Evaluation of Right Ventricular Tei Index (Index of Myocardial Performance) in Healthy Dogs and Dogs with Tricuspid Regurgitation

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ABSTRACT. Right ventricular (RV) Tei index (index of myocardial performance) has been demonstrated to be clinically useful in estimating RV function in various human cardiac diseases. The purposes of this study were to validate the correlation between RV Tei index and RV function obtained by cardiac catheterization in healthy dogs, and to evaluate the RV Tei index in dogs with tricuspid regurgitation (TR). In healthy dogs, the RV Tei index significantly correlated with the RV peak +dP/dt (r=–0.80, p<0.0001) and –dP/dt (r=0.69, p=0.0001). In normal dogs, the RV Tei index was not significantly correlated with heart rate, body weight, and age. The RV Tei index significantly increased in dogs with moderate to severe TR (0.39 ± 0.35, p=0.0015), filariasis (0.46 ± 0.16, p=0.0131), and trivial to mild TR and severe mitral regurgitation (MR; 0.61 ± 0.14, p=0.0017) when compared with the normal dogs (0.17 ± 0.10). In addition, the RV Tei index in dogs with TR significantly increased in association with pulmonary hypertension [PH(–), 0.19 ± 0.09; PH(+), 0.65 ± 0.14; respectively p<0.0001]. Our study has demonstrated that RV Tei index is a feasible approach to estimate RV function in dogs and is not influenced by heart rate, body weight, and aging. Further investigations are required to clarify the clinical significance of RV Tei index in dogs with right-sided cardiac diseases.

KEY WORDS: canine, echocardiography, right ventricular function, Tei index, tricuspid regurgitation.

Right ventricular (RV) function plays an important role in determining cardiac output and functional capacity in humans [1, 28]. RV dysfunction has been observed in various cardiac disorders such as pulmonary hypertension (PH) [17, 37], idiopathic dilated cardiomyopathy (DCM) [22], and heart failure [7, 8, 27].

RV function can be evaluated by cardiac catheterization with RV peak +dP/dt, Tau and RV ejection fraction. However, this method is invasive, and it is difficult to evaluate the RV function due to the complex structural geometry, mechanical properties, and contraction pattern of the right ventricle [12, 16].

A decade ago, the Tei index (index of myocardial performance) derived from pulsed Doppler echocardiography was proposed in human medicine [36, 39]. The Tei index is defined as the sum of isovolumetric contraction time (ICT) and isovolumetric relaxation time (IRT) divided by ejection time (ET), and it has been reported to reflect comprehensive cardiac function, including systolic and diastolic performances, in humans [36, 39]. The Tei index is a simple and reproducible technique, and is relatively independent of heart rate [4, 39] and age [19]. In addition, the Tei index has been demonstrated to be clinically useful in estimating the prognosis in human patients with primary PH [37, 44], DCM [9], cardiac amyloidosis [38], and myocardial infarction [32]. It could be used for evaluating the RV function as well as the left ventricular function that is unrelated to the complex RV geometric structure [10, 11, 19, 24, 33–35, 37, 44].

In small animal medicine, RV dysfunction is suspected in dogs with various cardiac diseases such as left-sided heart failure, pulmonary stenosis, tricuspid dysplasia, dirofilaria-sis, idiopathic cardiomyopathy, cor pulmonale, and idiopathic or secondary PH [2]. In these cardiac diseases, the evaluation of RV dysfunction may be useful in comprehending cardiac conditions because RV dysfunction may be associated with the severity of clinical symptom and morbidity similar to human reports [6–8, 22, 27, 37]. In the cases where RV dysfunction is suspected, detection using current methods is clinically difficult. A few reports on the canine RV function derived from echocardiography have been described [2, 5, 26], and some reports have described the canine RV function using invasive methods in experimental models [18, 30, 31, 43]. The RV Tei index in normal dogs was reported to be relatively independent of body weight and heart rate [2]. However, to our knowledge, there have been no studies for assessing the association between RV Tei index and RV function in dogs. In addition, the RV Tei index has not yet been evaluated in clinical cases of canine right-sided heart diseases.

