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Usefulness of Conventional and Tissue Doppler Echocardiography to Predict Congestive Heart Failure in Dogs with Myxomatous Mitral Valve Disease

J.-H. Kim and H.-M. Park

Background: Systolic and diastolic functions have been evaluated to predict outcome in congestive heart failure (CHF). Recently, tissue Doppler imaging (TDI) has become useful for the estimation of myocardial function in cardiac diseases of humans and animals.

Objective: This study was designed to assess whether myocardial function as assessed by TDI is associated with the occurrence of CHF in dogs with myxomatous mitral valve disease (MMVD) and whether additional information is gained over conventional Doppler variables.

Animals: Forty-one privately owned dogs (15 healthy dogs and 26 dogs with MMVD) were included. Dogs with MMVD were divided into non-CHF (n = 10) and CHF groups (n = 16).

Methods: Conventional echocardiographic examinations were performed. In addition, TDI-derived variables, including radial and longitudinal velocities, strain, and strain rate were assessed.

Results: Several (12 of 47, 26%) conventional and tissue Doppler echocardiography variables were significant predictors of CHF in a univariate analysis ($P < .05$). However, TDI-derived $E/E_{m\ sept}$ was the only load-independent significant predictor of CHF ($P < .05$) after multivariate logistic regression analysis. The $E/E_{m\ sept}$ cut-off value of >18.7 had a sensitivity of 56% and specificity of 90% in predicting CHF in dogs with MMVD.

Conclusions and Clinical Importance: The combination of TDI of the mitral annulus and mitral inflow velocity provided better estimates of diastolic dysfunction in dogs with MMVD and CHF. Additional study is warranted to assess TDI-derived $E/E_{m\ sept}$, an index of diastolic function that could contribute to the management of dogs with MMVD and CHF.

Key words: Acquired valvular disease; Canine; E/E_m; Tissue Doppler imaging.

Myxomatous mitral valve disease (MMVD) is the most commonly acquired cardiac disease in dogs, and severe complications can occur including death caused by congestive heart failure (CHF).[1–3] An accurate diagnosis of CHF in dogs can be difficult because clinical signs are nonspecific.[4] However, left atrial (LA) pressure increases with increasing early diastolic (E) filling rate as CHF progresses and masks early diastolic dysfunction.[3]

Tissue Doppler imaging (TDI) is considered to be more sensitive than conventional echocardiography in human medicine because TDI can detect early myocardial dysfunction in patients with left ventricular (LV) volume overload induced by mitral regurgitation (MR).[5] TDI also has been conducted in healthy dogs, as well as in dogs with different cardiac diseases.[6–9] In small animal medicine, a report using pulsed wave

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Abbreviations:

A	transmitral peak late diastolic velocity
A'	tissue Doppler-derived peak late diastolic velocity
CD	color Doppler
CHF	congestive heart failure
CW	continuous wave
E/A ratio	ratio of the transmitral peak early diastolic velocity to the transmitral peak late diastolic velocity
$E/E_{m\ lat}$	ratio of the transmitral peak early diastolic velocity to the tissue Doppler-derived peak early diastolic velocity at the left ventricular posterior wall's basal segment
$E/E_{m\ sept}$	ratio of the transmitral peak early diastolic velocity to the tissue Doppler-derived peak early diastolic velocity at the interventricular septal basal segment
EF	ejectional fraction
$E_{m\ lat}$	tissue Doppler-derived peak early diastolic velocity at the left ventricular posterior wall's basal segment
$E_{m\ sept}$	tissue Doppler-derived peak early diastolic velocity at the interventricular septal basal segment
E	transmitral peak early diastolic velocity
E'	tissue Doppler-derived peak early diastolic velocity
FS	fractional shortening
IVS	interventricular septum
LA/Ao	ratio of the left atrial diameter to the aortic diameter
LA	left atrium
LVIDd inc%	percentage increase in left ventricular internal diameter in diastole
LVIDs inc%	percentage increase in left ventricular internal diameter in systole
LV	left ventricle
LVPW	left ventricular posterior wall
MMVD	myxomatous mitral valve disease
MR	mitral regurgitation
non-CHF	noncongestive heart failure
PW	pulsed wave
ROI	region of interest
S'	tissue Doppler-derived peak systolic velocity
SR	strain rate
St	strain
TDI	tissue Doppler imaging
TTP	time-to-peak

(PW) TDI demonstrated that the ratio of the transmitral E velocity to the tissue Doppler-derived peak early diastolic velocity (E/E_m) value in dogs with MR and CHF increases significantly in comparison to dogs without CHF.[10] However, diagnostic guidelines for color Doppler (CD) TDI have not been well established in dogs with MMVD and CHF.

Strain (St) and strain rate (SR) imaging are relatively new ultrasound modalities based on TDI that allow a quantitative assessment of segmental myocardial contraction or stretching and the rate of deformation, respectively.[11,12]

The aim of the present study was to compare TDI variables with those of conventional echocardiography in healthy dogs and those with MMVD, with and without CHF. We determined useful conventional and TDI-derived echocardiographic variables of myocardial function including St imaging for diagnosing CHF in dogs with MMVD. Furthermore, we identified a clear cut-off value for these conventional echocardiographic and CD TDI-derived diagnostic variables in dogs with MMVD and CHF.

