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Dexmedetomidine Produces Similar Alterations in the Determinants of Left Ventricular Afterload in Conscious Dogs before and after the Development of Pacing-induced Cardiomyopathy

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Background: The authors tested the hypothesis that intravenous dexmedetomidine produces alterations in left ventricular (LV) afterload that are deleterious to cardiac performance in conscious dogs with pacing-induced cardiomyopathy.

Methods: Dogs ($n = 8$) were fitted with instruments for long-term measurement of LV and aortic blood pressure, aortic blood flow, and subendocardial segment length and received dexmedetomidine (1.25, 2.5, and 5 $\mu\text{g}/\text{kg}$) in a cumulative manner before and after 19 ± 3 (mean \pm SEM) days of rapid LV pacing. LV afterload was measured with aortic input impedance [$Z_{in}(\omega)$] and quantified with a three-element Windkessel model. Hemodynamics and $Z_{in}(\omega)$ were assessed under control conditions and 5 and 60 min after administration of each dose.

Results: Dexmedetomidine caused early and late decreases in heart rate, the maximum rate of increase of LV pressure, mean aortic blood flow, and stroke volume in dogs before and after pacing. Dexmedetomidine caused similar early increases in total arterial resistance and decreases in total arterial compliance in dogs before and after pacing. Early dexmedetomidine-induced increases in resistance and decreases in compliance caused similar reductions in mean aortic blood flow in cardiomyopathic compared with healthy dogs. Resistance and compliance returned to control values, and characteristic aortic impedance decreased late after dexmedetomidine in healthy

dogs. In contrast, resistance remained elevated late after dexmedetomidine in dogs with dilated cardiomyopathy.

Conclusions: Dexmedetomidine causes similar alterations in hemodynamics and LV afterload in conscious dogs with and without pacing-induced cardiomyopathy. (Key words: α_2 -Adrenoceptor agonists; signal processing; power spectrum analysis.)

INTRAVENOUS administration of the selective α_2 -adrenoceptor agonist dexmedetomidine causes an arterial pressor-depressor response in the normal cardiovascular system.¹⁻³ The initial hypertension occurs in part by direct stimulation of postsynaptic α_2 -adrenoceptors in arteriolar vascular smooth muscle,^{1,2,4} an action that increases systemic vascular resistance. Later reductions in arterial pressure result from a decline in central sympathetic or an increase in parasympathetic nervous system activity mediated by medullary α_2 -adrenergic⁵ or imidazoline⁶ receptors.⁷ Although knowledge of the relative early and late effects of dexmedetomidine on systemic vascular resistance may be qualitatively useful, the arterial forces that oppose left ventricular (LV) ejection cannot be precisely described using systemic vascular resistance, because this index has been shown to inadequately quantify LV afterload *in vivo*.⁸ Specifically, systemic vascular resistance ignores the frequency dependence of arterial pressure and blood flow, the viscoelastic properties of the blood and arterial vasculature, and the potential effects of arterial wave reflection. In contrast, aortic input impedance [$Z_{in}(\omega)$] incorporates these important features of the arterial system and provides a comprehensive description of LV afterload in the presence of volatile^{9,10} and intravenous^{11,12} anesthetics and cardiovascular disease.^{10,12,13} The current investigation examined the effects of dexmedetomidine on the determinants of LV afterload evaluated with $Z_{in}(\omega)$ and quantified with a three-element Windkessel model of the

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arterial circulation in a model of dogs fitted with instruments for long-term monitoring of dilated cardiomyopathy produced by 19 ± 3 (mean \pm SEM) days of chronic, rapid LV pacing. These results were directly compared with those obtained in identical experiments conducted in the same dogs before pacing was initiated.

Materials and 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) no. 85-23, revised 1996).

Surgical Instrumentation

The surgical implantation of instruments has been described in detail.^{9,10,14} 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 subendocardial segment length (ultrasonic crystals). Platinum pacing electrodes were sutured to the epicardial surface of the LV free wall. All instruments were tunneled between the scapulas and firmly secured *via* several small incisions. The pericardium was left open, the chest wall closed in layers, and the pneumothorax evacuated by a chest tube. All dogs received $5 \mu\text{g}/\text{kg}$ intravenous fentanyl for analgesia as needed after surgery and were allowed to recover a minimum of 7 days before the experiments began. 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 negative 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 contin-

uously on a polygraph and simultaneously digitized and recorded on a computer.

