The Relationship between Invasive Hemodynamic Measurements and Tissue Doppler-Derived Myocardial Velocity and Acceleration during Isovolumic Relaxation in Healthy Dogs

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ABSTRACT. This study investigated the feasibility of using the values of tissue Doppler imaging (TDI)-derived myocardial velocity during isovolumic relaxation (V_{IR}) and myocardial acceleration during isovolumic relaxation (ACC) obtained from the left ventricular (LV) free wall to evaluate LV relaxation in normal dogs. Seven dogs were anesthetized, and dobutamine or esmolol was infused at a rate of 5.0 and 10.0 $\mu\text{g/kg/min}$ or 100 and 500 $\mu\text{g/kg/min}$, respectively, via a cephalic vein. The order of drug administration (dobutamine or esmolol) was assigned to each dog. Simultaneous pulsed-Doppler (PD) echocardiography, TDI and hemodynamic measurements were performed. Compared with the baseline values, dobutamine significantly increased dP/dt min , but significantly shortened τ . Similarly, esmolol significantly decreased dP/dt min , but significantly prolonged τ . Compared with the baseline values, dobutamine significantly increased V_{IR} and ACC, and esmolol significantly decreased V_{IR} and ACC. Both dP/dt min and τ were significantly correlated with TDI-derived IVRT ($r=-0.43$ and 0.74), V_{IR} ($r=0.85$ and -0.49) and ACC ($r=0.84$ and -0.52). These results indicate that the TDI-derived V_{IR} and ACC values obtained from the LV free wall can potentially be used to assess LV relaxation in dogs.

KEY WORDS: canine, diastolic function, left ventricle, tissue Doppler imaging.

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Impaired relaxation is common in human patients and dogs with chronic heart failure [1, 5, 10, 27, 29]. Information regarding left ventricular (LV) diastolic function can be used to assess disease severity and prognosis in patients with heart failure [21, 23]. Several parameters measured by tissue Doppler imaging (TDI)-derived early and late diastolic myocardial velocities are indicators of diastolic function in dogs, providing diagnostic information and describing the severity of heart disease [4, 6, 29]. Similarly, TDI-derived isovolumic relaxation time (IVRT) can potentially be used as an indicator of LV diastolic function in humans and dogs with heart disease [3, 9, 17, 28].

Recently, strain rate imaging-derived myocardial velocity during isovolumic relaxation (V_{IR}) was found to be a useful parameter for dyskinesia in an animal model with myocardial ischemia [8]. Similarly, V_{IR} detected by pulsed-TDI may be a useful indicator of ischemia in patients with coronary artery disease [25]. Furthermore, Hashimoto *et al.* reported that strain rate imaging-derived myocardial acceleration during isovolumic relaxation (ACC) is correlated with ventricular diastolic function and is independent of preload in sheep [12, 13]. Because strain rate imaging measures only the velocity contribution from the myocardium, it may reflect regional function only. In contrast, because TDI measures velocity resulting from all longitudinal motion between the point of measurement and the ultrasound trans-

ducer, it is likely to reflect global cardiac function. Thus, pulsed-TDI-derived V_{IR} and ACC may be used as an additional screening method to identify diastolic function in dogs. However, the relationship between invasive measurements of LV diastolic function and pulsed-TDI-derived V_{IR} and ACC measurements in dogs is unknown.

Thus, the purpose of this study was to investigate the feasibility of using pulsed-TDI-derived V_{IR} and ACC measurements obtained from the LV free wall to evaluate LV relaxation in normal dogs.

MATERIALS AND METHODS

Animals: Seven healthy mongrel male dogs that were 1 to 5 years old and weighed 7 to 15 kg were used in this study. The dogs were housed individually in cages and fed commercial dry food with free access to water. The study followed the Guidelines for Institutional Laboratory Animal Care and Use of the School of Veterinary Medicine at Kitasato University, Japan.