The purposes of this study were to validate the correlation between the RV Tei index and the RV function obtained by cardiac catheterization in healthy dogs, and to evaluate the RV Tei index in dogs with tricuspid regurgitation (TR).

MATERIALS AND METHODS

Validation of correlation between RV Tei index and RV...
function obtained by catheterization (Experiment 1): Five female Beagle dogs (body weight between 10.0 kg and 13.0 kg) were used in this series. Physical examination, complete blood count (CBC), serum biochemistry, electrocardiogram (ECG), thoracic radiography and echocardiography confirmed that the dogs were healthy. All dogs were cared for in accordance with the guidelines for the care and use of laboratory animals approved by College of Bioresource Science, Nihon University.

Each dog was premedicated with midazolam hydrochloride (0.2 mg/kg, intravenous injection [IV]) and butorphanol tartrate (0.2 mg/kg, IV) and was intubated after induction with thiopental sodium (12.5 mg/kg, IV). General anesthesia was maintained by inhalation of isoflurane (1.5%) and oxygen (2 l/min) under mechanical ventilation (respiratory rate, 10 breaths/min; inspiratory pressure, 10–15 cmH₂O; end-expiratory carbon dioxide partial pressure, 40 mmHg) along with the intravenous administration of pancuronium bromide (0.04–0.05 mg/kg).

Each dog was placed in dorsal recumbency, and the neck was clipped and aseptically prepared for surgery. After a midline incision of the neck, a 6-Fr micromanometer-tipped catheter (PC-460, Millar Instruments Inc., Houston, U.S.A.) was directly inserted into the isolated left jugular vein, and it was advanced into the RV chamber under fluoroscopic guidance.

After changing the dog’s position to left lateral recumbency, hemodynamic and echocardiographic measurements were simultaneously recorded in a blinded manner with the dog under a transient respiratory arrest. The RV pressure profiles were recorded for 5 sequential cardiac cycles during the echocardiographic measurement of RV inflow. The peak rates of RV pressure rise (RV peak +dP/dt) and decline (RV peak -dP/dt) were calculated and averaged from the RV pressure data.

The diagnostic ultrasound machine Power Vision 8000 (SSA-390A, Toshiba Medical Systems, Tokyo, Japan) was used for the echocardiographic measurements. The RV inflow profiles were obtained by pulsed Doppler echocardiography for 5 sequential cardiac cycles. Following the measurement of the RV inflow profiles, the RV outflow profiles were obtained for 5 sequential cardiac cycles. The sample volume was set at 2-mm width. The sample points were located at the level of the tips of the tricuspid valve leaflets in the left parasternal RV inflow view for the measurement of RV inflow, and at the level of the base of pulmonary valve in the left parasternal RV outflow view for the measurement of RV outflow [40].

The RV Tei index was calculated as follows: from the end of atrial contraction (A) wave to the start of the early diastolic (E) wave was defined as interval a, and the RV ejection time (ET) was defined as interval b for 5 sequential cardiac cycles. These values were averaged, and ICT + IRT was calculated by subtracting interval b from interval a. Eventually, the Tei index, (ICT + IRT)/ET, was calculated as (a-b)/b (Fig. 1).

These measurements were repeated with changes in cardiac inotropy or lusitropy using continuous rate infusion of dobutamine (3–10 µg/kg/min) or intravenous bolus injection of propranolol (0.1–0.2 mg/kg).

