

Prognostic Value of Left Atrial Function in Dogs with Chronic Mitral Valvular Heart Disease

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Background: A strong correlation between left atrial (LA) dysfunction and the severity of cardiac disease has been described in human patients with various cardiac diseases. The role of LA dysfunction in dogs with chronic mitral valvular heart disease (CMVHD) has not been addressed.

Objectives: To investigate the correlation between LA function and the prognosis of dogs with CMVHD.

Animals: Thirty-eight client-owned dogs with CMVHD.

Methods: Prospective clinical cohort study. Dogs were divided into 2 groups (survivors and nonsurvivors) based on the onset of cardiac-related death within 1 year. Physical examination and echocardiographic variables were compared between the groups. For the assessment of the comparative accuracy in identifying patients with cardiac-related death, receiver operating characteristic (ROC) curves and multivariate logistic analysis were used.

Results: The highest accuracy was obtained for the LA active fractional area change (LA-FAC_{act}), with an area under the ROC curve (AUC) of 0.95, followed by the left atrial to aortic root ratio (LA/Ao), with an AUC of 0.94; peak early diastolic mitral inflow velocity (*E*), with an AUC of 0.85; and LA total fractional area change (LA-FAC_{total}), with an AUC of 0.85. In the multivariate logistic regression analysis, LA-FAC_{act} emerged as the only independent correlate of cardiac-related death within 1 year (odds ratio = 1.401, *P* = .002).

Conclusions and Clinical Importance: Regarding both the size and function, the LA has a strong correlation with the prognosis of dogs with CMVHD. The most significant independent predictor of mortality in this study was LA-FAC_{act}.

Key words: Cardiac-related death; Dog; Echocardiography; Left atrial emptying fraction.

Chronic mitral valvular heart disease (CMVHD) is the most common heart disease in dogs. This disease is caused by progressive myxomatous degeneration of the mitral valve, leading to incomplete coaptation of the leaflets and valvular regurgitation.^{1,2} The reported prevalence of this disease in small dogs ranges from 14% to over 40%, depending on the breed.^{3–5} Although most dogs with CMVHD remain asymptomatic for years or even for life,^{6–9} the progression of mitral regurgitation (MR) can cause severe congestive heart failure, leading to death in some dogs.

Predicting the onset of congestive heart failure or cardiac-related death is of clinical importance. To date, many studies have investigated the prognostic factors for survival or disease worsening in dogs with CMVHD.^{9–12} The high prognostic value of the degree of left atrial (LA) dilatation has been demonstrated in dogs with CMVHD.^{10–12} Chronic and hemodynamically

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Abbreviations:

<i>A</i>	late diastolic mitral inflow velocity
<i>A_m</i>	late diastolic velocity of the septal mitral annulus
AUC	area under the receiver operating characteristic curve
CI	confidence interval
CMVHD	chronic mitral valvular heart disease
<i>E_m</i>	early diastolic velocity of the septal mitral annulus
<i>E</i>	peak early diastolic mitral inflow velocity
FS	fractional shortening
LA/Ao	left atrial to aortic root ratio
LA-FAC _{act}	left atrial active fractional area change
LA-FAC _{pass}	left atrial passive fractional area change
LA-FAC _{total}	left atrial total fractional area change
LA	left atrial
LA _{max}	maximum area of the left atrium at ventricular end-systole
LA _{min}	minimum area of the left atrium at ventricular end-diastole
LA _p	left atrium at onset of the P wave on the ECG
LVIDd inc%	percent increase in left ventricular diameter in diastole
LVIDd	left ventricular diameter in diastole
LVIDsinc%	percent increase in left ventricular diameter in systole
LVIDs	left ventricular diameter in systole
LV	left ventricular
MR	mitral regurgitation
ROC	receiver operating characteristic

significant MR results in volume overload, which is first characterized by LA enlargement. Echocardiography can be used to measure LA size noninvasively; traditionally, LA size is measured by using linear M-mode or two-dimensional (2D) methods. The left atrial to aortic root ratio (LA/Ao) determined from the right parasternal short axis view is the most commonly used

method for detecting LA enlargement in veterinary clinical practice, and it has been demonstrated to be a reliable method to detect LA enlargement.^{13,14}

