Evaluation of Left Ventricular Tei Index (Index of Myocardial Performance) in Healthy Dogs and Dogs with Mitral Regurgitation

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ABSTRACT. The left ventricular (LV) Tei index (index of myocardial performance) has been demonstrated to be clinically useful in estimating comprehensive LV function, including the systolic and diastolic performances, in various human cardiac diseases. The purposes of this study were to validate the correlation between the LV Tei index and LV function obtained by cardiac catheterization in healthy dogs, and to evaluate the LV Tei index in dogs with naturally occurring mitral regurgitation (MR). In healthy dogs, the LV Tei index was significantly correlated with the LV peak +dP/dt (r = –0.89) and LV peak –dP/dt (r = 0.87). The LV Tei index significantly increased in dogs with MR compared with normal dogs and significantly increased with progressively more severe clinical signs due to heart failure. The elevation of the LV Tei index in dogs with symptomatic MR appears to be associated with shortening of ejection time. The LV Tei index significantly increased with age and was not correlated with heart rate and body weight in normal dogs. In conclusion, our study demonstrated that the LV Tei index was measurable in dogs and not influenced by heart rate and body weight. The LV Tei index significantly increased with the progression of clinical signs in MR dogs. In particular, the elevation of the LV Tei index in dogs with symptomatic MR due to shortening of ejection time may suggest LV systolic dysfunction and the decrement of forward stroke volume.

KEY WORDS: canine, echocardiography, left ventricular function, mitral regurgitation, Tei index.

FULL PAPER

Internal Medicine

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Mitrval regurgitation (MR) due to a progressive myxomatous degeneration and rupture of the chordae tendineae is the most commonly acquired cardiac disease in dogs [3, 4]. The MR causes left ventricular (LV) volume overload and remodeling (eccentric hypertrophy) that have been demonstrated to have an impact on LV function in experimental canine models [15, 20, 30].

Echocardiography is a predominant noninvasive modality that provides a large variety of useful information on isolated LV systolic and diastolic function in human [11] and small animal patients [10]. In dogs with MR, however, it is difficult to evaluate LV function using conventional echocardiographic indices such as fractional shortening (FS), peak early diastolic wave velocity (E), peak atrial contraction wave velocity (A) of LV inflow, and the ratio of E to A (E/A); this is because the existence of MR leads to a change in the loading conditions of the diseased heart. In addition, some reports have demonstrated that systolic and diastolic dysfunctions coexist in the majority of human patients with congestive heart failure [6, 12, 21].

The Tei index (index of myocardial performance) derived from pulsed Doppler echocardiography was proposed for use in human medicine [24, 27]. The index is defined as the sum of the isovolumetric contraction time (ICT) and the isovolumetric relaxation time (IRT) divided by the ejection time (ET) (Fig. 1) and it has been reported to reflect comprehensive cardiac function, including systolic and diastolic performances, in human patients [24, 27]. The Tei index is a simple and reproducible technique and relatively independent of heart rate (HR) [2, 22, 26, 27], age [7, 9], and systemic blood pressure [2, 26, 27]. Moreover, the index has been demonstrated to be clinically available to estimate the prognosis in human patients with dilated cardiomyopathy (DCM) [5], cardiac amyloidosis [26], myocardial infarction [23], and primary pulmonary hypertension [25, 31]. In addition, a few reports have described the application of the Tei index to human patients with MR due to mitral valvular myxomatous degeneration [1, 14].

In small animal medicine, the LV Tei index was reported to correlate with the severity of disease, and may be of value in the early diagnosis of affected dogs during screening for the presence of DCM [18]. However, to our knowledge, there are no studies that have assessed the association between the LV Tei index and LV function in dogs. In addition, the LV Tei index has not yet been evaluated in clinical cases of canine spontaneous MR.

The purposes of this study were to validate the correlation between the LV Tei index and the LV function obtained by cardiac catheterization in healthy dogs, and to evaluate the LV Tei index in dogs with MR.

