Development and evaluation of a composite echocardiographic score for predicting pulmonary hypertension severity in dogs

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Abstract

Background: Tricuspid regurgitation peak velocity (pTRV) is commonly used to estimate pulmonary arterial systolic pressure in dogs but is not always obtainable. Echocardiographic changes may suggest pulmonary hypertension (PH) probability, but not all of them equally reflect severity.

Hypothesis/Objectives: Develop a composite echocardiographic score predicting pTRV in dogs.

Animals: Client-owned dogs ($n = 118$) undergoing echocardiography for various cardiorespiratory reasons.

Methods: Multicenter retrospective study of dogs with identifiable tricuspid regurgitation. Echocardiographic findings were categorized into 6 *a priori* variables consisting of structural and flow-related abnormalities. Variable weighting was explored using regression analysis and cut-off scores were established for predicting pTRV ≥ 3.4 and ≥ 4.3 m/s using receiver operating characteristic (ROC) curves, and the predictive performance of the PH score also was assessed. Correlations between PH score and pTRV were analyzed, and intra- and interrater measurement reliability was evaluated.

Results: A final weighted PH score (25-point) incorporated semiquantification of right ventricular (RV) wall thickening (0/1/2 points), RV dilatation (0/2/4/6), right atrial (RA) enlargement (0/2/4/6), pulmonary artery enlargement (0/2/4/6), interventricular septal flattening (0/2/4), and midsystolic notching of RV outflow (0/1). In dogs without severe left atrial enlargement (LAE), 89% of cases were correctly stratified (area under the curve [AUC], 0.95), whereas performance was limited in dogs with postcapillary PH and marked LAE. Five-fold cross-validation identified final recommended thresholds of 3 (predicting pTRV ≥ 3.4 m/s) and 9 (pTRV ≥ 4.3 m/s). The PH score correlated with pTRV ($r_s = 0.88$, $P < .001$) and showed excellent intra- and inter-rater agreement (intraclass correlation coefficient [ICC] > 0.95).

Conclusions and clinical importance: The PH score may serve as a complementary tool for evaluating PH in dogs, particularly in those without severe LAE.

Introduction

Pulmonary hypertension (PH) is characterized by abnormally increased pulmonary arterial pressure (PAP), defined as mean PAP $\geq$ 20 mmHg in people.[1–3] The development of PH may result from increased pulmonary blood flow, increased pulmonary vascular resistance, increased pulmonary venous pressure, or a combination of these factors.[1,3,4] In dogs, PH can be idiopathic, or more commonly arise from numerous underlying diseases, including left heart disease, parasitic infections, congenital shunts, pulmonary thromboembolic disease, pulmonary capillary hemangiomatosis, PH secondary to respiratory disease or hypoxia, and other miscellaneous causes.[2,5–12] Direct PAP measurement using cardiac catheterization is the gold standard for PH diagnosis and classification,[12] but because of its invasiveness and the need for sedation or anesthesia, it is impractical for routine use or regular monitoring in client-owned dogs. Consequently, echocardiography has become the main noninvasive modality for indirect PH assessment. The most common echocardiographic approach for diagnosing and stratifying PH severity indirectly estimates systolic PAP from tricuspid regurgitation (TR) spectral Doppler tracings, utilizing the simplified Bernoulli equation.[1,8,13,14] Moreover, numerous echocardiographic changes secondary to PH also can be evaluated, including pulmonary artery enlargement, right ventricular (RV) hypertrophy or dilatation, rapid increase in pulmonary flow with or without midsystolic notching, systolic interventricular septal flattening, RV systolic dysfunction, and decreased right pulmonary artery distensibility.[1,2,15–18] These findings aid clinicians in determining the likelihood of PH.

Despite the frequent use of peak tricuspid regurgitation velocity (pTRV) for estimating systolic PAP in dogs, the absence and poor signal quality of TR are major impediments to this approach.[14,16,17] It may be particularly difficult to acquire good Doppler alignment to TR flow in dogs with clinical signs such as coughing or increased respiratory effort because of PH or underlying diseases.[2] Interference with the expanded lung makes image quality particularly problematic in dogs with respiratory disease. Alternative echocardiographic findings secondary to PH from various anatomic sites have been studied to address diagnostic constraints or the absence of a TR tracing and aid in prediction of PH, including right pulmonary artery distensibility index,[7,16,19,20] right pulmonary artery size,[21] tricuspid annular plane systolic excursion,[15,22–25] pulmonary vein-to-right pulmonary artery ratio,[17,26] left ventricular eccentricity index,[18] RV internal diameter, RV area, RV fractional area change, and RV strain.[23,27–29] The current American College of Veterinary Internal Medicine (ACVIM) consensus statement guidelines on PH in dogs propose a classification based on both pTRV and the number of distinct anatomic sites showing echocardiographic changes.[2] Nevertheless, structural and flow-related abnormalities at a given anatomical site may develop across a wide range of PAP and thus may not reliably indicate the severity of PH.[1,30] Although a comprehensive evaluation incorporating different anatomic sites helps in assessing the probability of PH, specific echocardiographic changes may not equally reflect PH severity.

