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Cardiovascular Effects of Xenon in Isoflurane-anesthetized Dogs with Dilated Cardiomyopathy

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Background: Clinical interest in xenon has been rekindled recently by new recycling systems that have decreased its relative cost. The cardiovascular effects of xenon were examined in isoflurane-anesthetized dogs before and after the development of rapid left ventricular (LV) pacing-induced cardiomyopathy.

Methods: Dogs (n = 10) were chronically instrumented to measure aortic and LV pressure, LV subendocardial segment length, and aortic blood flow. Hemodynamics were recorded, and indices of LV systolic and diastolic function and afterload were determined in the conscious state and during 1.5 minimum alveolar concentration isoflurane anesthesia alone and combined with 0.25, 0.42, and 0.55 minimum alveolar concentration xenon in dogs with and without cardiomyopathy.

Results: Administration of xenon to healthy dogs anesthetized with isoflurane decreased heart rate and increased the time constant (τ) of isovolumic relaxation but did not alter arterial and LV pressures, preload recruitable stroke work slope, and indices of LV afterload. Chronic rapid LV pacing increased the baseline heart rate and LV end-diastolic pressure, decreased arterial and LV systolic pressures, and produced LV systolic and diastolic dysfunction. Administration of xenon to isoflurane-anesthetized, cardiomyopathic dogs did not alter heart rate, arterial and LV pressures, myocardial contractility,

and indices of early LV filling and regional chamber stiffness. More pronounced increases in τ were accompanied by increases in total arterial resistance during administration of xenon to isoflurane-anesthetized cardiomyopathic compared with healthy dogs.

Conclusions: The results indicate that xenon produces minimal cardiovascular actions in the presence of isoflurane in dogs with and without experimental dilated cardiomyopathy. (Key words: Aortic compliance; power spectral analysis; Windkessel.)

THE anesthetic properties of the noble gas xenon were first described more than 50 yr ago.^{1,2} Unlike nitrous oxide, xenon is chemically inert, does not undergo biotransformation,³ and is devoid of teratogenic effects.⁴ Xenon has a blood gas partition coefficient (0.14)⁵ less than nitrous oxide (0.47), provides rapid induction and emergence from anesthesia,⁶⁻⁹ and exerts analgesic effects¹⁰ by suppressing spinal dorsal horn neurons¹¹ independent of μ_2 -adrenergic or opioid receptors.¹² Despite these advantageous properties, xenon has not been used routinely for clinical anesthesia in the United States because it is more expensive than nitrous oxide and volatile anesthetics. Recently, more efficient manufacturing techniques and development of low-flow administration and recycling systems have reduced the potential relative cost of xenon and rekindled interest in its clinical use.^{8,13,14}

Xenon causes minimal cardiovascular effects,^{6-8,15,16} appears to preserve myocardial contractility *in vivo*,⁷ and attenuates increases in plasma epinephrine and cortisol concentrations associated with surgical stimulation.¹⁵ Although these data suggest that xenon does not substantially alter hemodynamics in the normal cardiovascular system, the effects of this anesthetic gas on systemic hemodynamics, left ventricular (LV) function, and LV afterload have not been characterized in experimental models of, or patients with, heart failure. The current investigation examined the cardiovascular actions of xenon in dogs fitted with instruments for long-term monitoring before and after the development of rapid LV pacing-induced cardiomyopathy. The cardiovas-

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cular effects of xenon were examined during isoflurane anesthesia because the minimum alveolar concentration (MAC) of xenon is super-atmospheric (119%) in dogs.¹⁷ The experiments tested the hypothesis that xenon does not affect isoflurane-induced alterations in LV systolic and diastolic function and LV afterload.

Methods

All experimental procedures and protocols used in this investigation were reviewed and approved by the Animal Care and Use Committee of the Medical College of Wisconsin. All procedures conformed to the *Guiding Principles in the Care and Use of Animals* of the American Physiological Society and were performed in accordance with the *Guide for the Care and Use of Laboratory Animals* (DHEW [DHHS] publication [NIH] 85-23, revised 1996).