Materials and Methods

Animals and Procedures

Owners of the dogs gave informed consent before the dogs entered the study, and the Institutional Animal Care and Use committee of Konkuk University approved the study protocol. This study prospectively evaluated 15 healthy dogs and 26 dogs with MMVD that presented to the Konkuk University Veterinary Medical Teaching Hospital between November 2011 and April 2012.

All dogs included in this study underwent history taking, full clinical assessment, hematologic and biochemical profile evaluation, blood pressure,[a] thoracic radiography, electrocardiography (ECG[b]), and echocardiography at the time of presentation. The diagnosis of MMVD was based on guidelines in a previous report.[2]

Diagnosis and Classification of CHF

On the day of presentation, all dogs included in the MMVD group were divided into 4 classes of CHF based on the CHIEF classification,[1,13–15] ranging from A to D based on clinical and diagnostic examinations (Table 1). Class B I and B II were categorized as the non-CHF group (n = 10), and class C II, C III, and D IV were categorized as the CHF group (n = 16) for statistical analyses. Eleven of 16 dogs with CHF had previously received conventional medical treatment with diuretics and angiotensin-converting enzyme inhibitors from referring veterinary clinicians, whereas the remaining 5 had not yet received treatment at the time they were first presented to our hospital.

Conventional Echocardiography and Doppler Examinations

Conventional examinations were performed by a single experienced veterinarian (JK) with an ultrasound unit (HD15[c]) equipped with 3.0–8.5 MHz phased-array transducers. Left ventricular end-diastolic internal dimension (LVIDd) and end-systolic internal dimension (LVIDs) were measured from the M-mode. The percentage increases in LVID during diastole (LVIDd inc%) and systole (LVIDs inc%) were calculated based on guidelines in a previous report.[16] Measurements of the aorta and LA diameter were made by M-mode[17] using a short-axis right-sided parasternal view obtained at the level of the aortic valve. The LV ejection fraction (EF) was calculated by using the Teichholz method and the M-mode images. PW was used to record transmitral flow in the apical 4-chamber view.[18] Mitral inflow measurements included peak early (E) and peak late (A) diastolic velocities and the E/A ratio. CW Doppler was used to analyze the MR jet, and Doppler-derived dP/dt and −dP/dt were determined based on guidelines in a previous report.[19] Briefly, dP/dt was determined by measuring the mean rate of pressure increase of the MR jet between 1 and 3 m/s. Inversely, −dP/dt was determined by measuring the mean rate of pressure decrease of the MR jet between 3 and 1 m/s (Fig 1). All Doppler and M-mode recordings were obtained at a sweep speed of 100 mm/s. The average of 3 measurements was determined for each patient.

TDI and Strain Imaging

Two-dimensional color TDI examinations were performed by a single experienced veterinarian (JK) with the same ultrasound unit used for conventional echocardiography. All TDI examinations were conducted using standard views and techniques according to guidelines in a previous study.[3] The TDI data were analyzed off-line using commercially available software

Table 1. Clinical signs, radiographic signs, and cardiac medications based on CHIEF classification of CHF in dogs with MMVD in this study.

CHF	Study Group	Definition	Clinical Signs	Radiographic Signs	Cardiac Medication
MMVD without CHF (n = 10)	B I (n = 5)	Structural heart disease but no clinical signs of CHF	No	Cardiomegaly is mild or absent	Not receiving treatment
	B II (n = 5)		No	Cardiomegaly is present	Not receiving treatment
MMVD with CHF (n = 16)	C II (n = 5)	Clinical and radiographic signs of left or right CHF	Yes (present or past)	Cardiomegaly, left or right CHF	Receiving treatment for CHF with signs of CHF decreased or absent
	C III (n = 5)		Yes	Cardiomegaly, left or right CHF	Not yet receiving treatment
	D IV (n = 6)	End-stage CHF	Yes	Cardiomegaly, left or right CHF	Receiving standard treatment but refractory end-stage CHF

This scoring system was adopted with some modifications from the method previously described.[1,14–16]

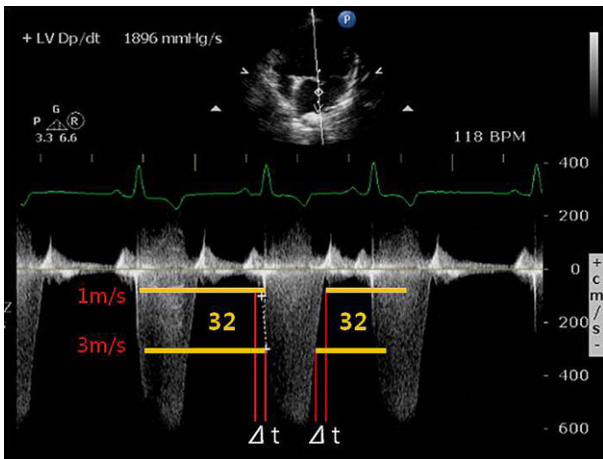CHF, congestive heart failure; MMVD, myxomatous mitral valve disease.

Fig 1. Determination of Doppler-derived dP/dt and −dP/dt from the CW Doppler spectrum of the MR jet obtained from a dog with MR.

(QLAB quantification software).[c] The region of interest (ROI) on the right parasternal short-axis view was positioned between the papillary muscles at a width of 0.5 cm and a length extending from the endocardium to the epicardium for radial LV segment (Fig 2A). In the longitudinal view, the ROI was placed within the interventricular septum (IVS) and LV with a width of 0.5 cm and a length extending from the apical or basal region to one third the length of each wall for the apical and basal segments, respectively (Fig 3A). Peak values of variables during 3–5 consecutive cardiac cycles were averaged.

