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Evaluation of Plasma NT-proBNP Concentration in Dogs with Chronic Mitral Valve Insufficiency

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Abstract : This study aimed to evaluate the plasma concentration of NT-proBNP in dogs with different stages of heart failure by chronic mitral valve insufficiency (CMVI). Fifty small-breed dogs with CMVI and 7 healthy control dogs without cardiac disease and critical systemic diseases were included in the study population. As a preliminary study, we compared the plasma concentrations of N-terminal pro-brain natriuretic peptide (NT-proBNP) and the echocardiographic parameters between dogs of the International Small Animal Cardiac Health Council (ISACHC) classes. Then, we evaluated the associations between NT-proBNP and echocardiographic parameters. Plasma NT-proBNP levels showed a significant difference among the ISACHC groups. In the comparison between echocardiographic parameters and NT-proBNP, NT-proBNP were found to be associated with left atrium/aorta (LA/AO), early diastolic transmitral flow (E) velocity, late diastolic transmitral flow (A) velocity, end diastolic volume index (EDVI). Our study found plasma NT-proBNP might be useful to predict the disease progression in dogs with CMVI.

Key words **:** Echocardiography, NT-proBNP, A flow velocity, dogs, CMVI.

Introduction

Echocardiography and cardiac biomarker are one of the most reliable non-invasive diagnostic methods for diagnosing heart diseases and heart failure in human and veterinary medicine (13,14,15). To date, several cardiac biomarkers have been found to be reliable and practicable for the diagnosis of heart failure (14,35). N-terminal pro-brain natriuretic peptide (NT-proBNP) is considered one of the critical indicators in the prediction and management of congestive heart failure due to systolic and diastolic dysfunction in humans, dogs and cats (14,26,42). With regard to echocardiography, transmitral flow indices and tissue Doppler imaging together with conventional echocardiography are considered to be accurate and reliable way to evaluate hemodynamic abnormalities in patient with heart diseases, as well as systolic and diastolic dysfunction (13,52).

The aim of this study was to identify the relationship between NT-proBNP and conventional echocardiographic indices in dogs with different stages of heart failure by chronic mitral valve insufficiency (CMVI). We hypothesized that dogs with the plasma levels of NT-proBNP in dogs with CMVI would have statistically significant relation with one of transmitral flow indices or TDI indices.

Materials and methods

Study design

This study was designed to evaluate the relationship between NT-proBNP and echocardiographic parameters in dogs with CMVI. First of all, we compared the echocardiographic parameters and plasma concentrations of NT-proBNP with the International Small Animal cardiac Health Council (ISACHC) classes in this study population, thereby making it possible to determine whether the data distributions in this study are consistent with those of previous studies. Second, we statistically analyzed the relationship between NT-proBNP and echocardiographic parameters.

Study population

The study population composed 57 client-owned dogs (mean age: 10.4 ± 2.93 years; range: 4-15 years) with or without CMVI. The owner's consent for the participation of each dog was obtained before enrollment to the study. All dogs underwent physical examination, echocardiography, complete blood count and chemistry panel. We excluded dogs that have clinically relevant systemic diseases such as renal failure and hypertension. The potential influence of age and body weight on NT-proBNP other than control group was limited by including only small breed dogs (≤ 12 kg)

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older than 7 years. Seven dogs served as healthy controls, judged as normal on the basis of blood biochemistry, echocardiography, blood pressure, and electrocardiography. The diagnosis of CMVI was made on the basis of clinical signs, X-ray data, and echocardiographic findings, according to guidelines (2) for the diagnosis of CMVI in dogs. The dogs with CMVI were then divided into 3 groups [ISACHC class I (class Ia and class Ib): asymptomatic; ISACHC class II: symptomatic; ISACHC class III (class IIIa and class IIIb), advanced to refractory], according to the criteria proposed by the ISACHC for the functional classification of heart failure (20). All dogs with CMVI were being medicated for heart disease depending on its severity, with drugs, such as enalapril, furosemide, spironolactone, pimobendan, digoxin, and amlodipine. The clinical characteristics of the 57 recruited dogs are presented in Table 1.