Each dog was anesthetized with propofol (6.0 mg/kg, IV) and intubated following sedation with butorphanol (0.2 mg/kg, IV) and atropine (0.025 mg/kg, SC). Anesthesia was maintained with 2.0% isoflurane in oxygen. The dog was positioned in left lateral recumbency. Respiratory rate was maintained with an artificial ventilator (KV-1a, Kimura Medical Instrument Co., Ltd., Tokyo, Japan), and the arterial partial pressure of carbon dioxide (PaCO_2) and heart rate were monitored. Under fluoroscopic guidance, a high-fidelity 3.5-F micromanometer-tipped catheter (Model

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SPR-524, Millar Instruments, Houston, TX, U.S.A.) was placed through the right carotid artery into the LV. The peak systolic left ventricular pressure (LVPS), end-diastolic left ventricular pressure (LVEDP), time constant of isovolumic relaxation (τ ; τ) and peak positive and negative first derivatives of the LV pressure (dP/dt max and dP/dt min, respectively) were recorded continuously. Hemodynamic data were recorded using the commercial analysis software package supplied with the system (Notocord HEM 3.1 software; Croissy sur Seine, France).

After completing the procedures, a 20- to 30-min stabilization period was allowed to establish a baseline condition for the hemodynamic and echocardiographic measurements.

Drug administration: Dobutamine (Dobutrex®, Shionogi & Co., Osaka, Japan) was infused at a rate of 5.0 or 10 $\mu\text{g}/\text{kg}/\text{min}$ for 5 min via a cephalic vein [23]. Similarly, esmolol (Brevibloc®, Maruishi Pharmaceutical Co., Ltd., Osaka, Japan) was infused at a rate of 100 or 500 $\mu\text{g}/\text{kg}/\text{min}$ for 5 min via a cephalic vein [3]. The adrenergic agents were dissolved in sterile saline and administered with an infusion pump. Four dogs were administered dobutamine and esmolol, and three dogs were administered esmolol and dobutamine. After completing the first drug, a stabilization period of at least 30 min was provided to reestablish a baseline condition. Following baseline recording, the other drug was administered.

Echocardiography: Standard pulsed-Doppler (PD) and TDI velocities were obtained from the apical long-axis view. Transthoracic echocardiography was performed using an ultrasonographic system (SONOS 5500 system, Hewlett Packard, Littleton, MA, U.S.A.) with a 12-MHz probe. Time-interval measurements were made using the internal analytical package of the ultrasound unit. The mean values of 3 consecutive cardiac cycles were calculated to obtain the PD and TDI measurements.

PD echocardiography (filter, 600 Hz; gain, 60%; sweep speed, 100 mm/sec) was used to measure the transmitral flow (TMF) velocity with the sample volume positioned at the tip of the opened mitral valve leaflets. The peak E wave and peak A wave TMF velocities were measured, and the ratio of the E wave to the A wave (E/A ratio) was calculated. The ejection time (ET) was measured from onset to the end of aortic outflow. PD-derived IVRT was calculated by subtracting the time interval between the peak of the R wave and the end of the ET from the time interval between the peak of the R wave and the onset of the E wave [7, 11]. The isovolumic contraction time (IVCT) was calculated by subtracting the ET and PD-derived IVRT from the time interval between the cessation of the mitral valve A wave and the onset of mitral valve E wave in the next cardiac cycle [7, 11].

The TDI program was adjusted from the standard PD mode. The filter was set to 50–100 Hz and was adjusted to exclude high-frequency signals. The gain was set to 10–20% and was minimized to allow for a clear signal with minimal background noise. The sweep speed was 100 mm/sec. A 2-mm sample volume was placed at the LV free wall

Fig. 1. Tissue Doppler imaging (TDI)-derived V_{IR} and ACC. S': mitral annular systolic velocity. E': mitral annular early diastolic velocity. A': mitral annular late diastolic velocity. V_{IC} : mitral annular velocity during isovolumic contraction. V_{IR} : mitral annular velocity during isovolumic relaxation. ACC: mitral annular acceleration during isovolumic relaxation. AT: acceleration time.

