

## Pulmonary Vein-to-Pulmonary Artery Ratio is an Echocardiographic Index of Congestive Heart Failure in Dogs with Degenerative Mitral Valve Disease

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**Background:** Early recognition of left-sided congestive heart failure (CHF) in dogs with degenerative mitral valve disease (DMVD) is important because it influences medical therapy, timing of follow-up, and outcome.

**Hypothesis:** Pulmonary vein diameter-to-pulmonary artery diameter ratio (PV/PA) measured by echocardiography can predict CHF.

**Animals:** Ninety-eight client-owned dogs, 37 controls, and 61 dogs with DMVD.

**Methods:** Prospective clinical cohort study. History, physical examination and Doppler-echocardiography were performed. Dogs were classified as International Small Animal Cardiac Health Council class I, II or III. Congestive heart failure was identified in a subset of 56 dogs based on radiographic findings. The PV/PA was measured in bidimensional (2D) and M-mode by 2 investigators blinded to the radiologists' conclusions.

**Results:** Interobserver coefficients of variation for PV/PA acquisition and measurement were <10%. The PV/PA in control dogs was approximately 1 and increased with class of heart failure. The presence of CHF could be best predicted by measuring PV/PA in 2D echocardiography (cut-off, 1.7; area under the curve, 0.98; CI, 0.97–0.98;  $P < .001$ ) with a sensitivity of 96% and a specificity of 91%.

**Conclusion and clinical importance:** The PV/PA is a simple and reproducible echocardiographic variable that increases with class of heart failure and may help discriminate dogs in CHF from asymptomatic dogs with DMVD. Additional studies are required to determine whether PV/PA might provide additional information in the integrated interpretation of Doppler-echocardiographic indices of left ventricular filling pressures and could be used for rapid assessment of CHF in dogs in a critical care setting.

**Key words:** Canine; Congestion; Diagnosis; Pulmonary vein.

Degenerative mitral valve disease (DMVD) is the most common form of acquired heart disease in dogs.<sup>1</sup> The course of the disease is highly variable with most dogs spending several years in an asymptomatic state. Approximately one-third of affected dogs develop congestive heart failure (CHF) and die.<sup>2</sup> Early recognition of CHF is important because it enables initiation of conventional therapy in accordance with expert recommendations,<sup>3</sup> the avoidance of life-threatening situations, and limitation of hospitalization costs. Clinical variables, such as resting respiratory rate, can predict cardiac decompensation,<sup>4</sup> but no clinical sign is CHF-specific. Thoracic radiography is considered the clinical “gold standard”, but important interreader variability exists. Diagnosis of CHF should not rely solely on radiographic determination of pulmonary edema.<sup>5,6</sup> The

### Abbreviations:

2D	bidimensional
ACEI	angiotensin converting enzyme inhibitor
AUC	area under the curve
Ao	aorta
BW	body weight
CHF	congestive heart failure
CI	confidence interval
CV	coefficient of variation
DMVD	degenerative mitral valve disease
E/A	maximal velocity of early left ventricular diastolic filling/maximal velocity of active filling
EDVI	indexed end-diastolic volume
IQR	interquartile range
ISACHC	international Small Animal Cardiac Health Council
LA	left atrium
nLVIDd	normalized left ventricular internal diameter in diastole
MM	m-mode
NT-proBNP	n-terminal probrain natriuretic peptide
PA	pulmonary artery
PV	pulmonary vein
PV/PA	pulmonary vein to pulmonary artery ratio
SD	standard deviation
TR	tricuspid regurgitation
VHS	vertebral heart score

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N-terminal probrain natriuretic peptide (NT-proBNP) biomarker may contribute to the diagnosis of CHF. The NT-proBNP concentration correlates with DMVD severity<sup>7,8</sup> and has been shown to help distinguish dogs with respiratory signs caused by CHF from those with respiratory disease.<sup>9,10</sup> However, a wide overlap exists between asymptomatic dogs and dogs in CHF,<sup>9,11,12</sup>

and a small proportion of healthy dogs have high concentrations of NT-proBNP.<sup>13</sup> Furthermore, day-to-day<sup>14</sup> and interbreed<sup>15</sup> variations exist. Doppler echocardiography may confirm DMVD diagnosis and detect dogs in CHF. In dogs with DMVD, peak E to isovolumic relaxation time ratio and diastolic functional class are sensitive markers of CHF.<sup>16</sup> However, these measurements require operator expertise. All of these single diagnostic tools have their own limitations, and obtaining a definitive diagnosis often relies on a combination of test results.<sup>10,16</sup> Therefore, the development of an additional, easy-to-measure, echocardiographic index might improve early recognition of CHF in dogs.