Radial Motion in the LV. Left ventricle radial velocities were measured from the right parasternal short-axis view at the level of the papillary muscles. Peak velocities were determined in systole (S′) and in early (E′) and late diastole (A′) (Fig 2A). Peak systolic SR and St also were determined (Fig 2B,C). Peak St was measured in systole, and peak SR was determined during systole and during early and late diastole. For measurement of time-to-peak (TTP), the time period from the beginning of the R wave on the ECG to the peak of the waveform was measured in millisecond for systolic velocities, SR, and St.

Longitudinal Motion in the LV and IVS. Left ventricle and IVS longitudinal velocities were assessed in basal and apical segments from the left apical 4-chamber view. Peak velocities were measured in systole and in early and late diastole (Fig 3A). E/E_m was calculated. In addition, SR and St were determined in LV and IVS (Fig 3B,C). Basal peak St was determined in systole and basal peak SR was determined in systole, and early and late diastole. TTP was measured for the systolic velocities SR and St.

Statistical Analysis

Data were analyzed by a software program[d] and expressed as medians and interquartile ranges. The Kruskal-Wallis test was used to compare the 3 groups. When significantly different values ($P < .05$) were observed, Tukey's test using ranks was applied for posthoc analysis to determine which groups were different. The Mann-Whitney *U*-test was used for pair-wise comparisons between groups. The associations between conventional and TDI-derived echocardiographic variables were investigated using Spearman's rank correlation. Logistic regression analysis and a receiver operating characteristic curve were used to determine variables predictive of CHF in dogs with MMVD. A $P < .05$ was considered significant.
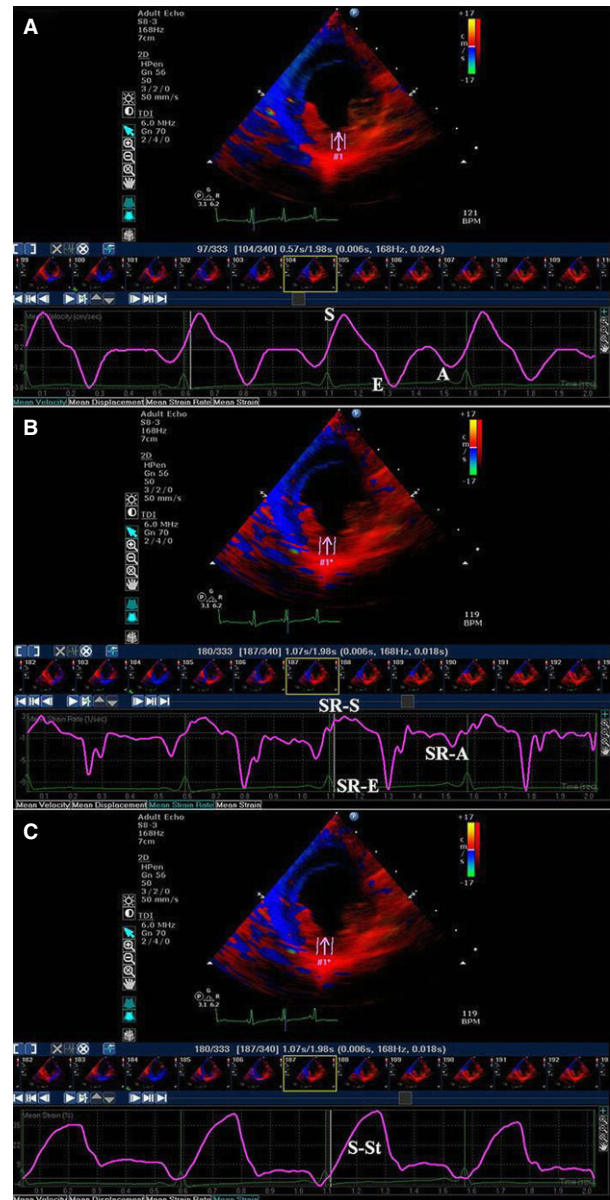

Fig 2. Radial tissue Doppler velocity **(A)**, SR **(B)**, and St **(C)** of the LV wall in a control dog. Note the ROI was positioned between the papillary muscles on the right parasternal short-axis view. S, systolic velocity; E, E wave velocity; A, A wave velocity; SR, strain rate; St, strain; ROI, region of interest; LV, left ventricle.