of the mitral valve annulus, and the peak myocardial velocity was measured during systole (S'), early diastole (E') and late diastole (A'). The ratio of the E' wave to the A' wave (E'/A' ratio) was subsequently calculated. The duration of the S' wave was measured from the onset to the end of the S' wave. The duration of the TDI-derived IVCT was measured from the end of the A' wave to the onset of the S' wave [21]. Similarly, the TDI-derived IVRT was measured from the end of the S' wave to the onset of the E' wave [3]. V_{IR} was measured as the peak velocity of the positive wave between the end of the systolic ejection phase and the beginning of the early diastolic relaxation phase (Fig. 1) [19, 25]. The presence of V_{IR} was judged as a positive wave in all dogs and situations. ACC, which is the slope of the upstroke of the isovolumic relaxation wave, was calculated as the peak V_{IR} divided by the acceleration time, which was measured from the onset to the peak velocity of V_{IR} (Fig. 1). The intra- and inter-assay coefficients of variation (CV) for V_{IR} and ACC are shown in Table 1.

Table 1. Intra- and inter-assay coefficients of variation for V_{IR} and ACC in healthy dogs

CV values	Observer (n)	Dog (n)	V_{IR} (%)	ACC (%)
Intra-day	1	5	11.3	11.5
Inter-day	1	4	9.6	14.8
Inter-observer	3	5	6.8	14.5
Intra-observer	1	5	5.0	12.4

CV values (%) = SD values/mean values $\times$ 100. V_{IR} and ACC were calculated from 3 consecutive cardiac cycles at baseline. The inter-day CV values for V_{IR} and ACC were the results from 5 dogs evaluated by a single observer on 3 occasions every other week. The intra-day CV values for V_{IR} and ACC were the results from 4 dogs evaluated by a single observer on 3 occasions at 8-hr intervals during one day. The inter-observer CV values for V_{IR} and ACC were the results from 5 dogs. Each dog was evaluated by 3 observer's respectively. The intra-observer CV values for V_{IR} and ACC were the results from 5 dogs evaluated by a single observer at 3 times on one occasion. CV values were calculated for each dog at each point. CV: coefficients of variation. V_{IR} : myocardial velocity during isovolumic relaxation. ACC: myocardial acceleration during isovolumic relaxation.

Statistical analyses: The data are described as mean $\pm$ standard deviation (SD) values. Changes in the hemodynamic and echocardiographic measurements were compared using a one-factor repeated-measures analysis of variance. Significant differences were tested using of the post-hoc Tukey's multiple comparison test. Spearman's nonparametric correlation analysis was applied to compare the changes in echocardiographic measurements to the changes in dP/dt min values and τ . A P value of < 0.05 was considered significant. Forward stepwise regression analysis was used to determine the hemodynamic parameters that were best correlated with dP/dt min or τ . A value of $F > 2.0$ was considered statistically significant.

RESULTS

Compared with the baseline, the heart rate increased significantly with dobutamine at 10 $\mu\text{g/kg/min}$, whereas it did not change with esmolol (Table 2). Similarly, following dobutamine administration, the LVPs significantly increased from baseline at each dose, whereas the LVEDP remained unchanged. At 500 $\mu\text{g/kg/min}$ esmolol, the LVPs significantly decreased from baseline, whereas the LVEDP significantly increased. Compared with the baseline value, dP/dt max significantly increased following dobutamine administration and decreased significantly with esmolol, regardless of the dose. Similarly, dP/dt min was increased significantly with dobutamine and decreased significantly with esmolol, regardless of the dose. All doses of do-

butamine significantly shortened τ from its baseline value, whereas all doses of esmolol significantly prolonged it.

