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Comparative Effects of Esmolol and Verapamil in a Model of a Supraventricular Tachydysrhythmia

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Supraventricular tachydysrhythmias are a commonly encountered clinical problem after cardiothoracic surgery. Current choices for acute drug therapy of these dysrhythmias include intravenous verapamil as well as esmolol, but no data yet exist comparing the relative negative dromotropic (atrioventricular [A-V] nodal blocking) and negative inotropic effects of these agents. The purpose of this study was to compare the effects of esmolol with those of verapamil on systemic hemodynamics, coronary blood flow, and cardiac contractility at doses that produce a similar ventricular response rate in an animal model of a supraventricular tachydysrhythmia. Rapid electrical stimulation (800 impulses/min) of the left atrium in 14 dogs resulted in a rapid and irregularly irregular ventricular rhythm. Esmolol or verapamil were administered by bolus and then infusion to incrementally slow the average ventricular rate. Regional myocardial contractility was measured using the end-systolic pressure-length relationship (Ees). At drug doses that produced similar decreases in ventricular rate, esmolol produced a greater decrease in contractility (Ees: 284 ± 46 to 40 ± 22 mmHg/mm, LV dp/dt:2,400 ± 450 to 1,360 ± 450 mmHg/sec) compared with that following verapamil (Ees: 297 ± 57 to 116 ± 25 mmHg/mm, LV dp/dt: 2,040 ± 580 to 1,950 ± 520 mmHg/sec). This was accompanied by a modest decrease in cardiac output in the esmolol group (2,880 ± 940 to 2,290 ± 730 ml/min) compared with an unchanged cardiac output as ventricular rate slowed in verapamil-treated animals. Stroke volume increased significantly in the verapamil-treated animals (10.9 ± 4.0 to 18.5 ± 4.6 ml), but remained unchanged following esmolol. Neither drug produced adverse effects on perfusion pressure nor left anterior descending coronary blood flow in the doses employed in this model. The differential effects of esmolol and verapamil on contractility may have important implications when used to control the ventricular response to supraventricular tachydysrhythmias in the presence of impaired ventricular function. (Key words: Heart: ventricular function, dysrhythmias. Pharmacology, calcium-entry blocking drug: verapamil. Sympathetic nervous system, antagonists: esmolol.)

SUPRAVENTRICULAR TACHYDYSRHYTHMIAS such as atrial fibrillation and atrial flutter commonly occur after otherwise uncomplicated cardiothoracic surgery.[1–4] In the absence of an accessory pathway, atrioventricular conduction is the primary determinant of the ventricular response (rate) for rhythms such as atrial fibrillation or flutter. Patients with otherwise normal myocardial function may tolerate the loss of atrial contribution to diastolic filling as well as the decrease in coronary blood flow and increase in myocardial work associated with rapid ventricular rates. However, in many patients with advanced cardiac disease, the development of rapid ventricular rates may be associated with myocardial ischemia, decreased cardiac output, and/or pulmonary congestion, and therapy to modulate the ventricular response to supraventricular tachydysrhythmias may be warranted.

Acute drug therapy currently employed in the postoperative management of these dysrhythmias includes β-adrenergic blocking agents such as esmolol and the calcium-entry blocking drug verapamil. Both of these agents prolong atrioventricular conduction (negative dromotropy), slow the ventricular response in many types of supraventricular tachydysrhythmias, and have been recommended for their treatment.[5–11]

The effects of these two drug classes are, however, mediated by different mechanisms. Beta-adrenergic blocking agents slow the spontaneous rate of pacemaker cells and antagonize the effect of adrenergic stimulation on the atrioventricular node and, to a lesser extent, on the ventricular muscle and His–Purkinje system.[12] Calcium-entry blocking drugs inhibit calcium movement in tissues, including the atrioventricular nodal area,[12] that are slow-current–dependent. They also can inhibit calcium movement in vascular smooth muscle and increase both coronary and systemic blood flow.

In addition to the negative dromotropic and chronotropic effects of β-adrenergic and calcium-entry blocking agents, these drugs also produce a negative inotropic effect. When either of these agents is used to control ventricular rate in patients with poor ventricular function, the associated decreases in the contractile state of the heart may be detrimental. No studies to date have compared the dromotropic efficacy of esmolol *versus* verapamil with their negative inotropic properties. Accordingly, the purpose of this study was to compare the effects of esmolol with those of verapamil on systemic hemodynamics, coronary blood flow, and regional as well as global cardiac contractility at doses that produce a similar ventricular response rate in an animal model of a supraventricular tachydysrhythmia.