Measuring NT-proBNP

Venous blood samples were taken from the external jugular vein of 12-hour-fasted dogs just before echocardiographic examination. These samples were then transferred directly into tubes containing ethylene diaminetetra acetic acid and centrifuged within 30 min of collection. The supernatant was placed into transport tubes provided by a laboratory (Idexx Laboratories, Westbrook, ME, USA), which were shipped overnight on dry ice within 2 week of collection for the measurement of NT-proBNP by a commercial laboratory. The plasma NT-proBNP concentration was measured using a commercially available assay (Cardiopet proBNP, Idexx Laboratories, Westbrook, ME, USA). The operators performing the NT-proBNP assays were blinded to the patients' clinical information.

Echocardiography

Each dog was unsedated and positioned first in right and then in left lateral recumbency for echocardiographic examination. Transthoracic echocardiography was performed using a commercially available system (Vivid 7, GE Healthcare, Milwaukee, WI, USA) to obtain standard 2-dimensional, pulse-Doppler (PD), M-mode left ventricular measurements (parameters measured: LA, left atrial diameter; EF, ejection fraction; FS, fractional shortening; IVSd, diastolic interventricular septal dimension in diastole; IVSs, interventricular septal dimension in systole; LVIDd, left ventricular internal dimension in diastole; LVIDs, left ventricular internal dimension in systole; LVPWd, left ventricular posterior wall thickness in diastole; LVPWs, left ventricular posterior wall thickness in systole; EDV, end diastolic volume; ESV, end systolic volume; EDVI, end diastolic volume index; ESVI, end systolic volume index). Three consecutive cardiac cycles were used for analysis, using mean values.The right parasternal projection was used to measure the left atrial (LA) and aortic root (AO) diameters during systole and diastole, respectively, using short-axis 2-dimensional views at the level of the aortic valve, and the LA/AO ratio was calculated. Doppler studies were performed from the left apical 4-chamber view. To minimize the background noise and clarify the blood flow and tissue signals, the gain and filter settings for each dog were adjusted. Trans-mitral velocities were measured by means of PD with the sample volume positioned at the tips of the mitral valve leaflets, through which the peak early (E) velocity, last (A) velocity, E/A ratio, and deceleration time (DT) of the early mitral inflow were obtained. All evaluated parameters are shown in Tables 2.

Statistical analysis

Statistical analyses were performed using commercially available statistical software (SPSS version 19.0 for Windows; SPSS Inc., San Diego, CA, USA). Continuous variables are presented as mean ± standard deviation (SD). The statistical methods used were one-way analysis of variance (ANOVA), and Pearson's coefficient of correlation. If statistical significance was obtained between groups, multiple comparisons (Scheffe post hoc test) were used to detect significant differences. Differences among the ISACHC groups in NT-proBNP, conventional echocardiographic variables were evaluated by 1-way ANOVA. Pearson's coefficient of correlation was used to evaluate the strength of the association between NT-proBNP and echocardiographic imaging-derived variables such as conventional echocardiographic variables and TDI-derived variables, which were visualized using a scatter plot and linear regression line. Multiple linear

Table 1. Demographic characteristics of the study population

	ISACHC class			
	Control	Class I	Class II	Class III
n (57)	7	12	19	19
Age	5.4 ± 1.4	10.2 ± 2.5	10.8 ± 2.1	12.0 ± 2.2
Sex	M(3), F(4)	M(3), F(9)	M(6), F(13)	M(13), F(6)
BW	6.0 ± 1.3	4.0 ± 1.6	5.6 ± 2.4	4.8 ± 2.5
Breeds				
Cocker spaniel			3	1
CKCS			2	
Chihuahua			1	
Cross breed		1		
Maltese	2	9	7	12
Miniature Poodle			1	
Pekingese			2	
Pomeranian			1	1
Schnauzer	1	1	1	1
Shih-Tzu	1	1	1	2
White terrier	2			
Yorkshire Terrier	1			2

All data are expressed with the mean value (± SD).
BW, body weight; M, male; F, female; CKCS, Cavalier King Charles Spaniel

regression analysis was performed on echocardiographic variables showing a significant association with NT-proBNP to evaluate the independent predictors of NT-proBNP. For all comparisons, $p < 0.05$ was considered statistically significant, unless stated otherwise.

Results

Study populations

The breeds of dogs included in this study were as follows: Maltese (52.6%), Shih tzu (8.8%), American cocker spaniel (7.0%), Miniature schnauzer (5.3%), Pekingese (3.5%), White terrier (3.5%), Miniature poodle (3.5%), cross breed (1.8%), Chihuahua (1.8%), Cavalier King Charles spaniel (1.8%), and Pomeranian (3.5%). The majority of the dogs were adults, female, and small-breed (Table 1). The mean body weight was 4.8 ± 2.4 kg.