Although dobutamine increased the E wave at each dose and the A wave at 10 $\mu\text{g/kg/min}$, esmolol decreased the E wave at 500 $\mu\text{g/kg/min}$ and the A wave at each dose (Table 3). Consequently, neither drug affected the E/A ratio. IVCT was shortened significantly following dobutamine administration compared with the baseline, whereas IVRT tended to shorten; the difference, however, was not significant. In contrast, both IVCT and IVRT were significantly prolonged following administration of 500 $\mu\text{g/kg/min}$ esmolol. ET was significantly shortened by both 10 $\mu\text{g/kg/min}$ dobutamine and 500 $\mu\text{g/kg/min}$ esmolol.

The effects of the inotropic agents on TDI are shown in Fig. 2 and Table 4. Dobutamine significantly increased the S', E' and A' velocities, whereas esmolol significantly decreased the S' and E' velocities. Consequently, the E'/A' ratio decreased significantly with esmolol at 500 $\mu\text{g/kg/min}$. Dobutamine significantly shortened the TDI-derived IVCT compared with the baseline, whereas esmolol at 500 $\mu\text{g/kg/min}$ produced a significant prolongation. The TDI-derived IVRT was significantly shorter than the baseline value following administration of 10 $\mu\text{g/kg/min}$ dobutamine, but it was significantly prolonged by administration of 500 $\mu\text{g/kg/min}$ esmolol. V_{IR} was detected as a positive wave in all dogs. V_{IR} increased significantly from baseline with 10 $\mu\text{g/kg/min}$ dobutamine, whereas esmolol significantly decreased it. Dobutamine significantly increased ACC compared with the baseline, whereas esmolol significantly

Table 2. Changes in hemodynamic values during inotrope administration

	Dobutamine			Esmolol		
	Baseline	5 $\mu\text{g/kg/min}$	10 $\mu\text{g/kg/min}$	Baseline	100 $\mu\text{g/kg/min}$	500 $\mu\text{g/kg/min}$
HR (bpm)	87 $\pm$ 11	87 $\pm$ 21	116 $\pm$ 34*	97 $\pm$ 16	92 $\pm$ 12	97 $\pm$ 7
LVPs (mmHg)	79 $\pm$ 8	109 $\pm$ 19†	113 $\pm$ 15†	77 $\pm$ 5	71 $\pm$ 5	57 $\pm$ 9‡
LVEDP (mmHg)	9 $\pm$ 2	9 $\pm$ 3	9 $\pm$ 3	9 $\pm$ 2	10 $\pm$ 2	14 $\pm$ 1‡
+dP/dt (mmHg/sec)	1161 $\pm$ 166	2593 $\pm$ 726‡	3335 $\pm$ 424‡	1166 $\pm$ 136	926 $\pm$ 153‡	563 $\pm$ 101‡
-dP/dt (mmHg/sec)	-1161 $\pm$ 254	-1777 $\pm$ 207‡	-1916 $\pm$ 373‡	-1103 $\pm$ 237	-885 $\pm$ 161†	-435 $\pm$ 100‡
τ (msec)	44 $\pm$ 8	36 $\pm$ 9*	30 $\pm$ 4‡	44 $\pm$ 6	54 $\pm$ 8†	91 $\pm$ 11‡

All data are normally distributed and are described as means $\pm$ SD. HR: heart rate. LVPs: left ventricular systolic pressure. LVEDP: left ventricular end-diastolic pressure. dP/dt max: peak positive first derivatives of the LV pressure. dP/dt min: peak negative first derivatives of the LV pressure. * $P < 0.05$ vs. baseline, † $P < 0.01$ vs. baseline, ‡ $P < 0.001$ vs. baseline.