Results

Study Group Characteristics

Forty-one dogs of 10 different breeds were prospectively enrolled in the study. They were composed of 18 (44%) males and 23 (56%) females. Eleven dogs with MMVD and CHF were treated with furosemide (11) and enalapril (11). No significant differences were observed among the groups for age, body weight, systolic blood pressure, or sex. Heart rates were significantly lower in the control group ($P < .05$) than in the non-CHF and CHF groups (median, 120 bpm for
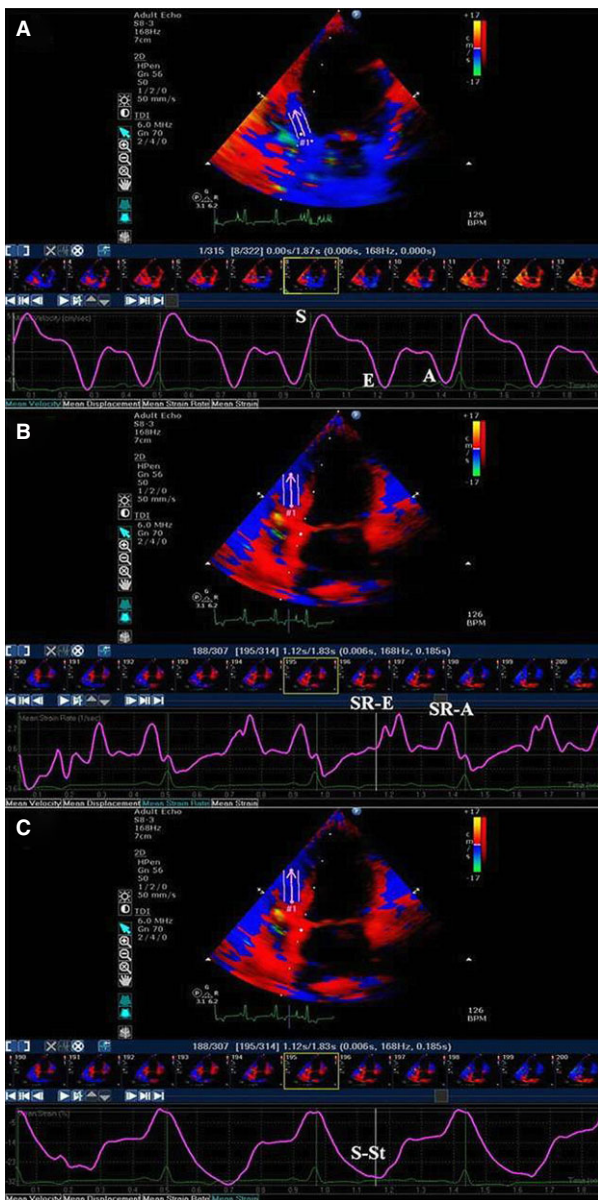
Fig 3. Longitudinal basal tissue Doppler velocities **(A)**, SR **(B)**, and St of the IVS wall in a control dog. Note the ROI was placed on the basal or apical region within the IVS and LV walls on the left parasternal apical 4-chambered view. Arrows represent sample segments located within the LV and IVS walls. SR, strain rate; St, strain; IVS, interventricular septum; ROI, region of interest; LV, left ventricle.

Table 2. Characteristics of the study population.

| Characteristics | Control Dogs (n = 15) | MMVD Dogs (n = 26) | |
		Non-CHF (n = 10)	CHF (n = 16)
Age (years)[a]	9 (5–16)	10 (7–14)	10 (6–15)
Body weight (kg)[a]	4.2 (2.1–25.0)	5.2 (2.3–17.2)	4.0 (1.5–13.0)
Sex (n)[b]			
Male	4	2	3
Castrated male	3	2	4
Female	6	2	2
Spayed female	2	4	7
Breed, n (%)[b]			
Maltese	0	12 (46)	
Yorkshire Terrier	6 (40)	1 (4)	
Shih-tzu	1 (7)	5 (19)	
Mixed	2 (13)	3 (12)	
Schnauzer	1 (7)	3 (12)	
Pomeranian	2 (13)	0 (0)	
Pekinese	1 (7)	1 (4)	
Cocker spaniel	0 (0)	1 (4)	
Chihuahua	1 (7)	0 (0)	
Jindo	1 (7)	0 (0)	
Heart rate (beats/min)[a]	120 (102–162)	150 (108–156)[c]	153 (102–216)[c]
Systolic blood pressure (mmHg)[a]	134 (118–149)	161 (122–173)	149 (132–201)
Medications (n)[b]			
ACEI	0	0	11
Diuretics	0	0	11
Serum sodium (mmol/L)	153 (148–159)	155 (148–159)	153 (142–164)

ACEI, angiotensin-converting enzyme inhibitor.
[a]Data are expressed as median with range.
[b]Data are expressed as the total number of dogs (n).
[c]$P < .05$ versus the control group (Mann-Whitney U-test).

ratio and mitral A velocity were significantly higher in the CHF group than in the non-CHF and control groups ($P < .01$ and $P < .05$, respectively). Lastly, dP/dt, $-$dP/dt, fractional shortening (FS), and EF values were not significantly different among the groups (Table 3).

TDI and Strain Imaging

Peak systolic tissue velocities, St, SR, and systolic St TTP were measured for radial LV motion in the right parasternal short-axis view (Table 4). Radial St was the only variable that differed significantly among groups ($P < .01$).

Peak systolic St and SR and systolic St TTP also were measured for longitudinal motion of the IVS and LV using the left apical 4-chamber view (Tables 5, 6). Nine (9/27 [33%]) variables showed significant differences ($P < .05$) on longitudinal tissue Doppler and strain imaging, and higher values were observed in the CHF group than in the non-CHF and control groups for 4

control group and 150 and 153 bpm for the non-CHF and CHF groups, respectively). Selected characteristics of the study population are shown in Table 2.