MATERIALS AND METHODS

Validation of the correlation between the LV Tei index
The Tei index, \( \frac{ICT + IRT}{ET} \), is calculated as \( \frac{a-b}{b} \), where interval \( a \) is the time between the cessation and onset of the mitral inflow and interval \( b \) is the ejection time of the left ventricular outflow.

\[ \text{Tei index} = \frac{ICT + IRT}{ET} = \frac{a-b}{b} \]

Fig. 1. The Tei index, \( \frac{ICT + IRT}{ET} \), is calculated as \( \frac{a-b}{b} \), where interval \( a \) is the time between the cessation and onset of the left ventricular outflow.

and LV function determined by catheterization (Experiment 1): Seven female beagles [body weight (BW) between 8.6 and 13.0 kg] were used in this series. A 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 the College of Bioresource Science, Nihon University.

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 right carotid artery; it was advanced into the LV chamber under fluoroscopic guidance. After changing the dog’s position to left lateral recumbency, hemodynamic and echocardiographic measurements were simultaneously blindly recorded with the dog under transient respiratory arrest.

A diagnostic ultrasound machine (Nemio SSA-550A; Toshiba Medical Systems, Tokyo, Japan) was used for the echocardiographic measurements. The LV inflow profiles were obtained by pulsed Doppler echocardiography for 5 sequential cardiac cycles. Following the measurement of the LV inflow profiles, the LV outflow profiles were obtained for 5 sequential cardiac cycles. The 2-mm width sample volume was used. The sample points were located at the level of the tips of the mitral valve leaflets in the left apical four chamber view; this was at the level of the base of the aortic valve in the left apical LV outflow tract view used for the measurement of the LV outflow [29]. The LV Tei index (Fig. 1) was calculated as follows. The distance between the end of peak A and the start of peak E for the LV inflow was defined as interval \( a \), and the LV ET for the LV outflow was defined as interval \( b \). The ICT + IRT was calculated by subtracting interval \( b \) from interval \( a \). The LV Tei index, \( \frac{ICT + IRT}{ET} \), was calculated as \( \frac{a-b}{b} \).

The LV pressure profiles determined by catheterization were recorded for 5 sequential cardiac cycles during the echocardiographic measurement of the LV inflow. The peak rates of LV pressure rise (LV peak +dP/dt) and decline (LV peak –dP/dt) were calculated and averaged from the LV pressure data.

These measurements were repeated with changes in cardiac inotropy and lusitropy using continuous rate infusion of dobutamine (3–10 \( \mu \)g/kg/min) or IV propranolol (0.2–0.4 mg/kg).

Evaluation of the LV Tei index in clinical cases with MR (Experiment 2): A total of 198 dogs referred to the Animal Medical Center of Nihon University between October 2003 and November 2005 were included in the series. All the dogs were evaluated by a 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 198 dogs, 125 were diagnosed as being free of cardiac diseases; these animals were classified as the normal group. In the remaining 73 dogs, MR attributable to chronic mitral valve disease was identified by echocardiography. The dogs with MR were divided into 4 groups based on the modified New York Heart Association functional classification of heart failure (NYHA class)—NYHA I (n=29), NYHA II (n=26), NYHA III (n=11), and NYHA IV (n=7) [17]. In addition, NYHA I and II were categorized as asymptomatic MR, and NYHA III and IV were classed as symptomatic MR. Echocardiography was performed using the Nemio SSA-550A diagnostic ultrasound machine.

Echocardiographic measurements were obtained without sedation and anesthesia. The intervals \( a \) and ET used for the LV Tei index calculation were derived as mentioned above for experiment 1. The intervals \( a \) and ET were measured with an error range of precedence R-R intervals on ECG that was set at less than 10% during the 2-stage measurements of LV inflow and outflow. In addition, FS, the ratio of left atrial to aortic diameters (LA/Ao), E, A, and E/A were recorded.

