Volume loading–related changes in tissue Doppler images derived from the tricuspid valve annulus in dogs

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Objective—To investigate the relationship between preload and tricuspid valve annulus–derived tissue Doppler imaging (TDI) as an index of right ventricular (RV) filling in dogs.

Animals—7 Beagles.

Procedures—Peak systolic RV pressure and RV end-diastolic pressure (RVEDP) were measured in anesthetized dogs. Pulsed Doppler was used to measure tricuspid valve inflow and pulmonary valve outflow velocities. The TDI velocities were measured at the lateral corner of the tricuspid valve annulus. Lactated Ringer’s solution was infused at 200 mL/kg/h for 60 minutes via the cephalic vein.

Results—IV infusion significantly increased heart rate, RV pressure, and RVEDP. Early diastolic flow (E-wave) and ejection time significantly increased. The myocardial performance index (MPI) significantly decreased. Intravenous infusion significantly increased the ratio of the E-wave (peak myocardial velocity during early diastole) to the A-wave (peak myocardial velocity during late diastole; E:A ratio) and myocardial velocity during systole (S′), early diastole (E′), and late diastole (A′). The TDI-isovolumic relaxation time and TDI-MPI decreased significantly. The RVEDP was correlated with late diastolic flow (A-wave), ratio of the E-wave to the A-wave (E:A ratio), E′-wave, A′-wave, S′-wave (peak myocardial velocity during systole), TDI-isovolumic relaxation time, TDI-MPI, and ratio of the E-wave to the E′-wave (E:E′ ratio). The A-wave and E:A ratio and TDI-derived isovolumic relaxation time, S′ duration, and E′-wave could predict the RVEDP.

Conclusions and Clinical Relevance—The TDI velocities were affected by RV filling pressure in healthy dogs, whereas other TDI profiles, such as MPI and E′:A′ ratio, were independent of acute filling abnormalities. (Am J Vet Res 2008;69:33–38)
al reported that TDI-derived early diastolic myocardial velocity correlated with LV-derived negative dP/dt in clinically normal dogs and that a decrease in E:A ratios and an increase in E'/A' ratios were related to severity of heart failure in dogs. The advantage of TDI-derived myocardial velocities is that they can identify patients with pseudonormalization, which is frequently encountered with the PD technique. Nevertheless, it remains unclear whether the RV-TDI profiles are influenced by the loading conditions in clinically normal dogs. Therefore, the purpose of the study reported here was to investigate the relationship between preload and tricuspid valve annulus-derived TDI as an index of RV filling in anesthetized dogs.

Materials and Methods

Animals—Seven male Beagles 1 to 2 years of age and weighing 8 to 12 kg were studied. The dogs were caged individually, fed commercial dry food, and had free access to water. This study followed the Guidelines for Institutional Laboratory Animal Care and Use of the School of Veterinary Medicine at Kitasato University, Japan.

After sedation with butorphanol (0.2 mg/kg, IV) and atropine (0.023 mg/kg, SC), the dogs were anesthetized with propofol (6.0 mg/kg, IV) and intubated. Anesthesia was maintained with 2.0% isoflurane in oxygen. The dogs were positioned in the left lateral recumbent position. The respiratory rate was maintained with an artificial ventilator. The end-tidal PaCO₂ was monitored and maintained between 35 and 45 mm Hg, and the heart rate was monitored by use of an ECG. The RV and PAP were measured with a 6-F Swan-Ganz catheter passed via the right jugular vein under fluoroscopic guidance. The catheter was connected to strain-gauge manometers to measure blood pressure, RVPs, RVEDP, PAPs, and PAPed. After completing the procedures, a 20- to 30-minute stabilization period was provided to establish a stable baseline condition for echocardiographic and hemodynamic measurements. As a baseline, all measurements were recorded before examination.

Echocardiography—Transthoracic echocardiography was performed with an ultrasonographic unit and a 12-MHz probe. Echocardiographic measurements were made during the expiratory phase. The echocardiograms were analyzed by use of the commercial analysis software package supplied with the system. The mean of 3 cardiac cycles was calculated. Because intraday and interday variability of the RV-TDI variables has been reported, all examinations were conducted in the daytime and once in each dog. Data were stored digitally and analyzed off-line by a single observer.