Our aim was to develop a semiquantitative echocardiographic scoring system for stratifying the probability of PH by predicting different TR velocity groups. First, in the exploration group of the study (group A), selected echocardiographic findings commonly obtained from routine imaging were utilized to propose the scoring system. The score was designed as a visual assessment-based tool, enabling rapid clinical application without the need for additional quantitative measurements. The predictive performance against pTRV of the resulting visual PH score (ie, its ability to estimate the presence of and classify the severity of PH) then was examined in a second performance-testing group (group B).

Materials and methods

Study design

Ours was a multicenter retrospective observational study involving 4 veterinary institutions. We utilized images retrieved from institutional databases, which were obtained during routine echocardiographic examinations performed solely for clinical purposes. All analyses were conducted after completion of data collection from all participating centers. No additional procedures were performed on dogs for research purposes, and the study did not influence clinical decision-making. Therefore, based on the regulations of the participating institutions, animal care and use approval and owner consent were not required.

Echocardiographic images and video clips from client-owned dogs undergoing cardiorespiratory evaluations for various reasons between January 2017 and August 2023 were eligible for screening. Clinical databases from 4 centers were reviewed to identify cases with a well-visualized TR spectral Doppler signal, characterized by a well-demarcated holosystolic flow envelope having a contour that complied with guideline-based standards.[2] Data regarding breed, age, sex, body weight, and final diagnosis were obtained from the attending veterinarians for each case. To ensure consistency in TR velocity measurement, all pTRV were re-measured by a single trained resident at the dense outer edge of the spectral envelope, avoiding fine linear signals, in accordance with the 2020 ACVIM consensus guidelines.[2] All echocardiographic images were evaluated by 1 blinded experienced cardiologist (with 15 years of experience in small animal cardiology and echocardiography) and 1 non-blinded trained resident (cardiopulmonary medicine/internal medicine) to reach a consensus on the presence of remodeling or other echocardiographic features commonly associated with PH as described in the literature.[1,2,8,17,30–32] In cases of disagreement, a third blinded experienced cardiologist (with > 20 years of experience in small animal cardiology and echocardiography) was consulted, and consensus was reached by joint review. Echocardiographic findings that could be directly identified by visual assessment were selected for developing a scoring system. Severity for each echocardiographic finding was categorized into prespecified, study-defined visual ordinal categories, arbitrarily stratified *a priori* to facilitate consistent visual assessment, and adapted from previous studies related to PH in dogs and the ACVIM consensus statement guidelines.[1,2,30] The detailed definitions are summarized in Table 1. The scoring system was intentionally designed by visual assessment, with all categorical severity thresholds defined to facilitate rapid assessment based on easily recognizable visual cues. When an anatomical structure was compared with an adjacent reference structure, whole numbers or fractional integer multiples were assigned to facilitate visual estimation without using calipers or performing quantitative measurements.

Table 1 Definitions of visual severity categories for each echocardiographic variable included in the PH score, and the corresponding weighted point values in the 25-point PH scoring system.

Findings	Categorical severity	Definition	Score
RV dilatation	Normal	RVID less than or equal to 50% of LVID	0
	Mild	RVID greater than 50% of LVID	2
	Moderate	RVID greater than or equal to 75% of LVID but less than LVID	4
	Severe	RVID greater than LVID	6
RV wall thickening	Normal	RV wall thickness thinner than LV wall thickness	0
	Mild-to-moderate	RV wall thickness equal to LV wall thickness	1
	Moderate-to-severe	RV wall thickness thicker than LV wall thickness	2
RA enlargement	Normal	RAD less than LAD	0
	Mild	RAD equal to LAD	2
	Moderate	RAD greater than LAD but less than 1.5 times LAD	4
	Severe	RAD equal to or greater than 1.5 times of LAD	6
IVS flattening	Normal	No IVS flattening	0
	Subtle-mild	IVS deviation toward the LV without a visually flat septal contour	2
	Moderate-to-severe	IVS visibly flattened or convex into the LV	4
PA enlargement	Normal	PA/Ao less than or equal to 1	0
	Mild	PA/Ao greater than 1 but less than 1.5	2
	Moderate	PA/Ao greater than or equal to 1.5 but less than 2	4
	Severe	PA/Ao greater than or equal to 2	6
RVOT flow profile	Normal	Absence of mid-systolic notching of RVOT profile	0
	Abnormal	Presence of mid-systolic notching of RVOT profile	1
		Total PH score: _____ (0-25)	

Abbreviations: IVS, interventricular septum; LAD, left atrial diameter; LV, left ventricle; LVID, left ventricular internal diameter; PA, pulmonary artery; PA/Ao, pulmonary artery to aorta ratio; PH, pulmonary hypertension; RA, right atrium; RAD, right atrial diameter; RV, right ventricle; RVID, right ventricular internal diameter; RVOT, right ventricular outflow tract.

