pISSN 1598-298X / eISSN 2384-0749
J Vet Clin 32(2) : 162-167 (2015)
http://dx.doi.org/10.17555/jvc.2015.04.32.2.162

Journal of Veterinary Clinics
www.ksvc.or.kr

Evaluation of Left Ventricular Tei Index in the Normal Dogs and Dogs with Mitral Valve Degenerative Disease

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(Accepted: April 10, 2015)

Abstract : Tei-index has been reported as one of reliable echocardiographic factors for evaluating cardiac function in human and small animals. In this study, Tei-index were measured and evaluated with other echocardiographic parameters in normal thirteen beagle dogs and thirty-one dogs with mitral valve degeneration. Normal range of Tei index with tissue Doppler obtained at septum and left ventricular free wall was 0.58 ± 0.07 and 0.60 ± 0.07, respectively. The values between septum and left ventricular free wall did not show significant difference. Tissue Doppler derived tei index showed better reproducibility and significantly lower values than the results obtained by pulsed wave Doppler. Tei index obtained in either method increased with the progression of clinical signs. Therefore, the increase of Tei index in dogs with mitral regurgitation is thought to be an useful factor reflecting left ventricular dysfunction.

Key words **:** left ventricular function, echocardiography, tissue Doppler, Tei index, dog.

Introduction

Left heart volume overload usually occurs depending on the progression of mitral regurgitation in dogs with mitral valve degeneration. As a result, left ventricular (LV) eccentric hypertrophy occurs and leads to LV dysfunction in advanced stage of mitral valve disease (1). Echocardiography is the noninvasive diagnostic method that provides variety of information of left ventricular systolic and diastolic function in veterinary and human medicine (7). Fractional shortening (FS), early diastolic mitral valve inflow (E wave) and ratio of early (E) to late (A) diastolic mitral valve inflow (E/A ratio) have been most commonly used to assess myocardial function in the dog by conventional echocardiography. However, these parameters have the limitation to reflect exactly cardiac function. One important limitation of FS is that depends on cardiac loading condition other than intrinsic myocardial contractility (7). Disadvantage of E wave and E/A ratio, used to assess the diastolic function, is that they cannot differentiate normal from pseudonormal state (7,17).

The myocardial performance index (MPI), also called Tei index, is another echocardiographic parameter for the assessment of global myocardial function and includes both diastolic and systolic time intervals (19). The index defined as the sum of isovolumic contraction time (IVCT) and isovolumic relaxation time (IVRT) divided by ejection time (ET). Tei index can be calculated from pulsed-wave Doppler (PW) and tissue Doppler image (TDI). The advantage of the Tei index using TDI is that the same cardiac cycle can be used since TDI records myocardial motion during systole and diastole (8). The Tei index has been known as a simple and reproducible technique and relatively independent of heart rate (HR), age, and systemic blood pressure in human medicine (8,13). In addition, this index can provide prognostic information in patients with valvular aortic stenosis, dilated cardiomyopathy and mitral regurgitation in men (3,9,21,24). In veterinary medicine, it was reported that the LV Tei index derived from PW significantly increased with the progression of clinical signs in dogs with mitral regurgitation (MR) (22). However, to our knowledge, there are no studies that assessed Tei index by TDI in clinical cases of canine MR.

The purposes of this study were to determine the normal reference values of LV Tei index and evaluate the reproducibility by tissue Doppler method. In addition, this study is aimed to evaluate the changes of LV Tei index and the correlation with other echocardiographic parameters in dogs with mitral valve degeneration disease (MVDD).

Materials and Methods

Animals

Thirteen beagles weighing from 7.0 to 11.5 kg were used for the evaluation of normal Tei index in this study. A physical examination, complete blood count, serum biochemistry, electrocardiogram, thoracic radiography, and echocardiography were performed to evaluate the health status on all dogs. Additionally, a total of 32 dogs referred to Veterinary Medical Teaching Hospital, Chungnam National University with evidence of MVDD by echocardiography were also included. These dogs also underwent a physical examination, complete blood count, serum biochemistry, electrocardiogram,