Pulsed Doppler echocardiography was used to measure the tricuspid valve inflow velocity in the 4-chamber view with the sample volume positioned at the tip of the tricuspid valve leaflets. Then, the tricuspid valve E-wave and A-wave and the E:A ratio were measured. Pulmonary valve outflow Doppler measurements were made with the sample volume placed just below the pulmonary valve in the apical long-axis view. The E-wave was measured from the onset to the end of the pulmonary valve outflow. Time interval measurements were performed with the internal analysis package of the ultrasonography unit. The intervals were determined by 2 carefully placed vertical cursors that were moved with a track ball. On the basis of the PD recordings, the MPI was calculated in the standard way as the total isovolumic (contraction and relaxation) time divided by the ET.

The time from cessation of the tricuspid valve A-wave to the onset of the tricuspid valve E-wave of the next cardiac cycle (a) is equal to the total isovolumic time plus the ET (b). The MPI was calculated by use of the formula (a – b)/b (Figure 1). The IRT was calculated by subtracting the interval between the peak of the R wave and the end of the ET from the interval between the peak of the R wave and the onset of the E-wave. The ICT was calculated by subtracting the ET and IRT from the interval between cessation of the tricuspid valve A-wave and the onset of the tricuspid valve E-wave of the next cardiac cycle.

<table>
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<tr>
<th>Variable</th>
<th>Baseline</th>
<th>10 minutes</th>
<th>20 minutes</th>
<th>30 minutes</th>
<th>40 minutes</th>
<th>50 minutes</th>
<th>60 minutes</th>
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<tr>
<td>HR (beats/min)</td>
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<td>106 ± 14</td>
<td>111 ± 13†</td>
<td>114 ± 111</td>
<td>118 ± 123</td>
<td>119 ± 104</td>
<td>115 ± 81†</td>
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<td>RVPs (mm Hg)</td>
<td>14 ± 4</td>
<td>21 ± 6*</td>
<td>21 ± 6*</td>
<td>24 ± 8†</td>
<td>26 ± 5†</td>
<td>27 ± 7†</td>
<td>26 ± 8†</td>
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<tr>
<td>RVEDP (mm Hg)</td>
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<td>5 ± 7*</td>
<td>6 ± 8*</td>
<td>6 ± 10*</td>
<td>7 ± 7†</td>
<td>7 ± 9*</td>
<td>5 ± 9†</td>
</tr>
<tr>
<td>PAPs (mm Hg)</td>
<td>13 ± 6</td>
<td>18 ± 8</td>
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<td>23 ± 8†</td>
<td>24 ± 7†</td>
<td>24 ± 9†</td>
<td>23 ± 8†</td>
</tr>
<tr>
<td>PAPed (mm Hg)</td>
<td>4 ± 5</td>
<td>7 ± 7</td>
<td>9 ± 6</td>
<td>11 ± 7*</td>
<td>13 ± 7*</td>
<td>15 ± 10*</td>
<td>13 ± 9†</td>
</tr>
</tbody>
</table>

*Significantly (P < 0.05) different from baseline value. †Significantly (P < 0.01) different from baseline value. ‡Significantly (P < 0.001) different from baseline value. HR = Heart rate.
The TDI program was set to PD mode. Filters were set to exclude high-frequency signals. The gain was minimized to allow a clear tissue signal with minimal background noise. The TDI velocities were obtained from the 4-chamber view of each dog. By use of the 4-chamber view, a 2-mm sample volume was placed at the lateral corner of the tricuspid valve annulus. The S’-wave, E’-wave, and A’-wave were measured (Figure 1). The E’:A’ ratio and E:E’ ratio were calculated. On the basis of the TDI recordings, the duration of the S’-wave was measured from its onset to the end of the S’-wave. The ICT was measured from the end of the A’-wave to the onset of the S’-wave. The IRT was measured from the end of the E’-wave to the onset of the E’-wave. The modified MPI obtained from the TDI was calculated as (ICT + IRT)/S’-wave duration.

Volume overload—Preload was increased by infusing lactated Ringer’s solution at 200 mL/kg/h for 60 minutes via the cephalic vein, which is a modification of the dosage reported by Cheung et al. An echocardiographic examination was performed at 10-minute intervals. During the IV infusion, the influence of volume overloading on the hemodynamic variables was monitored, and the mean PAPed was approximately 10 mm Hg above baseline. After all of the procedures, the dogs were administered furosemide (2 mg/kg, IV) and allowed to recover from anesthesia.