Table 3. Changes in pulsed-Doppler measurements during inotrope administration

	Dobutamine			Esmolol		
	Baseline	5 $\mu\text{g/kg/min}$	10 $\mu\text{g/kg/min}$	Baseline	100 $\mu\text{g/kg/min}$	500 $\mu\text{g/kg/min}$
E wave (cm/sec)	44 $\pm$ 8	63 $\pm$ 8‡	77 $\pm$ 7‡	49 $\pm$ 8	46 $\pm$ 9	33 $\pm$ 6‡
A wave (cm/sec)	23 $\pm$ 9	28 $\pm$ 13	48 $\pm$ 21‡	30 $\pm$ 11	25 $\pm$ 10†	22 $\pm$ 9‡
E/A ratio	2.4 $\pm$ 1.5	3.0 $\pm$ 2.5	2.5 $\pm$ 2.8	2.1 $\pm$ 1.5	2.4 $\pm$ 1.9	1.8 $\pm$ 1.0
IVCT (msec)	50 $\pm$ 19	15 $\pm$ 17‡	0 $\pm$ 17‡	46 $\pm$ 24	47 $\pm$ 13	68 $\pm$ 12†
IVRT (msec)	34 $\pm$ 17	30 $\pm$ 15	26 $\pm$ 12	40 $\pm$ 13	34 $\pm$ 13	69 $\pm$ 17‡
ET (msec)	216 $\pm$ 20	211 $\pm$ 16	192 $\pm$ 29†	207 $\pm$ 11	206 $\pm$ 14	190 $\pm$ 12†

All data are normally distributed and are described as means $\pm$ SD. E wave: peak early diastolic velocity. A wave: peak late diastolic velocity. IVCT: isovolumic contraction time. IVRT: isovolumic relaxation time. ET: ejection time. * $P < 0.05$ vs. baseline, † $P < 0.01$ vs. baseline, ‡ $P < 0.001$ vs. baseline.

Fig. 2. Representative recordings of mitral annular motion velocity using tissue Doppler imaging (TDI) at baseline (left), with dobutamine (center) and with esmolol (right). AT: acceleration time. V_{IR} : annular velocity during isovolumic relaxation.

Table 4. Changes in tissue Doppler imaging (TDI) measurements during inotrope administration

	Dobutamine			Esmolol		
	Baseline	5 $\mu\text{g/kg/min}$	10 $\mu\text{g/kg/min}$	Baseline	100 $\mu\text{g/kg/min}$	500 $\mu\text{g/kg/min}$
S' (cm/sec)	5.2 ± 1.0	$10.0 \pm 1.4^\ddagger$	$12.9 \pm 2.0^\ddagger$	5.2 ± 1.1	$4.0 \pm 0.7^*$	$2.8 \pm 0.5^\ddagger$
E' (cm/sec)	6.2 ± 1.0	$10.3 \pm 1.2^\ddagger$	$10.8 \pm 1.5^\ddagger$	6.2 ± 0.9	5.6 ± 1.1	$3.9 \pm 0.8^\ddagger$
A' (cm/sec)	3.4 ± 1.1	5.8 ± 3.4	$6.2 \pm 2.5^*$	3.9 ± 1.5	3.9 ± 1.7	3.3 ± 1.2
E'/A' ratio	2.0 ± 0.9	2.3 ± 1.3	2.2 ± 1.4	1.8 ± 0.7	1.7 ± 1.0	$1.4 \pm 0.8^*$
IVCT (msec)	57 ± 10	$25 \pm 9^\ddagger$	$17 \pm 9^\ddagger$	51 ± 12	61 ± 10	$77 \pm 16^\ddagger$
IVRT (msec)	72 ± 16	61 ± 13	$50 \pm 7^\ddagger$	68 ± 12	84 ± 18	$93 \pm 21^\ddagger$
V_{IR} (cm/sec)	3.6 ± 0.5	5.1 ± 1.1	$7.1 \pm 2.3^\ddagger$	3.7 ± 0.4	$2.8 \pm 0.4^\ddagger$	$2.5 \pm 0.3^\ddagger$
ACC (cm/sec ²)	85.4 ± 17.2	$145.1 \pm 47.9^*$	$224.7 \pm 50.6^\ddagger$	104.6 ± 24.0	$70.7 \pm 12.0^\ddagger$	$55.6 \pm 6.4^\ddagger$

All data are normally distributed and are described as means $\pm$ SD. E' : ventricular early diastolic velocity. A' : ventricular late diastolic velocity. S' : ventricular systolic velocity. IVCT: isovolumic contraction time. IVRT: isovolumic relaxation time. V_{IR} : myocardial velocity during isovolumic relaxation. ACC: myocardial acceleration during isovolumic relaxation. * $P < 0.05$ vs. baseline, $^\ddagger P < 0.01$ vs. baseline, $^\ddagger P < 0.001$ vs. baseline.

decreased ACC.