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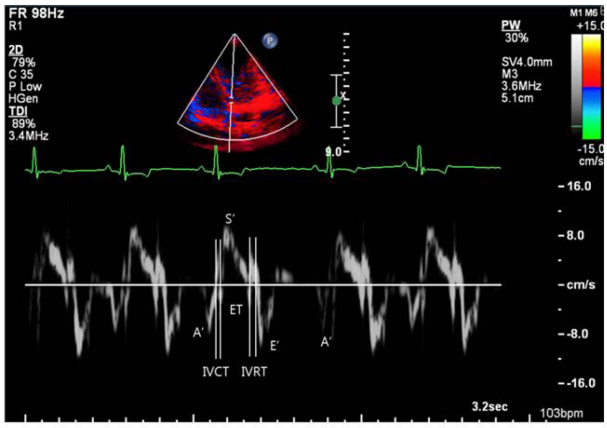
thoracic radiography, and echocardiography. All dogs were diagnosed as MVDD by echocardiography. The dogs with MVDD were divided into 3 groups based on the International small animal cardiac health council (ISACHC) classification. This study was approved by the Institutional Laboratory Animal Care and Use Committee of Chungnam National University.

Echocardiography

Echocardiographic examinations were performed without sedation or anesthesia with ultrasonographic unit (IU22®, Phillips, Bothwell, USA) in normal beagles and dogs with MR. Values for each parameter were obtained by averaging measurements from three consecutive cardiac cycles. M-mode examination was performed at the papillary muscle level of the right parasternal short axis view, and fractional shortening was obtained.

The pulsed Doppler gate was placed at the tips of the mitral leaflets to obtain transmitral inflow profiles from the left apical four-chamber view. For PW examinations, mitral inflow velocities were recorded from the apical four chamber view by placing the 2-mm pulsed-wave Doppler sample volume at the tip of mitral leaflets. The interval of mitral closure to opening time (MCO) was measured between from end to onset of the mitral inflow. Then a pulsed Doppler study of LV outflow was made placing the sample volume just below the aortic valve in the LV outflow view. ET was measured from the onset to the end of LV outflow. Tei index was calculated by the following formula: (MCO-ET)/ET (Fig 1). Mitral valve inflow velocity for E, A and ratio of between E/A ratio were also recorded.

TDI was performed by activating the TDI function in the same echocardiographic setting. A 2-mm site of sample volume was used. In the apical four-chamber view, the TDI cursor was placed at the septal and lateral side of the mitral annulus. The wall filter setting was adjusted to exclude high frequency blood flow signals and a Doppler velocity range of −20 cm/s to 20 cm/s was used. The systolic velocity duration was measured as ET, and the time between the end of the systolic velocity and the beginning of early diastolic velocity as IVRT, and the time between the end of the late diastolic velocity and the beginning of systolic velocity as IVCT. Tei index was calculated as the sum of IVRT and IVCT divided by ET (19). In addition, myocardial velocity for S', E' and A' were measured, and then E/E' and E/IVRT ratio were calculated.



$$\text{Tei index} = \frac{\text{IVCT} + \text{IVRT}}{\text{ET}}$$

Fig 1. Tissue Doppler time intervals and myocardial velocity were measured from mitral anuulus of setum and lateral wall. ET, ejection time; IVCT, isovolumic contraction time; IVRT, isovolumic relaxation time; S', myocardial velocity of systole; E', myocardial velocity of early diastole, A', myocardial velocity of late diastole.

Reproducibility

Intraobserver variability was assessed in thirteen dogs of normal group by repeating the measurements on 7 days apart by the same observer under the same basal conditions. To test the interobserver variability, the measurements were performed by two examiners who were unaware of the results of the first examination. Variability was calculated as the mean percentage error, derived as the difference between the two sets of measurements, divided by the mean observations. Interobserver and intraobserver reliability were expressed as intraclass correlation coefficient (ICC) (14). An ICC < 0.40 is considered as poor agreement, 0.41-0.59 as fair agreement, 0.60-0.74 as good agreement and 0.75-1.00 as excellent agreement.

Statistical analysis

All data were expressed as mean value ± SD. Differences between TDI-Tei index and PW-Tei index were evaluated by paired *t*-test. Comparisons between groups of parametric values were tested by ANOVA. The Pearson correlation coefficient was used for analysis of linear correlation between echocardiographic values. Statistical signification was defined as $p < 0.05$.