The pulmonary vein-to-pulmonary artery ratio (PV/PA) is a novel echocardiographic variable that might distinguish dogs in CHF from those in a compensated state.<sup>17</sup> In dogs with progressive DMVD leading to CHF, we would anticipate that increased pulmonary venous pressure associated with venous enlargement would cause an increase in the PV/PA ratio. Therefore, we first established normal values for PV, PA, and the PV/PA ratio in control dogs of various sizes and determined the correlation between the PV/PA ratio assessed by bidimensional (2D) and M-mode (MM) echocardiography. Thereafter, we assessed the effect of the class of heart failure on this ratio and determined if PV/PA could be used to identify CHF in dogs with DMVD.

## Material and Methods

### Dogs

Control and diseased dogs were prospectively recruited (from October 2011 until May 2015) at the Clinical Veterinary Hospital of the University of Liège. Inclusion criteria for affected dogs included the presence of a typical heart murmur and an echocardiographic diagnosis of DMVD, characterized by degenerative changes of the mitral valve leaflets, mitral valve prolapse and the presence of systolic regurgitant flow.<sup>18</sup> Control dogs were recruited during routine consultations or belonged to staff members. A thorough history was taken for all dogs before physical examination and Doppler echocardiography. Dogs with evidence of a concomitant disease were excluded. Dogs with DMVD were classified into class I, II, or III according to the International Small Animal Cardiac Health Council (ISACHC) classification system.<sup>19</sup> Class I was defined as subclinical heart disease without (IA) or with (IB) evidence of left cardiomegaly. Class II was defined as mild to moderate CHF in the presence of radiographic abnormalities consistent with pulmonary edema. Class III was defined as overt, severe CHF.

### Doppler Echocardiography

Transthoracic 2D, MM echocardiography and conventional Doppler echocardiography were performed by 2 trained observers (1 board-certified cardiologist [KME] and 1 cardiology resident [ACM]) using an ultrasound unit<sup>a</sup> equipped with 2.2–3.5 and 5.5–7.5 MHz phased-array transducers. Dogs were placed in right and left lateral recumbency and a simultaneous 1-lead electrocardiogram was recorded. Standard right parasternal (long and short axis) and left apical parasternal views were used for data acquisition. Left atrial size was assessed in the right parasternal long axis view using the septal-to-caudal dimension of the left atrium (LAmin) and in right parasternal short axis at the level of the aorta (LA). Both measurements were taken at the end of systole

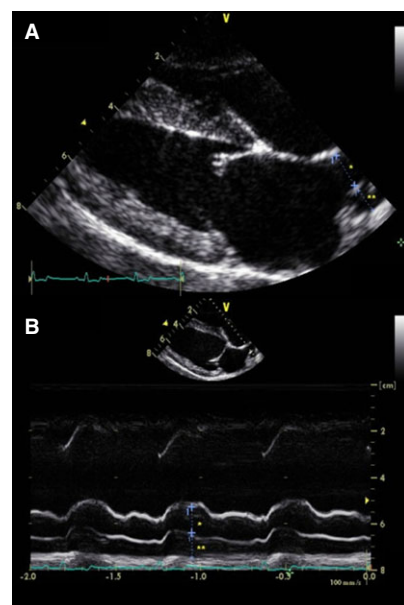
and were normalized using aortic diameter (Ao) (LAmin/Ao and LA/Ao, respectively). End-diastolic left ventricular volume was calculated from the right parasternal long axis view using modified Simpson's rule<sup>20</sup> and indexed to body surface area (EDVI). Left ventricular end-diastolic diameter was measured in MM from a left ventricular short axis view at the level of chordae tendinae and indexed to body weight using the Cornell method (nLVIDd).<sup>21</sup> Mitral inflow was recorded using pulsed-wave Doppler from the left apical parasternal 4-chamber view (E, A and E/A). The tricuspid valve was systematically evaluated for evidence of regurgitation. If a tricuspid regurgitant (TR) jet was visible, its velocity was recorded and transformed into a pressure gradient according to the modified Bernoulli equation. Pulmonary hypertension was defined as a TR pressure gradient >36 mmHg (TR > 3 m/s). All measurements were performed off-line by a single trained investigator (KME) blinded to clinical signs and thoracic radiographic scores.

