Repeatability and reproducibility of right ventricular Tei index valves derived from three echocardiographic methods for evaluation of cardiac function in dogs

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OBJECTIVE
To evaluate repeatability and reproducibility of right ventricular Tei index (RTX) values derived from dual pulsed-wave Doppler, conventional pulsed-wave Doppler, and tissue Doppler echocardiography and to investigate relationships and repeatability among the 3 methods in healthy dogs.

ANIMALS
6 healthy adult Beagles.

PROCEDURE
Echocardiography was performed on each dog on different days for 2 weeks (3 times/d) by 2 echocardiographers. Intraobserver within- and between-day and interobserver coefficients of variation (CVs) and intraclass correlation coefficients (ICCs) for RTXs derived from dual pulse-waved Doppler (RTX_{DPD}), conventional pulsed-wave Doppler (RTX_{PD}), and tissue Doppler (RTX_{TD}) methods were determined. Degrees of agreement among RTX values derived from the 3 methods were assessed by modified Bland-Altman analysis.

RESULTS
Least squares mean (95% confidence interval) RTX_{TD} was 0.50 (0.46 to 0.54), which was significantly higher than that for RTX_{DPD} (0.27 [0.23 to 0.31]) and RTX_{PD} (0.25 [0.21 to 0.29]). Agreement between RTX_{DPD} and RTX_{PD} was good (bias [mean difference], 0.04 [95% confidence interval, –0.03 to 0.10]). The RTX_{DPD} had high within-day (CV, 6.1; ICC, 0.77) and interobserver (CV, 3.5; ICC, 0.83) repeatability, but between-day repeatability was not high. The RTX_{TD} had high within-day repeatability (CV, 6.0; ICC, 0.80), but between-day and interobserver repeatability were not high. Within-day, between-day, and interobserver repeatability of RTX_{PD} were not high.

CONCLUSIONS AND CLINICAL RELEVANCE
RTX_{DPD} measurement was a repeatable and reproducible method of cardiac evaluation in healthy dogs. The RTX_{TD} values were significantly higher than the RTX_{DPD} and RTX_{PD} values; therefore, RTX values derived from different echocardiographic methods should be interpreted with caution. (Am J Vet Res 2016;77:715–720)

Pulmonary hypertension has been recognized as a clinical problem for many years in veterinary medicine. Routine accurate clinical diagnosis of pulmonary hypertension in dogs specifically has been markedly enhanced by the widespread use of echocardiography. However, systematic assessment of function of the right chambers of the heart is not uniformly carried out. This lack of consistency is due in part to the high amount of attention given to evaluation of the left chambers of the heart, a lack of familiarity with ultrasonographic techniques available for imaging the right chambers, and a paucity of ultrasonographic studies providing reference intervals for size and function of the right chambers. To date, reference intervals and repeatability of right-chamber heart function indices for echocardiographic evaluation, such as peak systolic tricuspid annulus velocity, tricuspid annulus plane systolic excursion, and systolic longitudinal right ventricular strain, have been reported. In addition, right-chamber heart function tests involving echocardiography have been used in clinical settings for dogs. These indices, however, provide an assess-

ABBREVIATIONS
CI Confidence interval
CV Coefficient of variation
DPD Dual pulsed-wave Doppler
ICC Intraclass correlation coefficient
ICT Isovolumic contraction time
IRT Isovolumic relaxation time
LS Least squares
RTX Right ventricular Tei index
RTX_{DPD} Right ventricular Tei index derived from DPD echocardiography
RTX_{TD} Right ventricular Tei index derived from tissue Doppler echocardiography
RTX_{PD} Right ventricular Tei index derived from conventional pulsed-wave Doppler echocardiography

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mment of only the regional or overall systolic function of the right chambers.

The Tei index (also called the myocardial performance index) is an index of overall myocardial function, including systolic and diastolic performance. This measurement involves a simple technique, and it correlates well with both the systolic and diastolic function of the right ventricle. Therefore, it has been used to evaluate right ventricular function and provide information on severity and prognosis for dogs with cardiac disease.

The Tei index has been derived from conventional pulsed-wave Doppler and tissue Doppler echocardiography. However, an important limitation exists in that values derived from conventional pulsed-wave Doppler cannot be calculated in a single cardiac cycle; therefore, the Tei index is influenced by heart rate fluctuations (ie, respiratory sinus arrhythmia). On the other hand, tissue Doppler echocardiography can be used to simultaneously record diastolic and systolic phases, but values measured by use of that method in dogs are reportedly different from those obtained via conventional pulsed-wave Doppler echocardiography.

