 30 beats/min (medetomidine group).

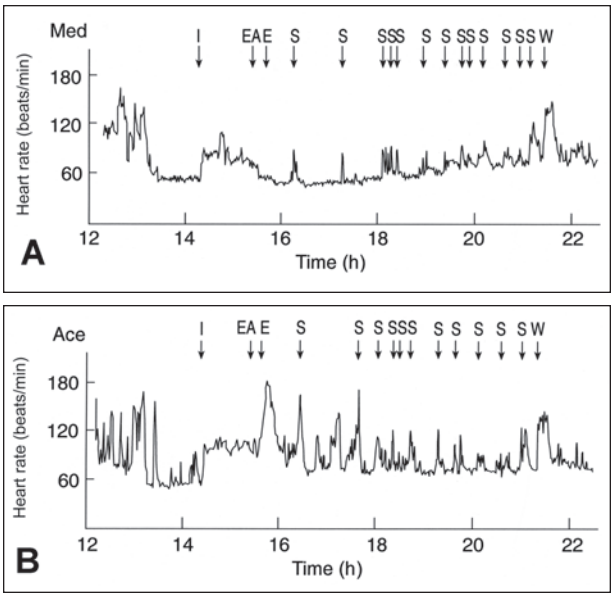

Figure 2—Representative printouts of perioperative heart rates recorded every 2 minutes by means of 24-hour ambulatory electrocardiography in 2 dogs undergoing ovariohysterectomy following premedication with medetomidine (Med; A) or acepromazine (Ace; B) and anesthesia with isoflurane. I = Induction of anesthesia. EA = End of isoflurane administration. E = Extubation. S = Times when dog was seen sitting or standing. W = Time when the dog was taken for a walk outside.

Maximum heart rates were similar for the 2 groups. Mean maximum heart rates during the 24-hour recording period were 178 beats/min (95% CI, 169 to 187 beats/min) for dogs given medetomidine and 186 beats/min (95% CI, 179 to 193 beats/min) for dogs given acepromazine. In most dogs, maximum heart rate was recorded about the time the dog was moved to the surgical suite or when the dog was taken outside for a walk after surgery. In 4 dogs given acepromazine, maximum heart rate was recorded during the early recovery phase.

Analysis of printouts of heart rate recorded every 2 minutes (**Figure 2**) showed that in dogs given medetomidine, low heart rates were especially apparent during the preoperative sedation phase but also during the immediate postoperative recovery period shortly after isoflurane administration was discontinued. However, in every dog, heart rate was > 60 beats/min whenever the dog was seen to be physically active (eg, sitting or standing up). Among dogs given acepromazine, heart rates were more variable, especially around the time of extubation when short-term increases in heart rate of > 20 beats/min were more frequently observed. Such short-term increases in heart rate were observed in 17 of the 20 dogs given acepromazine but in only 5 of the 21 dogs given medetomidine.

Cardiac conduction disturbances—The number of episodes of second-degree atrioventricular block was significantly greater among dogs given medetomidine than among dogs given acepromazine (**Table 1**). For dogs given medetomidine, most episodes of atrioventricular block identified during the preoperative sedation period occurred within the first 30 minutes after administration of medetomidine and butorphanol. Both Mobitz type I and II block were seen, but third-degree atrioventricular block was not identified in any of the dogs. In 5 dogs (3 in the medetomidine group and 2 in the acepromazine group), atrioventricular block occurred in bigeminy or

Table 1—Frequencies and temporal pattern of ventricular premature complexes (VPCs) and second-degree atrioventricular (AV) block in healthy dogs undergoing ovariohysterectomy following premedication with medetomidine (n = 21) or acepromazine (20).

	VPCs				AV block			
	Medetomidine		Acepromazine		Medetomidine		Acepromazine	
Recording period	No. of dogs	No. of VPCs*	No. of dogs	No. of VPCs*	No. of dogs	No. of blocks*	No. of dogs	No. of blocks*
Prior to premedication	2	8 (6–10)	1	1	1	10	1	3
Following premedication	3	4 (1–98)	1	2	20	11 (2–70)	13	4 (1–15)
Anesthesia and surgery	0	0	1	2	4	28.5 (1–150)	2	29.5 (11–48)
Postoperative period								
First hour	3	2 (2–60)	3	1 (1–1)	8	15 (1–50)	3	1 (1–26)
Second and third hours	3	2 (1–20)	1	3	5	20 (8–33)	0	0
Fourth through sixth hours	3	8 (1–12)	1	2	2	10 (5–15)	2	6 (2–10)
Subsequent night (10 PM–8 AM)	11	8 (1–54)	10	2 (1–42)	5	8 (3–15)	7	5 (1–41)
Next day (8 AM–12 AM)	3	2 (1–15)	3	2 (1–2)	1	1	4	3.5 (1–10)
Total recording period	11	8 (3–198)	13	4 (1–42)	20	14.5 (2–240)	17	5 (1–76)