### Acquisition and Reproducibility of PV/PA Ratio

For PV/PA measurement, a right parasternal long axis 4-chamber view was optimized to simultaneously visualize a longitudinal section of the medial PV and the right PA in cross-section and recorded. Measurements of PV and PA diameters were taken in MM as previously described<sup>17</sup> and in 2D. Dimensions were obtained by tracing a line perpendicular to the medial PV and passing through the center of the adjacent right PA. For both measurements, we used the inner edge-to-inner edge method at the end of the T wave (Fig 1). Three measurements were averaged. Interobserver variability of PV/PA image acquisition and of PV/PA measurement were assessed separately in 10 and 20 dogs, respectively.

### Thoracic Radiography

Thoracic radiographs (right lateral, left lateral, and dorso-ventral projections) were taken in a subset of dogs. A board-certified



**Fig 1.** Illustration of pulmonary vein diameter (\*) and right pulmonary artery diameter (\*\*) measurements in bidimensional (A) and M-mode (B) using the inner edge to inner edge method.

radiologist (GB) and a radiologist with extensive expertise (ALE) reviewed the images independently. All studies were randomly ordered and radiologists were blinded to the animal's identification, the date of examination, the initial interpretation of images, and the echocardiographic findings. A radiographic composite CHF score was assigned to each patient. This score was based on 3 main criteria: evidence of cardiomegaly, lung pattern, and pulmonary venous congestion. Specifically, cardiomegaly criteria were subdivided as follows: qualitative assessment of the cardiac silhouette, vertebral heart score,<sup>22</sup> and presence of left atrial enlargement. A cardiomegaly score of 0 was given when the cardiac silhouette was considered normal; a score of 1 was given when moderate cardiomegaly was present; and, a score of 2 was given when severe cardiomegaly was present. Lung pattern was assessed with a score varying from 0 to 3, with 0 corresponding to a normal lung pattern, 1 to a moderate to severe interstitial pattern, 2 to a localized alveolar pattern, and 3 to a diffuse alveolar pattern. Venous congestion also was assessed with a score between 0 and 2, with 0 corresponding to the absence of venous congestion, 1 for moderate venous congestion (not evident in all pulmonary veins), and 2 for severe venous congestion. A final cumulative score between 0 and 7 was allocated to each dog. The final radiographic assessment also determined if CHF was present or absent. Results of the 2 radiologists were compared and, if there was disagreement with regard to the presence or absence of CHF, images were reviewed by both radiologists together to provide a final consensus.

### Statistical Analysis

Statistical analysis was performed using the *xlstat*<sup>b</sup> software. Statistical significance was set at  $P < .05$ . Normality was tested using the Shapiro–Wilk test. Continuous data were expressed as median values with interquartile range (IQR, 25th to 75th percentiles). The interobserver variability of image acquisition and measurements was calculated using coefficients of variation (CV) with the formula:  $CV = \text{standard deviation of measurement}/\text{mean of measurement} \times 100$  (%). The PV/PA measurements obtained from 2D and MM were compared using a paired Mann–Whitney log rank test. Nonlinear regression analyses were used to identify and quantify relationships between PV or PA and body weight. Proportions were compared by a chi-squared test. A Mann–Whitney log rank test was used to compare continuous demographic data between control and affected dogs, and PV/PA between asymptomatic and CHF dogs. Pearson or Spearman correlations were used, according to data distribution, to test the strength of the relationship between PV/PA measured by the 2 methods and other echocardiographic parameters. A Kruskal–Wallis test with

Bonferroni's adjustment (corrected  $P$  value .005) was used to compare PV/PA among classes of heart failure. Receiver-operating characteristic (ROC) curve analysis was used to determine the diagnostic accuracy of PV/PA and to define cut-off values for each prediction.