Surgical Instrumentation

The surgical implantation of instruments was described in detail before.¹⁸⁻²⁰ Briefly, during general anesthesia and using aseptic techniques, a left thoracotomy was performed in mongrel dogs to place instruments to measure aortic pressure (heparin-filled catheter), aortic blood flow (transit time flow transducer), LV pressure (high fidelity, miniature micromanometer), the maximum rate of increase of LV pressure ($+dP/dt_{max}$), and LV anterior wall subendocardial segment length (ultrasonic crystals). A hydraulic vascular occluder was placed around the inferior vena cava for the abrupt alteration of LV preload required to generate a series of LV pressure-segment length diagrams. Platinum pacing electrodes were sutured to the epicardial surface of the LV free wall. All instrumentation was firmly secured, tunneled between the scapulas, and exteriorized *via* several small incisions. The pericardium was left open, the chest wall closed in layers, and the pneumothorax evacuated by a chest tube. Each dog was fitted with a jacket to prevent damage to the instruments and catheters. The pacing electrodes were attached to a programmable pacemaker that was housed in a jacket pocket. All dogs received intravenous fentanyl (5 μ g/kg) for analgesia as needed after surgery and were allowed to recover a minimum of 7 days before the experiments. All dogs were treated with intramuscular antibiotics (40 mg/kg cephalothin and 4.5 mg/kg gentamicin) and trained to stand quietly in a sling during hemodynamic monitoring. End-systole and end-diastole were measured 30 ms before peak neg-

ative LV dP/dt and immediately before the onset of LV isovolumic contraction, respectively. The percentage of segment shortening (%SS) was calculated using the equation $\%SS = (\text{end-diastolic segment length} - \text{end-systolic segment length}) \cdot 100 \cdot (\text{end-diastolic segment length})^{-1}$. Hemodynamic data were recorded continuously on a polygraph and simultaneously digitized and recorded on a computer.

Experimental Protocol

Dogs ($n = 10$; weight range, 24-34 kg) were fasted overnight. Fluid deficits were replaced with 0.9% saline (500 ml), and intravenous fluids were continued at 3 $\text{ml} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ for the duration of each experiment. After instruments were calibrated, baseline systemic hemodynamics were recorded in the conscious state. LV pressure, segment length, aortic blood pressure, and aortic blood flow waveforms were recorded to analyze LV diastolic function and aortic input impedance [$Z_{in}(\omega)$]. A series of LV pressure-segment length diagrams were recorded during abrupt reduction of LV preload *via* the inferior vena caval hydraulic vascular occluder for subsequent analysis of LV systolic function, as previously described.²⁰

After inhalational induction and tracheal intubation, anesthesia was maintained with 1.5 MAC isoflurane (end-tidal concentration = 1.92%) during positive-pressure ventilation in an air-and-oxygen (25%) mixture. The MAC values of isoflurane and xenon assumed in this investigation were 1.28% and 119%, respectively.^{17,21} Hemodynamic measurements were repeated after 30 min equilibration. Dogs then received 30%, 50%, and 65% xenon (MG Industries, Malvern, PA) in a sequential manner in addition to 1.5 MAC isoflurane. The inspired concentration of nitrogen was decreased as the concentration of xenon was increased to maintain a constant inspired oxygen concentration at 25%. Hemodynamic waveforms were recorded at end-expiration after 20 min equilibration at each dose of xenon. Thus the entire duration of anesthesia was 90 min. End-tidal concentrations of isoflurane and xenon were measured at the tip of the endotracheal tube using a portable mass spectrometer (Marquette Medical Systems, Milwaukee, WI) that was specifically calibrated to detect xenon. The mass spectrometer was calibrated with known standards before and during experimentation. Acid base status and arterial blood gas tensions were maintained at conscious levels by adjusting the air and oxygen concentrations and respiratory rate throughout each experiment.

After the completion of experiments in healthy dogs,

the LV of each dog was paced continuously at rates between 220 and 240 beats/min, as previously described.^{18,20} Dogs were paced for 16 ± 3 days (mean \pm SEM) to develop LV dysfunction. A state of myocardial dysfunction was assumed when left ventricular end-diastolic pressure was ≥ 20 mmHg in the conscious state with the pacemaker off. Dogs were fasted overnight before experimentation, and fluid deficits were replaced as described before. LV pacing was discontinued for the duration of the experiment. Systemic hemodynamics and LV pressure, segment length, aortic blood pressure, and aortic blood flow waveforms were recorded in sinus rhythm in the conscious state and during isoflurane anesthesia in the presence and absence of xenon, as described above. Thus a total of 20 experiments were performed that compared the effects of isoflurane and xenon before and after the development of rapid LV pacing-induced cardiomyopathy in the same 10 dogs.