Data were obtained by means of 24-hour ambulatory electrocardiography. Duration of the period prior to premedication was approximately 1 hour, duration of the period following premedication was approximately 1.3 hours, and duration of the anesthesia and surgery period was approximately 1.2 hours. Number of episodes of second-degree AV block was significantly ($P < 0.05$) greater in dogs given medetomidine.

*Data are given as median (range).

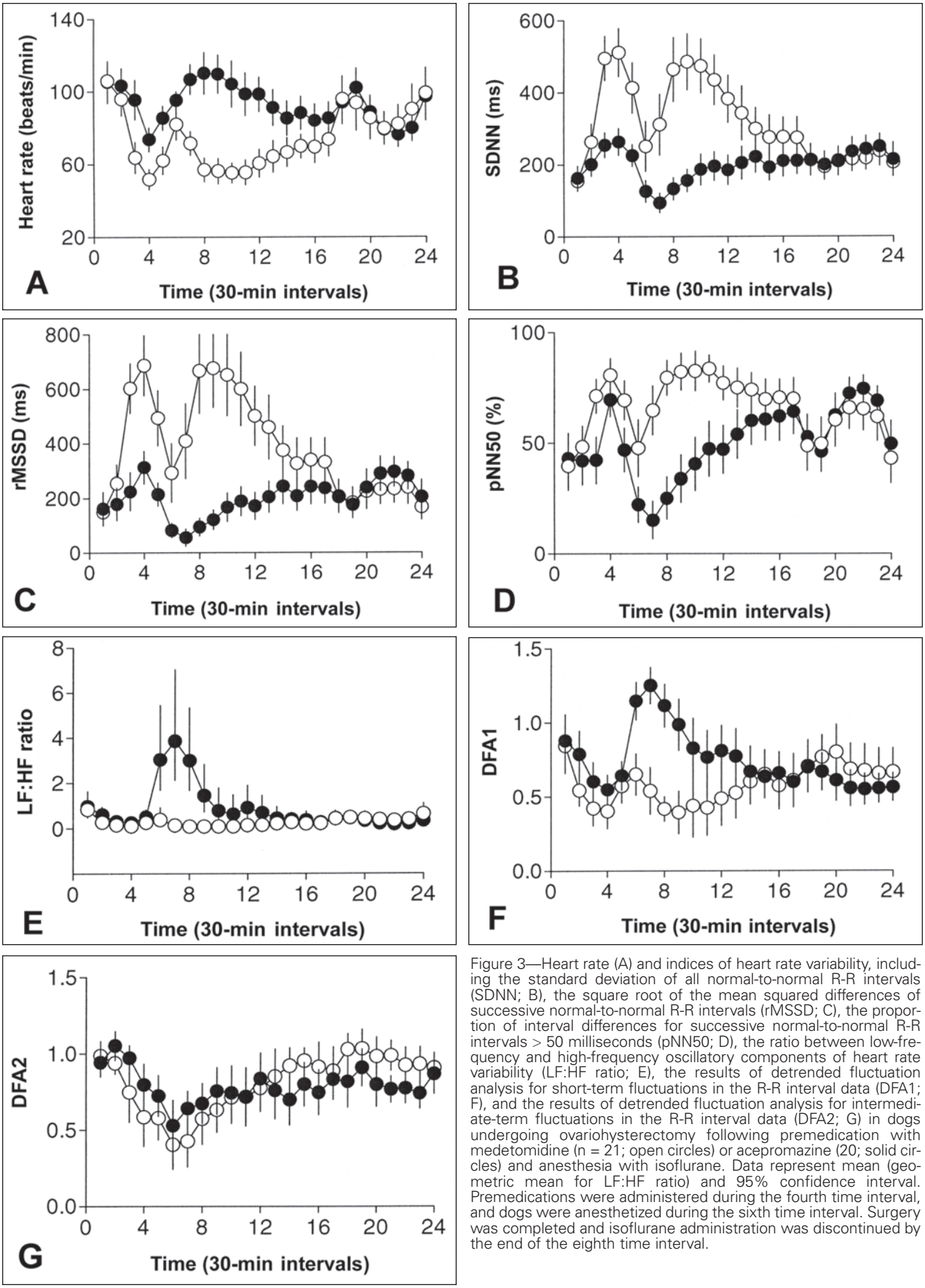

Figure 3—Heart rate (A) and indices of heart rate variability, including the standard deviation of all normal-to-normal R-R intervals (SDNN; B), the square root of the mean squared differences of successive normal-to-normal R-R intervals (rMSSD; C), the proportion of interval differences for successive normal-to-normal R-R intervals > 50 milliseconds (pNN50; D), the ratio between low-frequency and high-frequency oscillatory components of heart rate variability (LF:HF ratio; E), the results of detrended fluctuation analysis for short-term fluctuations in the R-R interval data (DFA1; F), and the results of detrended fluctuation analysis for intermediate-term fluctuations in the R-R interval data (DFA2; G) in dogs undergoing ovariohysterectomy following premedication with medetomidine (n = 21; open circles) or acepromazine (20; solid circles) and anesthesia with isoflurane. Data represent mean (geometric mean for LF:HF ratio) and 95% confidence interval. Premedications were administered during the fourth time interval, and dogs were anesthetized during the sixth time interval. Surgery was completed and isoflurane administration was discontinued by the end of the eighth time interval.

trigeminy. For all dogs, the maximum rate of atrioventricular block was 31/min; this represented a dog in the medetomidine group.

Number of VPCs was not significantly different between groups. For all dogs, maximum rate of VPCs was 6/min. Couplets or triplets were seen in 5 dogs (1 to 4/dog). Neither ventricular tachycardia nor the R-on-T phenomenon was observed. In general, VPCs were unifocal and were not detected in any dog during the induction of anesthesia or around the time of extubation. The VPCs recorded during the night