Statistical Analyses: The data are expressed as mean values ± standard deviation. A simple linear regression analysis was used for validating the correlation between the LV...
Tei index and LV peak +/- dP/dt in experiment 1 and the correlation between the LV Tei index and HR, BW, and age in the normal group in experiment 2. A one-way analysis of variance in conjunction with a post hoc test (Scheffe’s test) was used to compare the LV Tei index and other echocardiographic parameters among the groups in experiment 2. Statistical significance was defined as $p<0.05$.

**RESULTS**

**Experiment 1:** The measurement of the echocardiographic parameters for the LV Tei index was feasible in all the dogs irrespective of change in the contractile and lusitropic condition. Prior to the changes in the contractile and lusitropic status, the following measurements were obtained: LV Tei index, $0.48 \pm 0.11$; interval a, $323 \pm 39$ msec; ET, $218 \pm 16$ msec; ICT + IRT, $105 \pm 27$ msec; E, $57.7 \pm 14.8$ cm/sec; A, $20.8 \pm 13.3$ cm/sec; and E/A, $3.8 \pm 2.3$.

The LV Tei index was significantly correlated with the LV peak +dP/dt ($r = -0.89$, Fig. 2–1) and LV peak –dP/dt ($r = 0.87$, Fig. 2–2). Peak E was significantly correlated with the LV peak –dP/dt ($r = 0.76$). In contrast, there were no significant correlations between either peak A or E/A and the LV peak –dP/dt.

**Conventional echocardiographic indices in experiment 2:** The conventional echocardiographic indices are summarized in Table 1. The LV Tei index and other echocardiographic parameters were measurable in all the 198 dogs. No significant differences were found in HR and BW among the NYHA classes. However, there were significant differences in age between the normal group and NYHA group I, II, and III.

There were no significant differences in FS among the 5 groups. LA/Ao and peak E significantly increased with the progression of clinical signs due to MR, with the exception that there was no significant difference between the normal group and NYHA I. E/A was significantly decreased in NYHA II.

**Tei index in experiment 2:** Table 2 shows the LV Tei index and other Doppler time intervals. The LV Tei index significantly increased with the progression of clinical signs (NYHA class) due to MR (NYHA I, $0.47 \pm 0.16$; NYHA II, $0.59 \pm 0.17$; NYHA III, $0.68 \pm 0.19$; NYHA IV, $0.94 \pm 0.41$) compared with the normal group ($0.38 \pm 0.10$, Fig. 3). However, the LV Tei index for NYHA I was not significantly different from that for the normal group. The ET was significantly shorter in the dogs with symptomatic MR compared with the normal group and the dogs with asymptomatic MR. The ICT + IRT was significantly longer in the dogs with MR when compared with the normal group. There were no significant differences in interval a among the 5 groups.

**Relationship between echocardiographic indices and HR, BW, and age in experiment 2:** In the normal group, there were no significant correlations between the LV Tei index and either HR (Fig. 4–1, Table 3) or BW (Fig. 4–2). However, the LV Tei index was significantly correlated with age.

**DISCUSSION**

In human medicine, the LV Tei index has been demonstrated to be correlated with both the systolic (peak +dP/dt) and the diastolic function (peak –dP/dt and Tau) in patients with DCM or ischemic heart diseases [28]. In experiment 1 of the present study, the LV Tei index was demonstrated to reflect the LV systolic and diastolic functions in anesthetized healthy dogs. Thus, as in humans, the LV Tei index has the potential for evaluating comprehensive cardiac function in dogs.

In experiment 2, the LV Tei index significantly increased with the progression of clinical signs due to MR compared with the normal group. The elevation of the LV Tei index associated with NYHA class was thought to depend largely
on the shortening of the ET in addition to the slightly elongation of the ICT + IRT. The ET was also shown to change with the progression of NYHA class; however, the ET was significantly correlated with HR. The alteration of ET associated with HR might be attributable to the sympathetic activation and excitement. In contrast, the LV Tei index did not significantly changed by HR in experiment 2. The LV Tei index is thought to become the better echocardiographic index compared with the ET.