Determination of Indices of Left Ventricular Function and Afterload

The slope (M_w) of the regional preload recruitable stroke work relation derived from a series of LV pressure-segment length waveforms was used to quantify myocardial contractility.²² The time constant of LV isovolumic relaxation (τ) was calculated using the derivative method.²³ The peak rate of increase of myocardial segment length during early LV filling (dL/dt_{max}) was determined by differentiating the segment length waveform. A regional chamber stiffness constant (K) was derived from the LV pressure-length relation during diastole assuming a simple elastic model.²⁴ LV afterload was quantified with $Z_{in}(\omega)$ spectra and interpreted using a three-element Windkessel model of the arterial circulation, as previously described.¹⁸⁻²⁰ Briefly, digitized, steady state aortic blood pressure and blood flow waveforms were transformed from the time to the frequency (ω) domain using power spectral analysis to determine $Z_{in}(\omega)$. Each calculated $Z_{in}(\omega)$ spectrum was corrected for the phase responses of the aortic pressure and blood flow transducers.¹⁹ Characteristic aortic impedance (Z_c) was determined as the average magnitude of $Z_{in}(\omega)$ between 2 and 15 Hz. Total arterial resistance (R) was calculated as the difference between the magnitude of $Z_{in}(\omega)$ at zero Hz and Z_c . Total arterial compliance (C) was determined directly from steady state aortic pressure and blood flow waveforms using a previously validated formula.²⁵ For the purpose of calculating C , end-systole was defined as occurring at the dicrotic notch of the aortic pressure waveform.

Statistical Analysis

Statistical analysis of the data within and between groups in the conscious state and during isoflurane and xenon anesthesia before and after the development of pacing-induced cardiomyopathy was performed by analysis of variance with repeated measures followed by application of two-tailed Student's t test with Duncan's adjustment for multiplicity. Probability values < 0.05 were considered significant. All data are expressed as mean \pm SEM.

Results

As shown in table 1, 1.5 MAC isoflurane increased heart rate and decreased mean arterial pressure, LV systolic pressure, cardiac output, and stroke volume. Left ventricular end-diastolic pressure was unchanged. Isoflurane decreased M_w , $+dP/dt_{max}$, and %SS, consistent with a direct negative inotropic effect (fig. 1). Decreases in $-dP/dt_{min}$, dL/dt_{max} , and K occurred during isoflurane anesthesia, but τ remained unchanged (fig. 2). Isoflurane also reduced R and increased C (fig. 3). Characteristic aortic impedance (Z_c) was unchanged. Xenon caused minimal additional hemodynamic effects when this gas was administered to healthy dogs anesthetized with isoflurane (table 1). Xenon decreased heart rate and increased end-diastolic segment length. Arterial and LV pressures, cardiac output, and stroke volume were unchanged. Indices of LV systolic function and LV afterload also remained unchanged when xenon was added to 1.5 MAC isoflurane (figs. 1 and 3). Increases in τ and decreases in the magnitude of $-dP/dt_{min}$ occurred in healthy dogs that received isoflurane and xenon. Indices of early LV filling and regional chamber stiffness remained unchanged, however.

Chronic, rapid LV pacing increased baseline heart rate (sinus rhythm), LV end-diastolic pressure, and end-diastolic and end-systolic segment lengths and decreased arterial and LV systolic pressures (table 2). Cardiac output and indices of LV afterload were unchanged after 16 ± 3 days of pacing. Decreases in M_w , $+dP/dt_{max}$, and %SS were observed, consistent with a reduction in myocardial contractility (fig. 1). Diastolic dysfunction (increases in τ and K and decreases in the magnitude of $-dP/dt_{min}$; fig. 2) was also observed in conscious, cardiomyopathic dogs.

The hemodynamic effects of isoflurane in dogs with dilated cardiomyopathy were similar but not identical to those observed in healthy dogs before pacing was initi-