Dual pulsed-wave Doppler echocardiography allows Doppler signals at 2 points to be simultaneously measured, setting 2 separate sample volumes in 1 image. Therefore, measurement of the RTX during the same cardiac cycle is possible, which may overcome the limitations associated with a conventional pulsed-wave Doppler approach. In human medicine, the intra- and interobserver reliability of RTX are high. In addition, RTX values are higher than RTX and RTX values. However, to the authors’ knowledge, no reports exist on RTX measurement in dogs. Moreover, degrees of agreement among RTX values derived from the 3 echocardiographic methods have not been reported for dogs.

The purpose of the study reported here was to evaluate the repeatability and reproducibility of RTX, RTX, and RTX measurements in healthy dogs. In addition, we also sought to investigate statistical relationships among RTX, RTX, and RTX.

Materials and Methods

Dogs
Six laboratory Beagles (2 females and 4 males) between 1 and 3 years of age and weighing between 9.5 and 13.0 kg were used in this study. All dogs were determined to be healthy with unremarkable heart anatomy and myocardial function on the basis of complete physical, ECG, and standard echocardiographic examinations (including M-mode, pulsed-wave Doppler, and color flow Doppler imaging). All procedures were approved by the Laboratory Animal Experimentation Committee, Graduate School of Veterinary Medicine, Hokkaido University.

Echocardiographic measurements
Conventional echocardiographic examinations were performed by 1 echocardiographer (KN), who used an ultrasonographic machine equipped with a sector probe (3 to 7 MHz). Unsedated dogs were manually restrained for evaluation in left and right lateral recumbency. An ECG trace (lead II) was recorded simultaneously with echocardiographic imaging and automatically measured heart rate. All dogs were confirmed healthy by echocardiographic examination.

The RTX was derived from DPD, conventional pulsed-wave Doppler, and tissue Doppler findings by 2 echocardiographers (KN and TM). For this process, RTX was defined as the sum of the ICT and IRT, divided by ejection time (Figure 1). For each RTX, mean values of 3 separate cardiac cycles were used to assess repeatability. Each RTX value was calculated after image acquisition.

To calculate RTX, tricuspid inflow and pulmonary artery flow were measured simultaneously by means of DPD echocardiography with a left parasternal short-axis view, and ICT and IRT were derived by subtracting the ejection time from the amount of time that elapsed between cessation of the tricuspid valve A wave to the onset of the tricuspid valve E wave in 1 image (Figure 1). Ejection time was measured from the beginning of one to the beginning of the next pulmonary arterial spectrum.

To calculate RTX, tricuspid valve inflow was measured from a left parasternal short-axis view. Next, pulmonary arterial flow was measured from a left parasternal short-axis view. Finally, ICT and IRT were derived by subtracting ejection time from the amount of time that elapsed between cessation of the tricuspid valve A wave (late diastolic flow) to the onset of the tricuspid valve E wave (early diastolic flow) in 2 separate images (Figure 1). No attempt was made to match R-R intervals for the in- and outflow signals because, in the authors’ experience, it is difficult to match R-R intervals in clinical settings.

To calculate RTX, the tricuspid valve peak systolic annular velocity, peak early diastolic velocity, and late diastolic velocity were determined by tissue Doppler echocardiography with a apical 4-chamber view. Then, ICT and IRT were derived by subtracting the duration of the late systolic annular velocity wave for the tricuspid valve from the time that elapsed between the end of the late diastolic velocity wave and onset of the early diastolic velocity wave for the same valve on the basis of tissue Doppler recordings (Figure 1).

Statistical analysis
Power calculations for sample size determination were made on the basis of data from a previous study. Presuming a similar intraobserver within-day, intraobserver between-day, and interobserver ICC, it was estimated that a sample size of 6 dogs would be required to provide a power of 90% to detect an ICC of 0.75 with the null hypothesis that the ICC would be 0, an α value of 0.05, and 3 measurements/technique/dog.

Statistical analysis programs were used to develop a linear mixed model, with measurement time (1 to 9 times), method (DPD, tissue Doppler, and pulsed-
wave Doppler techniques), and their interaction as
categorical fixed effects and dog identity as a random
effect. The $F$ test was performed to assess the effect of
measurement time and method on RTX. Multiple com-
parisons were made by obtaining the LS mean of 1 ob-
server’s (KN) measurements and applying the Tukey
honest significant difference test to assess differences
among methods. The all-pairs Tukey test allows signifi-
cance tests of all combinations of pairs, and the result-
ing honest significant difference intervals are greater
than those provided with the Student pairwise $t$ test
for least significant differences.