The previous report on the LV Tei index in human cases with MR revealed that the LV Tei index did not increase in organic MR (mainly mitral valve prolapse) without LV dysfunction attributable to LV dilation (volume-overload), in contrast to secondary (functional) MR with LV dysfunction.

Table 1. Characteristics and the values of conventional echocardiographic measurements in the normal group (n=125) and dogs with MR (n=73)

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>NYHA I</th>
<th>NYHA II</th>
<th>NYHA III</th>
<th>NYHA IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>125</td>
<td>29</td>
<td>26</td>
<td>11</td>
<td>7</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>114 ± 24</td>
<td>116 ± 23</td>
<td>111 ± 22</td>
<td>128 ± 29</td>
<td>146 ± 30</td>
</tr>
<tr>
<td>BW (kg)</td>
<td>11.1 ± 10.3</td>
<td>8.6 ± 4.7</td>
<td>9.1 ± 7.5</td>
<td>6.8 ± 3.0</td>
<td>9.5 ± 10.4</td>
</tr>
<tr>
<td>Age (years)</td>
<td>5.4 ± 3.9</td>
<td>10.6 ± 3.0</td>
<td>11.4 ± 2.8</td>
<td>10.9 ± 3.6</td>
<td>9.2 ± 5.0</td>
</tr>
<tr>
<td>FS (%)</td>
<td>39 ± 7</td>
<td>39 ± 6</td>
<td>42 ± 9</td>
<td>45 ± 5</td>
<td>43 ± 11</td>
</tr>
<tr>
<td>LA/Ao</td>
<td>1.26 ± 0.13</td>
<td>1.26 ± 0.11</td>
<td>1.54 ± 0.21</td>
<td>1.65 ± 0.37</td>
<td>2.11 ± 0.45</td>
</tr>
<tr>
<td>E (cm/sec)</td>
<td>65 ± 13</td>
<td>58 ± 12</td>
<td>74 ± 25</td>
<td>85 ± 27</td>
<td>122 ± 29</td>
</tr>
<tr>
<td>E/A</td>
<td>1.3 ± 0.4</td>
<td>1.1 ± 0.3</td>
<td>1.0 ± 0.3</td>
<td>1.1 ± 0.5</td>
<td>1.4 ± 0.4</td>
</tr>
</tbody>
</table>

a) Significant difference with respect to the normal group. b) Significant difference with respect to NYHA I. c) Significant difference with respect to NYHA II. d) Significant difference with respect to NYHA III. HR, heart rate; BW, body weight; FS, fractional shortening; LA/Ao, the ratio of left atrial to aortic diameters; E, peak early diastolic wave velocity of left ventricular inflow; E/A, the ratio of E to peak atrial contraction wave velocity.

Table 2. Characteristics and the values of echocardiographic measurements in the normal group (n=125) and dogs with MR (n=73)

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>NYHA I</th>
<th>NYHA II</th>
<th>NYHA III</th>
<th>NYHA IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV Tei index</td>
<td>0.38 ± 0.10</td>
<td>0.47 ± 0.16</td>
<td>0.59 ± 0.17</td>
<td>0.68 ± 0.19</td>
<td>0.94 ± 0.41</td>
</tr>
<tr>
<td>Interval a (ms)</td>
<td>236 ± 30</td>
<td>254 ± 30</td>
<td>250 ± 28</td>
<td>246 ± 41</td>
<td>233 ± 26</td>
</tr>
<tr>
<td>ET (ms)</td>
<td>171 ± 20</td>
<td>174 ± 20</td>
<td>159 ± 24</td>
<td>150 ± 36</td>
<td>126 ± 36</td>
</tr>
<tr>
<td>ICT + IRT (ms)</td>
<td>64 ± 17</td>
<td>80 ± 26</td>
<td>91 ± 19</td>
<td>96 ± 15</td>
<td>107 ± 15</td>
</tr>
</tbody>
</table>

a) Significant difference with respect to the normal group. b) Significant difference with respect to NYHA I. c) Significant difference with respect to NYHA II. d) Significant difference with respect to NYHA III. ET, ejection time; ICT, isovolumetric contraction time; IRT, isovolumetric relaxation time.