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Materials and Methods

Instrumentation

The protocol was approved by the Institutional Animal Care and Use Committee. Fourteen overnight-fasted, heartworm-free, mongrel dogs of either sex with an average weight of 21.4 ± 4.5 kg (SD) were anesthetized with sodium pentobarbital (25 mg/kg intravenously [iv]). After tracheal intubation, the animals were positioned supine and the lungs mechanically ventilated (Harvard Apparatus, South Natick, MA) at a rate of 10/min, a tidal volume of 20 ml/kg and an fractional inspired O_2 concentration (FI_{O_2}) = 1.0. Rectal temperatures were continuously monitored; warmed iv fluids administered *via* the right external jugular vein and a thermal blanket were used to maintain the animal's temperature between 37 and 38.5° C. A catheter was inserted into the left common carotid artery and advanced into the ascending aorta 1 cm above the aortic valve. Neuromuscular blockade was established and maintained with incremental doses of pancuronium, and ventilation was adjusted to achieve blood gases of Pa_{O_2} greater than 400 mmHg, Pa_{CO_2} = 35 ± 3 mmHg, and a *p*H = 7.37 ± 0.05 (*p*H blood gas analyzer, Model 1301, Instrumentation Laboratory, Lexington, MA).

A supplemental dose of sodium pentobarbital (15 mg/kg iv) was administered 30 min after the induction dose, just before performing bilateral thoracotomies at the fourth intercostal space. Anesthesia was maintained with a continuous infusion of pentobarbital 1 $mg \cdot kg^{-1} \cdot h^{-1}$ begun after the supplemental bolus. The sternum was then split after ligation of the mammary arteries. Umbilical tapes were placed around the inferior vena cava and the midthoracic aorta to act as snares for nonpharmacologic manipulation of preload and afterload. The pericardial sac was opened and the heart suspended in a pericardial cradle. A catheter was inserted into the right atrium and a 10-cm, 1.07-mm (ID) rigid polyethylene catheter was placed through the ventricular apex for a distance of 1.5 cm into the left ventricular cavity. The aortic root was dissected free; an appropriately sized electromagnetic flow probe (Gould SP7515; 16 or 18 mm) was placed and aortic flow was measured using a flowmeter (Model 2201, Gould Instruments, Oxnard, CA). The left anterior descending coronary artery (LAD) just distal to its first diagonal branch was dissected off the epicardium and encircled with an electromagnetic flow probe (Gould SP7517; 2–2.5 mm) placed around the vessel and then connected to a flowmeter (Model 2201, Gould Instruments). Two 5-mm piezoelectric crystals (Triton Technologies, San Diego, CA) were placed approximately 10 mm apart and 10 mm from the LAD in the minor axis of the left ventricular epicardial surface. The minor axis was defined as a plane midway along and perpendicular to a line from the left ventricular apex to the aortic root. Subendocardial fiber length was measured from the crystals using a sonomicrometer (Model 120, Triton Technologies). Needle electrodes were placed for ECG recording of leads II and AVF, and pacing electrodes were attached to the left atrial appendage and connected to a pulse generator (Model 5320, Medtronic Inc., Minneapolis, MN).

Right atrial, left ventricular, and aortic pressures were measured using pressure transducers zeroed at the level of the left atrium (Model P25XL, Spectramed Inc., Oxnard, CA). Recordings were made on an eight-channel polygraph (Model 3800, Gould Instruments) and simultaneously collected by analog-to-digital conversion (Model 2801A, Data Translation, Marlboro, MA) at a rate of 100 Hz on a microcomputer (Advanced Logic Research, Irvine, CA).

Protocol

The animals received an intravenous infusion of 6% hetastarch in 0.9% sodium chloride sufficient to raise right atrial pressure to 5 mmHg, and maintained with an infusion of 0.9% sodium chloride. A supraventricular tachydysrhythmia was induced by pacing the left atrial appendage at a rate of 800 pulses per minute, using a pulse width of 2 ± 0.4 msec at a current of 2–4 mA. Ten minutes after initiating the supraventricular dysrhythmia, baseline hemodynamic parameters were recorded. In addition, left ventricular pressure-segment length loops were generated from data collected during 5–7-s occlusions of the thoracic aorta and the inferior vena cava, consecutively.