**Evaluation of RV Tei index in clinical cases with TR (Experiment 2):** Eighty-six dogs referred to the Animal Medical Center of Nihon University between April 2001 and August 2004 were included in the series. All the dogs were evaluated by physical examination, CBC, serum biochemistry, thoracic radiography and echocardiography. In the cases suspected of having arrhythmia, ECG was performed. The dogs with ventricular premature contraction (VPC) and any type of atrioventricular (AV) block were excluded from this series. Of the 86 dogs, 53 were diagnosed as free of cardiac diseases and were classified as normal dogs. In the remaining 33 dogs, TR was identified by echocardiography. Of the 33 dogs with TR, 4 concurrently had severe mitral regurgitation (MR) and left-sided heart failure, 6 had fibrillation and 2 had DCM. The remaining 21 dogs had moderate to severe TR with trivial to mild MR. In addition, the dogs with TR were divided into 2 categories: dogs without PH [PH(–)] and with PH [PH(+)]. PH was assumed on the basis of the following echocardiographic findings: essential parameters were maximal TR jet velocity of not less than 2.8 m/sec and no existence of RV outflow tract stenosis. In addition, relative dilation of the main pulmonary artery as compared with the aorta, appearance of another peak or notch in the latter half of RV outflow profiles and maximal pulmonary regurgitant jet velocity of not less than 2.2 m/sec were referred [3, 14, 20, 21, 29, 41]. Diagnostic ultrasound machines, Nemio (SSA-550A, Toshiba Medical Systems, Tokyo, Japan) and EUB-565A (Hitachi Medical Corporation, Tokyo, Japan), were used for the echocardiographic measurements. The echocardiographic measurement was performed without
sedation and anesthesia. The Doppler intervals a and b for the RV Tei index were obtained as mentioned above.

Statistical analyses: Data are expressed as mean value ± standard deviation. A simple linear regression analysis was used for validating the correlation between the RV Tei index and RV peak +/– dP/dt in experiment 1 as well as to correlate between the RV Tei index and heart rate and body weight and aging in normal dogs in experiment 2. One-way analysis of variance and post hoc test (Scheffe’s test) were used to compare the RV Tei index and other echocardiographic parameters among the groups in experiment 2. Statistical significance was defined as p<0.05.

RESULTS

Experiment 1: The echocardiographic measurements for RV Tei index were feasible in all the healthy dogs irrespective of change in the contractile and lusitropic conditions. In the healthy anesthetized dogs, the RV Tei index was 0.26 ± 0.06, interval a was 274 ± 45 msec, interval b (ET) was 217 ± 30 msec, and interval a-b (ICT + IRT) was 57 ± 17 msec, prior to the changes in the contractile and lusitropic status.

The RV Tei index significantly correlated with the RV peak +dP/dt (Fig. 2–1) and –dP/dt (Fig. 2–2).

Experiment 2: The RV Tei index was measurable in all the 86 dogs (Table 1). In the normal dogs, the RV Tei index was not significantly correlated with heart rate, body weight, and age (Figs. 3–1, -2, and -3). The RV Tei index significantly increased in dogs with moderate to severe TR (0.39 ± 0.35), filariasis (0.46 ± 0.16), and trivial to mild TR and severe MR (0.61 ± 0.14) when compared with the normal dogs (0.17 ± 0.10; Fig. 4). In addition, the RV Tei indices in 2 dogs with DCM (0.75 and 0.64) were higher than those in the normal dogs. As for the other Doppler intervals in normal dogs, interval a was significantly longer in dogs with filariasis (270 ± 33 msec), interval b (ET) was significantly shorter in dogs with moderate to severe TR (173 ± 31 msec) and trivial to mild TR and severe MR (154 ± 17 msec). Interval a-b (ICT + IRT) was significantly longer in dogs with moderate to severe TR (61 ± 49 msec), filariasis (84 ± 28 msec), and trivial to mild TR and severe MR (93 ± 11 msec).

In this series, of the 33 dogs with TR, 19 were categorized as PH(+) and 14 as PH(−). The age of the TR dogs with PH(+) and PH(−) was greater than those of the normal dogs (Table 2). The heart rate and body weight showed no significant differences among the 3 groups. The RV Tei index in PH(+) (0.65 ± 0.24) was significantly elevated in comparison to those in the normal dogs and PH(−) (0.19 ± 0.09; Fig. 5). Interval a was significantly longer in PH(+) than in normal dogs and PH(−). Interval b (ET) was significantly shorter in PH(+) than in normal dogs and PH(−). Interval a-b (ICT + IRT) was significantly longer in PH(+) than in normal dogs and PH(−). The maximal TR velocity and RV to RA pressure gradient increased significantly in PH(+) (357 ± 53 cm/sec) than in PH(−) (245 ± 18 cm/sec).
DISCUSSION