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Table 1. Hemodynamic Effects of Isoflurane and Xenon in Normal Dogs

	n	Conscious	Isoflurane 1.5 MAC			
			ISO only	+30% Xe	+50% Xe	+65% Xe
HR (beats · min ⁻¹)	10	84 ± 2	127 ± 4*	115 ± 5*,†	110 ± 5*,†	108 ± 4*,†,‡
MBP (mmHg)	10	104 ± 4	63 ± 4*	65 ± 5*	66 ± 5*	63 ± 5*
LVSP (mmHg)	9	125 ± 4	81 ± 5*	80 ± 7*	81 ± 6*	78 ± 6*
LVEDP (mmHg)	9	8 ± 1	7 ± 2	6 ± 1	7 ± 1	7 ± 1
-dP/dt _{min} (mmHg · s ⁻¹)	9	-2,352 ± 69	-1,331 ± 103*	-1,300 ± 138*	-1,230 ± 127*	-1,100 ± 109*,†,‡
CO (l · min ⁻¹)	8	2.4 ± 0.3	2.1 ± 0.2*	2.0 ± 0.2*	2.0 ± 0.2*	2.0 ± 0.2*
SV (ml)	8	29 ± 3	16 ± 1*	18 ± 1*	18 ± 2*	18 ± 2*
EDL (mm)	8	20.7 ± 0.8	18.3 ± 1.1*	18.7 ± 1.1*	19.0 ± 1.0*	19.1 ± 1.1*,†
ESL (mm)	8	16.3 ± 1.1	15.6 ± 1.1	15.7 ± 1.1	15.8 ± 1.1	16.2 ± 1.1
L _w (mm)	7	13.2 ± 1.1	13.8 ± 1.4	13.9 ± 1.4	13.8 ± 1.2	14.1 ± 1.5
ET _{ISO} (%)	10	—	1.9 ± 0.0	1.9 ± 0.0	1.9 ± 0.0	1.9 ± 0.0
ET _{Xe} (%)	10	—	—	32 ± 1	51 ± 1	65 ± 1

Data are mean ± SEM.

Xe = xenon; ISO = isoflurane; HR = heart rate; MBP = mean arterial pressure; LVSP and LVEDP = left ventricular systolic and end-diastolic pressures, respectively; -dP/dt_{min} = peak rate of decrease of left ventricular pressure; CO = cardiac output; SV = stroke volume; EDL = end-diastolic segment length; ESL = end-systolic segment length; L_w = length intercept of preload recruitable stroke work relationship; ET_{ISO} = end-expired isoflurane concentration; ET_{Xe} = end-tidal xenon concentration.

* $P < 0.05$ versus conscious.

† $P < 0.05$ versus 1.5 MAC isoflurane.

‡ $P < 0.05$ versus 1.5 MAC isoflurane and 30% xenon.

ated (table 2). Isoflurane decreased arterial and LV pressures, cardiac output, and stroke volume. In contrast to the findings in normal dogs, no change in heart rate occurred during isoflurane anesthesia in cardiomyopathic dogs. Isoflurane also decreased myocardial contractility (e.g., M_w , $+dP/dt_{max}$, and %SS), dL/dt_{max} , and K but did not alter τ in dogs after pacing. Isoflurane alone increased C but did not affect R and Z_c in cardiomyopathic dogs. Heart rate, arterial and LV pressures, cardiac output, and stroke volume were unchanged by the administration of xenon to isoflurane-anesthetized, cardiomyopathic dogs. No change in M_w occurred, but $+dP/dt_{max}$ and %SS were reduced during isoflurane and xenon anesthesia. An increase in τ and a decrease in the magnitude of $-dP/dt_{min}$ were observed in cardiomyopathic dogs that received isoflurane and xenon. No changes in dL/dt_{max} and K were observed. Xenon increased R and attenuated isoflurane-induced increases in C in cardiomyopathic dogs. Z_c remained unchanged.

Discussion

Several previous investigations have inferred that xenon causes minimal cardiovascular effects. Fractional area change of the LV mid-papillary short axis remained constant during 65% xenon anesthesia in patients undergoing cholecystectomy or hysterectomy.⁷ These findings sug-

gested that xenon does not affect myocardial contractility in humans. Most recently, xenon was shown to maintain heart rate and arterial pressure at constant levels in women undergoing gynecologic surgery, findings that were identical to those observed during nitrous oxide-sevoflurane or nitrous oxide-isoflurane anesthesia combined with epidural local anesthetics.⁹ Hemodynamics, cardiac output, and systemic and pulmonary vascular resistances remained constant, and plasma epinephrine concentrations were reduced during xenon anesthesia in barbiturate-anesthetized pigs.¹⁶ Xenon also did not affect systemic and pulmonary hemodynamics in acutely instrumented dogs anesthetized with α -chloralose and thiopental,²⁶ results that were identical to those observed when nitrous oxide was administered. These latter two studies^{16,26} indirectly suggested that xenon anesthesia may be well tolerated in the presence of preexisting LV dysfunction because the experimental preparations used in these studies are associated with profound depression of cardiac performance *in vivo*.²⁷