The study population was divided into an exploration group (group A) and a performance-testing group (group B). The allocation of dogs into the 2 groups was performed sequentially in 2 steps. First, the entire study population was stratified based on the presence or absence of a pTRV $\geq$ 3.4 m/s to ensure balanced representation of dogs with higher and lower pTRV in both groups. Second, random allocation to the 2 groups was conducted using the Excel "RAND()" function. Dogs were assigned a random number, sorted in ascending order, and then sequentially allocated in alternating fashion to group A and group B. Group A (the exploration group) was used to develop the PH score and determine the relative weighting of each echocardiographic variable. The categorical severity of each echocardiographic feature in this group was assigned by the same trained resident who was not blinded to pTRV. Each assignment was subsequently reviewed by an experienced cardiologist to verify the appropriateness of the severity classification, based on the predefined criteria listed in Table 1. The association between each echocardiographic variable and pTRV was analyzed using multiple linear regression. Based on the strength of these associations, weighting values were derived from the resulting regression coefficients and subsequently normalized to facilitate categorical scaling and the assignment of integer scores for each variable. Group B (the performance-testing group) was used to evaluate how accurately the PH score classified dogs into different pTRV categories and to assess its overall accuracy in predicting pTRV. In addition, we compared the score's accuracy between dogs with and without severe left atrial (LA) enlargement, defined as a LA-to-aorta ratio $\geq$ 2, to evaluate the potential impact of concurrent left heart remodeling on the PH score's performance.

A subset of echocardiographic images, contributed by all 4 centers and encompassing a wide range of pTRV values, was used to assess intra- and interobserver reliability of the PH score. Variability analysis was performed 3 months after the main analysis. Intraobserver variability was evaluated by a single experienced cardiologist who repeated the scoring of all 24 cases after a 1-week interval. Interobserver variability was assessed by 3 raters (2 cardiologists and 1 trained resident), each independently scoring the same anonymized image sets. To ensure blinding to pTRV values, the spectral Doppler images of TR were removed before scoring. All raters were instructed to assign scores for each variable based on the predefined visual criteria, without using calipers or performing quantitative measurements.

Finally, 3 additional analyses were performed on the full study population (groups A and B pooled). The predictive performance of the PH score was evaluated by comparing its accuracy in dogs with precapillary vs postcapillary PH. For this comparison, dogs with PH of uncertain etiology and those with pTRV < 3.4 m/s were excluded. In addition, the correlation between pTRV and the PH score was examined. To examine robustness, a 5-fold cross-validation was conducted across the full study population as an additional internal consistency check.

Echocardiography and pulmonary hypertension classification

Transthoracic echocardiographic examinations with a well-demarcated holosystolic flow envelope of the TR spectral Doppler signal were screened for inclusion in the study. Echocardiography

was performed by cardiologists or by residents or graduate students under the direct supervision of a cardiologist at each center (EPIQ 7, Philips; MyLab Eight, Esaote; Affiniti 50, Philips; Aplio ARTIDA, Toshiba; Vivid IQ, General Electric). The inclusion criteria were as follows: (1) each dog must have had a complete two-dimensional (2D), M-mode, and Doppler echocardiographic examination. A complete examination was defined as one that included standard imaging planes recommended by the 1993 ACVIM echocardiography committee of the specialty of cardiology, such as right parasternal long-axis, right parasternal short-axis, left apical, and left cranial views.[33] The imaging data obtained from these views had to be sufficient for cardiologists to integrate this information with other clinical findings to establish a cardiovascular diagnosis; (2) the stored 2D images or video clips were required to include the right parasternal long-axis 4-chamber view, the short-axis papillary muscle or chordae tendineae view, the short-axis heart base aorta/left atrium view, and the right parasternal short-axis pulmonary artery view, allowing quick assessment of right heart remodeling changes for evaluating the PH score defined in the study. Remodeling of the RV was assessed by reviewing both the right parasternal long-axis 4-chamber view and the short-axis papillary muscle or chordae tendineae view across the cardiac cycle. Right atrial (RA) remodeling was evaluated solely from the long-axis 4-chamber view. Interventricular septal (IVS) flattening was assessed from the short-axis view at the level of the papillary muscles or chordae tendineae. Pulmonary arterial enlargement was evaluated in the right parasternal short-axis view of the pulmonary trunk throughout the cardiac cycle; (3) Doppler images or video clips must have captured the TR and RV outflow spectral profiles; (4) the pTRV must have been recorded; (5) other supportive clinical and echocardiographic findings must have aided in determining the presence or absence of PH; and (6) the cause of PH must have been determined by the attending veterinarian using the classification scheme outlined in the ACVIM consensus statement on PH in dogs, which categorizes PH into 6 groups.[2] Precapillary PH was defined by increased PAP associated with increased pulmonary vascular resistance in the absence of increased LA pressure, and postcapillary PH was defined by increased PAP associated with increased pulmonary arterial wedge pressure secondary to left-sided heart disease.[2] In the absence of invasive cardiac catheterization, precapillary PH refers to dogs with an underlying disease known to cause precapillary PH (eg, respiratory disease, pulmonary thromboembolic disease, and heartworm disease) and without echocardiographic evidence of left heart disease, with the exception of mild mitral valve disease (mild mitral regurgitation and LA-to-aorta ratio < 1.6). Postcapillary PH refers to cases with echocardiographic evidence of left heart disease and LA-to-aorta ratio ≥ 1.6, without concurrent precapillary disease diagnosed. Pulmonary hypertension of uncertain cause refers to cases with presumed concurrent post- and precapillary causes but for which hemodynamic confirmation sufficient to be classified as combined post- and precapillary PH was lacking.