Results

In the MVDD patients, Maltese (25%) and Shih-tzu (25%) were the most common breeds, followed by Schnauzer (12.5%), Yorkshire Terrier (9%), Miniature Poodle (9%), and Pomeranian (6%), and each one of Cocker Spaniel, Chihuahua, Miniature Pinscher, and mixed breed dog were included. Based on the ISACHC classification, twelve dogs were included in Class I, another twelve dogs in Class II, and eight dogs in Class III. Clinical features of normal dogs and dogs with MVDD are summarized in Table 1. The dogs in MVDD

Table 1. Characteristics in the normal and dogs with MVDD

	Normal	MVDD groups		
		Class I	Class II	Class III
Number	13	12	12	7
Age (years)	2.2 ± 1.5	10.9 ± 2.7[a)]	11.3 ± 2.3[a)]	13.0 ± 1.6[a)]
BW	8.5 ± 1.5	6.0 ± 1.8[a)]	5.1 ± 2.4[a)]	5.1 ± 1.0[a)]
HR	94 ± 18	124 ± 26[a)]	124 ± 20[a)]	157 ± 37[a,b,c)]

[a)]Significant difference with respect to the normal group. [b)]Significant difference with respect to Class I. [c)]Significant difference with respect to Class II. BW, body weight; HR, heart rate

Table 2. LV Tei index values in the normal and dogs with MVDD

Methods		Normal	MMVD group		
			Class I	Class II	Class III
Tissue Doppler	Lateral wall	0.58 ± 0.07	0.58 ± 0.06	0.70 ± 0.10[a,b)]	0.96 ± 0.15[a,b,c)]
	Septum	0.60 ± 0.07	0.57 ± 0.06	0.67 ± 0.08[a,b)]	0.86 ± 0.08[a,b,c)]
Pulsed-wave Doppler		0.52 ± 0.04	0.55 ± 0.05	0.68 ± 0.07[a,b)]	0.88 ± 0.13[a,b,c)]

[a)]Significant difference with respect to the normal group. [b)]Significant difference with respect to Class I. [c)]Significant difference with respect to Class II.

group were older than the normal group. Heart rate significantly increased as clinical symptoms become severe ($p < 0.05$).

Tei index of lateral wall and septum derived from TDI in normal 13 Beagle dogs were 0.58 ± 0.07 and 0.60 ± 0.07, respectively (Table 2). Tei index from TDI were higher than the value of 0.52 ± 0.04 by PW method ($p < 0.001$). There were no significant differences between the values of TDI Tei index measured from the lateral wall and septum. All cardiac measurements were independent from body weight (BW). Several time intervals such as IVRT ($p = 0.006$) and ET ($p = 0.03$) were significantly associated with heart rate (HR). Tei index, conversely, was relatively independent from the HR although it has been calculated from the time intervals ($p = 0.23$).

The strength of the agreement in the inter- and intraobserver variability is shown in Table 3. Overall intraobserver ICC values but A' velocity and A wave were good or excellent, indicating an acceptable level of intraobserver agreement. For the Tei index of TDI at the lateral wall, the interobserver ICC value of 0.80 was excellent, and good for the Tei index of TDI at the septum among the three researchers. However, the interobserver ICC values for the measurements of some echocardiographic factors (velocity of A' and E' and A wave) were poor, and several factors (ET of TDI septum and PW, E wave, and LV Tei index of PW method) were fair. Tei index and Doppler time intervals of MVDD patients were shown in Table 2 and 4. LV Tei index obtained in either method increased with the progression of clinical signs, and the values in class II and class III was significantly higher than those of normal group and class I. However, Tei index of Class I was not significantly different from that for the normal group. The ET derived from either method and MCO were significantly shortened with the increase of severity of the clinical signs. There was not significant difference in IVCT between normal and MVDD group, and among three classes of the MVDD group. The IVRT was significantly shortened in the Class I compared with normal, but increased in class III.

Table 3. Intraclass correlation coefficient (ICC) for the inter- and intra-observer analysis for each echocardiographic parameter

Contents			Intra-observer ICC	Inter-observer ICC
Tissue Doppler	Lateral wall	IVRT (ms)	0.87	0.74
		IVCT (ms)	0.79	0.71
		ET (ms)	0.97	0.72
		LV Tei index	0.92	0.80
		S' (cm/s)	0.89	0.73
		E' (cm/s)	0.87	0.79
		A' (cm/s)	0.37	−0.02
	Septum	IVRT (ms)	0.84	0.71
		IVCT (ms)	0.81	0.78
		ET (ms)	0.92	0.58
		LV Tei index	0.80	0.74
		S' (cm/s)	0.72	0.53
		E' (cm/s)	0.79	0.40
		A' (cm/s)	0.29	0.17
Pulsed-wave Doppler		MCO (ms)	0.95	0.66
		ET (ms)	0.96	0.43
		E wave (cm/s)	0.64	0.52
		A wave (cm/s)	0.50	−0.13
		LV Tei index	0.68	0.52
E/E'			0.69	0.32
E/IVRT			0.75	0.72