## Results

### Dogs

Ninety-eight dogs were enrolled in the study including 37 controls and 61 dogs with DMVD. In the control group, the most common breeds were crossbreed (7), Jack Russell Terrier (4), Beagle (3), Dachshund (3), West Highland white terrier (3), American Staffordshire (2), Labrador (2), and Yorkshire terrier (2). In dogs with DMVD, the most common breeds were Cavalier King Charles Spaniel (14), crossbreed (7), Jack Russell terrier (5), Bichon Frise (5), Beagle (4), Dachshund (3), Shih-Tzu (3), Chihuahua (3), Lhasa Apso (2), and Yorkshire terrier (2). Control dogs (6.1 years old; range, 3.9–9.6) were significantly younger and included more females (21/37) than affected dogs (10 years old; range, 8.6–12.3;  $P = .001$ ; female, 22/61;  $P = .045$ ). No significant difference was found for body weight. Demographic data, historical findings, and physical examination results for the DMVD dogs are summarized in Table 1. At presentation, 4 (25%) dogs of class IA and 5 (31%) dogs of class IB were being treated with an angiotensin converting enzyme inhibitors (ACEI). One dog of class IB was also receiving pimobendan (6%). In classes II and III, 13 (65%) and 4 dogs (44%), respectively, had received furosemide before examination. Fifteen (75%) dogs in class II and 4 (44%) dogs in class III were being treated with an ACEI, whereas 10 (50%) and 2 (22%) dogs were receiving pimobendan. Three (15%) dogs in class II and 2 (22%) dogs in class III had received spironolactone.

### PV/PA: Variability and Reference Intervals

Interobserver CV for image acquisition of PV, PA and PV/PA were, respectively, 8, 4 and 8% in 2D and 4, 5 and 7% in MM. Interobserver CV for PV, PA and

**Table 1.** Demographic data, history findings, and the results of physical examination in 61 dogs with degenerative mitral valve disease.

	ISACHC IA	ISACHC IB	ISACHC II	ISACHC III
Number	16	16	20	9
Age (years)	10.3 (6.0–11.6)	9.1 (8.5–11.0)	10.3 (9.0–12.4)	11.1 (7.5–12.3)
Body weight (kg)	10.4 (7.3–13.1)	11.4 (8.0–14.4)	8.4 (7.0–11.5)	7.6 (5.9–11.2)
Sex (male : female)	9 : 7	11 : 5	14 : 6	5 : 4
Cough (%)	1 (6)	4 (25)	13 (65)	8 (89)
Exercise intolerance (%)	1 (6)	/	13 (65)	7 (78)
Tachypnea/Dyspnea (%)	/	1 (6)	6 (30%)	8 (89)
Syncope (%)	/	/	6 (30)	2 (22)
RR (breaths/min)	28 (24–32)	24 (24–30)	36 (24–48)	52 (42–84)
HR (beats/min)	102 (80–120)	110 (88–120)	132 (120–147)	160 (120–180)
Murmur grade (0/6–6/6)	3 (1–4)	4 (3–4)	5 (4–6)	5 (4–5)

Median (IQR) for continuous data, median (range) for categorical data and number of dogs (%) for frequency data. HR, heart rate; IQR, interquartile range; ISACHC, International Small Animal Cardiac Health Council; RR, respiratory rate.

PV/PA measurements were, respectively, 7, 9 and 9% in 2D 6, 9 and 9% in MM.

In healthy dogs, PV and PA measured in 2D and MM were correlated with body weight; no correlation was found for PV/PA (Fig 2). No significant difference was observed between PV/PA obtained in 2D or MM and both methods were highly correlated ( $r = 0.90$ ;  $P < .001$ ; Fig 3). The PV/PA ratio for control dogs was 1.01 (range, 0.95–1.06) in 2D and 1.01 (range, 0.95–1.12) in MM.

**PV/PA and Class of Heart Failure**

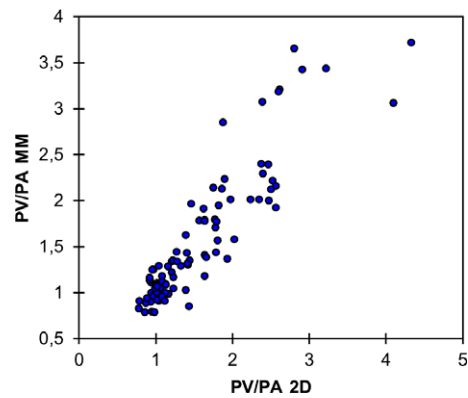
The PV/PA ratio increased with class of heart failure (Fig 4). The PV/PA ratio was significantly lower in control dogs compared to dogs with DMVD in ISACHC class IB (2D, 1.63; range, 1.42–1.76; MM, 1.60; range, 1.34–1.82), II (2D, 2.36; range, 1.89–2.53; MM, 2.02; range, 1.96–2.35) and III (2D, 2.55; range, 2.24–2.83; MM, 3.07; range, 1.78–3.43;  $P < .001$ ). The PV/PA also was lower in DMVD dogs in class IA (2D, 1.23; range, 1.14–1.40; MM, 1.15; range, 1.01–1.35) compared to dogs in class II ( $P < .001$ ) and III ( $P = .001$ ). Doppler-echocardiographic variables according to ISACHC class are summarized in Table 2. Regardless of the mode, PV/PA was correlated with other echocardiographic indices of left ventricular filling pressures such as the indexed left atrial and left ventricular sizes and the E/A ratio (Table 3).