Experimental Protocol

Dogs ($n = 8$; weight range, 24 to 31 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. Left ventricular afterload was quantified with $Z_{in}(\omega)$ spectra and interpreted using a three-element Windkessel model of the arterial circulation, as previously described.^{9,10,12} Briefly, digitized, steady state aortic blood pressure and blood flow waveforms were transformed from the time to the frequency (ω) domain using a 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.⁹ Characteristic aortic impedance (Z_c) was determined as the magnitude of $Z_{in}(\omega)$ between 2 and 15 Hz. Total arterial resistance was calculated as the difference between $Z_{in}(\omega)$ at zero Hz and Z_c . Total arterial compliance was determined directly from steady state aortic pressure and blood flow waveforms using a previously validated formula.¹⁵ To calculate compliance, end-systole was defined as occurring at the dicrotic notch of the aortic pressure waveform. Dogs received 1.25, 2.5, and $5 \mu\text{g}/\text{kg}$ intravenous dexmedetomidine over 10 min in a sequential manner (total cumulative doses = 1.25, 3.75, and $8.75 \mu\text{g}/\text{kg}$, respectively). Systemic hemodynamics and LV pressure, aortic pressure, and aortic blood flow waveforms were recorded 5 min (early) and 60 min (late) after administration of each dose of dexmedetomidine.

After the completion of the experiments, the LV of the each dog was paced continuously at rates between 220 and 240 beats/min, as previously characterized.^{10,14} Dogs were brought to the laboratory on each day after pacing was initiated to monitor the development of pacing-induced cardiomyopathy. Pacing was discontinued during and restarted immediately after this brief period of daily hemodynamic monitoring. Dogs were paced for 19 ± 3 (mean \pm SEM) days to develop LV dysfunction. Dogs were fasted overnight before experimentation, and fluid deficits were replaced as described before. Left ventricular pacing was discontinued for the duration of the experiment. Systemic hemodynamics and LV pressure, aortic blood pressure, and aortic blood flow waveforms were recorded in sinus rhythm before and 5 and 60 min after