Other cardiac parameters were summarized in Table 5. Fractional shortening (FS) was significantly increased in MVDD groups compared to normal group, but there were no remarkable changes among MVDD groups. E wave and E/IVRT ratio were significantly higher in Class III. E/A ratio was decreased in Class I and II than normal group, but significantly increased in Class III. E/E' ratio was measured more higher in MVDD than normal group, and it was especially significantly higher in Class III.

The correlation between Tei index and other echocardiographic parameters are shown in Table 6. Tei index obtained by either method was partially related to E, E/A ratio and E/E' ratio.

Discussion

Several studies have previously demonstrated that systolic and diastolic time intervals are closely related to either systolic or diastolic left ventricular (LV) performance (3). Tei reported pulsed wave Doppler derived index, which combines systolic and diastolic time intervals (19). Since then, Tei index could be measured by tissue Doppler echocardiography, which is a new ultrasound technique, and it correlated well with conventional Tei index in normal and patient groups (21).

In human study of heart failure patients, TDI-Tei index had a stronger correlation with NYHA functional classes and

Table 4. LV echocardiographic measurements obtained from normal and dogs with MVDD

Methods		Time intervals	Normal	MMVD group		
				Class I	Class II	Class III
Tissue Doppler	Lateral wall	IVRT (ms)	61 ± 10	50 ± 12[a)]	55 ± 14	64 ± 12[b)]
		IVCT (ms)	47 ± 10	41 ± 6	45 ± 15	41 ± 11
		ET (ms)	182 ± 18	159 ± 17[a)]	139 ± 13[a,b)]	112 ± 17[a,b,c)]
	Septum	IVRT (ms)	63 ± 13	50 ± 14[a)]	55 ± 15	63 ± 10[b)]
		IVCT (ms)	46 ± 9	42 ± 10	43 ± 15	41 ± 11
		ET (ms)	180 ± 16	161 ± 14[a)]	141 ± 14[a,b)]	121 ± 13[a,b,c)]
Pulsed-wave Doppler		MCO (ms)	268 ± 29	238 ± 26[a)]	222 ± 31[a)]	205 ± 37[a,b)]
		ET (ms)	183 ± 18	153 ± 16[a)]	131 ± 18[a,b)]	108 ± 14[a,b,c)]

[a)]Significant difference with respect to the normal group. [b)]Significant difference with respect to Class I. [c)]Significant difference with respect to Class II.

Table 6. Correlation between Tei index and cardiac parameters

		FS	E	E/A	E/E'	E/IVRT
Tissue Doppler Tei index	Lateral wall	$r = 0.16$ $p = 0.30$	$r = 0.49$** $p = 0.001$	$r = 0.39$** $p = 0.009$	$r = 0.42$** $p = 0.004$	$r = 0.01$ $p = 0.52$
	Septum	$r = 0.10$ $p = 0.52$	$r = 0.35$* $p = 0.02$	$r = 0.32$* $p = 0.044$	$r = 0.26$ $p = 0.09$	$r = 0.001$ $p = 0.99$
PW Tei index		$r = 0.30$ $p = 0.06$	$r = 0.43$** $p = 0.004$	$r = 0.15$ $p = 0.34$	$r = 0.33$* $p = 0.03$	$r = 0.18$ $p = 0.25$

*$p < 0.05$, **$p < 0.01$

ejection fraction than did PW-Tei index (3,9). In addition, TDI-Tei index had higher specificity, sensitivity, negative and positive predictive value, and diagnostic accuracy in congestive heart failure (9). In patients with isolated organic mitral regurgitation, the TDI-Tei is found to correlate well with ejection fraction and plasma brain natriuretic peptide (BNP) levels, and may be considered as a new echocardiographic parameter for the assessment of global ventricular function during follow up of patient with mitral regurgitation (12).