Conventional Echocardiography

Of 11 parameters evaluated, 7 were significantly different (7/11 [64%]) among the 3 groups ($P < .05$). The LVIDd inc%, LVIDs inc%, mitral E velocity, and E/A were significantly higher in dogs with MMVD than in control dogs ($P < .01$). Similarly, the LA/Ao

Table 3. Clinical and conventional echocardiography and Doppler variables in dogs with MMVD and healthy controls.

| Variables | Control (n = 15) | Dogs with MMVD | | P-Value |
		Non-CHF (n = 10)	CHF (n = 16)	
Heart rate (beats/min)	120 (102–162)[a]	150 (108–156)[b]	153 (102–216)[b]	<.01**
LVIDd inc%	−2.4 (−5.6 to 1.4)[a]	11.0 (6.4–18.3)[b]	38.5 (31.1–49.1)[b]	<.01**
LVIDs inc%	−16.1 (−19.5 to −3.2)[a]	−5.25 (−6.90 to 2.5)[b]	15.8 (9.0–23.9)[b]	<.01**
LA/Ao	1.1 (1.1–1.2)[a]	1.2 (1.1–1.3)[a]	1.4 (1.3–2.1)[b]	<.01**
FS (%)	42.4 (40.7–45.7)[a]	42.95 (40.4–48.0)[a]	46.9 (42.4–49.5)[a]	.14
EF (%)	70.2 (62.5–79.3)[a]	73.8 (71.9–75.2)[a]	74.0 (70.6–78.5)[a]	.55
Mitral E wave (m/s)	64.2 (54.5–68.5)[a]	73.4 (67.7–95.0)[b]	104.7 (99.3–139.0)[b]	<.01**
Mitral A wave (m/s)	59.0 (57.8–68.5)[a]	68.0 (55.–82.0)[a]	79.6 (65.8–84.5)[b]	.04*
Mitral E/A	1.0 (1.0–1.1)[a]	1.2 (1.1–1.2)[b]	1.6 (1.2–1.9)[b]	<.01**
Velocity of MR jet (m/s)	NA	4.0 (4.0–5.0)[a]	5.0 (5.0–5.0)[b]	<.01**
dP/dt (mmHg/s)	NA	3,141 (2,370–3,168)[a]	2,265 (1,818–2,904)[a]	.09
−dP/dt (mmHg/s)	NA	1,552 (1,034–1,821)[a]	1,051 (846–1,344)[a]	.54

Values are medians (IQR) (*$P < .05$; **$P < .01$). Values with different superscript letters indicate significant differences between groups.
LVIDd inc%, percentage increase in left ventricular internal diameter in diastole; LVIDs inc%, percentage increase in left ventricular internal diameter in systole; LA/Ao, ratio of left atrial diameter to aortic diameter; FS, fractional shortening; EF, ejectional fraction; E, early diastole; A, late diastole; E/A, ratio of the peak early to the peak atrial mitral inflow velocities; MR, mitral regurgitation.

Table 4. Radial tissue Doppler and strain imaging variables in dogs with MMVD and healthy controls.

| Variables | Control (n = 15) | MMVD Dogs (n = 26) | | P-Value |
		Non-CHF (n = 10)	CHF (n = 16)	
Systolic S' wave velocity (cm/s)	5.45 (4.65–6.18)[a]	5.90 (5.30–6.05)[a]	6.41 (5.10–7.06)[a]	.41
Diastolic E' wave velocity (cm/s)	−3.58 (−3.98 to −3.31)[a]	−2.49 (−5.08 to −2.21)[a]	−3.67 (−4.78 to −2.99)[a]	.74
Diastolic A' wave velocity (cm/s)	−3.15 (−3.55 to −2.86)[a]	−2.75 (−3.42 to −2.32)[a]	−2.74 (−3.56 to −2.18)[a]	.31
E'/A'	1.10 (1.0–1.3)[a]	1.2 (0.7–1.5)[a]	1.5 (1.0–2.0)[a]	.22
Strain (%)	38.0 (29.0–42.8)[a]	38.89 (30.52–45.12)[a]	46.66 (41.5–60.0)[b]	.01**
Systolic strain rate (/s)	4.21 (3.56–4.56)[a]	4.74 (4.15–4.84)[a]	4.63 (4.35–5.29)[a]	.06
Systolic TTP (ms)	90.0 (75.0–109.0)[a]	100.5 (96.0–108.0)[a]	102.0 (90.5–116.0)[a]	.30
Strain TTP (ms)	209.0 (179.0–247.0)[a]	228.5 (198.0–253.0)[a]	215.0 (159.0–236.0)[a]	.45
Systolic strain rate TTP (ms)	94.0 (86.0–109.0)[a]	96.0 (86.0–105.0)[a]	98.0 (89.5–106.5)[a]	.85

Values are medians (IQR) (**$P < .01$). Values with different superscript letters indicate significant differences between groups.
TTP, time-to-peak; S', tissue Doppler-derived peak systolic velocity; E', tissue Doppler-derived peak early diastolic velocity; A', tissue Doppler-derived peak late diastolic velocity; E'/A', ratio of the peak early to the late diastolic velocity.

Table 5. Longitudinal IVS TDI and strain imaging variables in dogs with MMVD and healthy controls.