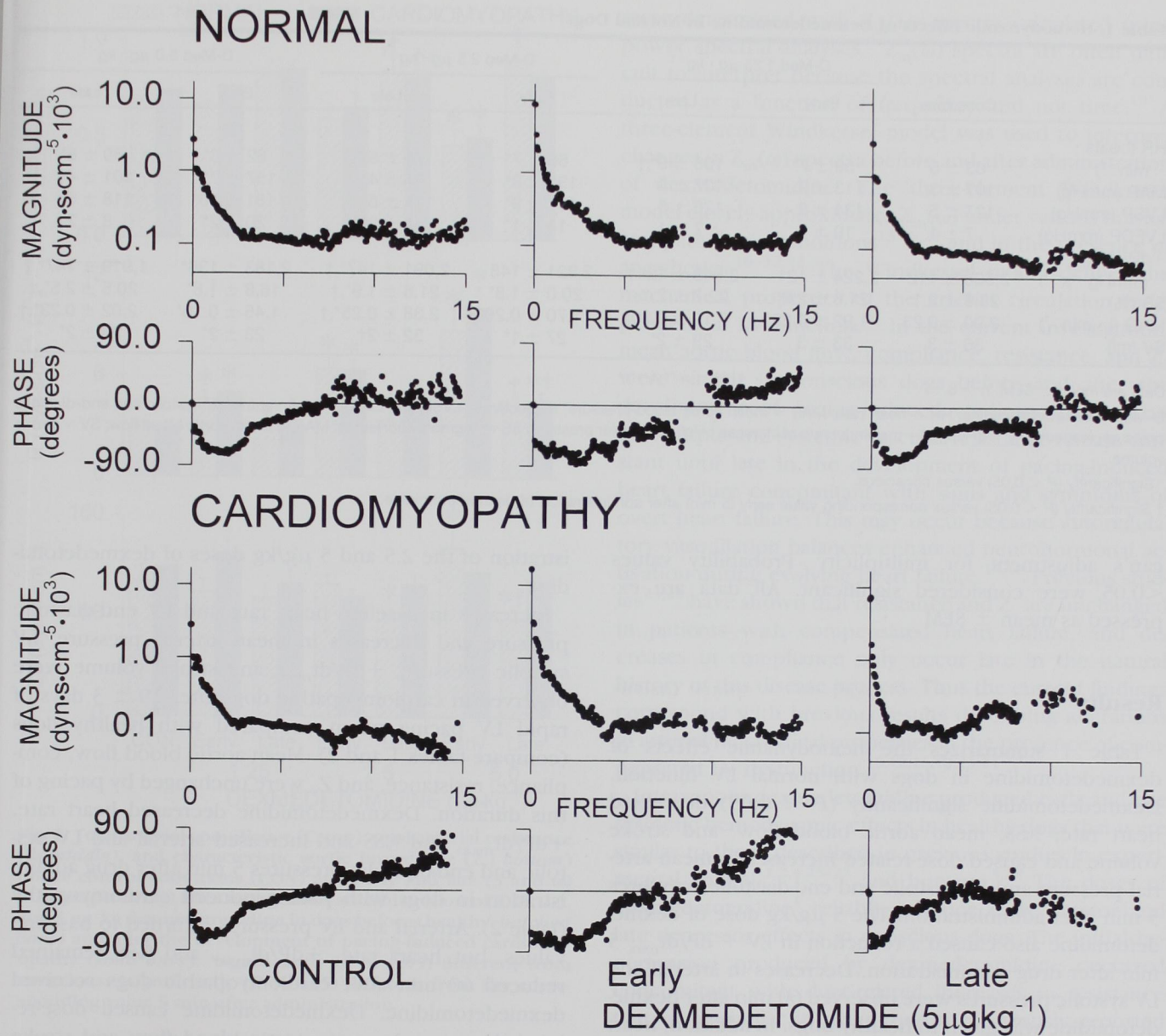


Fig. 1. Typical aortic input impedance magnitude and phase spectra obtained in conscious dogs before (top) and after (bottom) the development of pacing-induced cardiomyopathy. Spectra were obtained before and 5 min (early) and 60 min (late) after intravenous administration of dexmedetomidine (5 $\mu\text{g/kg}$).

administration of 1.25, 2.5, and 5 $\mu\text{g/kg}$ dexmedetomidine, as described before. Figure 1 shows typical $Z_{in}(\omega)$ spectra obtained in healthy and cardiomyopathic dogs before and after administration of dexmedetomidine. In all 16 experiments were performed that compared the effects of dexmedetomidine on hemodynamics and LV afterload before and after the development of rapid LV pacing-induced cardiomyop-

athy in the same eight dogs fitted with instruments for long-term monitoring.

Statistical Analysis

Statistical analysis of the data within and between groups before and after administration of dexmedetomidine was performed by analysis of variance with repeated measures, followed by Student's *t* tests with Dun-

Table 1. Hemodynamic Effects of Dexmedetomidine in Normal Dogs

	Conscious	D-Med 1.25 $\mu\text{g} \cdot \text{kg}^{-1}$		D-Med 2.5 $\mu\text{g} \cdot \text{kg}^{-1}$		D-Med 5.0 $\mu\text{g} \cdot \text{kg}^{-1}$	
		Early	Late	Early	Late	Early	Late
HR (beats \cdot min $^{-1}$)	83 \pm 6	59 \pm 7*	106 \pm 9*,†	60 \pm 7*	74 \pm 5†	62 \pm 6*	69 \pm 8*
MAP (mmHg)	107 \pm 3	113 \pm 7	107 \pm 4	137 \pm 8*	97 \pm 4*,†	157 \pm 7*	101 \pm 4†
LVSP (mmHg)	127 \pm 5	134 \pm 8	126 \pm 5	157 \pm 9*	114 \pm 6*,†	181 \pm 10*	118 \pm 6†
LVEDP (mmHg)	7 \pm 1	10 \pm 1	7 \pm 1	14 \pm 1*	7 \pm 2†	20 \pm 2*	8 \pm 2†
+dP/dt $_{\text{max}}$ (mmHg \cdot s $^{-1}$)	2,508 \pm 112	2,224 \pm 121	2,549 \pm 124†	2,321 \pm 148	2,091 \pm 147*,†	2,183 \pm 136*	1,919 \pm 147*,†
SS (%)	23.6 \pm 2.1	21.6 \pm 2.0*	22.7 \pm 2.1	20.0 \pm 1.8*	21.6 \pm 1.9*,†	16.8 \pm 1.6*	20.5 \pm 2.5*,†
MAQ (l \cdot min $^{-1}$)	2.90 \pm 0.23	1.92 \pm 0.23*	3.10 \pm 0.30†	1.70 \pm 0.20*	2.38 \pm 0.25*,†	1.45 \pm 0.16*	2.02 \pm 0.23*,†
SV (ml)	36 \pm 3	33 \pm 3	29 \pm 2*	27 \pm 1*	32 \pm 2†	23 \pm 2*	28 \pm 2*

Data are mean \pm SEM; n = 8.