In small animal medicine, there are few studies about LV TDI-Tei index. Baseline of LV TDI-Tei index of dogs was investigated in one study (5), where there might be some problems in accepting the normal value of Tei index because it was measured under anesthesia. In the previous study about in which effect of isoflurane on Tei index in dogs, Tei index had higher values in dogs under anesthesia than in conscious dogs. (18). Compared to other study (11), there was no difference between Tei index derived from lateral wall and ventricular septum unlike the previous study (11). In addition, PW-Tei index was significantly low compared to TDI-Tei index in both studies. According to the researches of TDI-Tei index of healthy subjects of human medicine, it was known that there are no differences between either by lateral wall or septum (16,20). Several studies of human medicine demonstrated that the TDI-Tei index correlates well with the PW-Tei index (21). However, another studies showed that the agreement between TDI-Tei index and the PW-Tei index was not good, because systolic intervals are longer and diastolic intervals are shorter when measured with TDI. The disagreement exists in healthy people, and it was increased on patients with prior myocardial infarction (9,16).

Table 5. Other cardiac parameters obtained from normal and dog with MVDD

	Normal	MVDD group		
		Class I	Class II	Class III
FS	39 ± 5	51 ± 7[a)]	53 ± 8[a)]	51 ± 8[a)]
E wave	81 ± 19	91 ± 25	104 ± 22	142 ± 47[a)]
E/A	1.8 ± 0.5	1.2 ± 0.4	1.3 ± 0.4	2.4 ± 1.4[b,c)]
E/E'	7.3 ± 1.9	10.8 ± 3.0[a)]	10.6 ± 3.3[a)]	15.3 ± 6.3[a,b,c)]
E/IVRT	1.4 ± 0.6	2.0 ± 0.8	2.1 ± 0.9	2.4 ± 1.0[a)]

[a)]Significant difference with respect to the normal group. [b)]Significant difference with respect to Class I. [c)]Significant difference with respect to Class II. FS, fractional shortening; E wave, early diastolic mitral valve inflow; E/A ratio, ratio between early (E) and lateral (A) mitral valve inflow; E/E', ratio of between early mitral valve inflow and early diastolic myocardial velocity; E/IVRT, ratio of between early mitral valve inflow and isovolumic relaxation time.

The results of the present study in which inter- and intraobserver variability, PW-Tei index showed relatively low agreement compared to TDI-Tei index measured either at lateral wall or septum. The inability to measure the mitral inflow and the LV outflow at the same time is a major limitation of PW-Tei index, so heart rate fluctuation could cause the variation of Tei index. The TDI can simultaneously record systolic and diastolic mitral annular velocities. Thus, the TDI-Tei index may reduce inaccuracy might be caused by HR change during examination, and has practical advantages over the PW-Tei index (8).

In this study, Tei index significantly increased with the progression of clinical signs in MVDD groups. The increase of

Tei index associated with ISACHC class was thought to depend on the shortening of the ET. The ET was also presented to strongly correlation with clinical signs. Decrease in the ET was reported both in human and dogs with MR due to the potential inability of the ventricle to maintain ejection (3,22). However, the ET was significantly affected ($r = -0.43$, $p < 0.01$) by heart rate unlike the Tei index ($r = 0.29$ p = ns). Therefore, the LV Tei index is thought the better echocardiographic parameter than ET.

In this study, the increase of the LV Tei index in dogs with MVDD might reflect LV dysfunction, in particular systolic dysfunction due to LV volume overload. FS is the most commonly used to assess systolic myocardial function in the dog by conventional echocardiography (7). However, FS depends on several factors other than intrinsic myocardial contractility, such as preload and afterload. MVDD is characterized by an increased preload due to MR. In addition, mitral valve lesion create a new pathologic pathway of low resistance for ejection of blood from the LV (7). Typically, MVDD progression is mainly characterized by a LV hyperdynamic state with elevated FS due to combined volume overload. Therefore, normal values for FS in dogs with severe MR suggest systolic dysfunction (7). However, early detection of systolic dysfunction through a FS is unclear. In this study, Tei index was no significantly different between in normal group and asymptomatic patient group (Class I) and significantly increased with progression of clinical sings in dogs with MVDD. Therefore, Tei index is better indicator of systolic dysfunction compared to FS, which exhibited no difference among the MVDD groups.