| Variables | Control Dogs (n = 15) | Dogs with MMVD (n = 26) | | P-Value |
		Non-CHF (n = 10)	CHF (n = 16)	
Basal S' wave velocity (cm/s)	4.88 (4.01–6.46)[a]	5.28 (4.78–5.97)[a]	6.34 (4.45–7.14)[a]	.50
Apical S' wave velocity (cm/s)	2.0 (1.7–2.5)[a]	2.1 (1.9–2.4)[a]	3.3 (2.1–4.8)[b]	.05*
Basal E' wave velocity (cm/s) = $E_{m\ sept}$	−3.3 (−3.8 to −2.6)[a]	−3.7 (−5.8 to −3.1)[a]	−4.4 (−7.0- −3.7)[b]	.03*
Apical E' wave velocity (cm/s)	−1.5 (−2.3 to −1.2)[a]	−2.3 (−3.0 to −1.3)[a]	−3.1 (−5.5 to −1.7)[a]	.10
Basal A' wave velocity (cm/s)	−3.20 (−3.89 to −2.87)[a]	−4.38 (−4.94 to −3.62)[a]	−4.26 (−5.36 to −3.20)[a]	.17
Apical A' wave velocity (cm/s)	−1.9 (−2.3 to −1.2)[a]	−2.4 (−2.5 to −1.6)[a]	−2.0 (−3.2 to −1.4)[a]	.49
Basal E'/A'	1.0 (0.8–1.2)[a]	1.0 (0.8–1.2)[a]	1.1 (0.9–1.3)[a]	.64
Apical E'/A'	1.0 (0.8–1.2)[a]	1.1 (0.7–1.6)[a]	1.4 (1.2–1.7)[b]	.05*
$E/E_{m\ sept}$	14.3 (11.3–15.5)[a]	16.6 (14.2–18.0)[a]	19.3 (17.7–25.5)[b]	<.01**
Strain (%)	−21.42 (−24.36 to −17.07)[a]	−22.03 (−25.89 to −17.48)[a]	−30.42 (−39.72 to −23.81)[b]	.05*
Strain rate (/s)	−2.58 (−3.49 to −1.53)[a]	−2.21 (−2.61 to −1.66)[a]	−2.78 (−3.90 to −1.91)[a]	.58
Systolic time-to-peak (ms)	87.0 (78.0–100.0)[a]	90.5 (83.0–98.0)[a]	95.5 (86.0–102.5)[a]	.55
Strain time-to-peak (ms)	207.0 (180.0–234.0)[a]	213.5 (190.0–234.0)[a]	233.0 (209.5–273.0)[a]	.27
Strain rate time-to-peak (ms)	89.0 (75.0–100.0)[a]	86.0 (71.0–100.0)[a]	87.0 (82.5–96.0)[a]	.83

Values are medians (IQR) (*$P < .05$; **$P < .01$). Values with different superscript letters indicate significant differences between groups.
IVS, interventricular septum; TDI, tissue Doppler imaging; MMVD, myxomatous mitral valve disease.

Table 6. Longitudinal LV TDI and strain imaging variables in dogs with MMVD and healthy controls.

| Variables | Control Dogs (n = 15) | Dogs with MMVD (n = 26) | | P-Value |
		Non-CHF (n = 10)	CHF (n = 16)	
Basal S' wave velocity (cm/s)	4.25 (3.99–5.11)[a]	4.54 (3.66–4.97)[a]	5.47 (3.96–6.44)[a]	.21
Apical S' wave velocity (cm/s)	2.5 (1.6–3.7)[a]	2.4 (2.1–2.5)[a]	2.3 (2.1–4.0)[a]	.71
Basal E' wave velocity (cm/s) = $E_{m\ lat}$	4.20 (3.52–5.79)[a]	4.67 (4.48–5.49)[a]	5.35 (4.99–6.00)[b]	.03*
Apical E' wave velocity (cm/s)	−1.7 (−2.6 to −1.4)[a]	−2.1 (−3.4 to −1.7)[a]	−2.4 (−3.6 to −2.0)[a]	.16
Basal A' wave velocity (cm/s)	−1.98 (−3.29 to −1.31)[a]	−2.58 (−3.10 to −2.03)[a]	−2.22 (−2.70 to −1.50)[a]	.63
Apical A' wave velocity (cm/s)	−1.24 (−1.65 to −1.00)[a]	−1.51 (−2.24 to −1.07)[a]	−1.58 (−1.91 to −1.22)[a]	.28
Basal E'/A'	1.20 (0.70–1.70)[a]	1.50 (1.30–1.50)[a]	1.85 (1.45–2.25)[b]	.04*
Apical E'/A'	1.50 (1.10–2.30)[a]	1.55 (1.40–2.00)[a]	1.85 (1.45–2.25)[a]	.90
Strain (%)	−17.3 (−22.6 to −11.3)[a]	−16.4 (−20.8 to −13.2)[a]	−25.2 (−33.9 to −15.5)[b]	.03*
Systolic strain rate (/s)	−2.03 (−2.70 to −1.35)[a]	2.39 (−2.98 to −1.74)[a]	−2.26 (−3.31 to −1.89)[a]	.34
Systolic time-to-peak (ms)	96.0 (85.0–102.0)[a]	100 (95.0–107.0)[a]	100.0 (92.5–113.0)[a]	38
Strain time-to-peak (ms)	271.0 (250.0–283.0)[a]	278.0 (251.0–283.0)[a]	236.0 (225.0–281.0)[a]	.14
Strain rate time-to-peak (ms)	91.0 (82.0–103.0)[a]	112.5 (100.0–125.0)[a]	110.5 (97.5–123.0)[b]	.02*

Values are medians (IQR) (*P < .05). Values with different superscript letters indicate significant differences between groups.

IVS, interventricular septum; TDI, tissue Doppler imaging; MMVD, myxomatous mitral valve disease.

systolic (IVS apical systolic velocity, IVS strain, LV strain, and LV SR TTP) and 5 diastolic (IVS basal E' wave velocity [$E_{m\ sept}$], IVS apical E'/A', $E/E_{m\ sept}$, LV basal E' wave velocity [$E_{m\ lat}$], and LV basal E'/A') variables. No differences were observed among the groups for any of the time parameters, except LV SR TTP.