D-Med = dexmedetomidine; HR = heart rate; MAP = mean aortic blood pressure, respectively; LVSP and LVEDP = left ventricular systolic and end-diastolic pressure, respectively; +dP/dt $_{\text{max}}$ = maximum rate of increase of left ventricular pressure; SS = segment shortening; MAQ = mean aortic blood flow; SV = stroke volume.

* Significantly ($P < 0.05$) versus conscious.

† Significantly ($P < 0.05$) versus corresponding value early (5 min) after administration of dexmedetomidine.

can's adjustment for multiplicity. Probability values < 0.05 were considered significant. All data are expressed as mean \pm SEM.

Results

Table 1 summarizes the hemodynamic effects of dexmedetomidine in dogs with normal LV function. Dexmedetomidine significantly ($P < 0.05$) decreased heart rate, %SS, mean aortic blood flow, and stroke volume and caused dose-related increases in mean arterial pressure and LV systolic and end-diastolic pressures 5 min after administration. The 5 $\mu\text{g}/\text{kg}$ dose of dexmedetomidine also caused a reduction in LV + dP/dt $_{\text{max}}$ 5 min after drug administration. Decreases in arterial and LV systolic pressures were observed 60 min after dexmedetomidine was given to healthy dogs. In addition, heart rate, +dP/dt $_{\text{max}}$, %SS, mean aortic blood flow, and stroke volume remained decreased compared with control 60 min after dexmedetomidine was administered. Dexmedetomidine caused dose-related increases in resistance (3,027 \pm 283 during control to 8,853 \pm 1,413 dyn \cdot s \cdot cm $^{-5}$ after 5 $\mu\text{g}/\text{kg}$; fig. 2). Decreases in compliance (0.70 \pm 0.08 during control to 0.47 \pm 0.08 ml/mmHg) and increases in Z_c (108 \pm 13 during control to 135 \pm 18 dyn \cdot s \cdot cm $^{-5}$) were also observed with the high dose of dexmedetomidine 5 min after administration. Resistance and compliance returned to control values 60 min after administration of dexmedetomidine in dogs before rapid LV pacing. Decreases in Z_c occurred 60 min after admin-

istration of the 2.5 and 5 $\mu\text{g}/\text{kg}$ doses of dexmedetomidine.

Increases in baseline heart rate and LV end-diastolic pressure and decreases in mean arterial pressure, LV systolic pressure, +dP/dt $_{\text{max}}$, and stroke volume were observed in cardiomyopathic dogs after 19 \pm 3 days of rapid LV pacing when compared with healthy dogs (compare tables 1 and 2). Mean aortic blood flow, compliance, resistance, and Z_c were unchanged by pacing of this duration. Dexmedetomidine decreased heart rate, +dP/dt $_{\text{max}}$, and %SS and increased arterial and LV systolic and end-diastolic pressures 5 min after drug administration in dogs with pacing-induced cardiomyopathy (table 2). Arterial and LV pressures returned to baseline values, but heart rate, +dP/dt $_{\text{max}}$, and %SS remained reduced 60 min after cardiomyopathic dogs received dexmedetomidine. Dexmedetomidine caused dose-related decreases in mean aortic blood flow and stroke volume in cardiomyopathic dogs. Mean aortic blood flow and stroke volume remained decreased 60 min after administration of the 2.5 and 5 $\mu\text{g}/\text{kg}$ doses of dexmedetomidine. Dose-related increases in resistance (3,000 \pm 316 during control to 10,220 \pm 1,295 dyn \cdot s \cdot cm $^{-5}$ after 5 $\mu\text{g}/\text{kg}$; fig. 2) occurred 5 min after cardiomyopathic dogs received dexmedetomidine. In contrast to the findings before rapid LV pacing was initiated, resistance remained elevated 60 min after administration of 5 $\mu\text{g}/\text{kg}$ dexmedetomidine in dogs after pacing. A reduction in compliance (0.75 \pm 0.06 during control to 0.51 \pm 0.07 ml/mmHg) was also observed 5 min after