In humans, RV dysfunction is observed in various right-sided cardiac disorders. The indicators of RV function were reported to be associated with the severity of clinical symptom, morbidity, and mortality in human patients with primary PH [6, 37], idiopathic DCM [22], and heart failure [7, 8, 27]. Likewise, dogs with right-sided heart diseases are thought to be at a potential risk of having RV dysfunction. In particular, PH, which indicates an increase in RV afterload, has been reported to be caused by heartworm disease [20, 21, 41], pulmonary arterial thromboembolism (pulmonary vascular obstruction) [20, 21], chronic severe left-sided heart failure (increased left atrial pressure) [20, 21], and longstanding pulmonary parenchymal diseases (alveolar hypoxia) [13, 20, 21]. In these cases, RV function may be impaired and associated with clinical manifestation and prognosis similar to human cases [6–8, 22, 27, 37]. Therefore, the investigation of RV function in dogs with right-sided heart diseases is thought to be of clinical value.

The results of experiment 1 revealed that the RV Tei index reflects the RV systolic and diastolic functions in healthy dogs. We used RV +/–dP/dt as reference values to evaluate RV systolic and diastolic functions. The RV peak +/–dP/dt are the most commonly used indices for assessing ventricular function [15, 23, 25, 42]. However, these indices are influenced by ventricular preload and afterload. Therefore, other invasive indices of the ventricular function, such as maximal elastance (Emax), preload recruitable stroke work, chamber stiffness, and the time constant of relaxation (Tau), may reduce the impact from ventricular preload and afterload [15, 25, 42].

The value of RV Tei index was higher in healthy dogs in experiment 1 (0.26 ± 0.06) than in normal dogs in experiment 2 (0.18 ± 0.12). In experiment 1, the general anesthesia was thought to impede the RV function. Additionally, hemodynamic alteration with consciousness and sympathetic activation may have the influence on the RV Tei index...
in experiment 2. Especially, experiment 2 had the potential of involving the interobserver error. All echocardiographic indices including RV Tei index have a possibility of intraobserver and interobserver error. Therefore, further investigations on those errors of RV Tei index in dogs are required.

The RV Tei index is considered an index of global myocardial performance and it reflects the combined systolic and diastolic functions; however, it is difficult to assess the impairment of isolated systolic or diastolic function. In this case, invasive cardiac catheterization is required to assess the isolated RV systolic or diastolic function. However, it is difficult to apply invasive cardiac catheterization in routine small animal practice. In contrast, the RV Tei index calculated by noninvasive echocardiography is a convenient technique and is useful for estimating comprehensive RV function independent of the structural geometry of the right ventricle.

The results of experiment 2 indicate that the RV Tei index in dogs is an independent indicator of heart rate, body weight and aging. The RV Tei index in normal dogs has been demonstrated to be relatively independent of body weight and heart rate [2]. In humans, the RV Tei index was reported to be uninfluenced by heart rate in normal subjects and patients with primary PH [37]. The RV Tei index increased in dogs with TR when compared with the normal dogs. In particular, the RV Tei index in dogs with PH markedly increased. The RV diastolic function was impaired by chronic PH (pressure overload) in experimental canine and lamb models [25, 31]. Tei et al. [37] reported that the RV Tei index, which is the strongest predictor of clinical status and survival, increased significantly in human patients with primary PH. Moreover, the RV Tei index was not correlated with RV pressure overload; however, it was correlated with parameters of RV function obtained by right heart catheterization in patients with PH [33, 37]. In addition, it was discussed that the increased afterload may not solely affect the RV Tei index, which is substantially related to the RV systolic and diastolic function [15]. The elevation of RV Tei index in TR dogs with PH may be caused by RV dysfunction that was mainly impaired by chronic PH in our study. Hence, use of the RV Tei index is thought to be important for the evaluation of RV dysfunction that may be associated with symptoms and prognosis. However, in the case of arrhythmia, including VPC and AV block, it is impossible to adapt the Tei index for evaluating RV dysfunction because the Tei index is cal-