The results of the present investigation indicate that xenon causes minimal cardiovascular effects during 1.5 MAC isoflurane anesthesia in healthy dogs. Xenon decreased heart rate but did not affect arterial and LV pressures, cardiac output, and stroke volume in isoflurane-anesthetized dogs. Tachycardia during isoflurane anesthesia results from baroreceptor reflex activation,²⁸ and declines in heart rate during administration of xenon may reflect attenuation

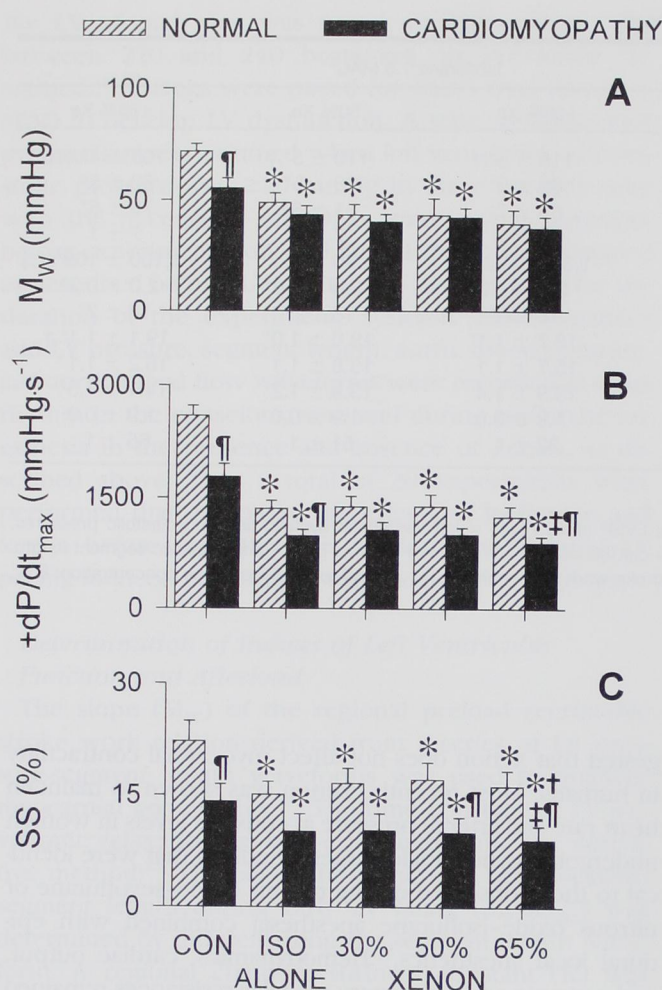


Fig. 1. Histograms illustrating (A) the effects of isoflurane (ISO) and xenon on preload recruitable stroke work slope (M_w), (B) the peak rate of increase of left ventricular pressure ($+dP/dt_{max}$), and (C) the percentage of segment shortening (%SS) in healthy (hatched bars) and cardiomyopathic dogs (solid bars) that received 1.5 MAC isoflurane in the presence and absence of 30, 50, and 65% xenon. * $P < 0.05$ versus conscious (CON); † $P < 0.05$ versus ISO alone; ‡ $P < 0.05$ versus ISO and 30% xenon; ¶ $P < 0.05$ versus corresponding values in healthy dogs.

of this baroreceptor response. Xenon did not alter M_w , a relatively heart rate- and load-insensitive index of inotropic state,²² in dogs anesthetized with 1.5 MAC isoflurane. Isovolumic ($+dP/dt_{max}$) and ejection phase (%SS and cardiac output) indices of contractile state also remained unchanged. These findings indicate that xenon does not affect intrinsic myocardial contractility in healthy dogs and support previous observations with transesophageal echocardiography during xenon anesthesia in humans.⁷ Isoflurane-induced reductions in dL/dt_{max} and K were unchanged by xenon, suggesting that this anesthetic gas does not alter

early diastolic LV filling or chamber compliance. In contrast, an increase in τ was observed during administration of 50% and 65% xenon and 1.5 MAC isoflurane in healthy dogs. These findings suggest that xenon causes modest prolongation of the isovolumic phase of relaxation concomitant with decreases in heart rate. Xenon also did not alter beneficial isoflurane-induced alterations of LV afterload. Isoflurane has been shown to produce reductions in R and increases in C .¹⁹ These changes in the determinants