were observed both in dogs seen to be physically active and in those lying down. The highest number of VPCs (198 VPCs during the 24-hour recording period) was recorded in a dog in the medetomidine group. Half (98/198) of the VPCs in this dog occurred during the preoperative sedation phase at a rate of approximately 1/min. During the 3 hours after surgery, this dog had 80 VPCs. Bigeminy was present on 10 occasions. This dog was the only individual seen to stand immediately after extubation and had a high heart rate (170 beats/min) around the time of extubation. Of the 10 Doberman Pinschers or German Shepherd Dogs included in the study, all but 2 had < 15 VPCs during the 24-hour recording period; the remaining 2 dogs had 40 and 42 VPCs during the 24-hour recording period.

The number of dogs that had sinus pauses > 2.0 seconds and median duration of the longest pauses were significantly greater among dogs given medetomidine (20 dogs; median duration of longest pause, 3.5 seconds; range, 2.2 to 7.5 seconds) than among dogs given acepromazine (14 dogs; median duration of longest pause, 2.5 seconds; range, 2.1 to 5.5 seconds). Pauses occurred during periods of low heart rate. In dogs given medetomidine, pauses occurred most often during the preoperative sedation or early recovery period. In dogs given acepromazine, pauses occurred most often during the night.

Indices of HRV—From approximately 6 hours after surgery to the end of the recording period, no systematic differences in HRV indices were detected between groups. Prior to this, time domain HRV indices (SD of all normal-to-normal R-R intervals, square root of the mean squared differences of successive normal-to-normal R-R intervals, and proportion of interval differences for successive normal-to-normal R-R intervals > 50 milliseconds) were higher among dogs given medetomidine than among dogs given acepromazine (**Figure 3**). During the anesthesia and surgery period, time domain HRV indices decreased in both groups. However, intraoperative time domain HRV indices were lower and the LF:HF ratio was higher among dogs given acepromazine than among dogs given medetomidine. Perioperative alterations were also detected in nonlinear HRV indices.