The animals then were randomized to receive either esmolol (E) or verapamil (V) in doses that had been shown in pilot experiments to produce similar decrements in ventricular rate using the above protocol. The E group (n = 7) received a bolus of 500 μg/kg of E followed by 50 $\mu g \cdot kg^{-1} \cdot min^{-1}$ for 10 minutes (E-I), then another 500 μg/kg, followed by 100 $\mu g \cdot kg^{-1} \cdot min^{-1}$ for 10 minutes (E-II), then another 500 μg/kg followed by 200 $\mu g \cdot kg^{-1} \cdot min^{-1}$ for 10 minutes (E-III). The V group received a bolus of 60 μg/kg followed by 1 $\mu g \cdot kg^{-1} \cdot min^{-1}$ for 10 minutes (V-I), then another 60 μg/kg followed by 2 $\mu g \cdot kg^{-1} \cdot min^{-1}$ for 10 minutes (V-II), then another 60 μg/kg followed by 4 $\mu g \cdot kg^{-1} \cdot min^{-1}$ (V-III). Ten minutes after each bolus, hemodynamic measurements were recorded and left ventricular pressure-segment length loops generated from these data as described above.

Determination of Regional Myocardial Contractility

Overlay plots of digitized data from left ventricular pressure-segment length loops were generated for at least

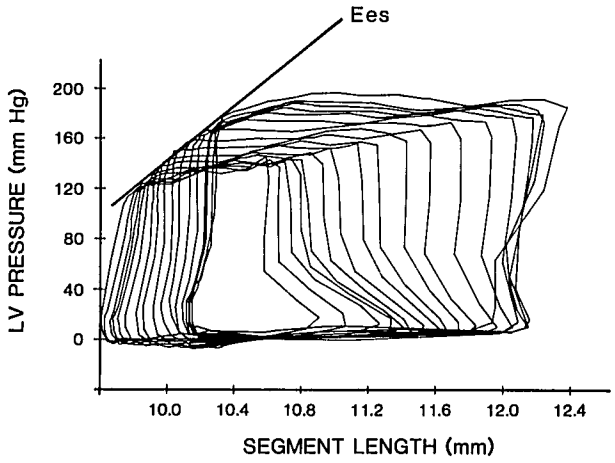

FIG. 1. Series of end-systolic pressure-length (ESPL) loops generated by preload reduction and afterload increases. The linearity and load independence of the ESPL relationship, designated E_{es} is demonstrated.

15–20 cardiac cycles for each of the following: no occlusion, thoracic aortic occlusion, and inferior vena caval occlusion. A best-fit line was generated by applying least-squares linear regression to the end-systolic pressure, end-systolic length data. The slope of this line was used as the load-independent index of regional myocardial contractility, the end-systolic pressure/length ratio, which is designated as Ees (fig. 1). This procedure was repeated in duplicate, and the mean of the values is reported.

Data Analysis

Measurements of mean ventricular rate, mean arterial pressure, right atrial pressure, aortic blood flow, LAD blood flow, and left ventricular systolic and end-diastolic pressures were made during at least ten cardiac cycles at baseline and after each of the drug infusions just before preload and afterload manipulations. Determination of left coronary perfusion pressure (diastolic aortic pressure—left ventricular end diastolic pressure), left ventricular stroke volume (aortic blood flow/ventricular rate), and systemic vascular resistance (79.9 • [mean arterial blood pressure − right atrial pressure]/mean aortic blood flow) also were performed at the above times. The first and second derivatives of the left ventricular pressure (LV dP/dt and V_{max}, respectively) were electronically differentiated.

For each hemodynamic variable, data were analyzed using a two-way analysis of variance (ANOVA) for repeated-measures design (treatment × dose). To account for effects of heart rate on the determination of Ees, LV dP/dt and V_{max}, data for these variables were analyzed using a two-way analysis of covariance for repeated-measures design, with heart rate as the covariable. Post-hoc testing was done when appropriate using the Tukey-a method. The null hypothesis was rejected if P was less than 0.05.