For the purposes of analysis, dogs were arbitrarily stratified based on pTRV results into 4 categories: < 2.5, 2.5 to < 3.4, 3.4 to < 4.3, and ≥ 4.3 m/s, following stratification commonly used in previous studies.[1,2,15,16,18] Because of the lack of a validated method for noninvasive RA pressure estimation in dogs, only pTRV and the derived pressure gradient were used to classify PH severity.

Statistical analysis

Statistical analyses were performed using SPSS (version 27, IBM Corp., USA) and R (version 4.5.0, R Core Team, 2024, Austria), with $P < .05$ considered significant. Normality of continuous variables was tested using the Shapiro–Wilk test. Data were expressed as mean ± SD (or 95% confidence interval [CI]) or median (range) and compared using *t*-tests or Mann–Whitney *U* tests, respectively. Categorical variables were analyzed using chi-squared or Fisher's exact tests. Baseline characteristics were compared between group A and group B using the same methods. In group A, a multiple linear regression model was constructed to predict pTRV based on categorical echocardiographic variables, and the resulting coefficients were used to determine the weight of each variable in the PH score. Residuals were checked for normality, and variance inflation factors > 4 indicated collinearity. Regression coefficients were divided by the smallest coefficient, rounded to assign integer weights, and multiplied by predefined severity levels to calculate the PH score.[34] Receiver operating characteristic (ROC) curve analysis then was performed to identify optimal PH score cut-offs for predicting pTRV ≥ 3.4 and ≥ 4.3 m/s using the Youden index.[35] In group B, the predefined PH score cut-offs from group A were applied to evaluate predictive performance. Accuracy was assessed by the percentage of correctly classified cases and ROC analysis (area under the curve [AUC]). The correlation between PH score and pTRV was assessed by Spearman rank correlation. Sample size was estimated using a one-way analysis of variance (ANOVA), assuming effect size as Cohen's $f = 0.5$ based on pTRV distributions adapted from previous data,[1] with $\alpha = 0.05$ and power = 0.80.

To assess the robustness of the PH score, 5-fold cross-validation was performed using the entire study population. Each of the 5 cross-validation splits used 80% of the data for training and 20% for testing, evaluating 2 PH severity thresholds (pTRV ≥ 3.4 and ≥ 4.3 m/s) with cut-offs derived from each training set applied to the corresponding test set to calculate classification accuracy. To assess intra- and inter-rater variability of the PH score, 12 dogs with pTRV < 3.4 m/s and 12 dogs with pTRV ≥ 3.4 m/s were randomly sampled from across the 4 institutions. Intra- and inter-rater reliability were quantified using intraclass correlation coefficients (ICCs) for absolute agreement.[36]

Results

Animals

A total of 264 dogs undergoing echocardiography for clinical suspicion of cardiopulmonary disease (eg, heart murmur, cough, respiratory distress, syncope, abnormal thoracic radiographic findings) or for other clinical purposes, including routine health examination or preanesthetic cardiopulmonary evaluation, initially were screened. Of these, 146 dogs were excluded, leaving 118 dogs in the final study population (Figure 1). The 4 institutes in the study contributed 81, 17, 11, and 9 dogs, respectively, to the final population. Median age and body weight were 12.0 years (range, 4.0-18.0 years) and 5.8 kg (range, 1.8-45.0 kg), respectively. Of the study population, 56% (66/118) were male. The included breeds were Maltese (23), Chihuahua (10), and Miniature Schnauzer (10), Poodle (9), Pomeranian (9), Spitz (4), Beagle (4), Shih Tzu (3), French Bulldog (2), Yorkshire Terrier (2), and Canarian Warren

Table 2 Baseline characteristics of the exploration and performance-testing groups.