Diagnostic Accuracy of Echocardiographic Variables for the Occurrence of CHF in Dogs with MMVD

Several variables (12/47 [26%]) of conventional and tissue Doppler echocardiography were significant predictors of CHF (P < .05) in a univariate analysis comparing the non-CHF and CHF groups. Among these were 6 (6/11 [55%]) conventional echocardiographic variables (E velocity, E/A, MR, LA/Ao ratio, LVIDd inc%, and LVIDs inc%) and 6 (6/27 [22%]) TDI-derived echocardiographic variables ($E/E_{m\ sept}$, $E_{m\ sept}$, $E_{m\ lat}$, radial strain, IVS St, and LV St) (Table 7). A

multivariate logistic regression analysis was conducted to investigate load-independent predictors of CHF in dogs with MMVD. The $E/E_{m\ sept}$ remained independently significant after adjusting for load-dependent echocardiographic variables in the multivariate logistic regression analysis (P < .05, Table 8).

A cut-off $E/E_{m\ sept}$ value >18.7 discriminated MMVD from CHF with 56% sensitivity and 90% specificity, and the area under the receiver operating characteristic curve was 0.77 (Fig 4 and Table 8).

Discussion

In this study, we collected data on conventional echocardiographic and TDI variables in dogs with MMVD with and without CHF. Assessment of myocardial function is of great importance in the diagnosis, treatment, and follow-up of CHF in dogs[1,6] and humans.[5] Generally, conventional and Doppler

Table 7. Univariate analysis of predicators of CHF in MMVD dogs.

| Variables | MMVD Dogs (n = 26) | | P-Value |
	Non-CHF (n = 10)	CHF (n = 16)	
Conventional echocardiography			
Mitral E velocity (cm/s)	73.4 (67.7–95.0)	104.7 (99.3–139.0)	<.01**
Mitral E/A	1.2 (1.1–1.2)	1.6 (1.2–1.9)	.02*
MR (m/s)	4.0 (4.0–5.0)	5.0 (5.0–5.0)	<.01**
LA/AO	1.2 (1.1–1.3)	1.4 (1.3–2.1)	.05*
LVIDd inc%	11.0 (6.40–18.30)	38.5 (31.10–49.10)	<.01**
LVIDs inc%	−5.25 (−6.90 to 2.5)	15.80 (9.00–23.90)	.02*
Tissue Doppler echocardiography			
$E/E_{m\ sept}$	16.6 (14.2–18.0)	19.3 (17.7–25.5)	.02*
IVS basal E' = $E_{m\ sept}$	−3.7 (−5.8 to −3.1)	−4.4 (−7.0 to −3.7)	.06*
LV basal E' = $E_{m\ lat}$	4.67 (4.48–5.49)	5.35 (4.99–6.00)	.05*
Radial strain	38.89 (30.52–45.12)	46.66 (41.47–60.02)	.03*
IVS stain	−22.03 (−25.89 to −17.48)	−30.42 (−39.72 to −23.81)	.04*
LV strain	−16.4 (−20.8 to −13.2)	−25.2 (−33.9 to −15.5)	.03*

Values are medians (IQR) (*P < .05; **P < .01).

CHF, congestive heart failure; MMVD, myxomatous mitral valve disease.

Table 8. Multivariate regression analysis and sensitivity and specificity of 5 predicators of CHF in dogs with MMVD.

Variables	Predictor	AUC	95% CI	Cut-off Points	Sensitivity (%)	Specificity (%)	P-Value
Conventional echocardiography	Mitral E/A	0.581	0.60–0.96	>1.2	75	80	.06
				>1.3	56	100	
Tissue Doppler echocardiography	Radial stain	0.588	0.36–0.82	>40.78	75	30	.46
				>44.71	50	30	
	IVS strain	0.681	0.46–0.90	< −31.9	50	70	.13
				< −27.5	69	70	
				< −25.5	69	60	
	LV strain	0.638	0.41–0.86	−17.8	56	50	.25
				−15.2	81	50	
	$E/E_{m\ sept}$	0.772	0.59–0.96	>18	63	80	.02*
				>18.7	56	90	
				>19.9	31	90	

Values are medians (IQR) (*$P < .05$).
AUC, area under curve; CHF, congestive heart failure; MMVD, myxomatous mitral valve disease.
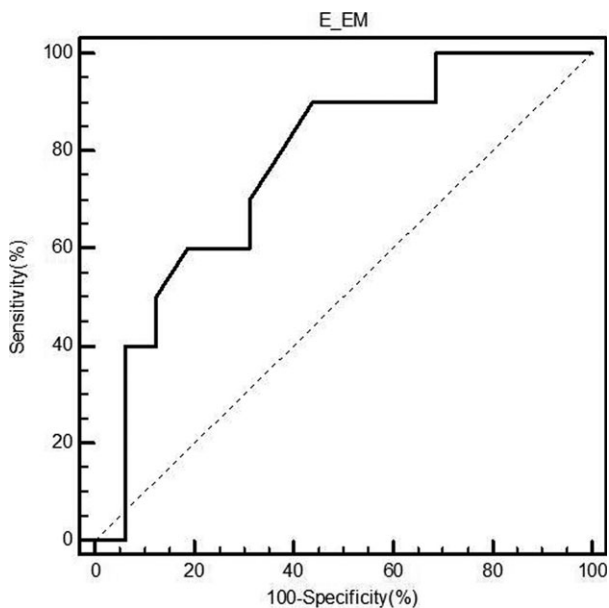