Results

Atrial pacing resulted in an irregularly irregular tachydysrhythmia with beat-to-beat variability in stroke volume and decreased aortic blood flow, as depicted in figure 2. Hemodynamic variables, Ees, LV dP/dt, and V_{max} did not differ between groups before drug administration or pacing (table 1). Administration of drug resulted in conversion to a regular ventricular rate response in 4 of 7 animals in each group.

Ventricular rate decreased with increasing levels of drug infusion in both groups. Progressively increasing doses of E and V were both associated with progressive declines in Ees as compared with baseline (fig. 3). E pro-

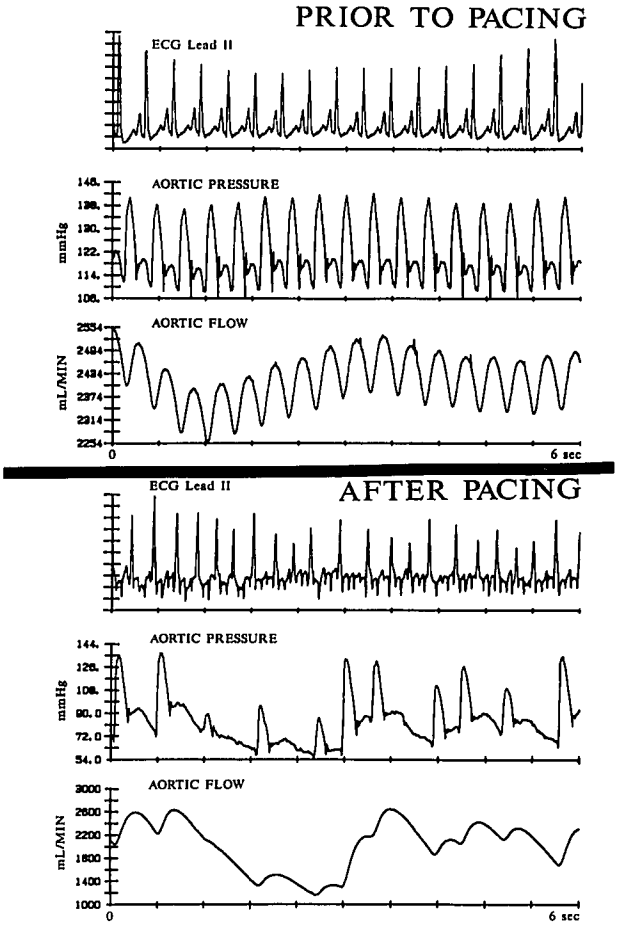

FIG. 2. Typical electrocardiographic and hemodynamic changes produced by rapid atrial pacing. (*Upper panel*) Before pacing, normal sinus rhythm with no significant beat-to-beat variability in stroke volume noted in mean aortic pressure waveform. (*Lower panel*) After pacing, ventricular response is irregularly irregular with large beat-to-beat variability in stroke volume and a decline in mean aortic flow.

TABLE 1. Hemodynamic Effects of Esmolol *Versus* Verapamil for Control of Ventricular Rate