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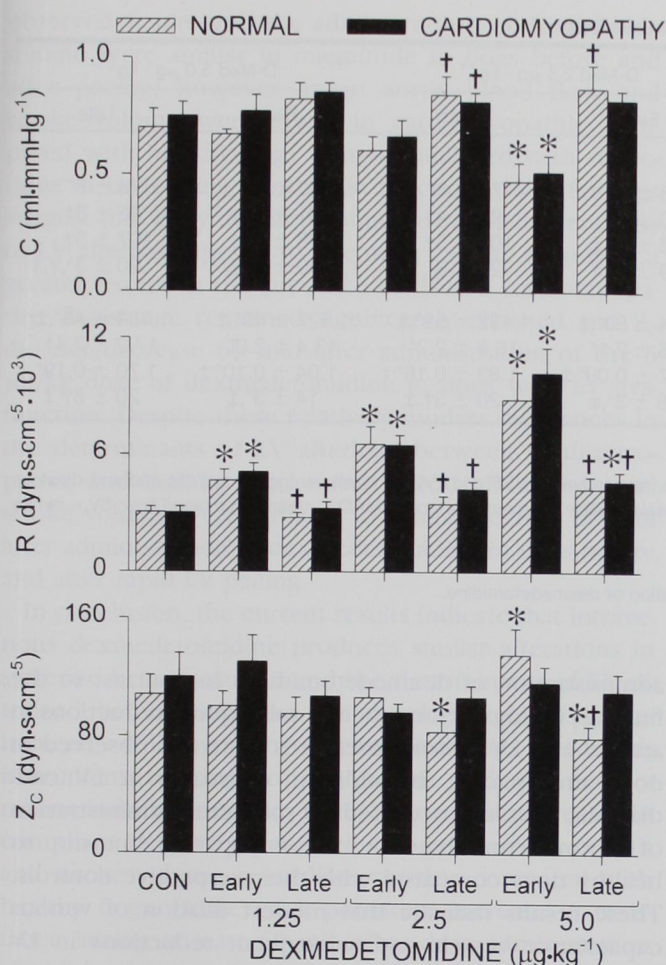


Fig. 2. Total arterial compliance (C; top), total arterial resistance (R; middle), and characteristic aortic impedance (Z_c ; bottom) under control conditions (CON) and early and late (5 and 60 min, respectively) after intravenous administration of 1.25, 2.5, and 5 $\mu\text{g}/\text{kg}$ dexmedetomidine in dogs before (healthy; hatched bars) and after the development of pacing-induced cardiomyopathy (solid bars). *Significantly ($P < 0.05$) different from conscious; †significantly ($P < 0.05$) different from the corresponding value 5 min after administration.

the high dose of dexmedetomidine. In cardiomyopathic dogs, Z_c was unchanged by dexmedetomidine.

Discussion

We examined the actions of intravenous dexmedetomidine on hemodynamics and LV afterload in an extensively validated model of compensated, dilated cardiomyopathy^{10,12,14,16-18} and compared these findings with those obtained in the same dogs fitted with long-term monitoring instruments before rapid LV pacing was initiated. The effects of dexmedetomidine on LV afterload

were determined with $Z_{in}(\omega)$ spectra calculated using power spectral analyses.⁹ $Z_{in}(\omega)$ spectra are often difficult to interpret because the spectral analyses are conducted as a function of frequency and not time.¹⁹ A three-element Windkessel model was used to interpret changes in $Z_{in}(\omega)$ spectra before and after administration of dexmedetomidine. The three-element Windkessel model closely approximates $Z_{in}(\omega)$ under various normal and pathologic conditions^{13,20,21} and in the presence of anesthetics.^{10-12,22} The Windkessel model defines the mechanical properties of the arterial circulation independent of LV function.²⁰ In the current investigation, mean aortic blood flow, compliance, resistance, and Z_c were similar in conscious dogs before and after the development of pacing-induced cardiomyopathy. Cardiac output and systemic vascular resistance remain constant until late in the development of pacing-induced heart failure concomitant with signs and symptoms of overt heart failure. This may occur because autoregulatory vasodilation balances enhanced neurohormonal activation during evolving heart failure.^{16,18} Previous studies^{23,24} have shown that resistance and Z_c are unchanged in patients with compensated heart failure, and decreases in compliance only occur late in the natural history of this disease process. Thus the current findings correspond with previous results describing alterations in arterial mechanical properties in the presence of compensated LV dysfunction.^{10,12,16,18,23,24}