The left atrium plays a key role in cardiac performance by modulating left ventricular (LV) filling with its reservoir function (expansion associated with the inflow of blood from the pulmonary veins during ventricular systole), conduit function (passage of blood from the pulmonary veins to the left ventricle during ventricular diastole), and booster pump function (augmentation of LV filling during atrial contraction).¹⁵ LV diastolic dysfunction, elevated filling pressure, LV hypertrophy, and MR are all potential contributors to ongoing LA morphologic and pathologic changes. Increased LA volume may be accompanied morphologic and pathologic changes. Increased LA volume may be accompanied by a progressive impairment in LA function, and both may precede symptom development and adversely affect prognosis. A strong correlation between LA dysfunction and the severity of cardiac disease has been described in human patients with various cardiac diseases.^{16–18} The role of LA dysfunction in dogs with CMVHD has not been addressed.

The purpose of this study was to investigate the correlation between LA function and survival time in dogs with CMVHD.

Materials and Methods

Animals

Thirty-eight client-owned dogs were prospectively studied. Dogs with CMVHD were consecutively selected between April 2010 and December 2013 at the Hokkaido University Veterinary Teaching Hospital. The diagnosis of CMVHD was confirmed by the presence of a left systolic apical heart murmur and the echocardiographic findings of systolic MR by color Doppler imaging with irregularly thickened mitral valve leaflets.

All dogs included in this study had undergone physical examination, blood tests, thoracic radiographs, and echocardiography, and were classified according to the American College of Veterinary Internal Medicine consensus statement.¹⁹ Dogs with atrial flutter or fibrillation and other concurrent acquired cardiac diseases, such as cardiomyopathy or infective endocarditis, or congenital cardiac diseases were excluded.

Classification

Dogs were divided into 2 groups for statistical analysis based on whether they survived for more than 1 year after the first echocardiographic examination (Group A, “survivors”) or experienced cardiac-related death within 1 year after the first echocardiographic examination (Group B, “nonsurvivors”). Cardiac-related death was defined as death occurring because of progression of clinical signs of heart failure without any other identifiable cause of death.

Conventional Echocardiography and Doppler Examination

Conventional 2D and M-mode echocardiographic and Doppler examinations were performed by an experienced veterinarian

(KN) with an ultrasound unit (HI VISION Preirus[®]) equipped with a 3–7 MHz phased array sector probe (EUP-S52[®]) in all dogs. Dogs were unsedated and gently restrained in left and right lateral recumbency during the examination. Measurements were obtained using the 2D-guided M-mode with concomitant ECG registration for the ventricles according to the guidelines of the American Society of Echocardiography.²⁰ The LA/Ao was obtained from the right parasternal short axis 2D view as previously described.¹⁴ The LV diameter in diastole (LVIDd) and LV diameter in systole (LVIDs) were measured from the M-mode echocardiogram from the right parasternal short axis 2D view.²¹ M-mode values were used to derive the fractional shortening (FS) and the percent increase in LVIDd (LVIDd inc%) and LVIDs (LVIDs inc%) according to the following equation²²: % increase = $100 \times (\text{observed dimension} - \text{expected normal dimension}) / \text{expected normal dimension}$. Expected normal dimensions were calculated according to the following equations²²: expected normal LVIDd = $1.53 \times (\text{body weight})^{0.294}$ and expected normal LVIDs = $0.95 \times (\text{body weight})^{0.315}$. From the left apical 4-chamber view, pulsed Doppler was used to measure the peak early (E) and late (A) diastolic mitral inflow velocity, and tissue Doppler was used to measure the early diastolic (E_m) and late diastolic (A_m) velocity of the septal mitral annulus.

Left Atrial Function Analysis with 2D Speckle Tracking Echocardiography

For LA function analysis, images of the 3 consecutive cardiac cycles from the left apical 4-chamber view were saved onto a hard drive for offline analysis. A frame corresponding to the time of the peak of the R wave on the ECG was selected as the indicator for left ventricular end-diastole, and the endocardium of the left atrium was manually traced in that frame. The area of the left atrium was then automatically calculated by the software (Left Atrial Tracking[®]) in each subsequent frame throughout the cardiac cycle to derive a time-left atrial area curve. The maximum area of the left atrium at ventricular end-systole (LA_{max}), area of the left atrium at the onset of the P wave on the ECG (LA_p), and minimum area of the left atrium at ventricular end-diastole (LA_{min}) were determined by the same software. Indicators of left atrial phasic function (reservoir, conduit, and booster) were calculated with the following equations: total fractional area change ($LA-FAC_{total}$) = $100 \times (LA_{max} - LA_{min}) / LA_{max}$; passive fractional area change ($LA-FAC_{pass}$) = $100 \times (LA_{max} - LA_p) / LA_{max}$; and active fractional area change ($LA-FAC_{act}$) = $100 \times (LA_p - LA_{min}) / LA_p$.²³