The following linear model was used for within- and
between-day and interobserver variability analyses:

$$Y_{ijkl} = \mu + \text{observer}_i + \text{day}_j + \text{dog}_k + (\text{observer} \times \text{dog})_{ik} + (\text{day} \times \text{dog})_{jk} + \epsilon_{ijkl}$$

where $Y_{ijkl}$ was the first value measured for dog $k$ on
day $j$ by observer $i$, $\mu$ was the general mean, observer,
was the differential effect (considered as fixed) of ob-
server $i$, dog$_k$ was the differential effect of dog $k$, (ob-
server $\times$ dog)$_{ik}$ represented the interaction between
the observer and dog, (day $\times$ dog) represented the in-

Figure 1—Echocardiographic images illustrating a technique used to measure RTX in dogs by means of DPD (A), pulsed-wave Doppler (B and C), and tissue Doppler (D) techniques. A—The upper waveform is tricuspid inflow, and the lower waveform is pulmonary artery flow. B—Tricuspid inflow is shown. C—Pulmonary artery flow is shown. D—Tricuspid valve annular velocity is shown. The simultaneously recorded ECG appears at the top. For all calculations, RTX = (a – b)/b, a = Interval from tricuspid valve closure to opening (pulsed-wave Doppler recordings) or the end of the A’ wave to the beginning of the E’ wave (tissue Doppler recordings). A = Tricuspid valve late diastolic flow. A’ = Tricuspid valve late diastolic velocity. b = Ejection time or S’ duration. E = Tricuspid valve early diastolic flow. E’ = Tricuspid valve early diastolic annular velocity. S’ = Tricuspid valve systolic annular velocity.
The interaction between day and dog, and ε_{ijkl} was the model error. The SD of within-day variability was estimated as the residual SD of the model, SD of between-day variability as the SD of the differential effect of day, and SD of interobserver variability as the SD of the differential effect of observer. The corresponding CVs were determined by dividing each SD by the mean.

The intraobserver within-day ICC was determined from data generated by the same observer (KN); this echocardiographer evaluated 6 dogs 3 times during the same day. The intraobserver between-day ICC was determined from data generated by 1 blinded observer (KN); on each of 3 days, this echocardiographer made 3 evaluations of the 6 dogs. The interobserver ICC was determined from data generated by 2 blinded observers (KN and TM) on the same day; these echocardiographers evaluated 6 dogs 3 times during the same day. Agreement was considered high when the CV was < 20% and the ICC was > 0.75.

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Differences among measurements derived from the 3 methods were evaluated by use of Bland-Altman analysis, with modification for repeated measures as described elsewhere. Mean differences (bias) and 95% CIs were calculated. Differences among methods were considered significant when the 95% CI did not contain 0. Values of P < 0.05 were considered significant. Results are summarized as LS mean (95% CI).

Differences among measurements derived from the 3 methods were evaluated by use of Bland-Altman analysis, with modification for repeated measures as described elsewhere. Mean differences (bias) and 95% CIs were calculated. Differences among methods were considered significant when the 95% CI did not contain 0. Values of P < 0.05 were considered significant. Results are summarized as LS mean (95% CI).

**Results**

Least squares means for variables associated with RTX as measured by 1 observer using the 3 echocardiographic methods were summarized (Table 1). The RTX_{TD} values were significantly higher than the RTX_{DPD} and RTX_{PD} values. In contrast, RTX_{DPD} did not differ significantly from RTX_{PD}. Intervals between tricuspid valve closure and opening and isovolumic time (sum of ICT and IRT) derived from the tissue Doppler method were longer than respective values derived from the DPD and pulsed-wave Doppler methods. No difference in LS mean heart rate was identified among the 3 methods.

Bland-Altman analysis revealed that RTX_{TD} values were significantly higher than RTX_{DPD} and RTX_{PD}.
values (Figure 2). However, agreement was good between RTX_{dpd} and RTX_{pd}.

Intraobserver within- and between-day and interobserver CVs and ICCs of RTX derived from the 3 methods were summarized (Table 2). The RTX_{dpd} had high (low CV and high ICC) within-day and interobserver repeatability, but between-day repeatability was not high. The RTX_{td} had high within-day repeatability, but between-day and interobserver repeatability were not high. The RTX_{pd} lacked high within- and between-day repeatability and interobserver repeatability.