Additional observations—During the first 6 hours after surgery, dogs tended to spend short periods in an upright position and were typically seen to sit or stand for only 1 to 3 minutes at a time. Time spent lying down during the first 6 hours after surgery was similar for the 2 groups. For dogs given medetomidine, median times spent lying down during each of the 6 hours after surgery were 59 minutes (range, 16 to 60 minutes), 59 minutes (range, 17 to 60 minutes), 53 minutes (range, 0 to 59 minutes), 58 minutes (range, 0 to 59 minutes), 59 minutes (range, 48 to 59 minutes), and 42 minutes (range, 3 to 59 minutes). For dogs given acepromazine, median times were 59 minutes (range, 37 to 60 minutes), 59 minutes (range, 31 to 65 minutes), 58 minutes (range, 45 to 60 minutes), 59 minutes (range, 52 to 60 minutes), 57 minutes (range, 0.5 to 60 minutes), and 44 minutes (range, 8 to 58 minutes).

Discussion

The bradycardia observed among dogs given medetomidine in the present study was not surprising, as similar heart rates have been documented in dogs given α_2-adrenoceptor agonists.[13,21] The continuous observations performed in the present study further underline the extent of medetomidine's effects in this regard but also demonstrate the ability for heart rate to increase, even when α_2-adrenoceptor agonists are used. In the present study, increases in heart rate were recorded not only during the anesthesia and surgery period but also in every dog during the postoperative period in response to increased behavioral activity. The ability to mount physiologic responses following α_2-adrenoceptor agonist administration has aroused interest on various occasions[22,23]; in humans treated with an α_2-adrenoceptor agonist, changes in heart rate and HRV in response to positional stimuli have been demonstrated.[24]

In the present study, perioperative perturbations in time domain HRV indices were documented in both groups. To some extent, these alterations followed the changes in heart rate, with higher values for HRV indices identified when heart rate was seen to decrease. Along with the occurrence of atrioventricular block and sinus pauses, these results imply that cardiac efferent vagal modulation was enhanced with both anesthetic regimens. This has been documented previously for α_2-adrenoceptor agonists[25,26] but has not clearly been stated for acepromazine.[14] Our data indicate that when administered as a premedication, medetomidine had greater effects on cardiac efferent vagal modulation than did acepromazine.

During anesthesia and surgery in the present study, heart rates increased and values for time domain HRV indices decreased with both preanesthetic protocols. Administration of isoflurane alone[27] and nociceptive stimuli[28] have been implicated to result in vagal withdrawal, and in human surgical patients, decreases in HRV indices have been a common finding.[4,5] The lower intraoperative time domain HRV indices recorded for dogs given acepromazine in the present study could reflect the effects of the greater amounts of anesthetics administered to these dogs, possibly partly mediated by baroreceptor-induced responses, but could also reflect the different analgesic properties of the 2 premedications. Medetomidine could have contributed to the attenuation of nociceptive impulses through its actions on central α_2-adrenoceptors.[12,22] In contrast, no analgesic effects have been demonstrated for acepromazine.[29] The tendency for decreased HRV during surgery following preoperative administration of medetomidine may represent a desired phenomenon. Exaggerated vagal tone accompanied by vagally mediated reflexes induced by

visceral manipulation have the potential to induce detrimental effects in surgical patients.

Compared with dogs given medetomidine in the present study, dogs treated with acepromazine had higher LF:HF ratios during the anesthesia and surgery period, which further suggests that cardiac sympathetic modulation was enhanced. The LF:HF ratio has been suggested to be a measure of sympathetic and parasympathetic balance,[6,8] with higher values representing decreased vagal or enhanced cardiac sympathetic efferent activities. In humans, increases in LF HRV and in the LF:HF ratio have been reported in association with surgical stimuli.[30] The present study, however, provides only general information about perioperative HRV characteristics, and in general, markers of cardiac sympathetic modulation are not clearly defined.[20] In addition, the frequency domain analysis method is especially vulnerable to unstable experimental conditions, which inevitably occurred in the present study. Nevertheless, it is of interest that in dogs given acepromazine, these kinds of intraoperative HRV characteristics were recorded even though simultaneous measures of heart rate did not reveal any clinically relevant episodes of tachycardia. This could suggest the value of using HRV as a more sensitive measure to evaluate perioperative physiologic status. In addition, despite the perturbations in HRV, our previous study[17] documented low and stable intraoperative plasma catecholamine concentrations for the medetomidine-treated dogs, which could further indicate the dissimilar role of overall sympathetic nervous system activity and cardiac vagal influences in modulating the heart rate behavior.