Statistical Analysis

Measurements are presented as the median and range. Variables were compared using the Mann-Whitney *U*-test for continuous variables and the chi-squared test for categorical variables (Fisher's exact test for 2 categorical variables and the likelihood ratio test for more than 2 categorical variables). The relationships among different parameters were assessed by Spearman's correlation analysis.

For the assessment of the comparative accuracy of different echocardiography variables in identifying patients with cardiac-related death, receiver operating characteristic (ROC) curves and the respective area under the ROC curve (AUC) were calculated for those variables with significance set at $P < .05$ in the Mann-Whitney *U*-test. Predictors of cardiac-related death within 1 year were assessed using binary logistic regression analysis. Echocardiographic variables with a $P < .01$ in univariate analyses were included in the multivariate model. Hosmer-Lemeshow statistics and accuracy rate were calculated to evaluate the fitness of the

model. All statistical analyses were performed with commercially available statistical software.^b A two-sided *P*-value <.05 was considered significant.

Results

Table 1 shows the demographic data, physical examination results, and radiographic and echocardiographic characteristics of the study population. There were no significant differences between patients in Groups A and B with respect to age, sex, body weight, heart rate, and vertebral heart scale (*P* > .05). The distribution of American College of Veterinary Internal Medicine classes between the 2 groups was significantly different (*P* < .001).

The incidence of pulmonary edema was significantly higher in Group B (58.3%) than Group A (7.7%) (*P* = .002). The use of angiotensin-converting enzyme (ACE) inhibitors (*P* = .035), pimobendan (*P* = .026),

and loop diuretics (*P* < .001) was significantly different between the 2 groups.

Results of conventional echocardiographic parameters are also shown in Table 1. There were significant differences in LA/Ao, LVIDd inc%, *E*, *E/A*, and *E/E_m* between the 2 groups. Two of the 3 LA function parameters, LA-FAC_{total} [37.1% (20.7–55.7%) versus 50.1% (35.5–64.7%); *P* = .001] and LA-FAC_{act} [14.9% (6.1–28.4%) versus 31.9% (13.9–50.0%); *P* < .001], significantly decreased in Group B compared to Group A.

The LA function parameters were significantly related to some of the assessed conventional echocardiographic parameters (Fig 1). Significant correlations were found between LA-FAC_{total} and LA/Ao (*r* = −0.535, *P* = .001), LVIDd inc% (*r* = −0.332, *P* = .042), LVIDs inc% (*r* = −0.577, *P* < .001), and *A_m* (*r* = 0.532, *P* = .001) (Table 2). The LA-FAC_{act} had a significant correlation with age (*r* = −0.330, *P* = .043), LA/Ao (*r* = −0.771,

Table 1. Clinical and echocardiographic characteristics of dogs in Groups A and B. Group A included dogs surviving for more than 1 year after echocardiographic examination; Group B included dogs experiencing cardiac-related death within 1 year.