**PV/PA and Radiographic Score**

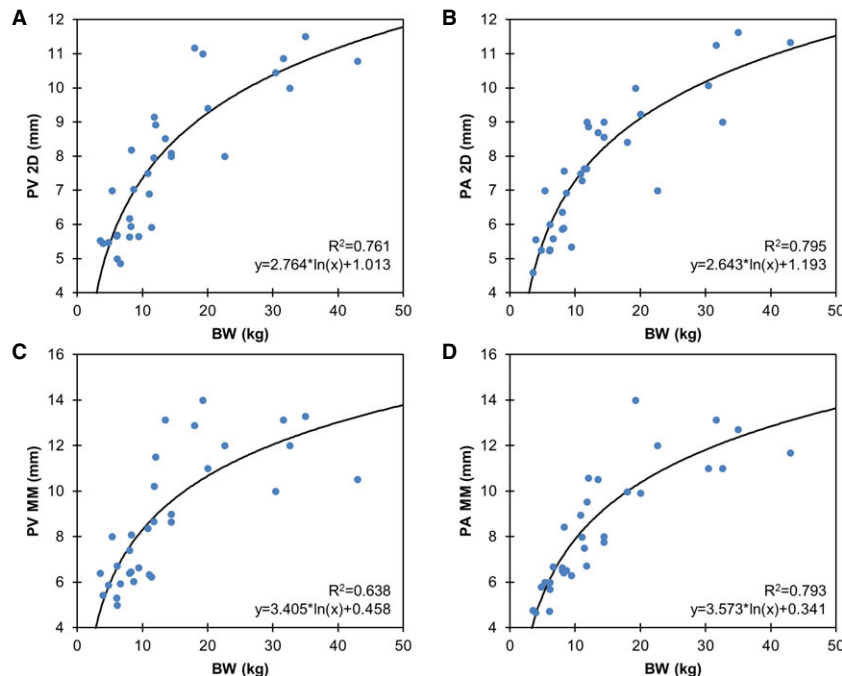
Thoracic radiographs were available for 13 controls and 43 (70%) dogs with DMVD. A radiographic

diagnosis of CHF was made in 39% of dogs with DMVD. The 13 control dogs had no evidence of CHF and had a total radiographic score of 0, 1, or 2. Dogs with a radiographic diagnosis of CHF had higher PV/PA ratios (2D, 2.39; range, 1.89–2.56; MM, 2.16; range, 1.86–2.63) than dogs without CHF on thoracic radiographs (2D, 1.19; range, 1.02–1.41; MM, 1.09; range, 0.96–1.35;  $P < .001$ ; Fig 5). The PV/PA was significantly correlated with radiographic composite score (2D,  $r = 0.66$ ;  $P < .001$ ; MM,  $r = 0.65$ ;  $P < .001$ ).

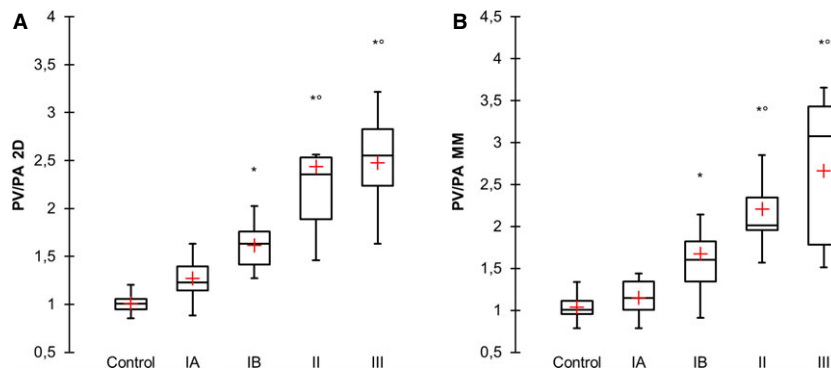
The receiver operating characteristic (ROC) curve analysis indicated that the PV/PA ratio measured in 2D and MM was useful to distinguish dogs with CHF (diagnosed by radiography) from dogs without CHF



**Fig 3.** Scatter plots of PV/PA ratio obtained in 2D and MM illustrating high correlation between both methods.  $r = 0.90$ ;  $P < .001$ . 2D, bidimensional; MM, M-mode; PV/PA, pulmonary vein diameter to pulmonary artery diameter.