	Esmolol (Rhythm)				
	Sinus	Paced	Paced	Paced	Paced
Drug Infusion ($mcg \cdot kg^{-1} \cdot min^{-1}$)	0	0	50	100	200
HR (bpm)	176 ± 19	227 ± 27	197 ± 31	182 ± 33	169 ± 28
CO ($ml \cdot min^{-1}$)	2,990 ± 830	2,880 ± 940	2,230 ± 920*	2,040 ± 840*	2,290 ± 730*
SV (ml)	17.3 ± 5.9	12.7 ± 4.1	11.6 ± 4.7	11.6 ± 4.5	13.8 ± 4.4†
LVEDP (mmHg)	3.1 ± 2.7	4.3 ± 3.1	5.5 ± 3.8	4.4 ± 2.8	4.5 ± 3.2
LVESP (mmHg)	125.6 ± 17.5	106.4 ± 14.9	94.6 ± 13.2	101.4 ± 11.8	102.1 ± 13.2
MAP (mmHg)	121.4 ± 21.5	83.5 ± 9.3	88.7 ± 13.2	93.7 ± 9.9	93.4 ± 15.9
SVR ($dyn \cdot s \cdot cm^{-5}$)	2,560 ± 720	1,840 ± 680	2,700 ± 1,260	3,310 ± 1,940*¶	2,630 ± 980
LVSW ($g \cdot m$)	47.3 ± 13.9	31.4 ± 12.5	26.3 ± 13.8	24.7 ± 10.3	27.7 ± 9.0
CPP (mmHg)	95.1 ± 3.9	73.7 ± 6.1	73.6 ± 13.2	79.9 ± 11.2	81.3 ± 13.3
CBF ($ml \cdot min^{-1}$)	32.0 ± 10.3	25.1 ± 13.6	21.1 ± 10.0	24.1 ± 9.8	24.1 ± 14.1
LV dP/dt ($mmHg \cdot s^{-1}$)	2,820 ± 700	2,400 ± 450	1,420 ± 540*§	1,320 ± 340*	1,360 ± 450*
V_{max} ($mmHg \cdot s^{-2}$)	793 ± 242	686 ± 186	358 ± 148*§	289 ± 56*¶	277 ± 88*†
	Verapamil (Rhythm)				
	Sinus	Paced	Paced	Paced	Paced
Drug Infusion ($mcg \cdot kg^{-1} \cdot min^{-1}$)	0	0	1	2	4
HR (bpm)	176 ± 27	235 ± 32	189 ± 27	171 ± 35	144 ± 36
CO ($ml \cdot min^{-1}$)	2,970 ± 980	2,520 ± 810	2,650 ± 840	2,610 ± 820	2,540 ± 410
SV (ml)	17.0 ± 5.0	10.9 ± 4.0	14.4 ± 4.9	16.1 ± 5.6*	18.5 ± 4.6*†
LVEDP (mmHg)	2.6 ± 1.6	3.8 ± 1.8	3.2 ± 2.8	4.1 ± 3.3	2.6 ± 1.9
LVESP (mmHg)	125.1 ± 15.0	109.6 ± 13.1	100.7 ± 14.8	105.0 ± 17.8	102.4 ± 13.1
MAP (mmHg)	109.1 ± 14.2	77.7 ± 14.8	83.0 ± 20.6	80.9 ± 22.5	81.1 ± 19.7
SVR ($dyn \cdot s \cdot cm^{-5}$)	2,320 ± 710	1,980 ± 840	1,900 ± 450	1,860 ± 500¶	1,890 ± 520
LVSW ($g \cdot m$)	42.9 ± 15.4	24.5 ± 6.8	29.8 ± 13.8	28.8 ± 13.6	27.4 ± 8.9
CPP (mmHg)	107.7 ± 16.7	65.8 ± 16.6	70.2 ± 23.0	68.6 ± 21.1	68.3 ± 21.0
CBF ($ml \cdot min^{-1}$)	33.1 ± 15.2	23.9 ± 9.4	22.1 ± 7.6	23.1 ± 6.9	24.1 ± 8.9
LVdP/dt ($mmHg \cdot s^{-1}$)	2,720 ± 640	2,040 ± 580	2,170 ± 620§	2,040 ± 650	1,950 ± 520
V_{max} ($mmHg \cdot s^{-2}$)	775 ± 218	686 ± 225	600 ± 140§	614 ± 159¶	586 ± 191†

HR = average ventricular rate over at least 10 beats; CO = cardiac output; SV = stroke volume; LVEDP = left ventricular end-diastolic pressure; LVESP = left ventricular end-systolic pressure; MAP = mean aortic pressure; SVR = systemic vascular resistance; LVSW = left ventricular stroke work; CPP = coronary perfusion pressure; CBF = coronary blood flow; LV dP/dt and V_{max} = 1st and 2nd derivatives of left ventricular pressure with respect to time.

Values are means ± SD.

* Significant difference within group from no drug during pacing; $P < 0.05$.

§,¶,† Significant differences between corresponding pairs (comparable levels of dromotropy); $P < 0.05$.

duced greater declines in Ees as compared with V at doses that produced comparable decreases in ventricular rate. Global markers of contractility (LV dP/dt and V_{max}) declined from baseline values at all levels of E infusion, whereas these parameters did not change from baseline in the animals receiving V (table 1).