NT-proBNP and echocardiographic parameters according to ISACHC classes

The plasma levels of NT-proBNP showed a significant difference among the groups. NT-proBNP was significantly higher in the ISACHC III group (1313.63 ± 962.43) than in control (303.14 ± 98.71), ISACHC I (236.33 ± 185.13) and ISACHC II (412.84 ± 319.12) groups (Fig 1). Free wall E/E’ was 9.46 ± 1.77 in control dogs, 11.98 ± 3.48 in ISCAHC I dogs, 11.92 ± 4.38 in ISACHC II dogs and 18.52 ± 8.41 in ISACHC III dogs, while septal wall E/E’ was 12.76 ± 4.59 in control dogs, 17.12 ± 7.31in ISCAHC I dogs, 16.31 ± 6.58 in ISACHC II dogs and 20.55 ± 7.56 in ISACHC III dogs. In the comparison of conventional echocardiography along the ISACHC classes, significant differences in LA dimension, LA/AO ($p < 0.001$), EF ($p < 0.05$), FS ($p < 0.05$), E ($p <$

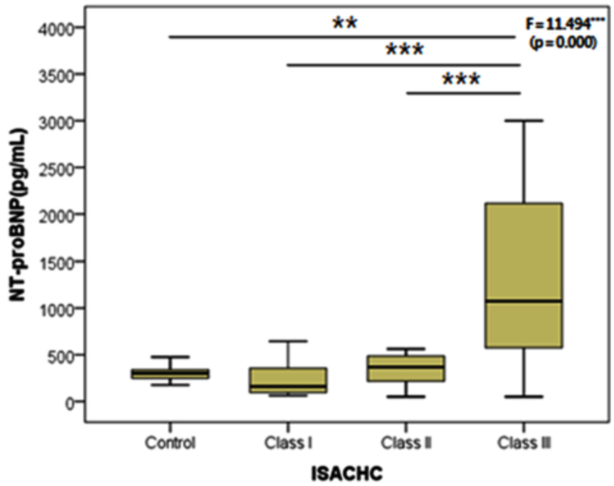

Fig 1. Comparison of NT-proBNP levels between ISACHC classes. The lines inside the boxes represent the median; the lower and upper edge of each box represents the 25th and 75th percentile, respectively; the lowest and highest lines represent the 10th and 90th percentiles, respectively (*p < 0.05, **p < 0.001, ***P < 0.001).

Table 2. Comparison of conventional echocardiographic variables in comparison between ISACHC classes

	ISACHC				P-value
	Control Mean ± SD	Class I Mean ± SD	Class II Mean ± SD	Class III Mean ± SD	
LA (cm)	1.73 ± 0.25^{a}	2.17 ± 0.41^{ab}	2.65 ± 0.48^{bc}	2.96 ± 0.71^{c}	0.000^{***}
LA/AO	1.31 ± 0.08^{a}	1.62 ± 0.36^{ab}	1.90 ± 0.22^{b}	2.31 ± 0.26^{c}	0.000***
EF (%)	73.11 ± 8.84^{a}	78.66 ± 11.67^{ab}	84.07 ± 6.89^{ab}	84.58 ± 8.20^{b}	0.015*
FS (%)	41.17 ± 6.35^{a}	47.04 ± 13.11^{ab}	51.86 ± 8.56^{ab}	53.7 ± 10.87^{b}	0.038*
E (m/sec)	0.60 ± 0.10^{a}	0.68 ± 0.09^{a}	0.85 ± 0.27^{a}	1.12 ± 0.33^{b}	0.000***
A (m/sec)	0.47 ± 0.09^{a}	0.63 ± 0.15^{ab}	0.83 ± 0.16^{b}	1.03 ± 0.25^{c}	0.000***
E/A	1.30 ± 0.28	1.13 ± 0.27	1.03 ± 0.35	1.16 ± 0.49	0.450
DT (m/sec)	84.40 ± 20.27	73.59 ± 18.41	91.99 ± 24.34	88.43 ± 26.04	0.233
IVSd	0.75 ± 0.16	0.67 ± 0.14	0.70 ± 0.19	0.59 ± 0.13	0.094
IVSs	1.00 ± 0.22	0.96 ± 0.18	1.04 ± 0.19	0.97 ± 0.19	0.615
LVIDd	2.24 ± 0.40^{ab}	2.06 ± 0.47^{a}	2.39 ± 0.63^{ab}	2.74 ± 0.54^{b}	0.012^{*}
LVIDs	1.33 ± 0.35	1.12 ± 0.45	1.20 ± 0.40	1.30 ± 0.46	0.645
LVPWd	0.67 ± 0.13	0.64 ± 0.08	0.70 ± 0.16	0.60 ± 0.11	0.146
LVPWs	1.05 ± 0.22	1.04 ± 0.21	1.15 ± 0.25	1.11 ± 0.22	0.616
EDV	17.82 ± 7.08^{ab}	14.92 ± 7.94^{a}	22.21 ± 14.95^{ab}	29.77 ± 14.32^{b}	0.020^{*}
ESV	4.89 ± 2.86	3.65 ± 3.32	4.10 ± 3.14	5.13 ± 4.17	0.671
EDVI	61.84 ± 25.46^{a}	57.1 ± 24.17^{a}	71.29 ± 40.22^{a}	123.11 ± 35.74^{b}	0.000^{***}
ESVI	17.11 ± 11.03	13.27 ± 11.99	12.40 ± 7.02	19.96 ± 12.71	0.170