Statistical analysis—Data are described as mean ± SD. The change in the loading conditions was compared with baseline by use of 1-factor repeated-measures ANOVA. The significance of the differences between the mean values at baseline and under each condition was tested by use of the Tukey multiple comparison test. Correlations between the RVEDP and echocardiographic measurements were determined via single regression analysis. A value of P < 0.05 was considered significant. Forward stepwise regression analysis was used to determine the RVEDP that correlated best with individual Doppler variables; a value of F > 2.0 was considered significant.

Results
The hemodynamic variables changed markedly with the volume overload (Table 1). Heart rate increased significantly (P < 0.001) from baseline. The RVPs and RVEDP increased significantly from baseline (P < 0.001 and P = 0.003, respectively). The PAPs and PAPed also increased significantly (both P < 0.001) from baseline.

Representative recordings of results of the PD echocardiography under acute volume overloading were obtained (Figure 2). The E-wave increased significantly (P < 0.001) from baseline, but the A-wave did not change (Figure 3). Moreover, the E:A ratio remained unchanged with volume overloading (Figure 4). The PD-ICT and PD-IRT shortened from baseline, but not significantly (Figure 5). In contrast, the ET was prolonged significantly (P < 0.001) from baseline, causing the PD-MPI to decrease significantly (P = 0.002) from baseline (Figure 6).

Representative recordings of the TDI under acute volume overloading were obtained (Figure 2). The E’-wave and A’-wave increased significantly (P < 0.001) from baseline, but the A-wave did not change (Figure 3). Similarly, the S’-wave increased significantly (P < 0.001) from baseline. The E’A’ ratio increased significantly (P = 0.006) from baseline with volume overloading (Figure 8). Although the TDI-ICT decreased from baseline, this...
was not significant; the TDI-IRT decreased significantly from baseline ($P < 0.001$; Figure 9). In contrast, the systolic myocardial velocity duration increased significantly ($P = 0.008$) from baseline, which caused the TDI-MPI to decrease significantly ($P < 0.001$) from baseline (Figure 6).

Results of the regression analyses between RVP and the echocardiographic variables were tabulated (Table 2). Significant correlations were found between RVEDP and the PD measurements, including the A-wave and E:A ratio. In addition, significant correlations were found between RVEDP and the TDI measurements, including the E’-wave, A’-wave, S’-wave, IRT, MPI, and E:

![Figure 4](image-url) Volume loading–related changes in the E:A ratio (mean ± SD) in 7 dogs.

![Figure 5](image-url) Volume loading–related changes in ET and isovolumic times (mean ± SD) in 7 dogs. See Figure 3 for key.

![Figure 7](image-url) Volume loading–related changes in TDI velocities (mean ± SD) in 7 dogs. See Figure 3 for key.

![Figure 6](image-url) Volume loading–related changes in the MPI (mean ± SD) in 7 dogs. See Figure 3 for key.

![Figure 8](image-url) Volume loading–related changes in the E’:A’ and E:E’ ratios (mean ± SD) in 7 dogs. See Figure 3 for key.

![Figure 9](image-url) Volume loading–related changes in the TDI-derived S’ duration and isovolumic times (mean ± SD) in 7 dogs. See Figures 2 and 3 for key.
E′ ratio. Stepwise regression analysis revealed that the PD-derived A-wave and E:A ratio and the TDI-derived IRT, systolic myocardial velocity duration, and E′-wave could predict the RVEDP ($r = 0.98; r^2 = 0.96; P < 0.001$; Table 3).