Intravenous dexmedetomidine produced early and late systemic hemodynamic effects in healthy dogs that were similar to those described in previous studies in experimental animals^{1,2,4,25-27} and humans.^{3,28} The doses of dexmedetomidine¹ reliably produce early pressor and late depressor effects in conscious dogs. The initial hypertension produced by dexmedetomidine occurred concomitant with dose-related increases in resistance that were similar in magnitude to previously reported increases in systemic vascular resistance in dogs fitted with instruments for long-term monitoring,¹ confirming that dexmedetomidine produces immediate arteriolar vasoconstriction. The increases in resistance were accompanied by an increase in Z_c and a reduction in compliance 5 min after administration of the 5 $\mu\text{g}/\text{kg}$ dose of dexmedetomidine. Characteristic aortic impedance makes a relatively small contribution to resistance, consistent with the concept that the aorta is a high-compliance, low-resistance component of the arterial circulation.¹⁹ However, the early dexmedetomidine-induced increase in Z_c suggests that increased aortic hydraulic resistance may contribute to early reductions in mean aortic blood

Table 2. Hemodynamic Effects of Dexmedetomidine in Cardiomyopathic Dogs

	Conscious	D-Med 1.25 $\mu\text{g} \cdot \text{kg}^{-1}$		D-Med 2.5 $\mu\text{g} \cdot \text{kg}^{-1}$		D-Med 5.0 $\mu\text{g} \cdot \text{kg}^{-1}$	
		Early	Late	Early	Late	Early	Late
HR (beats \cdot min $^{-1}$)	98 \pm 2‡	80 \pm 5‡	97 \pm 6†	78 \pm 7*	79 \pm 6*	70 \pm 5*	74 \pm 6*
MAP (mmHg)	91 \pm 3‡	102 \pm 3*	95 \pm 3†,‡	120 \pm 4*	94 \pm 4†	131 \pm 5*,‡	95 \pm 3†
LVSP (mmHg)	105 \pm 2‡	113 \pm 2*,‡	108 \pm 3†,‡	126 \pm 3*,‡	106 \pm 3†	136 \pm 4*,‡	107 \pm 3†
LVEDP (mmHg)	23 \pm 2‡	25 \pm 2‡	20 \pm 3†,‡	29 \pm 3*,‡	20 \pm 3*,†,‡	30 \pm 3*,‡	20 \pm 3*,†,‡
+dP/dt _{max} (mmHg \cdot s $^{-1}$)	1,725 \pm 54‡	1,472 \pm 52*,‡	1,633 \pm 50†,‡	1,524 \pm 50*,‡	1,452 \pm 59*,‡	1,527 \pm 40*,‡	1,480 \pm 45*,‡
SS (%)	19.1 \pm 2.5	17.7 \pm 2.2	18.0 \pm 2.5	14.6 \pm 2.1*	16.9 \pm 2.2*	13.4 \pm 2.0*	17.2 \pm 2.4†
MAQ (l \cdot min $^{-1}$)	2.49 \pm 0.21	1.56 \pm 0.13*	2.41 \pm 0.20†	1.37 \pm 0.09*,‡	1.83 \pm 0.16*,†	1.04 \pm 0.10*,‡	1.70 \pm 0.19*,†
SV (ml)	22 \pm 4†	18 \pm 3*,‡	22 \pm 4†	16 \pm 3*,‡	20 \pm 3†,‡	14 \pm 3*,‡	20 \pm 3†,‡

Data are mean \pm SEM; n = 8.

D-Med = dexmedetomidine; HR = heart rate; MAP = mean aortic blood pressure, respectively; LVSP and LVEDP = left ventricular systolic and end-diastolic pressure, respectively; +dP/dt_{max} = maximum rate of increase of left ventricular pressure; SS = segment shortening; MAQ = mean aortic blood flow; SV = stroke volume.

* Significantly ($P < 0.05$) versus conscious.

† Significantly ($P < 0.05$) versus corresponding value early (5 min) after administration of dexmedetomidine.