	Group A (n = 26)	Group B (n = 12)	<i>P</i> -Value
Age (years)	12 (8–14)	13 (7–15)	.053
Sex (female/male)	10/16	5/7	.284
Body weight (kg)	6.05 (2.5–14.1)	6.21 (2.95–9.8)	.588
Heart rate (bpm)	148 (88–186)	158 (92–212)	.172
ACVIM class ^a			
B1	11 (42.3%)	0 (0%)	<.001
B2	13 (50%)	2 (16.7%)	
C	2 (7.7%)	5 (41.7%)	
D	0 (0%)	5 (41.7%)	
Pulmonary edema ^a	2 (7.7%)	7 (58.3%)	.002
Vertebral heart scale	11 (9.5–12.5)	12.5 (9–13)	.067
Medication			
ACE inhibitor ^a	9 (34.6%)	9 (75%)	.035
Pimobendan ^a	5 (19.2%)	7 (58.3%)	.026
Loop diuretics ^a	3 (11.5%)	10 (83.3%)	<.001
Conventional parameters			
LA/Ao ^a	1.70 (1.22–2.81)	2.38 (1.92–3.75)	<.001
LVIDd inc% ^a	12.0 (−11.7 to 39.6)	28.7 (−1.4 to 81.8)	.002
LVIDs inc% ^a	−8.9 (−45.3 to 30.8)	5.83 (−15.4 to 47.0)	.038
FS	45.2 (26.3–67.6)	48.7 (41.2–50.8)	.283
<i>E</i> (m/s) ^a	0.84 (0.36–1.85)	1.29 (0.82–1.93)	<.001
<i>A</i> (m/s)	0.74 (0.42–1.31)	0.8 (0.53–1.17)	.566
<i>E/A</i> ^a	1.21 (0.54–3.78)	1.52 (1.01–2.59)	.011
<i>E_m</i> (cm/s)	6.45 (4.2–10.65)	8.2 (5.5–10.8)	.081
<i>A_m</i> (cm/s)	9.3 (4.5–13.7)	7.9 (4.3–11)	.727
<i>E/E_m</i> ^a	12.0 (7.9–31.9)	15.6 (9.1–35.1)	.042
LA function parameters			
LA-FAC _{total} ^a	50.1 (35.5–64.7)	37.1 (20.7–55.7)	.001
LA-FAC _{pass}	26.6 (11.8–36.7)	25.7 (15.5–38.1)	.914
LA-FAC _{act} ^a	31.9 (13.9–50.0)	14.9 (6.1–28.4)	<.001

Data are expressed as the median (range) or number (percentage).

A, late diastolic mitral inflow velocity; ACE, angiotensin-converting enzyme; ACVIM, American College of Veterinary Internal Medicine; *A_m*, late diastolic velocity of the septal mitral annulus; *E*, peak early diastolic mitral inflow velocity; *E_m*, early diastolic velocity of the septal mitral annulus; FS, fractional shortening; LA, left atrial; LA/Ao, left atrial to aortic root ratio; LVIDd inc%, percent increase in left ventricular diameter in diastole; LVIDs inc%, percent increase in left ventricular diameter in systole; LA-FAC_{act}, left atrial active fractional area change; LA-FAC_{pass}, left atrial passive fractional area change; LA-FAC_{total}, left atrial total fractional area change.

^aValues between Groups A and B differed significantly (*P* < .05).