In human medicine, increase of IVRT and Tei index (with normal values of IVCT) can be considered as a useful and reliable tool to identify LV diastolic dysfunction (4). However, in this study, IVRT decrease in Class I and Class II groups than normal group in spite of increase of other diastolic index such as E/E' ratio and E/IVRT ratio. The reason was that the IVRT was significantly affected ($r = -0.32$, $p = 0.04$) in heart rate, like other time intervals. Some of the patients with Class III, IVRT decreased, and Tei index closed to normal value (IVRT = 38ms, Tei index = 0.62). However, E/E' ratio and E/IVRT highly increased (E/E' ratio = 15.9, E/IVRT = 3.94). The reason was that IVRT decrease in end-stage diastolic dysfunction. In addition, in severe MR, IVCT and IVRT can be extremely short or non-existent due to the presence of an opening in the mitral valve area (7). Therefore, in that case, the Tei index seems to be inaccurate for assessing myocardial function.

E/E' ratio and E/IVRT have been shown to be correlated experimentally with LA pressure and LV end-diastolic pressure in the dog (1,7). An E/E' cut-off value of 13 could be used to identify congestive heart failure (22), and an E/IVRT ratio > 2.5 and an IVRT < 45ms in dogs with moderate to severe chronic MR are usually associated with the presence of congestive heart failure in thoracic radiographs (17). Therefore, in patients with severe myocardial dysfunction, Tei index must be interpreted together with these other parameters.

A major limitation of this study is that the number of experimental animals was small, and further study is required in a larger patient population. Moreover, normal group was composed only Beagle dogs. Difference in the Tei index between various dog breeds and age effect have not been exactly known. Another limitation of this study, we did not investigate in patients with or without medical treatment. Medications could play a role in improving ejection fraction by decrement of afterload, so it is expected to affect value of Tei index.

Tei index is a simple and reproducible measure of tissue Doppler or pulsed wave Doppler examinations, and is independent to heart rate and body weight. Especially, TDI-Tei index showed relatively good reproducibility compared with PW-Tei index. The Tei index significantly increased with severity of clinical signs in dogs with MVDD. In addition, in this study, Tei index is best indicator of myocardial function in MVDD compared to FS, E/E' and E/IVRT. Therefore, Tei index reflects global myocardial performance, and seems to be a useful predictor of clinical outcome in dogs with mitral valve degeneration disease.

Acknowledgment

This work was supported by research fund of Chungnam National University.

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정상 및 퇴행성이첨판 질환이 있는 개에서 조직도플러를 통한 좌심실 Tei index 의 평가

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요 약 : 좌심실의 용적과부하와 심할 경우 심근 기능부전을 일으키는 질병에서 Tei index 는 심근기능을 평가하는데 있어 비교적 측정이 쉽고 재현율이 양호하다고 보고된 심초음파 측정 요소이다. 본 연구에서는 정상 및 퇴행성 이첨판 질환이 있는 개에서 조직도플러와 펄스파 도플러를 통해 Tei index 값을 측정하고, 다른 초음파평가지표와 비교평가하였다. 정상 개에서 Tei index 측정을 위해 심혈관계에 이상이 없는 13마리의 비글견을 사용하였으며, 이첨판 역류를 진단받은 환자 31마리를 환자군으로 하여 각각의 환자는 임상증상에 따라 세 개의 그룹으로 나뉘어 각 측정치를 비교하였다. 본 실험 결과에서 대부분의 측정항목들이 좋은 신뢰도를 보였으며, Tei index 의 경우 조직도플러를 통한 Tei index 가 펄스파 도플러에 비해 좀 더 높은 신뢰도를 나타내었다. 본 실험에서 정상 개에서 Tei index 는 조직도플러의 심실외벽과 중격에서 각각 0.58 ± 0.07, 0.60 ± 0.07로 측정되었다. 조직도플러 검사 결과 중격과 좌심실벽 지점간에는 Tei index 의 차이가 나타나지 않았다. 펄스파도플러를 통해 측정한 Tei index 는 조직도플러를 통해 측정한 Tei index 에 비해 유의성 있게 낮게 측정되었다. 정상 및 퇴행성이첨판 질환이 있는 환자군에서 Tei index 는 두 가지 측정 방식 모두에서 이첨판 역류의 임상증상에 따라 그룹별로 유의적으로 증가하는 것으로 나타났다. 따라서, Tei-index는 이첨판 역류가 있는 개에서 좌심실 기능 저하를 반영하는 유용한 검사 요소로 생각된다.

주요어 : 좌심기능, 심초음파, 조직도플러, Tei-index, 개