*p < 0.05, **p < 0.01, ***p < 0.001
SD : standard deviation , Scheffe post hoc test, a < b < c

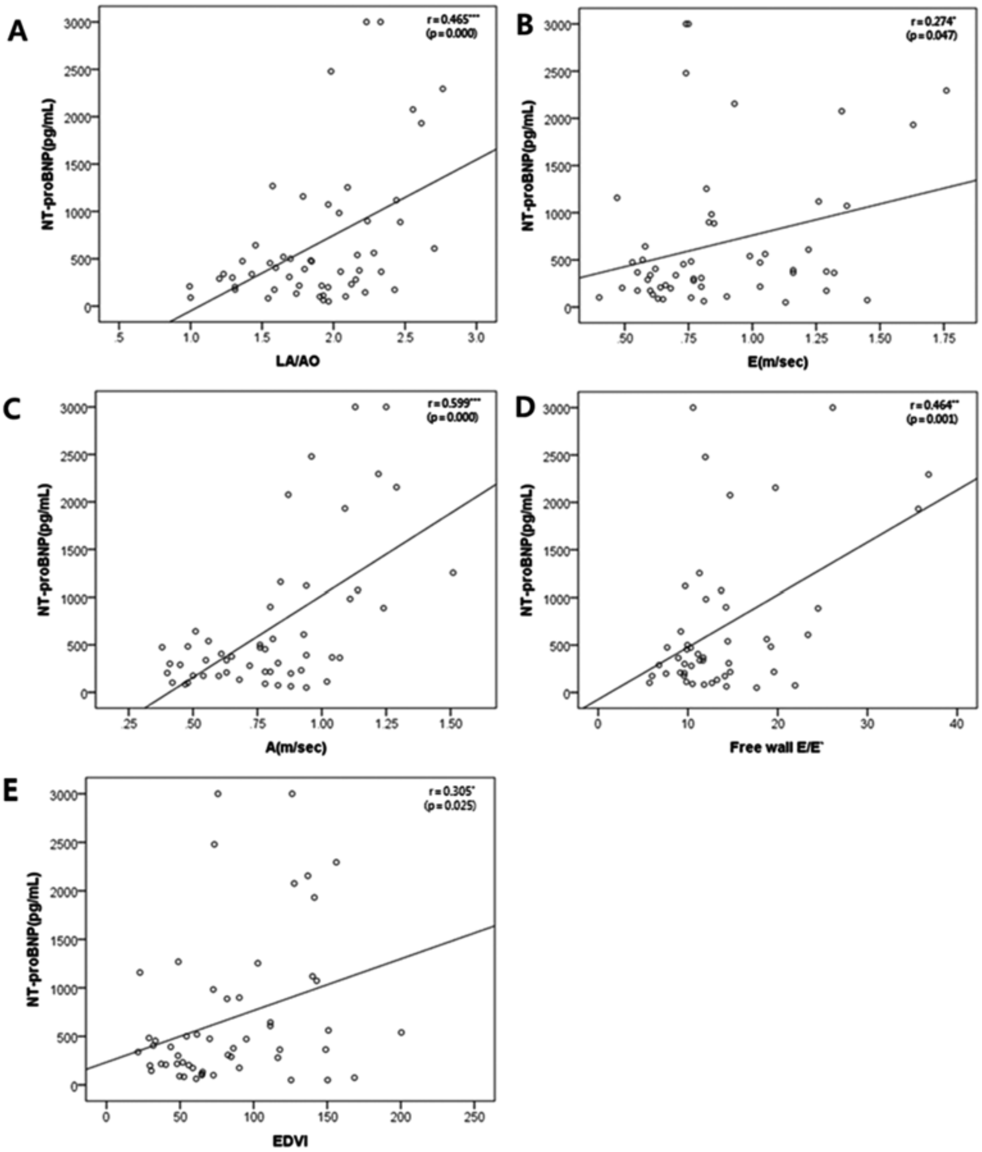

Fig 2. Correlations of NT-proBNP plasma concentrations with echocardiographic parameters in study population with CMVI. Among the parameters, LA/AO- ratio, E and A, free wall E/E', and EDVI were significantly associated with the plasma NT-proBNP levels. EDVI: End diastolic volume index, LA/AO ratio: left atrial to Aorta ratio.

0.001), A ($p < 0.001$), LVIDd ($p < 0.05$), EDV ($p < 0.05$) and EDVI ($p < 0.001$) were observed (Table 2).

Correlations between NT-proBNP and echocardiographic parameters

Fig 2 shows scatter plots with linear regression linefor NT-proBNP versus echocardiographic variables. Among the echocardiographic parameters listed in Tables 2 and 3, LA/AO ($r = 0.465$, $p < 0.001$), A velocity ($r = 0.599$, $p < 0.001$), E velocity ($r = 0.274$, p 0.047) and E/E' ratio ($r = 0.464$, $p < 0.001$) were significantly associated with plasma levels of NT-proBNP in this study population. However, in the multiple linear regression analysis, only A velocity ($\beta = 0.443$, $p < 0.006$) was an independent predictor of NT-proBNP (Table 3).

Discussion

In this study, we found that LA, LA/AO, EF, FS, E and A, EDV and EDVI increased as the ISACHC class increased. These findings are compatible with those of previous studies in dogs with CMVI (6,13,45,46). This suggests that volume overload, high left atrial blood pressure, and high left ventricular filling pressure develop as heart disease progresses (13,54). Interestingly, there was no apparent evidence of systolic or diastolic dysfunctionon the basis of echocardiographic findings. In terms of systolic dysfunction, the characteristic hemodynamic changes in mitral regurgitation, such as reduction of afterload, eccentric hypertrophy and volume overload may have masked systolic dysfunction (13,54).