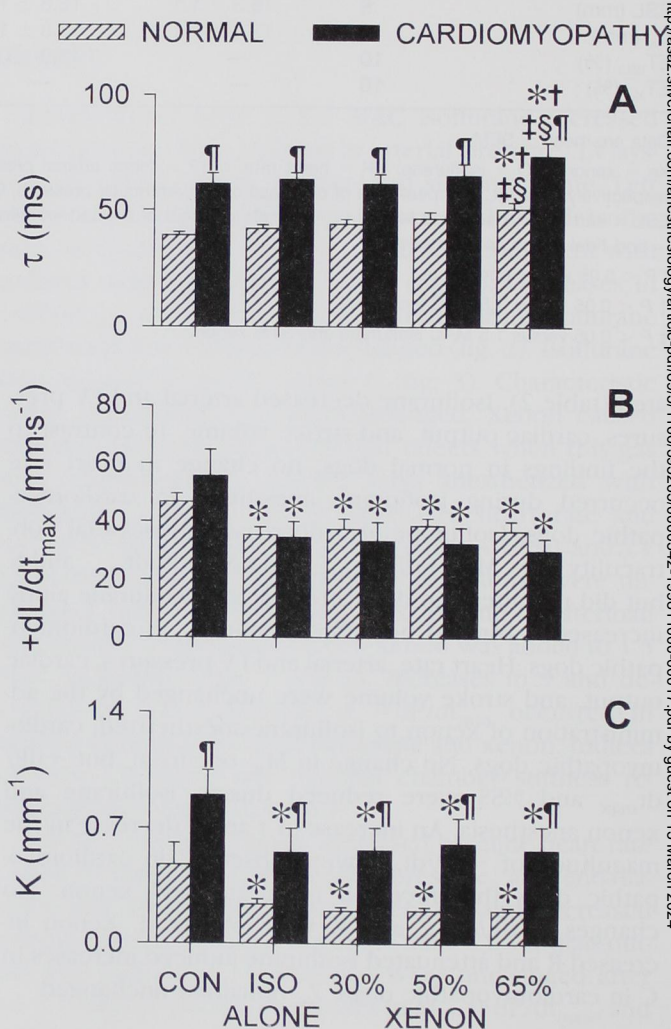


Fig. 2. Histograms illustrating (A) the effects of isoflurane (ISO) and xenon on the time constant of isovolumic relaxation (τ), (B) the peak rate of increase of segment lengthening (dL/dt_{max}), and (C) the regional chamber stiffness constant (K) in normal (hatched bars) and cardiomyopathic dogs (solid bars) receiving 1.5 minimum alveolar concentration isoflurane in the presence and absence of 30%, 50%, and 65% xenon. * $P < 0.05$ versus conscious (CON); † $P < 0.05$ versus ISO alone; ‡ $P < 0.05$ versus ISO and 30% xenon; ¶ $P < 0.05$ versus ISO and 50% xenon; ¶ $P < 0.05$ versus corresponding value in healthy dogs.

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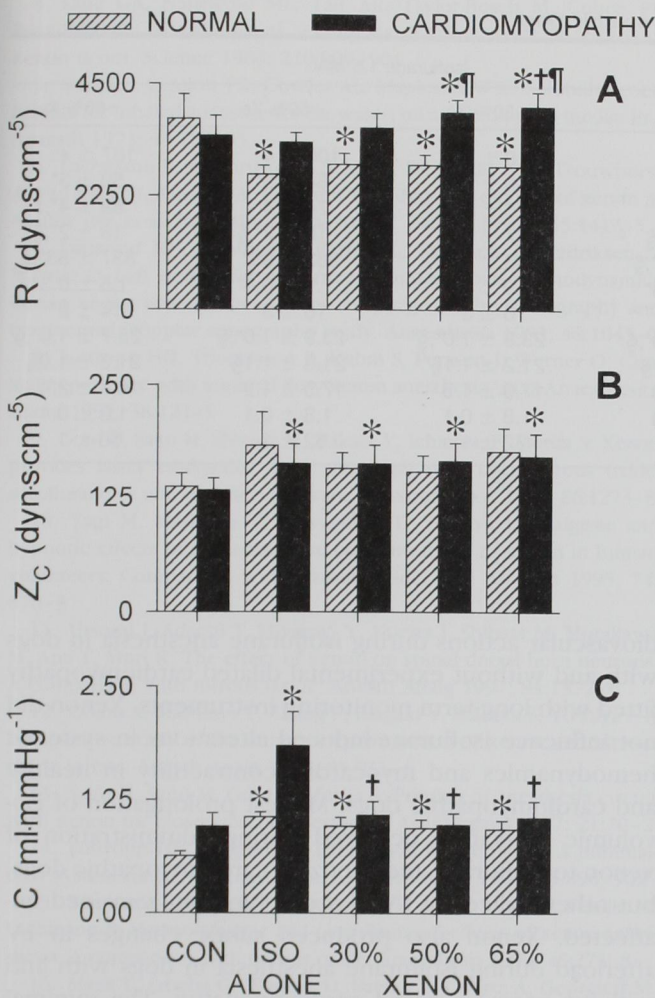