The results of regression analysis of the echocardiographic measurements and dP/dt min or τ are described in Figs. 3 and 4 and Table 5, respectively. The PD-derived IVRT was significantly correlated with dP/dt min and τ ($r = -0.60$ and 0.62). The dP/dt min was strongly correlated with the TDI-derived V_{IR} and ACC ($r = 0.85$ and 0.84), whereas it was weakly correlated with the IVRT ($r = -0.43$). Similarly, τ was strongly correlated with the TDI-derived IVRT ($r = 0.74$), whereas it was weakly correlated with V_{IR} and ACC ($r = -0.49$ and -0.52). Stepwise regression analysis showed that the E' velocity ($F = 41.1$), ACC ($F = 5.6$), PD-derived IVRT ($F = 4.6$) and heart rate ($F = 2.8$) could predict dP/dt min ($r = 0.94$, $r^2 = 0.88$, $P < 0.001$). In contrast, the PD-derived IVRT ($F = 21.0$), TDI-derived IVRT ($F = 7.5$), E' velocity ($F = 5.3$) and E'/A' ratio ($F = 4.8$) were equally able to predict τ ($r = 0.88$, $r^2 = 0.78$, $P < 0.001$).

DISCUSSION

Measurements of diastolic function during isovolumic relaxation have been used to assess active or intrinsic relaxation properties in human patients with heart failure [1, 10, 27]. Several studies have reported elevated LV filling pressures in patients with chronic heart failure, despite having normal LV systolic function [16, 26, 30]. In addition, LV diastolic function frequently becomes impaired before systolic function in human patients with heart disease [18]. Furthermore, diastolic dysfunction has been reported to be evident in dogs with dilated cardiomyopathy [4–6, 24]. In the present study, we investigated the feasibility of using the mitral annulus-derived time interval, velocity and acceleration obtained from pulsed-TDI during isovolumic relaxation in dogs.

TDI can be used to calculate the IVCT and IVRT over a single cardiac cycle under normal conditions [2, 3, 14]. In addition, TDI provides the timing elements necessary to cal-

Fig. 3. Correlations between the negative first derivative of the left ventricular pressure (dP/dt min) and tissue Doppler imaging (TDI)-derived IVRT (left), V_{IR} (center) and ACC (right). Significant correlations were observed between dP/dt min and the IVRT, V_{IR} , and ACC (all $P < 0.001$). IVRT: isovolumic relaxation time. V_{IR} : annular velocity during isovolumic relaxation. ACC: annular acceleration during isovolumic relaxation.

Fig. 4. Correlations between the time constant of isovolumic relaxation (τ) and tissue Doppler imaging (TDI)-derived IVRT (left), V_{IR} (center) or ACC (right). Significant correlations were observed between τ and the IVRT, V_{IR} and ACC ($P < 0.001$, respectively). IVRT: isovolumic relaxation time. V_{IR} : annular velocity during isovolumic relaxation. ACC: annular acceleration during isovolumic relaxation.

Table 5. Correlations between standard pulsed-Doppler (PD) or tissue Doppler imaging (TDI) measurements and the negative first derivative of the left ventricular pressure (dP/dt min) or time constant of isovolumic relaxation (τ)