Table 3. Multiple regression analysis for evaluating associations of clinical echocardiographic indices listed in Fig 2 with NT-proBNP levels

Independent variables	B	Beta	T-value	P-value
K	−1096.049			
LA/AO	410.490	0.239	1.275	0.210
E(m/sec)	−421.957	−0.163	−0.862	0.394
A(m/sec)	1264.115	0.443	2.925	0.006**
Free wall E/E'	28.794	0.248	1.505	0.140
EDVI	4.865	0.257	1.463	0.152
R^2		0.463		
Adjusted R^2		0.408		
F-value		8.394***		

Dependent Variable: NT-proBNP
*$p < 0.05$ **$p < 0.01$ ***$p < 0.001$

Although we did not include all possible echocardiographic criteria used in diagnosing diastolic dysfunction in humans, recent literatures imply that the echocardiographic criteria for the diagnosis of diastolic dysfunction in humans (37) cannot be directly extrapolated to dogs with CMVI (6,10,49). This is because some of the parameters such as iso-volumic relaxation time (IVRT), E, A, and E' and A' velocities can be affected by the hemodynamic changes associated with varying degrees of mitral regurgitation (6,10,13). Interestingly, Tsutsui *et al*. suggest that diastolic dysfunction in dogs with CMVI is unlikely because the reduction of diastolic function in these dogs is due to decrease in the extent of shortening instead of diastolic dysfunction, which is proven by the control dogs with normal diastolic function (49). This makes it difficult to determine whether patients with various degrees of CMVI have systolic or diastolic heart failure on the basis of echocardiographic parameters alone (6,13). Therefore, further studies are needed with regard to the diagnosis of diastolic dysfunction in dogs with CMVI. On the basis of the preliminary study involving echocardiographic parameters, we confirmed that the hemodynamic characteristics of this study population corroborate the results of previous studies in dogs with CMVI (6,13,45,46).