**Fig 2.** Scatter plots of BW to PV diameter measured in 2D (A) and MM (C) and BW to PA diameter measured in 2D (B) and MM (D) in 37 healthy dogs. 2D, bidimensional; BW, Body weight; MM, M-mode; PA, Pulmonary artery; PV, Pulmonary vein.



**Fig 4.** Box plot illustrating PV/PA ratio in bi-dimensional mode (A) and M-mode (B) according to heart failure classes. The whiskers indicate the range of values. The box contains the 25th–75th centiles. The line within the box indicates the median and the cross indicates the mean. 2D, bi-dimensional; MM, M-mode; PV/PA, pulmonary vein diameter to pulmonary artery diameter. \*Significantly different from control group ( $P < .001$ ). °Significantly different from ISACHC IA group ( $P = .001$ ).

**Table 2.** Echocardiographic variables for 61 dogs and radiographic scores for 43 dogs with different classes of heart failure.

	ISACHC IA	ISACHC IB	ISACHC II	ISACHC III
LA/Ao	1.39 (1.33–1.46)	1.61 (1.54–1.73)	2.28 (1.94–2.61)	2.48 (2.11–2.82)
LAmin/Ao	1.78 (1.67–1.81)	2.09 (1.99–2.26)	2.89 (2.50–3.22)	2.93 (2.69–3.5)
nLVIDd (cm/kg)	1.52 (1.40–1.60)	1.72 (1.60–1.84)	2.11 (2.01–2.27)	2.27 (2.04–2.31)
EDVI (mL/m <sup>2</sup> )	45.8 (38.1–53.3)	53.9 (46.0–62.0)	86.4 (75.0–90.8)	94 (89–105.4)
E/A	1.05 (0.78–1.29)	1.31 (1.01–1.38)	1.90 (1.56–2.41)	1.90 (1.7–2.26)
TR (mmHg)	23 (10.2–34) {6/16}	22.8 (17.3–33.0) {5/16}	36.9 (29.5–44.3) {13/20}	37.3 (27.0–49.7) {8/9}
Radiographic composite score	1 (0–3)	2 (0–4)	4 (1–7)	5 (4–7)

Median (IQR) for continuous data and median (range) for categorical data; {} = number of dogs with TR. Ao, Aorta; EDVI, Indexed end-diastolic volume; IQR, interquartile range; LA, Left atrium; nLVIDd, Normalized left ventricular internal diameter in diastole; TR, Tricuspid regurgitation.

**Table 3.** Correlation between PV/PA and other echocardiographic parameters.

	LA/Ao	LAmin/Ao	nLVIDd	EDVI	E/A
PV/PA 2D	0.77 (<0.001)	0.74 (<0.001)	0.76 (<0.001)	0.72 (<0.001)	0.62 (<0.001)
PV/PA MM	0.74 (<0.001)	0.75 (<0.001)	0.70 (<0.001)	0.62 (<0.001)	0.58 (<0.001)

Coefficient of correlation ( $P$  value).

2D, bidimensional; MM, M-mode; Ao, Aorta; EDVI, Indexed end-diastolic volume; LA, Left atrium; nLVIDd, Normalized left ventricular internal diameter in diastole.

(Fig 6). Area-under-the receiver-operating characteristic curves (AUC) was 0.98 (CI, 0.97–0.98) for both 2D and MM. A cut-off value of 1.7 in 2D and 1.6 in MM predicted CHF in DMVD dogs with sensitivity of 96% (CI, 77–100) and 87% (CI, 67–96) and specificity of 91% (CI, 75–97) and 94% (CI, 79–99), respectively.