**Discussion**

Evaluating RV function has an important role in predicting the prognosis and severity of disease in patients with tetralogy of Fallot, as well as in dogs with tricuspid valve regurgitation and pulmonary hypertension.\(^1\)\(^,\)\(^3\)\(^,\)\(^16\)\(^-\)\(^20\)

Given the difficulty in determining the RV endocardial surface, as well as the complexity of its shape, the conventional Doppler echocardiographic evaluation of RV systolic or diastolic function must be interpreted with caution. In human medicine, the usefulness of TDI derived from the tricuspid valve annulus velocity is reported in patients with RV dysfunction and provides clinical information on various functional variables in patients with heart failure.\(^7\)\(^,\)\(^19\)\(^,\)\(^21\)

Previously, we reported that RV-derived systolic myocardial velocity is significantly correlated with positive dP/dt in clinically normal dogs, whereas the RV-derived early diastolic and late diastolic myocardial velocities are significantly correlated with negative dP/dt valve.\(^1\) In addition, the peak systolic and diastolic tricuspid valve annulus velocities are effective predictors of survival and event-free survival.\(^7\)\(^,\)\(^18\)

In the present study, the tricuspid valve annulus–derived TDI velocities were increased markedly with volume overloading. Stepwise regression analysis revealed that the TDI-derived E′-wave was correlated with the RVEDP, but the S′- and A′-wave velocities, E′:A′ ratio, and E: E′ratio were not correlated. We have to consider 1 factor when explaining this result: the difference between a normal heart and a failing heart. Although tricuspid valve annulus velocities were accelerated by the Frank-Starling mechanism in clinically normal dogs, the failing myocardium may lead to a different response in dogs with chronic heart disease.\(^21\)

Therefore, our results suggested that the tricuspid valve annulus velocities are influenced by RV filling abnormalities in clinically normal dogs and that the clinical implications of the TDI findings must be interpreted with caution.

The MPI is a useful clinical index of global ventricular function and can be used to evaluate both systolic and diastolic function.\(^10\)\(^,\)\(^17\)\(^,\)\(^21\)

The PD-derived MPI has gained favor as a clinical examination for assessing cardiac function and is a useful predictor of the clinical outcome in patients with cardiac disease.\(^24\)\(^,\)\(^25\)

Teshima et al\(^9\) reported that the RV-derived MPI increased significantly in dogs with tricuspid valve regurgitation and microfilariasis. The main advantage of this index is that it appears to be independent of heart rate, body weight, and age in clinically normal dogs.\(^3\)\(^,\)\(^27\)

However, one of the main limitations of the PD-MPI is that it cannot be calculated over a single cardiac cycle because the interval between the end and onset of tricuspid valve inflow and the ET are measured sequentially. In contrast, the TDI can be used to determine the isovolumic contraction and relaxation and ETs over a single cardiac cycle under normal conditions.\(^3\)

In the present study, the PD- and TDI-MPI significantly decreased from baseline because volume overloading markedly prolonged the ET and decreased the total isovolumic time. The correlation coefficients between TDI-MPI and RVEDP were higher than for the PD-MPI. These results, which are consistent with a previous report,\(^9\) indicate that the PD-MPI in patients with pulmonary regurgitation does not differ from that in healthy individuals, although patients with heart disease have a significantly greater TDI-MPI than healthy individuals. In addition, a previous study\(^1\) found that inotropic agent–induced positive and negative dP/dt changes were significantly correlated with the RV-derived TDI-MPI in healthy dogs.\(^1\) Because the TDI can measure all of the variables within 1 cardiac cycle, the TDI-derived MPI may reduce the inaccuracy related to the heart rate. Furthermore, stepwise regression analysis in the present study revealed that MPI is not a predictor of acute RV filling abnormalities, which indicated that the MPI was independent of acute volume overloading in healthy dogs.

This study was conducted to investigate the response of dogs to acute volume overloading as an experimental method of replicating a filling abnormality. It has been reported that general anesthesia affects echocardiographic measurements.\(^13\)

Complete autonomic blockade was not used in the present study, and reflex autonomic changes might have affected the heart filling variables. In addition, Cheiboul et al\(^13\) reported that the intraday and interday coefficient of variation values of the TDI variables were observed at the tricuspid annulus in the dog.\(^13\)

Because the repeatability and reproducibility data were not analyzed in the present study, our results must be interpreted with caution.
Furthermore, chronic heart disease might lead to different responses. Although volume loading did not alter the PD-MPI in normal left ventricular function, it decreased with left ventricular dysfunction. Therefore, the TDI should be evaluated by testing the rate of changes in loading conditions and modulation of inotropic state on the myocardial performance index: comparison with conductance catheter measurements. Eur Heart J 2004;25:2238–2242.

References