Fig. 3. Histograms illustrating (A) the effects of isoflurane (ISO) and xenon on total arterial resistance (R), (B) characteristic aortic impedance (Z_c), and (C) total arterial compliance (C) in healthy (hatched bars) and cardiomyopathic dogs (solid bars) that received 1.5 minimum alveolar concentration isoflurane in the presence and absence of 30%, 50%, and 65% xenon. * $P < 0.05$ versus conscious (CON); † $P < 0.05$ versus ISO alone; ‡ $P < 0.05$ versus corresponding value in healthy dogs.

of LV afterload help to maintain cardiac output despite simultaneous reductions in contractility. Together the present findings indicate that xenon produces only very subtle cardiovascular actions during isoflurane anesthesia in healthy dogs.

The present results indicate that 16 ± 3 days of rapid LV pacing produces cardiovascular effects that are nearly identical to those we previously reported in chronically instrumented dogs.^{18,20,29} Conscious dogs with pacing-induced cardiomyopathy displayed increases in baseline heart rate, LV end-diastolic pressure, LV chamber dilatation, decreases

in arterial and LV systolic pressures, and LV systolic and diastolic dysfunction. Cardiac output and indices of LV afterload remained unchanged during pacing of this duration, as previously characterized.¹⁸ Reductions in cardiac output and total arterial compliance and increases in total arterial resistance do not occur until late in the development of pacing-induced heart failure because vasodilation resulting from reduced peripheral perfusion is balanced by enhanced sympathetic nervous system activity.^{30,31} Thus the present investigation examined the cardiovascular effects of isoflurane and xenon in a canine model of LV dysfunction before decompensation into frank heart failure had occurred.

Xenon caused minimal hemodynamic effects in cardiomyopathic dogs in the present investigation. Arterial and LV pressures, cardiac output, and stroke volume were unchanged during the administration of xenon to isoflurane-anesthetized cardiomyopathic dogs. In contrast to the findings in dogs before pacing, heart rate remained unchanged during isoflurane and xenon anesthesia in dogs after pacing. The lack of change in heart rate during administration of isoflurane with and without xenon may reflect altered baroreceptor reflex activity concomitant with basal increases in sympathetic and decreases in parasympathetic nervous system activity associated with evolving heart failure.³² M_w was unchanged during administration of xenon, indicating that this noble gas does not alter intrinsic myocardial contractility in the presence of preexisting LV dysfunction. In contrast, reductions in $+dP/dt_{max}$ and %SS occurred, but these indices of contractile state may have been adversely influenced by simultaneous increases in LV afterload.³³ Isoflurane alone increased C but did not alter R in dogs with dilated cardiomyopathy. These findings confirm our previous results¹⁸ and indicate that favorable reductions in arteriolar resistance do not occur during isoflurane anesthesia in the presence of pacing-induced cardiomyopathy. Xenon increased R and abolished the isoflurane-induced increase in C in cardiomyopathic dogs. These results suggest that xenon causes detrimental increases in LV afterload during isoflurane anesthesia. The afterload sensitivity of LV relaxation is enhanced in failing myocardium.²⁹ Thus increases in τ observed in cardiomyopathic dogs anesthetized with isoflurane and xenon may have occurred because of simultaneous increases in R.³⁴ Despite these increases in τ , dL/dt_{max} and K were unchanged during administration of xenon to isoflurane-anesthetized, cardiomyopathic dogs. These findings suggest that modest prolongation of the isovolumic relaxation phase of diastole did not affect early LV