<table>
<thead>
<tr>
<th>Table 1. The Doppler time intervals in the normal dogs and dogs with various cardiac diseases</th>
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<tbody>
<tr>
<td>Number</td>
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<tr>
<td>--------</td>
</tr>
<tr>
<td>RV Tei index</td>
</tr>
<tr>
<td>Interval a (msec)</td>
</tr>
<tr>
<td>Interval b (msec)</td>
</tr>
<tr>
<td>ICT + IRT (msec)</td>
</tr>
</tbody>
</table>

TR, tricuspid regurgitation; MR, mitral regurgitation; DCM, dilated cardiomyopathy; RV Tei index, (ICT + IRT)/ET; interval a, from the end of the atrial contraction wave to the start of the early diastolic wave; interval b, the ejection time of right ventricular outflow; ICT, isovolumetric contraction time; IRT, isovolumetric relaxation time; ET, ejection time.

Table 2. Characteristics and the values of echocardiographic measurements in normal dogs (n=53), TR dogs without PH (n=14), and TR dogs with PH (n=19)

<table>
<thead>
<tr>
<th>Normal</th>
<th>TR without PH</th>
<th>TR with PH</th>
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</thead>
<tbody>
<tr>
<td>Number</td>
<td>53</td>
<td>14</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>111 ± 27</td>
<td>118 ± 20</td>
</tr>
<tr>
<td>BW (kg)</td>
<td>10.3 ± 9.1</td>
<td>7.7 ± 4.1</td>
</tr>
<tr>
<td>Age (years)</td>
<td>4.3 ± 3.2</td>
<td>8.5 ± 4.1</td>
</tr>
<tr>
<td>RV Tei index</td>
<td>0.17 ± 0.10</td>
<td>0.19 ± 0.09</td>
</tr>
<tr>
<td>Interval a (msec)</td>
<td>226 ± 30</td>
<td>225 ± 33</td>
</tr>
<tr>
<td>Interval b (msec)</td>
<td>194 ± 23</td>
<td>190 ± 25</td>
</tr>
<tr>
<td>ICT + IRT (msec)</td>
<td>32 ± 19</td>
<td>35 ± 18</td>
</tr>
<tr>
<td>TR velocity (cm/sec)</td>
<td>NA</td>
<td>244 ± 18</td>
</tr>
</tbody>
</table>

TR, tricuspid regurgitation; PH, pulmonary hypertension; HR, heart rate; BW, body weight; RV Tei index, (ICT + IRT)/ET; interval a, from the end of the atrial contraction wave to the start of the early diastolic wave; interval b, ejection time of right ventricular outflow; ICT, isovolumetric contraction time; IRT, isovolumetric relaxation time; ET, ejection time; NA, not available.

a) Significant difference with respect to Normal. b) Significant difference with respect to TR without PH.
culated using time intervals. In experiment 2, clinical cases with arrhythmia were excluded. Therefore, further investigations on alternative noninvasive methods for evaluating the RV function are required in dogs with arrhythmia.

A potential limitation of the RV Tei index is the inability to obtain both RV inflow and outflow simultaneously by Doppler echocardiography. In the cases where the heart rate changes during 2 stage measurements of RV inflow and outflow, the accuracy of the RV Tei index is thought to decrease. In particular, respiratory arrhythmia may be detected in dogs in routine small animal practice; this has an impact on the R-R intervals of ECG. Then, in our study, the intervals a and b were measured with an error range of precedence R-R intervals that was set less than 10% during 2 stage. We believed that this measurement reduces the intrinsic error of the changes in the intervals due to respiratory arrhythmia. However, further study is required to determine the most suitable measurement under respiratory arrhythmia.

In conclusion, our study has demonstrated that the RV Tei index is feasible in dogs and is not influenced by heart rate, body weight, and aging. In addition, the RV Tei index increased in dogs with TR when compared with normal dogs. In particular, the RV Tei index markedly increased in dogs with PH. Further investigations are necessary to clarify the clinical significance of the RV Tei index in individual cardiac disorders in dogs.

REFERENCES