NT-proBNP is considered one of the most reliable and accurate biomarkers for the evaluation of heart failure in humans and in animals (7,9,18,19,35,44). Interestingly, our preliminary study showed a significant difference between the ISACHC III group and the other groups, which might be explained by the fact that all dogs other than those in the control group were medicated for the control of heart failure. Previous studies have also shown that the plasma levels of NT-proBNP can be reduced owing to the resolution of heart failure by cardiac medications (39,51), which is compatible with the findings of this study.

In veterinary field, Chetboul *et el*. (12) demonstrated that NT-proBNP were correlated with regurgitation fraction, LA/AO, EDVI, and FS out of conventional echocardiographic parameters other than transmitral flow indices. Other studies (34,41) also compared NT-proBNP with conventional echocardiographic parameters. However, all of these veterinary studies did not directly compared NT-proBNP with transmitral flow velocities (E flow and A flow velocities).

On the contrary, there have been many human studies demonstrating associations between NT-proBNP or BNP and echocardiographic parameters in patient with congestive heart failure (24,28,47,48). Interestingly, some human studies have shown different results from that of our study regarding the relation between NT-proBNP and LA/AO, E and A, EDVI and E/E' ratio, as well as inconsistencies in results between different human studies, depending on the types of heart disease examined (3-5,21,27,47,48). Despite these inconsistent results in human studies, similar conclusions to ours have also been drawn, as follows: 1) NT-proBNP is a sensitive marker for systolic or diastolic heart failure, and also reflects the severity of heart failure; 2) NT-proBNP levels were associated with at least one of the echocardiographic criteria used for diagnosing heart disease; 3) associations between NT-proBNP and echocardiographic criteria may differ depending on the hemodynamic changes associated with the heart diseases of the study population (3-5,21,27,47,48). In addition, the hemodynamic characteristics reflected in the echocardiographic parameters vary with each type of heart disease (15). The results obtained in the human heart are at variance with those of dog studies. However, the prevalence of primary mitral regurgitation in humans is low (estimated at 2-3%) (22) contrary to that in dogs (2). For these reason, in terms of comparing NT-proBNP with the echocardiographic parameters in patients with primary mitral regurgitation, there are very few human studies eligible to be compared with this present study. Thus, the interpretation of this study result shall focus on associations between hemodynamics of CMVI and plasma NT-proBNP, rather than comparing it with previous studies.

NT-proBNP, a biologically inactive metabolite and a remnant from the cleavage of proBNP to BNP, has higher plasma concentrations and longer half-life than BNP (25,35,44,48). The release of NT-proBNP and BNP is predominantly originated from the ventricles in response to myocardial wall stress associated with high left atrial pressure, high ventricular filling pressure and systolic or diastolic dysfunction (35). In this study, we found that the plasma concentrations of NT-proBNP were significantly associated with LA/AO, E and A, EDVI, and E/E'. Interestingly, using multiple regression analysis, only A was an independent predictor of NT-proBNP in this study population. According to previous studies, echocardiographic parameters such as LA/AO, E and A, EDVI and E/E' were associated with PCWP and LVEDP (10,17,36). Accordingly, an increase in these echocardiographic parameters may reflect increasing atrial pressure, volume overload, left ventricular filling pressure and LVEDP with increasing ISACHC class in the study population (5,6,13,17,31,33,35, 36,38). Consequently, increases in these hemodynamic indices may cause myocardial wall stress causing the release of NT-proBNP.

With regard to association between NT-proBNP, and LA/AO and EDVI, Cheboul *et al* (12) has alrealy reported similar results in dogs with CMVI. The LA/AO ratio has been widely used in evaluating the severity of CMVI because it shows characteristic hemodynamic features due to the progressive deformation of the valve structure causing regurgitation, volume overload, ventricular remodeling and myocardial dysfunction (2). Accordingly, LA/AO is known to progressively increase as regurgitation becomes worse. In addition, it is positively associated with the LVED that is considered one of the release factors of NT-proBNP in myocardium. With regard to EDVI, it is associated with mitral regurgitant volume and ventricular filling pressure in patients with mitral valve regurgitation, which can be indirectly used to evaluate the severity of CMVI (6,50). However, the dimension and volume of the left atrium and left ventricle do not proportionally reflect the pressure of the chambers because the compliance of the chamber wall, together with preload are considered critical factors in determining the chamber pressure (23,33, 38,43). In addition, the half-life of canine BNP is shorter at 20 min, while NT-proBNP has a slightly longer half-life than BNP (9). Accordingly, the associations of NT-proBNP with LA/AO and EDVI may be highly influenced by the compliance curve for the left atrium and left ventricle and the half-life of NT-proBNP (9,23).