PD	dP/dt min		τ	
	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>
E wave	0.85	0.001	-0.29	NS
A wave	0.63	0.001	0.03	NS
E/A ratio	0.14	NS	-0.25	NS
IVRT	-0.60	0.001	0.62	0.001
TDI	dP/dt min		τ	
	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>
E' wave	0.92	0.001	-0.61	0.001
A' wave	0.34	0.05	0.10	NS
E'/A' ratio	0.50	0.01	-0.31	NS
E/E' ratio	-0.19	NS	0.08	NS
IVRT	-0.43	0.01	0.74	0.001
V_{IR}	0.85	0.001	-0.49	0.01
ACC	0.84	0.001	-0.52	0.001

culate IVRT on a beat-to-beat basis [3, 14]. IVRT, which can provide information related to LV diastolic function, is correlated with dP/dt min and τ [12, 13, 15, 16, 22]. Several studies have demonstrated that the TDI-derived IVRT is prolonged in patients with LV diastolic dysfunction [9, 17, 28]. Our results demonstrate that pulsed-TDI-derived IVRT

is significantly shortened by dobutamine, but significantly prolonged by esmolol. Pulsed-TDI-derived IVRT was strongly correlated with dP/dt min and τ , which is consistent with previous reports [12, 13, 15, 16, 22].

V_{IR} has been demonstrated as a positive velocity spike during isovolumic relaxation [12, 13, 19]. When comparing different LV segments, TDI-derived positive V_{IR} can be used as an indicator of coronary artery disease in humans [25]. In addition, the strain rate imaging-derived peak myocardial acceleration during IVRT is correlated with LV dP/dt min in sheep [12, 13]. Our study showed that the TDI-derived V_{IR} is a positive wave in the LV free wall, which is consistent with previous reports. In addition, our results demonstrate that V_{IR} values derived from the mitral annulus are increased significantly with dobutamine, but decreased significantly with esmolol and are strongly correlated with dP/dt min and τ . Our data indicate that pulsed-TDI-derived positive V_{IR} measurements are a useful parameter for assessing LV relaxation in dogs.

Assessing myocardial acceleration during the isovolumic phase may be an attractive method to investigate cardiac function. For example, acceleration during isovolumic contraction is a good indicator of global LV systolic function in pigs, independent of preload and afterload changes and within a physiological range [31]. However, assessment of myocardial acceleration during isovolumic contraction seems to be very limited because it does not provide further

information about regional contractility in dogs with myocardial ischemia [20]. This conflict may be explained by methodological differences. Vogel *et al.* [31] measured global cardiac function by conductance catheterization, whereas Lyseggen *et al.* [20] measured regional myocardial motion by sonomicrometry.

Previous studies using strain rate imaging show that ACC is the acceleration of the myocardial velocity during isovolumic relaxation [12, 13]. ACC values derived from strain rate imaging are significantly affected by adrenergic agents and correlate with ventricular diastolic function in sheep [12, 13]. Our study showed that the ACC values derived from TDI were significantly increased by dobutamine, but significantly decreased by esmolol, and were strongly correlated with dp/dt min and τ . These results indicate that pulsed-TDI-derived ACC measurements can be used to assess LV relaxation in dogs.

Several limitations of the present study should be noted, including the confounding influence of LV translation and rotation during relaxation and our ability to determine the velocity at only a single point within the myocardium. In our study, the LV free wall-derived V_{IR} was a positive wave. However, there is some conflicting data indicating that V_{IR} is a negative wave or biphasic wave in dogs and humans, but that large positive V_{IR} values may indicate dyskinesia in the ischemic myocardium [8, 25]. These results may be explained by methodological differences such as in animal species, instruments and methods (strain rate imaging or TDI). Furthermore, septal TDI-derived V_{IR} and ACC may demonstrate different results under the same conditions. We cannot exclude the possibility that general anesthesia might have affected our echocardiographic measurements. Given that V_{IR} and IVRT are influenced by several factors, including age, preload condition and heart rate [19, 22], these values should be interpreted with caution. Finally, dogs with chronic heart disease may demonstrate a very different response under the same conditions.

Our data demonstrate that pulsed-TDI-derived V_{IR} and ACC measurements reflect invasive measurements of LV relaxation in normal dogs. Therefore, pulsed-TDI-derived V_{IR} and ACC values may be good indicators for noninvasive LV diastolic assessment. Additional studies are required to assess the practical utility of these approaches and to investigate whether the present findings are valid in dogs with heart disease.

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