Despite the differences in heart rates and indices of HRV, continuous electrocardiography did not reveal differences in the prevalence of perioperative VPCs between dogs given medetomidine and dogs given acepromazine in the present study. To some extent, this may demonstrate the moderately benign nature of the perioperative perturbations in physiologic status associated with both anesthetic protocols. On the other hand, the seemingly infrequent occurrence of VPCs in overtly healthy dogs[31] may complicate the documentation of significant differences. One dog that received medetomidine in the present study did have frequent VPCs that were associated with lower heart rates (approx 50 beats/min) and greater degrees of R-R interval variability, as evidenced by the ECG printouts, than recorded during other times in this dog. Ventricular premature complexes did not occur during the anesthesia period (heart rate, approx 80 beats/min), nor were they apparent during the early recovery period when the dog was seen standing and heart rate was approximately 80 beats/min. Observations in animals and humans have implicated enhanced cardiac sympathetic or decreased vagal influences as contributors to ventricular dysrhythmias.[32] In susceptible dogs, however, these types of arrhythmias have also been associated with low heart rates,[33] and some investigators have further suggested that overall autonomic nervous system balance has a role in the occurrence of ventricular events.[34,35] The present study did not allow us to draw any conclusions about the various factors, such as drug-related effects and patient factors, that may have contributed to the VPCs that were seen. Worth mentioning, however, is the fact that the only dog to have a high number of VPCs was also the one that had the lowest HRV during the preoperative phase and was regarded as a nervous individual in behavioral evaluations.

Nonlinear measures of HRV were included in the present study as a further measure of heart rate characteristics. The fact that changes in DFA1 and the LF:HF ratio were similar is in accordance with findings in humans[36] and may reflect the role of both vagal[37,38] and sympathetic[37] influences on this nonlinear index of HRV. The physiologic bases of these newer HRV indices, however, are yet to be fully discovered, and the similar values recorded for the 2 groups with respect to DFA2 may further underline the different aspects of heart rate behavior or physiologic status revealed when different analysis techniques are used. Anesthesia-related changes in beat-to-beat interval characteristics have been suggested as potential reflections of CNS depression and anesthetic depth,[39] and possibly, the perioperative alterations observed with DFA2 in the present study were influenced by such phenomena. The values for both groups decreased in relation to sedation and anesthesia. Nonetheless, further studies are warranted to explore factors that affect nonlinear HRV in dogs and the proper paradigms to be used in analysis programs. In the present study, values could not be obtained for some dogs, most of which had been given medetomidine. The data obtained from the other dogs, however, was considered worth reporting.

Some further limitations of the present study should be mentioned. The lack of control 24-hour ECG recordings confounds the analysis of the data obtained, especially with respect to arrhythmic events detected during the night. In addition, performing HRV analyses on ECG data containing arrhythmic events affects the estimation of HRV. No efforts were made to control the effects of respiration, which is known to modulate the beat-to-beat interval behavior.[20] However, respiratory rates for the 2 groups of dogs were similar in the present study; for instance, the mean (SD) respiratory rates among dogs given medetomidine during anesthesia and during the first postoperative hour were 14 (12) and 15 (6) breaths/min, respectively, and among dogs given acepromazine, 11 (8) and 12 (14) breaths/min, respectively (data derived from medical records).

In conclusion, the present study provides information on the extent and temporal pattern of perturbations in cardiac electrical activities and autonomic modulation in dogs undergoing elective surgery when either medetomidine or acepromazine is used as part of the preanesthetic medication. Under the conditions of the present study, greater influences on cardiac efferent vagal activities were documented for dogs premedicated with medetomidine. In dogs premedicated with acepromazine, our data suggest that there was more extensive vagal withdrawal and possibly greater increases in cardiac sympathetic influences. The 2 preanesthetic protocols, on the other hand, resulted also in similar physiologic characteristics, as reflected in certain HRV measures, the enhancement of intraoperative heart rate behavior, and the occurrence of VPCs. Further studies await the detailed characterization

of the contributors to the findings of the present study and their clinical importance. For instance, the bradycardic effects of medetomidine are to a certain extent dose dependent,[13] and the necessity of anticholinergic medication with α_2-adrenoceptor agonists is still somewhat controversial.[12,21] Acepromazine, on the other hand, is commonly administered with full opioid agonists in everyday practice, which may result in different analgesic and cardiovascular statuses. The differences between the 2 preanesthetic protocols subsided by 6 hours after surgery in the present study, which may assist in determining the optimal period for postoperative monitoring.

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f. Oxford Medilog 4500, Oxford Instruments, Hawthorne, NY.
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