Mitral inflow velocities such as E and A wave velocities, one of the candidate parameters for the noninvasive assessment of LV filling pressures or PCWP, do not solely reflect ventricular filling pressures because these parameters are influenced by age, heart rate, preload, diastolic function and other potentially interrelated factors (32). Some human and canine studies have shown that E/E’ proportionally reflects the LV filling pressures, PCWP and LVEDP in patients with myocardial diastolic dysfunction (17,30,36). However, it is still controversial whether or not E/E’ is useful predicting PCWP and LVEDP in various heart diseases (10,36). Brunch *et al* demonstrated that contrary to secondary mitral regurgitation, E/E’ did not reflect the LVEDP in patients with primary mitral valve regurgitation in which the preserved myocardial performance were reactive to increased preload (10). Even though Oyama *et al* (36) suggest that E/E’ reflects left atrial pressure in dogs with experimental mitral regurgitation, their study population unlike ours did not have adequate time for the natural remodeling associated with the progressive regurgitation, which is different from our study population.

Regarding the clinical importance of E in dogs with CMVI, the severity of mitral regurgitation is a critical determinant of increased early diastolic filling velocities (E wave velocity) (6). An E wave velocity exceeding 1.25-1.5 m/sec carries the likelihood of elevated filling pressure and a poor prognosis in dogs with CMVI (6,8), which may be consequently related to increased myocardial wall stress and NT-proBNP. Together with E, A likewise reflects atrial pressure, atrial function, atrial volume, and ventricular diastolic and systolic functions (1,43). In the case of CMVI without evident systolic or diastolic dysfunction, the role of atrial contraction dealing with volume remnant after the E may be critical and reflected in A wave velocity. This is supported by previous studies showing gradual increase of E and A in dogs with CMVI (45,46). However, it is difficult to explain why A is the only independent predictor of NT-proBNP in the study population. One possible explanation may be the fact that atrial volume overload and high atrial pressure are the main hemodynamic abnormalities in dogs with mitral regurgitation.

Our study has some limitations. Our patient population represents generally older (> 7 years old) and small-breed dogs, while the mean age of the control group in this study was 5.4 years. Echocardiographic parameters, including tissue Doppler indices can be influenced by factors such as age (29). In addition, previous studies have stressed the importance of IVRT in predicting left ventricular filling pressure (16,40). Some human studies have shown a positive association between IVRT and plasma concentrations of NT-proBNP (53). However, we did not evaluate IVRT in the present study.

In conclusion, we found that plasma NT-proBNP levels were significantly correlated with LA/AO, A and E, E/E’-ratio and EDVI. Other than E/E’-ratio, no TDI indices showed relationship with NT-proBNP. Interestingly, only A was found to be an independent predictor of NT-proBNP in dogs with CMVI. Thus, we believe that further studies directly comparing the catheter-measured LVEDP and PCWP with NT-proBNP and echocardiographic parameters are warranted.

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개의 만성 이첨판 폐쇄부전증 환자군에서 혈장 NT-proBNP 농도 평가연구

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요 약 : 본 연구는 개의 이첨판 폐쇄부전증(CMVI) 환자군에서 혈장 NT-proBNP농도를 평가한 연구이다. 본 연구를 위해 CMVI에 이환된 50마리와 건강한 대조군 7마리를 대상으로 일반적인 심초음파 검사와 혈중NT-proBNP농도를 측정하였다. 심부전의 심하기에 따라 분류된 환자군에서 측정된 NT-proBNP농도와 심초음파 인덱스의 상호관련성을 평가하였다. 혈중 NT-proBNP 농도는 심부전의 심하기에 따라 상승하였다. 또한 심초음파 인덱스중 left atrium/aorta (LA/AO), early diastolic transmitral flow (E) velocity, late diastolic transmitral flow (A) velocity, end diastolic volume index (EDVI) 등과 밀접한 관련성이 관찰되었다. 본연구는 이첨판 폐쇄부전증 환자의 예후를 평가하는데 중요할 것으로 보인다.

주요어 : 심초음파, NT-proBNP, A flow velocity, 개, 이첨판 폐쇄부전증