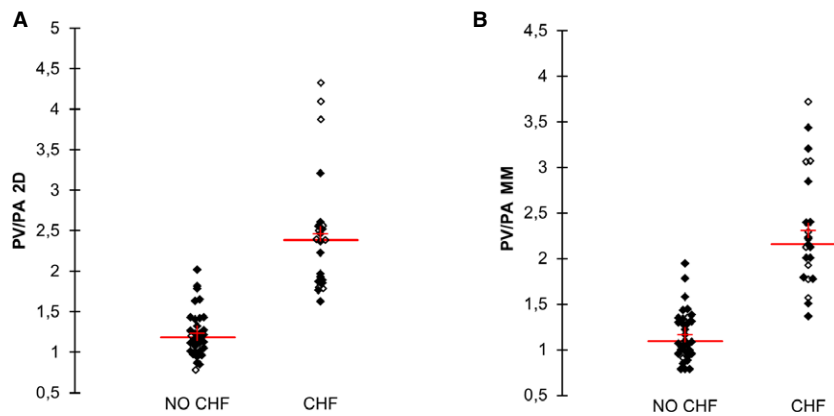
## Discussion

The diagnosis of CHF in dogs with DMVD relies on a combined interpretation of clinical signs and results of  $\geq 1$  diagnostic tools including thoracic radiography, NT-proBNP or Doppler echocardiography. Pulmonary venous congestion suggests increased pulmonary venous pressure, the trigger factor for development of pulmonary edema. The principal finding of our study is

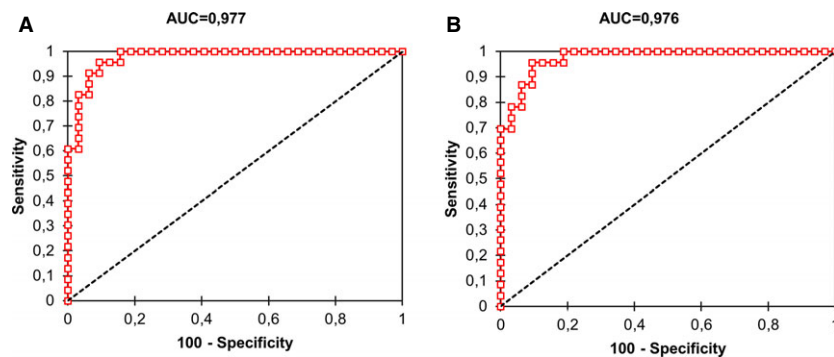
that, PV/PA, a new echocardiographic index of pulmonary venous congestion, increases with heart failure severity in dogs with DMVD. Using a cut-off value of 1.7 in 2D, PV/PA differentiates dogs with CHF from dogs without CHF with high accuracy using thoracic radiographs as the gold standard.

### Interobserver Variability and Normal Values of PV/PA

Assessment of observer variability is an essential step in the evaluation of the diagnostic value of a measurement. The interobserver CV for image acquisition and measurements ranged from 4 to 8% which indicated good to excellent reproducibility. We also found that both measurement methods were highly correlated. In



**Fig 5.** Median and scatter plots of PV/PA measured in 2D (A) or in MM (B) in 19 dogs with compensated DMVD and in 23 dogs with DMVD and radiographic evidence of CHF. White dots correspond to dogs with evidence of mild to moderate pulmonary hypertension (pressure gradient > 36 mmHg). 2D, bidimensional; CHF; Congestive heart failure; DMVD, degenerative mitral valve disease; MM, M-mode; PV/PA, pulmonary vein diameter to pulmonary artery diameter. \*Significantly different from groups without CHF ( $P < .001$ ).



**Fig 6.** Receiver-operating characteristic (ROC) curve illustrating PV/PA ratio measured in 2D (A) and M-Mode (B) that distinguishes asymptomatic from decompensated dogs with degenerative mitral valve disease. 2D, bidimensional; AUC, Area under the curve; PV/PA, pulmonary vein diameter to pulmonary artery diameter.

our study, suggested reference values for the PV/PA ratio in healthy dogs were approximately 1 in 2D and MM, based on data from 37 dogs. These reference ranges are in accordance with a previous report describing a mean PV/PA ratio of 1 in MM with SD of 0.11.<sup>17</sup> A PV/PA value of 1 might therefore be used in future studies as a reference value for healthy dogs.

### Diagnosis of CHF by PV/PA

Increased left ventricular filling pressure is a key feature of left-sided CHF, with therapeutic and prognostic significance, in dogs with DMVD. However, this hemodynamic variable cannot be directly measured in a non-invasive manner prompting a search for accurate surrogate markers. As DMVD progresses, the left atrium and ventricle gradually enlarge. Subsequently, left atrial pressure, which is dependent on the regurgitant volume, chamber compliance and pulmonary venous pressure, increases. This increase can lead, in a subset of dogs with DMVD, to left-sided CHF. In dogs with DMVD, left atrial size, as assessed by the ratio of LA/Ao, has been shown to increase with increasing class of heart failure,<sup>23</sup> to be associated with decreased