Aortic blood flow was decreased compared with baseline at all levels of E infusion, but was unchanged from baseline at all levels of V infusion. The left ventricular stroke volume was increased at the second and third infusion levels compared with baseline in the V group, but unchanged from baseline in the E group.

Mean arterial blood pressure did not differ between groups of animals nor within any group at any time compared with baseline (after pacing). Calculated systemic vascular resistance increased in the E group, and was greater than the V group at the second drug infusion level. Left anterior descending coronary artery blood flow and coronary perfusion pressure did not change from baseline within each group, nor were there any between-group differences at any level of drug infusion.

Discussion

Because of its pharmacokinetic profile, the depression of ventricular function and occasional excessive bradycardia following a single intravenous bolus of verapamil may persist for 4–6 h.[13,14] As such, a drug like esmolol, which has as rapid an onset of action but a much shorter half-life, may be preferable because dissipation of its ef-

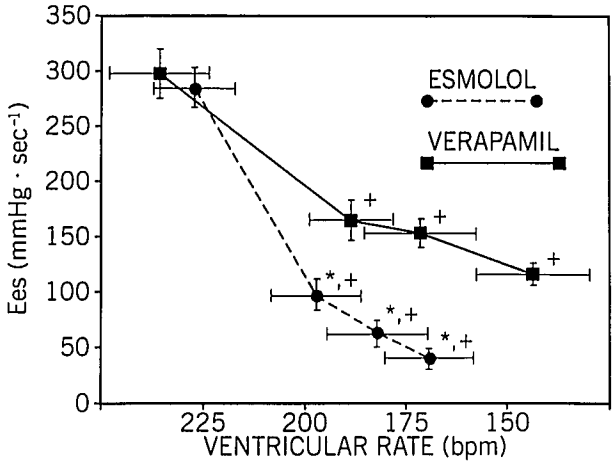

FIG. 3. The change in regional contractility (E_{es}) produced by doses of esmolol (E) and verapamil (V) producing similar degrees of dromotropy. Values are means ± SEM. *E was less than V at all doses ($P < 0.05$). †Difference from baseline within group ($P < 0.05$).

fects occurs within minutes after slowing or stopping its infusion. Other agents used for rate control of atrial fibrillation or flutter also have relatively long half-lives (*e.g.*, 2–4 h for propranolol). From a pharmacokinetic viewpoint, esmolol's rapid titration would appear to make it the most desirable agent for the control of ventricular rate in the setting of unstable cardiovascular states that commonly occur after heart surgery. However, the major findings of this study indicate that verapamil appears to be more specific than esmolol at prolonging atrioventricular conduction and slowing ventricular rate, producing less concomitant depression of myocardial contractility and cardiac output at comparable levels of negative dromotropy. Preferential uptake and binding of verapamil by the atrioventricular (A-V) nodal tissues has been suggested because the duration of the depressant effect on the A-V node considerably outlasts the duration of its hemodynamic actions.[15] In contrast, electrophysiologic studies have demonstrated a rapid reversal of blocking effects on discontinuation of esmolol. Our model does not allow determination of the relative ability of these drugs to cause conversion of dysrhythmias such as atrial fibrillation to sinus rhythm.

This study recorded significant decreases in contractility that were not accompanied by corresponding decrements of cardiac output in verapamil-treated animals. The improvement in ventricular filling as a result of lengthened diastolic time appears to compensate well for the impairment of contractility in the verapamil-treated animals, resulting in a net increase in stroke volume. The improvement in diastolic filling (preload) associated with slower ventricular rates did not provide the same degree of compensation for the greater negative inotropic effects of esmolol. When aortic flow or pressure decrease in the intact animal, there are compensatory increases in neural sympathetic cardiac stimulation as well as release of adrenal catecholamines. Therefore, any net hemodynamic changes are also the result of the interplay between the direct negative inotropic effects of these drugs and the positive inotropic effects of these compensatory mechanisms. The presence of β-adrenergic blockade may attenuate these mechanisms, which serve to preserve contractility and perfusion, whereas calcium entry blockade alone may not interfere with these sympathetically mediated compensations to as great a degree.