Fig 4. Receiver operating characteristic curve comparing sensitivity and specificity of the cut-off value for E/E_m sept as a diagnostic test to distinguish between CHF and non-CHF in dogs with MMVD.

echocardiography is performed on dogs and humans to noninvasively assess myocardial function.[10,20] In the present study, transmitral E velocity and E/A ratio were significantly higher in dogs with MMVD compared to healthy dogs, regardless of CHF ($P < .01$), in agreement with a previous study.[21] However, higher LA : Ao ratio and mitral A wave velocity indicating increased LA pressure was present in the CHF group compared with the non-CHF and control groups. As a result, pseudonormalization of transmitral inflow velocity is more commonly observed in dogs with MMVD and CHF than in dogs with MMVD without CHF or healthy dogs, because of increased LA pressure.[21–23] In addition, LVIDd inc%, a marker of LV preload, was significantly higher in dogs with MMVD than in healthy dogs ($P < .01$).

Recently, dP/dt and $−dP/dt$ have been proposed as noninvasive echocardiographic methods to assess LV function more accurately by CW Doppler echocardiography in humans.[24] However, this indirect method has not been well described in dogs with MMVD. We evaluated dP/dt and $−dP/dt$ in dogs with MMVD, and no significant difference was observed between the groups. The lack of a difference may be because of the higher heart rates in dogs than in humans because higher heart rates decreased the time between 1 and 3 m/s. Increasing sweep speed from 100 to 150 mm/s could be considered to overcome these problems.

Systolic dysfunction, as indicated by significantly higher LVIDs inc%, was present in dogs with MMVD compared with healthy dogs ($P < .01$). EF and FS did not differ significantly among the groups, which agreed with previous studies showing that these variables were relatively less sensitive indicators of systolic function.[21,25] Several studies have demonstrated that TDI-derived E' and A' velocity are correlated with LV diastolic function,[22,26] and that TDI-derived S' velocity is correlated with LV systolic function.[27,28] Although a previous study[1] reported that LV basal S' increases significantly in dogs with CHF compared with dogs without CHF and control dogs, it is difficult to evaluate whether or not the difference found in that study was because of inotropic drugs or other factors because dogs treated with inotropes were included. Another study[10] reported no difference in S' between dogs with MMVD with and without CHF, which agreed with our finding.

In human medicine, regional systolic St and SR are used as powerful noninvasive indices of systolic function.[29] However, alterations in systolic function as assessed by TDI-induced St and SR are still poorly understood in dogs with MMVD. In the present study, both radial and longitudinal St was higher in the CHF group than in the non-CHF and control groups. As a consequence, we demonstrated that TDI-derived St was a comparatively more sensitive indicator of systolic function than S'. Although TDI-derived indices generally are considered relatively load independent,[22]

$E_{m\ sept}$ was correlated with load-dependent variables such as LA/Ao ratio in our study. Therefore, a multivariate logistic regression analysis was conducted with conventional and tissue Doppler echocardiographic variables to further investigate the load-independent predictors of CHF in dogs with MMVD. After adjusting for load-dependent clinical and echocardiographic variables in a multivariate logistic regression analysis, $E/E_{m\ sept}$ remained independently significant. As a result, TDI-derived $E/E_{m\ sept}$ was the most reliable diagnostic marker of CHF in dogs with MMVD, regardless of the severity of volume overload.

In the present study, E/E_m was significantly higher in the CHF group than in the non-CHF group ($P < .05$). In contrast, another study reported no difference in E/E_m between dogs with MMVD with and without CHF, regardless of different filling pressures.[1] This difference might be because of breed differences, effects of medications, or examining different myocardial walls (IVS versus LVPW). An E/E_m cut-off value of 18.7 had 56% sensitivity and 90% specificity for identifying CHF in the present study. The E/E_m ratio was markedly higher than that reported in previous studies because of different TDI display techniques.[1,30] The first method available, PW TDI, measures maximum velocities, whereas CD TDI used in our study measures mean velocity, which could result in an increased ratio from the same myocardial segment.[1] Several issues remain when interpreting our data. First, the number of patients was relatively small, because we performed this study at a single center. The lack of significant differences among groups may be caused by an underpowered study. However, several significant results (12/47 [26%]) were observed in this population which was similar to results of a recent large prospective field study conducted in dogs with MMVD. Second, several variables may have been affected by medications. Although we excluded patients treated with inotropes or inodilators, diuretics may have decreased preload-dependent variables, and angiotensin-converting enzyme inhibitors may have decreased or delayed the onset of CHF. However, no significant differences were observed between dogs that were taking medications and those that were not on medications in this study. Lastly, values in this study were measured only on presentation. Thus, variables such as drugs, day differences, and physical activity could not be controlled. Despite these limitations, our results suggested possible cut-off values for several echocardiographic variables to distinguish dogs with MMVD and CHF from those with MMVD without CHF.

In conclusion, although 6 conventional and 6 TDI-derived variables were useful for predicting CHF, TDI-derived $E/E_{m\ sept}$ was the only load-independent predictor of CHF in dogs with MMVD.

TDI-derived $E/E_{m\ sept}$ which evaluates diastolic function could be an important predictor of CHF in dogs with MMVD and it may overcome the limitation of load-dependent conventional echocardiography. Additional investigations are necessary to clarify the clinical relevant changes of pulse TDI while managing the dogs with MMVD.

Footnotes

Acknowledgments

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