Variables	Exploration group (*n* = 59)	Performance-testing group (*n* = 59)	*P* value
Age (years)[a]	12.0 (range, 5.0-16.1)	12.0 (range, 4.0-18.0)	.77
BW (kg)[a]	6.1 (range, 1.8-45.0)	4.6 (range, 2.2-30.0)	.58
Female: number (%)	30 (51%)	22 (37%)	.14
pTRV (m/s)[b]	3.52 (95%CI, 3.29-3.74)	3.77 (95%CI, 3.42-4.11)	.23

Abbreviations: BW, body weight; pTRV, peak tricuspid regurgitation velocity. [a] Data are presented as median (range). [b] Data are presented as mean (95%CI).
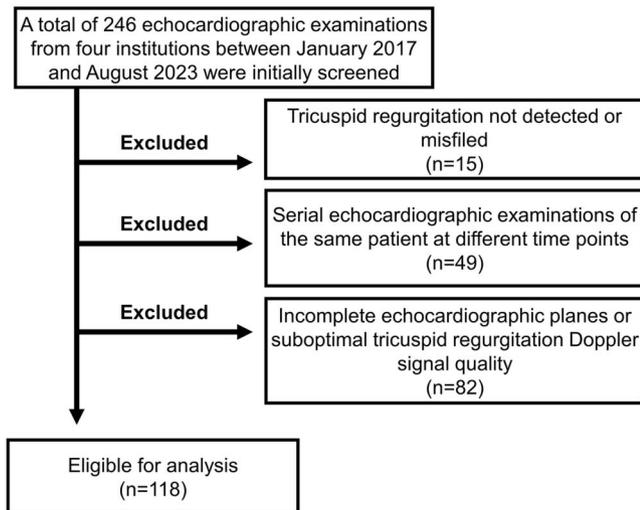

Figure 1 Flow diagram showing eligible dogs with ideally traced tricuspid regurgitation Doppler spectral signals and reasons for exclusion.

Hound (2). In addition, 1 dog each of the following breeds was represented: West Highland White Terrier, Shiba Inu, Scottish Terrier, Pug, Presa Canario, Pointer, Norfolk Terrier, Greyhound, German Shepherd, Welsh Corgi, English Cocker Spaniel, Cavalier King Charles Spaniel, Boston Terrier, Border Collie, Belgian Shepherd, and Airedale Terrier. Twenty-four dogs were mixed breed.

The median pTRV of the study population was 3.48 m/s (range, 1.01-6.92 m/s). Based on pTRV stratification, 65 of 118 dogs (55%) had results ≥ 3.4 m/s (high probability of PH), whereas 53 dogs (45%) had pTRV < 3.4 m/s, including 14 dogs with results < 2.5 m/s, a range typically not associated with PH. In dogs with pTRV ≥ 3.4 m/s and clinically diagnosed moderate-to-severe PH, the underlying cause was classified by the attending clinicians performing the echocardiography as group 1 (*n* = 1), group 2 (*n* = 16), group 3 (*n* = 18), group 4 (*n* = 1), group 5 (*n* = 10), and group 6 (*n* = 19), according to the ACVIM consensus statement guidelines of PH in dogs.[2] Of these 65 dogs, 40 (61.5%) were classified as having precapillary PH, 18 as postcapillary PH, and 7 as having PH of uncertain cause. The entire study population consisted of an exploration group and a second group used for performance assessment, with no significant differences in baseline characteristics between the 2 groups (Table 2).

Exploration group (group A)—development of PH score and variable weighting

Fifty-nine dogs were included in the exploration group to develop the PH scoring system based on echocardiographic variables associated with pTRV, which served as the outcome variable. Candidate variables listed in Table 3 showed no substantial multicollinearity and all were retained, yielding a regression model predicting pTRV with an R^2 of 0.71. To facilitate clinical application, variable weights were derived from the regression coefficients, normalized by dividing each coefficient by the smallest one and rounding to the nearest integer (Table 4). The final scoring system reflects both statistical associations and clinical interpretation, enabling semiquantitative assessment of PH severity. A simplified scoring framework then was constructed to integrate multiple echocardiographic findings into a total score for estimating PH severity (Figure 2 and Table 1).