Fig. 3. The LV Tei index in dogs with MR. The LV Tei index significantly increased in dogs with mitral regurgitation (MR) (NYHA II, III, and IV) when compared with normal dogs. The circles and bars represent the mean ± SD.

Fig. 4–1. Relationship between the LV Tei index and heart rate in normal dogs. The LV Tei index was not significantly correlated with heart rate (HR). ns, no significant.
On the other hand, the LV Tei index in human patients with organic MR has been reported to exhibit a slight but significant increase in comparison with that in normal subjects [14]. In addition, a decrease in the ET was reported both in human patients with MR and in canine MR models due to the potential inability of the ventricle to maintain ejection [8, 19]. In experiment 2, the elevation of the LV Tei index in dogs with MR might reflect LV dysfunction, in particular systolic dysfunction due to LV volume overload. Therefore, this index is potentially a better indicator of systolic function compared to FS, which exhibited no difference among the groups in experiment 2. However, it was also shown that human MR patients with a short ET had a low forward stroke index and forward ejection fraction, a large MR flow volume, and a high regurgitant fraction [16]. Therefore, the elevation of the LV Tei index might reflect not only LV systolic dysfunction but also the severity of MR and the decrement of the forward stroke volume. Further studies are required to define the influence of the afterload and preload on the LV Tei index in dogs with MR.

The systolic dysfunction due to LV volume overload demonstrated in humans has also been reported in canine MR models [15, 20, 30]. Moreover, the systolic dysfunctions observed both in vivo and in vitro were associated with clinical signs in canine MR models [30]. Therefore, systolic dysfunction has the potential to affect clinical signs and prognosis; consequently, it is important to evaluate the cardiac condition, including systolic function, using the LV Tei index in dogs with MR.

In experiment 2, the LV Tei index in the normal group was shown to be an independent indicator of HR and BW. In humans, the LV Tei index has been reported to be relatively uninfluenced by HR [2, 22, 26, 27]. However, the LV Tei index has a major limitation; this relates to the inability to obtain simultaneous measurements for both the LV inflow and outflow using Doppler echocardiography. Therefore, we had no alternative but to exclude the cases of VPC and AV block in experiment 2. Additionally, in clinical cases, some patients with MR may have respiratory arrhythmia. In experiment 2, the influence of the respiratory arrhythmia could be attenuated due to less than 10% of the difference of precedence R-R intervals on ECG in the measurements between LV inflow and outflow. This method is thought to be convenient and clinically useful in reducing the intrinsic error associated with changes in these intervals.

In experiment 2, the LV Tei index significantly increased with age. The LV Tei index has been demonstrated to be relatively uninfluenced by age in young patients (3 to 18 years) [7, 9]. However, there has been no report describing an association between the LV Tei index and age in older human patients. However, an age-related LV relaxation abnormality was reported in senescent beagles [13]. Therefore, the mild elevation of the LV Tei index in addition to the decrease of E/A in old dogs without cardiac disease may indicate a potential depression of LV diastolic function with age. Further investigations are required to clarify the age-related change of cardiac function in canine patients.

In conclusion, our study demonstrated that the LV Tei index was measurable in dogs. Additionally, the index was significantly inversely correlated with age in normal dogs. The LV Tei index was not significantly correlated with body weight (BW). ns, no significant.
not influenced by HR and BW. The LV Tei index significantly increased in dogs with symptomatic MR. In particular, the elevation of the LV Tei index due to shortening of the ET in dogs with symptomatic MR may suggest LV systolic dysfunction and the decrement of forward stroke volume.

REFERENCES