Table 2. Hemodynamic Effects of Isoflurane and Xenon in Cardiomyopathic Dogs

	n	Conscious	Isoflurane 1.5 MAC			
			ISO only	+30% Xe	+50% Xe	+65% Xe
HR (beats · min ⁻¹)	10	110 ± 6§	110 ± 4	110 ± 5	106 ± 4	107 ± 4
MBP (mmHg)	10	90 ± 3§	62 ± 3*	66 ± 3*	64 ± 3*	59 ± 3*
LVSP (mmHg)	9	106 ± 4§	71 ± 3*	76 ± 4*	74 ± 4*	69 ± 4*,‡
LVEDP (mmHg)	9	22 ± 1§	16 ± 2*,§	17 ± 2*,§	18 ± 2*,§	18 ± 2*,§
-dP/dt _{min} (mmHg · s ⁻¹)	9	1,680 ± 156§	927 ± 66*,§	1,043 ± 103*	963 ± 96*	837 ± 83*,‡
CO (l · min ⁻¹)	8	2.7 ± 0.4	1.7 ± 0.3*	1.9 ± 0.4*	1.7 ± 0.4*	1.5 ± 0.3*
SV (ml)	8	24 ± 3	15 ± 2*	16 ± 3*	16 ± 3*	14 ± 2*
EDL (mm)	8	24.8 ± 1.3§	23.7 ± 0.9*,§	23.9 ± 1.0*,§	23.9 ± 1.0*,§	23.7 ± 1.0*,§
ESL (mm)	8	21.0 ± 1.3§	21.0 ± 1.1§	21.2 ± 1.1§	21.3 ± 1.1§	21.3 ± 1.0§
L _w (mm)	7	16.2 ± 2.1	17.4 ± 1.9	17.0 ± 1.3	17.5 ± 1.2	16.7 ± 2.4
ET _{ISO} (%)	10	—	1.9 ± 0.0	1.8 ± 0.1	1.8 ± 0.1	1.9 ± 0.1
ET _{Xe} (%)	10	—	—	32 ± 1	52 ± 1	66 ± 1

Data are mean ± SEM. See table 1 for abbreviations.

* $P < 0.05$ versus conscious.

‡ $P < 0.05$ versus 1.5 MAC isoflurane and 30% xenon.

§ $P < 0.05$ versus corresponding value in normal dogs (Table 1).

filling, chamber stiffness, or stroke volume during isoflurane and xenon anesthesia.

The results of this study should be interpreted within the constraints of several potential limitations. The cardiovascular actions of xenon were examined in isoflurane-anesthetized dogs rather than alone because the MAC of xenon is super-atmospheric (119%) in dogs.¹⁷ End-tidal concentrations of xenon >65% (0.55 MAC) were not examined because the high flow of xenon required to achieve such concentrations was impractical. Thus, whether higher MAC of xenon produce cardiovascular effects in the presence of isoflurane could not be addressed by the present investigation. The presence of baseline isoflurane anesthesia must also be considered when the actions of xenon on systemic hemodynamics, LV function, and afterload are evaluated. Xenon effects could have been masked or attenuated by the presence of isoflurane. However, considerable capacity for further hemodynamic, functional, and afterload depression at anesthetic concentrations >1.5 MAC were previously demonstrated.^{19,35-37} The cardiovascular effects of isoflurane and xenon were studied in the presence of compensated LV dysfunction and may have been different in the presence of overt heart failure. The canine pacing-induced cardiomyopathy model used in the present investigation has been shown to be similar in many respects to human idiopathic dilated cardiomyopathy.³⁸ However, the present results may also have been different in LV dysfunction resulting from pressure- or volume-overload hypertrophy or infiltrative disease processes.

In conclusion, the results of the current investigation indicate that xenon (≤ 0.55 MAC) produces subtle car-

diovascular actions during isoflurane anesthesia in dogs with and without experimental dilated cardiomyopathy fitted with long-term monitoring instruments. Xenon did not influence isoflurane-induced alterations in systemic hemodynamics and myocardial contractility in healthy and cardiomyopathic dogs. Modest prolongation of isovolumic relaxation occurred during administration of xenon to isoflurane-anesthetized, cardiomyopathic dogs, but other indices of LV diastolic function remained unaffected. Xenon also produced subtle changes in LV afterload during isoflurane anesthesia in dogs with and without pacing-induced cardiomyopathy. The minimal cardiovascular effects of xenon are not accompanied by changes in global cardiac performance.

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