The PH score subsequently was applied to each dog in the exploration group. The median PH score was 3 (range, 0-21). The ROC curve analysis showed that the PH score distinguished dogs with pTRV < 3.4 m/s vs ≥ 3.4 m/s, and those with pTRV < 4.3 m/s vs ≥4.3 m/s, with AUCs of 0.96 (95% CI, 0.91-1.0; *P* < .001) and 0.97 (95% CI, 0.93-1.0; *P* < .001), respectively. The optimal PH score cut-offs, based on the Youden index, were 4 for predicting pTRV ≥ 3.4 m/s and 9 for predicting pTRV ≥ 4.3 m/s.

Performance testing of the PH score in group B

An additional 59 dogs were enrolled in group B and assigned the PH score to evaluate its predictive performance. The median PH score of group B was 3 (range, 0-23). The PH score had excellent discriminatory performance for distinguishing dogs with pTRV < 3.4 and ≥ 3.4 m/s (AUC, 0.95; 95% CI, 0.90-0.998; *P* < .001), as well as dogs with pTRV < 4.3 and ≥ 4.3 m/s (AUC, 0.98; 95% CI, 0.95-1.0; *P* < .001). Using the cut-offs of 4 and 9 derived from the exploration group, the PH score accurately predicted pTRV categories in 78% (46/59) of dogs.

Among these 59 dogs, 12 had a LA-to-aorta ratio ≥ 2. Dogs with LA-to-aorta ratio ≥ 2 had significantly lower classification accuracy compared with those without severe LA enlargement (33% vs 89%, *P* < .001). After excluding these 12 dogs, the PH score correctly predicted the pTRV category in 42 of the 47 dogs. Among the 5 misclassified dogs, 3 had a pTRV ≥ 3.4 m/s but a PH score < 4, and 2 had a pTRV < 3.4 m/s but a PH score ≥ 4. In contrast, the higher cut-off of 9 (corresponding to a pTRV ≥ 4.3 m/s) correctly identified all dogs in this subgroup.

The PH score between precapillary and postcapillary PH (groups A and B pooled)

After excluding dogs with PH of uncertain cause and those with pTRV < 3.4 m/s, 58 dogs were available for this comparison

Table 3 Distribution of echocardiographic severity categories by pTRV group.

Findings	Categorical severity	pTRV (m/s)		
		<3.4 (*n* = 53)	3.4 to < 4.3 (*n* = 34)	≥4.3 (*n* = 31)
RV wall thickening	Normal	35	11	7
	Mild-to-moderate	18	21	19
	Moderate-to-severe	0	2	5
RV dilatation	Normal	47	18	1
	Mild	6	12	7
	Moderate	0	4	17
	Severe	0	0	6
RA enlargement	Normal	52	26	3
	Mild	1	6	6
	Moderate	0	1	16
	Severe	0	1	6
PA enlargement	Normal	47	14	1
	Mild	6	17	12
	Moderate	0	3	12
	Severe	0	0	6
IVS flattening	Normal	53	32	8
	Subtle-mild	0	2	18
	Moderate-to-severe	0	0	5
Mid-systolic notching of RVOT profile	Normal	52	25	22
	Abnormal	2	9	9

Abbreviations: IVS, interventricular septum; PA, pulmonary artery; pTRV, peak tricuspid regurgitation velocity; RA, right atrium; RV, right ventricle; RVOT, right ventricular outflow tract.

Table 4 Multiple linear regression analysis of echocardiographic variables associated with peak tricuspid regurgitation velocity in the 59 dogs from the exploration group. Regression coefficients are normalized by dividing each by the smallest coefficient (0.259) and rounded to assign variable weights. The number of dogs exhibiting or not exhibiting each feature are shown as Yes/No.

Variable	Yes/No	Regression coefficient	Weighting	Variance inflation factor
RV wall thickening	30/29	0.259	1	1.08
RV dilatation	24/35	0.436	2	1.65
RA enlargement	17/42	0.395	2	2.37
PA enlargement	26/33	0.536	2	1.55
IVS flattening	7/52	0.616	2	1.58
Mid-systolic notching of RVOT profile	9/50	0.372	1	1.06

Abbreviations: IVS, interventricular septum; PA, pulmonary artery; RA, right atrium; RV, right ventricle; RVOT, right ventricular outflow tract.

(Table 5). The PH score had significantly higher diagnostic accuracy in dogs with precapillary PH compared with those with postcapillary PH ($P < .001$). For the 18 dogs with postcapillary PH, the PH score correctly classified all 4 dogs with LA-to-aorta ratio < 2 (4/4, 100% accuracy), whereas classification accuracy was low in the 14 dogs with LA-to-aorta ratio ≥ 2 (3/14, 21.4%).