survival time<sup>2,7,24</sup> and to predict CHF.<sup>16,24</sup> A similar scenario might be expected for pulmonary vein size, but this has not been studied in dogs. We anticipate that in the absence of congenital heart disease (left-to-right shunt or pulmonic stenosis) and in the absence of pulmonary hypertension, the right pulmonary artery diameter should be relatively stable. Therefore, in uncomplicated DMVD, an increase of PV diameter (and PV/PA) is expected. In this study, PV/PA increased with increasing class of heart failure. Furthermore, dogs identified to be in CHF by thoracic radiography had higher PV/PA values than did asymptomatic dogs. The increase of PV/PA is likely related to pulmonary vein enlargement. This variable had an AUC >0.9 indicating excellent diagnostic performance for CHF detection. A PV/PA value >1.7 in 2D predicted CHF with an accuracy >90%, a sensitivity of 96%, and a specificity of 91%. This variable had an AUC > 0.9, indicating excellent diagnostic performance for CHF detection. Theoretically, the presence of concurrent pulmonary hypertension could contribute to false negative results by decreasing the PV/PA ratio. In our study, the presence of pulmonary hypertension did not interfere with CHF diagnosis performed by echocardiographic

assessment of PV/PA. Other factors that might influence PV/PA values include an absence of venous congestion as sometimes is observed in acute CHF caused by chordae tendinae rupture, differences in pulmonary venous tone or compliance, and the presence of an abnormally small or large PA.

### **Comparison with Other Doppler-echocardiographic Indices of CHF**

Each Doppler-echocardiographic-derived surrogate measure for left ventricular filling pressure has its own limitations. Evaluation of filling pressures depends on an integrated interpretation of volume overload remodeling indices as well as indices of left ventricular filling. In our study, PV/PA correlated with left atrial and ventricular size, echocardiographic parameters of volume overload already known to identify CHF.<sup>24</sup> We also showed that in dogs with DMVD, PV/PA was correlated with mitral E/A ratio. Transmitral flow patterns may identify diastolic dysfunction and increased left ventricular filling pressures, but these variables are interrelated.<sup>25</sup> The diagnostic accuracy of E/A for CHF detection may be limited in dogs with DMVD because of the large influence of volume overload on left ventricular filling. Furthermore, the influence of preload on early diastolic tissue velocity ( $E'$ ) in mitral regurgitation explains why identification of CHF using the E/ $E'$  ratio is less accurate in DMVD than in dilated cardiomyopathy.<sup>16</sup> The ratio between E and the isovolumetric relaxation time has been shown to be the optimal Doppler index for identifying CHF in dogs with DMVD.<sup>16</sup> However, these measurements require Doppler mode and a high level of expertise, and can prolong the duration of echocardiographic examination. On the contrary, the PV/PA ratio is relatively simple to obtain by conventional 2D or MM echocardiography.

### **Limitations**

This study has several limitations. Left ventricular filling pressures were not directly measured and thoracic radiography was used as the gold standard to assess the presence or absence of CHF. The sensitivity and specificity of thoracic radiography are unknown and are observer dependent.<sup>5,6</sup> Second, a majority of dogs in CHF were on treatment to decrease venous pressure before their examination, and this could have confounded interpretation of both Doppler-echocardiographic variables and thoracic radiographs. Third, the relatively small population studied rendered the study underpowered especially for comparison of PV/PA among classes of heart failure. Additional studies evaluating the accuracy of PV/PA to predict CHF in DMVD dogs using the pre-established cut-off value are indicated.

### **Conclusion**

Despite these limitations, our study has demonstrated that PV/PA is a simple and reproducible echocardiographic variable that can be obtained by 2D or MM

echocardiography. In DMVD dogs, PV/PA increases with increasing stage of heart failure. Using a cut-off value of 1.7 in 2D, PV/PA permitted accurate discrimination of dogs in CHF from asymptomatic dogs. Additional studies are required to determine if PV/PA might provide additional information in the integrated interpretation of Doppler-echocardiographic indices of left ventricular filling pressure. This measure also could have potential value in the rapid assessment of CHF in dogs in a critical care setting.

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## **Footnotes**

<sup>a</sup> Vivid I, General Electric Medical System, Waukesha, WI

<sup>b</sup> Xlstat 2014.6.01, Addinsoft, Paris, France

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*Conflict of Interest Declaration:* Authors disclose no conflict of interest.

*Off-label Antimicrobial Declaration:* Authors declare no off-label use of antimicrobials.

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