**Table 2—Within- and between-day (1 observer) and interobserver (2 observers) CVs and ICCs for 3 echocardiographic methods of RTX measurement in healthy adult Beagles (n = 6) performed 3 times/d for 3 days.**

<table>
<thead>
<tr>
<th>Method</th>
<th>Within-day CV (%)</th>
<th>Within-day ICC</th>
<th>Between-day CV (%)</th>
<th>Between-day ICC</th>
<th>Interobserver CV (%)</th>
<th>Interobserver ICC</th>
</tr>
</thead>
<tbody>
<tr>
<td>DPD</td>
<td>6.1</td>
<td>0.77</td>
<td>8.4</td>
<td>0.73</td>
<td>3.5</td>
<td>0.83</td>
</tr>
<tr>
<td>Tissue Doppler</td>
<td>6.0</td>
<td>0.80</td>
<td>7.7</td>
<td>0.63</td>
<td>2.4</td>
<td>0.62</td>
</tr>
<tr>
<td>Pulsed-wave Doppler</td>
<td>20.7</td>
<td>0.62</td>
<td>20.7</td>
<td>0.35</td>
<td>19.1</td>
<td>0.65</td>
</tr>
</tbody>
</table>

Agreement was considered high when the CV was < 20% and the ICC was > 0.75.

The RTX_{td} values were higher than the RTX_{dpd} and RTX_{pd} values of the dogs of the present study. This finding was consistent with findings of previous studies involving humans and dogs. The higher RTX_{td} was mainly attributable to the longer interval between tricuspid valve closure and opening and isovolumic time derived from the tissue Doppler method, compared with values obtained with DPD and pulsed-wave Doppler methods. The reason for differences between RTX_{td} and other RTX measurements may have been related to differences in methods used and measurement sites. The RTX_{td} is measured by use of intervals based on myocardial motion, whereas the RTX_{dpd} and RTX_{pd} are measured by use of intervals based on blood flow. Moreover, RTX_{td} is measured only at the right ventricular inlet portion, in contrast to RTX_{dpd} and RTX_{pd}, which are measured at both the right ventricular inlet and outlet portions. Therefore, RTX_{td} may be unrelated to the overall right ventricular function. It is important to consider that RTX_{td} had higher reference values than did RTX_{dpd} and RTX_{pd}; therefore, Tei indexes should not be used interchangeably.

In humans with right ventricular overload, RTX_{dpd} is a better predictor of exercise capacity than is RTX_{td} and RTX_{pd}. Therefore, in dogs with right ventricular overload, as occurs with pulmonary hypertension, RTX_{dpd} may also be a better predictor of right heart dysfunction. Additional studies are needed to validate the clinical usefulness of RTX_{dpd} measurement in dogs with right heart dysfunction.

The present study had several limitations. First, a small number of healthy laboratory Beagles was used; therefore, caution should be exercised when attempting to extrapolate the repeatability and reproducibility data to dogs with right heart dysfunction. Indeed, in humans, the degree of disagreement among RTX values in patients with heart disease is higher than that in healthy subjects. Second, no reference standard of the right ventricular function, such as cardiac catheterization, was evaluated in the present study. Therefore, we could not assess which of the 3 methods for RTX measurement was superior. Additional studies are needed to validate the correlation between RTX and right ventricular function obtained by cardiac catheterization and other noninvasive echocardiographic
indices, such as tricuspid valve annular plane systolic excursion or fractional area change. Third, DPD echocardiography is a novel application of ultrasonography that is available on only few ultrasonographic systems, so the usefulness of RTX_{DPD} measurement may be limited in clinical settings.

The study reported here revealed that RTX_{DPD} measurement was a feasible and reliable method for evaluation of cardiac function in a small number of healthy dogs. The RTX_{DPD} values were not significantly different from the RTX_{TD} values; however, RTX_{TD} values were significantly higher than RTX_{DPD} and RTX_{PD} values. Therefore, RTX values derived from different methods should be interpreted with caution and not used interchangeably because values differ with each method. Investigations involving dogs with heart disease are warranted to determine the clinical applicability of RTX_{DPD} measurement.

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Footnotes
a. HI VISION Preirus, Hitachi Medical Corp, Chiba, Japan.
b. EUP-S52, Hitachi Medical Corp, Chiba, Japan.
c. JMP version 8.0, SAS Institute Inc, Cary, NC.
d. SPSS, version 21, SPSS Inc, Chicago, III.

References