Assessment of predictive robustness using cross-validation (groups A and B pooled)

Five-fold cross-validation supported the internal consistency and robustness of the PH score, yielding a mean classification accuracy of 0.86 ± 0.10 for predicting pTRV ≥ 3.4 m/s and 0.95 ± 0.04 for predicting pTRV ≥ 4.3 m/s. Cross-validation identified a final

recommended cut-off of 3 for predicting pTRV ≥ 3.4 m/s, whereas the cut-off of 9 for predicting pTRV ≥ 4.3 m/s remained consistent across cross-validation splits. Applying these final thresholds to the performance-testing group (group B) confirmed that classification performance essentially was unchanged compared to the preliminary thresholds.

Correlation between PH score and pTRV (groups A and B pooled)

In the entire study population, the PH score showed positive correlation with pTRV ($r_s = 0.88$, $P < .001$). After excluding dogs with severe left heart remodeling (LA-to-aorta ratio ≥ 2), the correlation improved ($r_s = 0.92$, $P < .001$; Figure 3).
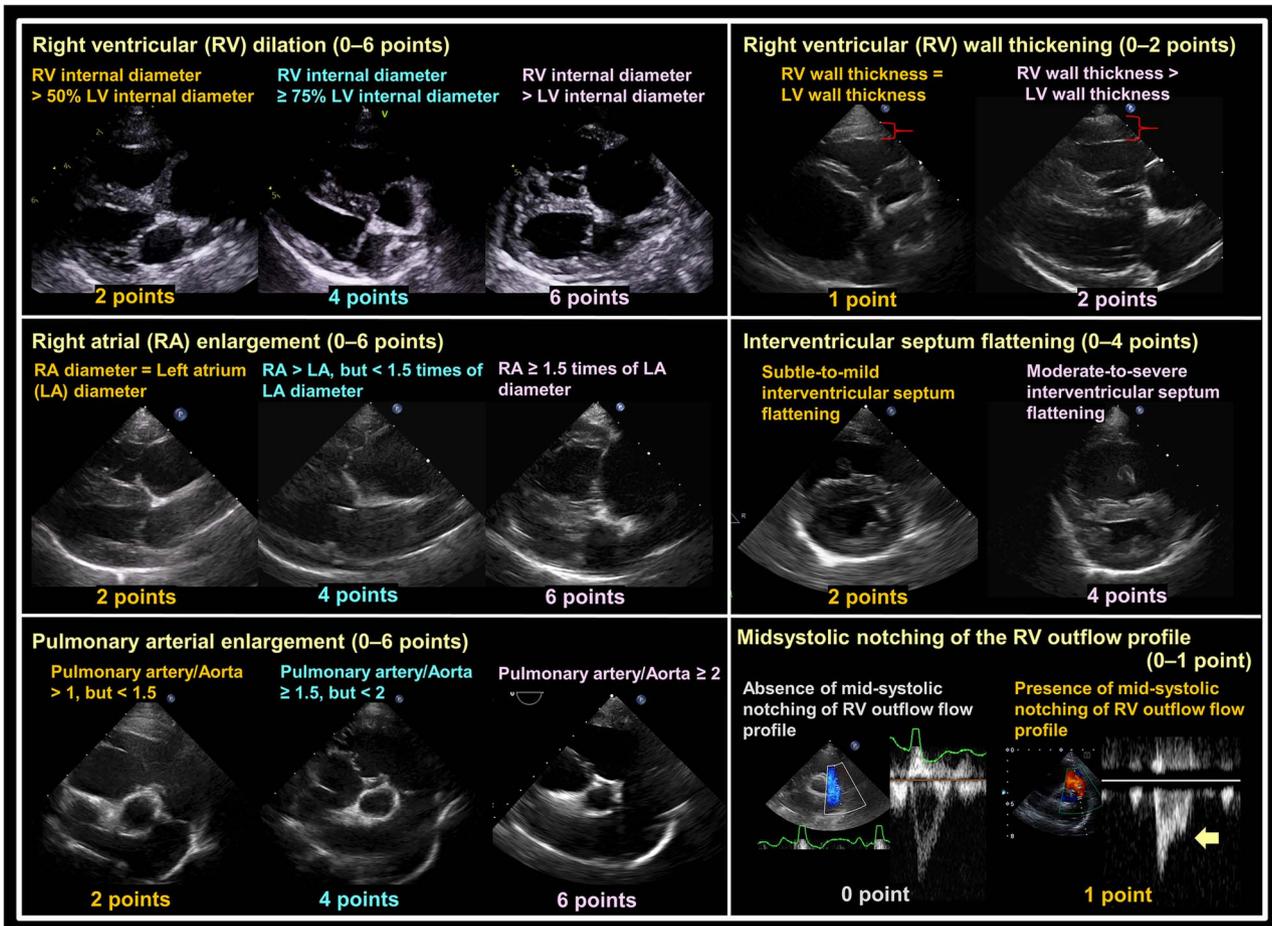
Figure 2 The 25-point PH score after weight adjustment, incorporating RV wall thickening, RV dilatation, right atrial enlargement, pulmonary artery enlargement, interventricular septum flattening, and midsystolic notching of the RV outflow profile. Abbreviations: PH = pulmonary hypertension; RV = right ventricular.