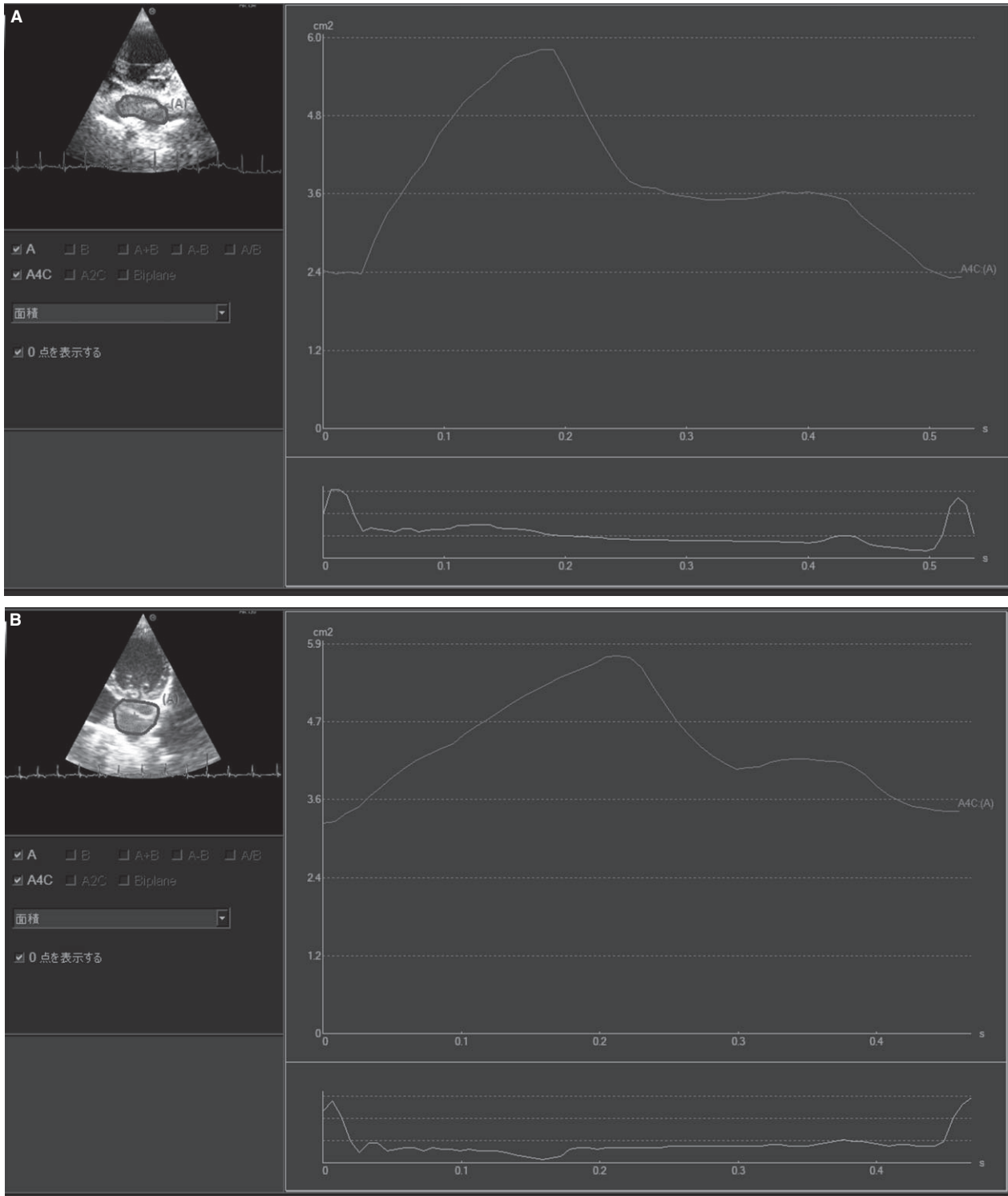


Fig 1. Time-left atrial area curves of a dog in Group A (A) and Group B (B). The upper graph represents the time-left atrial area curve and the lower represents the ECG tracing. The dog in Group B has a lower LA-FAC_{total} and LA-FAC_{act} than the dog in Group A.

$P < .001$), LVIDd inc% ($r = -0.562$, $P < .001$), LVIDs inc% ($r = -0.500$, $P = .001$), E ($r = -0.551$, $P < .001$), E/A ($r = -0.437$, $P = .006$), and A_m ($r = 0.461$, $P = .004$) (Table 2).

For the comparative assessment of the accuracy of conventional echocardiographic parameters and LA function parameters in identifying the dogs with short survival times, ROC curves and the corresponding

Table 2. Correlates of left atrial function parameters.

	%LAEF _{total}		%LAEF _{pass}		%LAEF _{act}	
	<i>P</i> -Value	<i>r</i>	<i>P</i> -Value	<i>r</i>	<i>P</i> -Value	<i>r</i>
Age	.231		.932		.043	-0.330
Body weight	.205		.264		.659	
Heart rate	.530		.023	0.378	.873	
LA/Ao	.001	-0.0535	.962		<.001	-0.771
LVIDd inc%	.042	-0.332	.370		<.001	-0.562
LVIDs inc%	<.001	-0.577	.140		.001	-0.500
FS	.064		.011	0.408	.963	
<i>E</i>	.133		.069		<.001	-0.551
<i>A</i>	.482		.976		.634	
<i>E/A</i>	.136		.197		.006	-0.437
<i>E_m</i>	.96		.389		.355	
<i>A_m</i>	.001	0.532	.127		.004	0.461
<i>E/E_m</i>	.611		.124		.051	
%LA _{total}			<.001	0.586	<.001	0.846
%LA _{pass}	<.001	0.586			.401	
%LA _{act}	<.001	0.846	.401			

A, late diastolic mitral inflow velocity; *A_m*, late diastolic velocity of the septal mitral annulus; *E*, peak early diastolic mitral inflow velocity; *E_m*, early diastolic velocity of the septal mitral annulus; FS, fractional shortening; LA/Ao, left atrial to aortic root ratio; LVIDd inc%, percent increase in left ventricular diameter in diastole; LVIDs inc%, percent increase in left ventricular diameter in systole; %LAEF_{act}, left atrial active emptying fraction; %LAEF_{pass}, left atrial passive emptying fraction; %LAEF_{total}, left atrial total emptying fraction.