‡ Significantly ($P < 0.05$) versus corresponding value in normal dogs (table 1).

flow and stroke volume in healthy dogs. In addition, the decrease in compliance observed early after administration of the high dose of dexmedetomidine further suggests that the α_2 -adrenoceptor agonist attenuates the beneficial rectifying characteristics of the aorta. Total arterial compliance is determined primarily by the mechanical properties of the proximal aorta.²⁹ However, compliance is also inversely related to mean aortic pressure,^{19,30} and pronounced increases in aortic pressure resulting from arteriolar vasoconstriction may be partially responsible for the decrease in compliance produced by the 5 $\mu\text{g}/\text{kg}$ dose of dexmedetomidine in dogs before rapid LV pacing. Nevertheless, this decrease in compliance indicates that the aorta does not store and redistribute LV ejection energy as efficiently during systole and diastole, respectively. Resistance and compliance returned to control values and Z_c declined modestly 60 min after administration of dexmedetomidine to healthy dogs. Thus it is likely that persistent reductions in mean aortic blood flow and stroke volume observed 60 min after administration of dexmedetomidine occurred as a result of decreases in heart rate and LV systolic function (e.g., +dP/dt_{max} and %SS) and not because of adverse increases in LV afterload.

The effects of intravenous dexmedetomidine on hemodynamics and LV afterload in cardiomyopathic dogs were similar but not identical to those observed before rapid LV pacing was initiated. Decreases in heart rate, +dP/dt_{max}, and %SS and increases in arterial and LV systolic and end-diastolic pressures occurred early after

administration of dexmedetomidine. In contrast to the findings in dogs before pacing, subsequent reductions in arterial and LV systolic pressures were not observed in dogs after pacing. In addition, decreases in LV end-diastolic pressure occurred 60 min after administration of dexmedetomidine to cardiomyopathic but not to healthy dogs compared with their respective controls. These results indicate that modest dilation of venous capacitance vessels and subsequent reductions in LV preload are important late effects of dexmedetomidine in dogs with dilated cardiomyopathy. Reductions in heart rate and +dP/dt_{max} were also observed 60 min after intravenous administration of dexmedetomidine in dogs after chronic rapid LV pacing. These findings suggest that the α_2 -adrenoceptor agonist exerts effects on autonomic nervous system activity in dogs with compensated LV dysfunction that are similar to those observed in healthy dogs.^{1,2} The relative increases in sympathetic and decreases in parasympathetic nervous system tone that are known to occur in developing heart failure^{16,18} to maintain adequate cardiac output are antagonized by dexmedetomidine. Dose-related increases in resistance were observed 5 min after administration of dexmedetomidine, suggesting that vasoconstriction produced by direct activation of peripheral α_2 -adrenoceptors in arteriolar vascular smooth muscle is preserved. A decrease in compliance also occurred 5 min after administration of the 5 $\mu\text{g}/\text{kg}$ dose of dexmedetomidine, indicating that aortic distensibility is adversely affected as well. The increases in resistance and the decrease in compliance

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observed 5 min after the administration of dexmedetomidine were similar in magnitude in dogs before and after pacing; however, mean aortic blood flow and stroke volume were lower in cardiomyopathic compared with healthy dogs. When combined with reductions in underlying contractile function, these findings suggest that early dexmedetomidine-induced alterations in LV afterload appear to attenuate cardiac output to a greater extent in the presence of dilated cardiomyopathy. Resistance remained significantly elevated and Z_c did not decrease 60 min after administration of the 5 $\mu\text{g}/\text{kg}$ dose of dexmedetomidine in dogs with LV dysfunction. Despite these relatively modest differences in the determinants of LV afterload between cardiomyopathic and healthy dogs, mean aortic blood flow and stroke volume were reduced to similar degrees 60 min after administration of dexmedetomidine in dogs before and after rapid LV pacing.

In conclusion, the current results indicate that intravenous dexmedetomidine produces similar alterations in systemic hemodynamics and the determinants of LV afterload before and after the development of pacing-induced cardiomyopathy in conscious dogs fitted with instruments for long-term monitoring. Early dexmedetomidine-induced increases in resistance and decreases in compliance caused greater reductions in cardiac output and stroke volume in cardiomyopathic compared with healthy dogs. However, a persistent increase in resistance lasting at least 60 min after drug administration also did not appear to contribute to sustained decreases in cardiac performance in the presence of LV dysfunction.

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