Esmolol is cardioselective, although some β_2-adrenergic blocking effects on vascular smooth muscle may be expected at higher doses. These latter effects may result in a small degree of unmasked α-adrenergic tone, which increases systemic vascular resistance and opposes a fall in perfusion pressure as cardiac output declined in the esmolol-treated animals. This is consistent with other data demonstrating similar maintenance of blood pressure, probably because of compensatory vasoconstriction, associated with reduced contractility after comparable doses of esmolol in anesthetized dogs.[16] This increase in afterload may contribute to the greater decrease in cardiac output (and contractility) in the animals receiving esmolol. The relative depression of cardiac output and contractility by esmolol compared with verapamil also may be influenced by the degree of sympathetic tone in any given experimental model. For example, esmolol might theoretically be more negatively inotropic in the presence of high sympathetic tone; conversely, a smaller difference in myocardial depression between esmolol and verapamil might occur in the presence of low basal sympathetic tone. The dromotropic state of the atrioventricular node also depends on endogenous sympathetic tone, so that a β-adrenergic blocker might have greater electrophysiologic effects at high levels of sympathetic tone. Although our model does not allow us to confirm or refute such hypotheses, they remain important considerations when interpreting the results of this study.

Because baroreceptor reflexes and autonomic nervous system function are somewhat affected by barbiturate anesthesia, it is possible that the hemodynamic responses to the cardiovascular drugs tested represent a balance between their direct properties and the reflex stimulation of sympathetic tone related to pentobarbital anesthesia. The contribution of basal barbiturate anesthesia to the hemodynamic effects of low doses of verapamil in acutely instrumented dogs is limited and not significantly different than in conscious animals.[17] Nonetheless, extrapolation of the data from this study to the clinical setting is limited because of potential interactions of the basal anesthetic, species differences, the influence of acute instrumentation

in open-chested animals, and the presence of unimpaired ventricular function in this model.

In the presence of a well-maintained perfusion pressure, there was little change in LAD coronary artery blood flow in either drug group. Although drug effects on coronary vascular resistance could affect global myocardial blood flow, this was not examined in this study. Coronary blood flow might be expected to change because of decreases in heart rate or direct coronary vasodilating effects in the case of verapamil. Autoregulation of coronary blood flow in association with unchanged pressure-volume work (LVSW, table 1) and the relatively small doses of verapamil used in this study may be partly responsible for the lack of significant changes in coronary blood flow.

The measurement and meaning of contractility as defined in this model deserve additional comment. As noted above, the end-systolic pressure-length (ESPL) relationship was used as a sensitive and relatively load-independent method of quantifying regional myocardial contractility. The ESPL relationship has been established as an index of contractility in nonischemic canine hearts.[18-20] Furthermore, regional myocardial function was monitored in the anteroapical region of the left ventricle, which has been shown to be more dynamic and more sensitive to negative inotropic interventions than the basal region.[21] It should be noted that the ESPL relationship is a measure of regional contractility in contrast to the end-systolic pressure-volume (ESPV) relationship, which reflects global contractility. In the absence of regional ischemia, changes in the ESPL relation are proportional to changes in the ESPV relation when myocardial contractility is altered.[18,19] The presence of ischemia within or outside of the region in which myocardial segment lengths are used to generate the ESPL relationship invalidates this relationship to ESPV data. Because our model was nonischemic, a measure of regional contractility (Ees) might be expected to reflect global changes in contractility. Although myocardial depression may shift the line defined by the ESPL relation without changing its slope,[20] we did observe significant changes in Ees that corresponded to other measures of contractility such as LV dP/dt and V_{max}.

In summary, these data suggest that when doses of verapamil and esmolol producing similar degrees of negative dromotropy are compared in a canine model of supraventricular tachydysrhythmias, esmolol has a more deleterious effect on myocardial contractility. Depression of contractility represents a decrease in the potential to deliver a certain flow. This potential may be modified by factors such as heart rate, preload, and afterload conditions. These factors often change in the dynamic setting of the intact cardiovascular system, either because of compensatory reflexes, pathophysiologic states, or external modulation (by the clinician). It is therefore possible to have significant depression of contractility that can be accommodated without causing an insufficient cardiac output. In general, the function of the heart as a pump is more important and not synonymous with contractility. However, decreased contractility may have significant clinical importance in the patient with advanced cardiovascular disease, especially those who already have impaired ventricular function.

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