AUC were calculated. As shown in Table 3, the highest accuracy was obtained for LA-FAC_{act}, which had an AUC of 0.95, a sensitivity of 91%, and a specificity of 96%, followed by the LA/Ao, which had an AUC of 0.94, a sensitivity of 100%, and a specificity of 88%. The *E/A* had the lowest accuracy, with an AUC of 0.74, a sensitivity of 73%, and a specificity of 72%, whereas the LVIDs inc% had the second lowest accuracy, with an AUC of 0.77, a sensitivity of 73%, and a specificity of 76%. Although *E*, LA-FAC_{total}, and LVIDd inc% had the same AUC of 0.85, they differed in sensitivity (82%, 82%, and 73%, respectively) and specificity (84%, 76%, and 84%, respectively).

Based on the results of univariate analysis, the variables LA/Ao, *E*, LA-FAC_{total}, and LA-FAC_{act} were selected for multivariate logistic regression analysis (Table 4). In the multivariate logistic regression analysis, LA-FAC_{act} emerged as the only independent correlate of cardiac-related death within 1 year in our study population (odds ratio = 1.401; 95% confidence interval (CI), 1.132–1.735; *P* = .002) (Table 4).

Discussion

The findings of this study indicate that LA size and function are strongly correlated with early death in dogs with CMVHD. Although several echocardiographic parameters were significantly different between the 2 groups, LA-FAC_{act}, the parameter corresponding to the booster pump function, was the most significant independent predictor of mortality in this study.

Table 3. Area under the receiver operating characteristic curve (AUC) and optimal diagnostic cutoffs between Groups A and B.

	AUC	95% CI	Se	Sp	Cutoff	<i>P</i> -Value
%LAEF _{act}	0.95	0.88–1.00	0.91	0.96	24.0	<.0001
LA/Ao	0.94	0.85–1.00	1.00	0.88	2.06	<.0001
<i>E</i>	0.85	0.71–0.98	0.82	0.84	1.17	.001
%LAEF _{total}	0.85	0.70–0.99	0.82	0.76	45.6	.001
LVIDd inc%	0.85	0.72–0.98	0.73	0.84	26.2	.001
LVIDs inc%	0.77	0.62–0.92	0.73	0.76	-2.2	.011
<i>E/A</i>	0.74	0.58–0.91	0.73	0.72	1.36	.022

%LAEF_{act}, left atrium active emptying fraction; LA/Ao, left atrial to aortic root ratio; *E*, peak early diastolic mitral inflow velocity; %LAEF_{total}, left atrium total emptying fraction; LVIDd inc%, percent increase in left ventricular diameter in diastole; LVIDs inc%, percent increase in left ventricular diameter in systole; *A*, late diastolic mitral inflow velocity; Se, sensitivity; and Sp, specificity.

Many studies have reported the value of echocardiography for predicting survival time and providing prognostic indicators in dogs with CMVHD.^{9–12,24} Although the recent advancements in ultrasound equipment, such as tissue Doppler imaging and strain imaging, have facilitated more detailed analysis of cardiac ventricular function, assessment of LA size with LA/Ao using conventional B-mode remains one of the most important echocardiographic methods to evaluate the severity and prognosis of CMVHD.^{24–26} To the best of our knowledge, this study is the first report demonstrating that LA function analysis could be the most reliable prognostic indicator in dogs with CMVHD.

In our study, significant increases in LA/Ao were observed in nonsurvivor dogs, and the LA/Ao had a moderate and strong correlation with the reservoir and booster pump functions, respectively. However, LA enlargement does not always result in its functional incompetence. During chronic MR, the left atrium enlarges in size and the LA chamber becomes more compliant. Thus, the enlarged left atrium appears to exert an important compensatory mechanism by buffering the rise in pressure in the atrium and by

Table 4. Binary logistic regression analysis for cardiac-related death within 1 year.

Variables	Univariate Analysis			Multivariate Analysis
	OR	95% CI	<i>P</i> -Value	<i>P</i> -Value
LA/Ao	0.956	0.929–0.984	.002	.372
<i>E</i>	0.019	0.001–0.326	.006	.705
%LAEF _{total}	1.164	1.049–1.291	.004	.179
%LAEF _{act}	1.401	1.132–1.735	.002	.002

CI, confidence interval; *E*, peak early diastolic mitral inflow velocity; LA/Ao, left atrial to aortic root ratio; OR, odds ratio; %LAEF_{act}, left atrial active emptying fraction; %LAEF_{total}, left atrial total emptying fraction.

providing an adequate ventricular filling volume. Moreover, it has been demonstrated that the Frank-Starling mechanism is also operative in the left atrium and that LA output increases as atrial volume increases, which contributes to maintaining a normal stroke volume.²⁷ The increased atrial response to early-stage LV filling impairment is characterized by augmented reservoir and booster pump functions according to the Frank-Starling mechanism. At end-stage LV dysfunction, however, the atrial reservoir and the booster pump functions decline.²⁸ Therefore, the analysis of atrial function, as well as its size, is required to evaluate the severity and prognosis of dogs with CMVHD.

During LV systole, pulmonary venous inflow distends the left atrium, which acts as a reservoir by storing energy in the form of pressure.²⁹ The LA reservoir function is determined mainly by LA compliance (stiffness) and LV systolic function (systolic apical motion of the LV base facilitates LA filling) and, to a lesser extent, by right ventricular systole (pulmonary venous inflow).^{15,29} Decreased LA reservoir function has been described in human patients with severe MR.¹⁸ Similarly, this study showed that severe MR is associated with a significant reduction in LA reservoir function. This reduced function may be caused partly by reduced LV systolic function because %LVEF_{total} had a mild correlation with the FS of the left ventricle in this study. However, the ultrastructural changes in the LA myocardium, including the presence of interstitial fibrosis and myocyte hypertrophy in patients with severe MR, may reduce LA compliance, resulting in reservoir dysfunction.³⁰

The LA functions as a conduit after the reservoir phase, allowing a passive transfer of blood from the pulmonary veins toward the left ventricle. The LA conduit function is determined mainly by LA elasticity and afterload. Although impaired LA conduit function was observed in human patients with severe MR,³¹ there was no difference between the conduit function of survivors and nonsurvivors in this study. The clinical utility of evaluating LA conduit function in dogs with CMVHD is still uncertain.

Active LA contraction, the booster pump function, finalizes LV filling during late diastole. It depends on LA afterload (LV compliance and end-diastolic filling pressure) and LA intrinsic contractility. In this study, impaired LA booster pump function was observed to a greater degree in nonsurvivor dogs, and it was the most significant independent predictor of mortality in this study; it may be related to the decreased LA contractility and increased LA afterload. These results are congruent with findings from human patients with hypertrophic cardiomyopathy and MR. In those studies, it was demonstrated that parameters of booster pump function had the highest correlation with the severity of the disease.^{16,30}

Mitral A_m velocity with tissue Doppler imaging, another parameter of atrial function, had moderate correlations with LA-FAC_{total} and LA-FAC_{act} (reservoir and booster pump function, respectively). In

humans, several studies have demonstrated that A_m velocity can be used as a rapid and accurate marker of global atrial function.^{32,33} The A_m velocity correlates with other parameters of atrial function, including the peak A velocity, atrial ejection fraction, and atrial ejection force.³³ Moreover, A_m velocity has been shown to provide important prognostic information in patients with various cardiac diseases.³⁴ In this study, there was no significant difference in A_m velocity between the survivor and nonsurvivor dogs, reflecting a lower value for this prognostic predictor in dogs with CMVHD.

Some limitations of this study must be considered. First, no invasive assessment of LA mechanical properties or afterload was performed to prove the determinations of reduced LA function, which must be the focus of further specific studies. Second, the number of dogs studied was small, rendering the study underpowered to detect differences between groups. Last, it is possible that medication use influenced the echocardiographic parameters and survival time. The use of ACE inhibitors, pimobendan, and loop diuretics was significantly higher in the nonsurvivors. Because this study included dogs in various clinical stages, it was impossible to standardize the treatment.

In conclusion, both LA size and function are strongly correlated with the prognosis of dogs with CMVHD. Booster pump function was the most significant independent predictor of mortality in this study. The assessment of LA function can provide further insights about the pathophysiology and prognosis in dogs with CMVHD.

Footnotes

^a Hitachi Medical Corp., Chiba, Japan

^b IBM SPSS Statistics, version 21; IBM Corp., Chicago, IL

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Conflict of Interest Declaration: The authors disclose no conflict of interest.

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