Table 5 Diagnostic accuracy of the PH score in dogs with precapillary vs postcapillary PH.

	Precapillary PH	Postcapillary PH
Exploration group (group A)	18/19 (94.7%)	4/9 (44.4%)
Performance-testing group (group B)	18/21 (85.7%)	3/9 (33.3%)
All dogs (groups A and B pooled)	36/40 (90.0%)	7/18 (38.9%)
		LA:Ao < 2.0 4/4 (100%)
		LA:Ao ≥ 2.0 3/14 (21.4%)

Abbreviations: LA:Ao, left atrium to aorta ratio; PH, pulmonary hypertension.

Reliability

The PH score had excellent agreement, with ICCs > 0.95 for both intra- and inter-rater assessments. All individual scoring variables had ICCs > 0.85, except for right ventricular wall thickening (Table 6).

Discussion

The visual PH score effectively stratified dogs into different pTRV-based categories in the performance testing group, particularly in the absence of severe LA enlargement. By integrating 6 echocardiographic findings, including RV wall thickening, RV size, RA enlargement, pulmonary artery enlargement, systolic flattening of the IVS, and the RV outflow tract profile, the PH score provided a practical semiquantitative framework for predicting pTRV. In the 25-point scoring system, a cut-off score of 9 correctly classified all dogs with pTRV ≥ 4.3 m/s without misclassification.

The PH score correlated positively with pTRV in our study. Although PH diagnosis should not rely solely on TR velocity estimated by the simplified Bernoulli equation,[2,12] pTRV still was chosen as the primary criterion for classifying PH severity in our study, because it remains the most commonly used method for estimating systolic PAP in previous studies of dogs.[5,6,8,10,16–18,22–25,27,29] Furthermore, when available, pTRV has been shown to have superior repeatability compared with
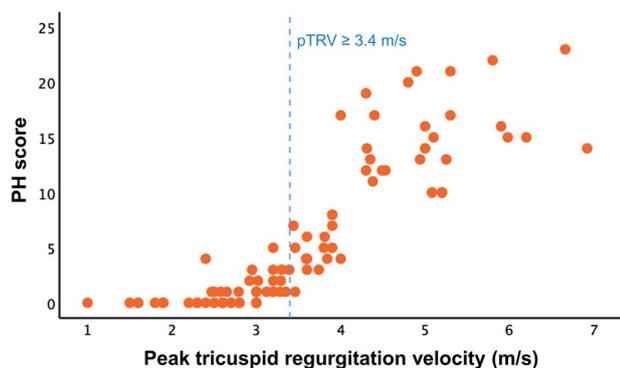
Figure 3 Scatter plot illustrating the positive correlation between the PH score and pTRV in cases without significant left atrial enlargement. The dashed vertical line represents the pTRV threshold of 3.4 m/s. Abbreviations: PH = pulmonary hypertension; pTRV = peak tricuspid regurgitation velocity.

Table 6 Intra- and inter-rater agreement for the PH score and individual echocardiographic manifestations.

	ICC	95%CI
Intrarater		
The 25-point PH score	0.998	0.995-0.999
Right ventricular wall thickening	0.861	0.680-0.939
Right ventricular dilatation	0.982	0.956-0.992
Right atrial enlargement	0.983	0.961-0.993
Pulmonary arterial enlargement	1.000	
Interventricular septum flattening	0.946	0.871-0.977
Mid-systolic notching of right ventricular outflow profile	1.000	
Interrater		
The 25-point PH score	0.991	0.983-0.996
Right ventricular wall thickening	0.636	0.287-0.830
Right ventricular dilatation	0.981	0.964-0.991
Right atrial enlargement	0.967	0.934-0.985
Pulmonary arterial enlargement	0.972	0.946-0.987
Interventricular septum flattening	0.952	0.905-0.977
Mid-systolic notching of right ventricular outflow profile	0.889	0.775-0.949

Abbreviations: ICC, intraclass correlation coefficients; PH, pulmonary hypertension.

other echocardiographic measurements.[14] However, PAP estimation based on pTRV is not without limitations. For example, studies have shown that PAP estimated from TR velocity on echocardiography had poor agreement with systolic PAP measured using right heart catheterization in dogs with myxomatous mitral valve disease with mild and moderate systolic PAP.[12] In addition, in clinical cases, pTRV measurement may not always be obtainable, and Doppler alignment with the TR jet may be suboptimal.[17] These shortcomings in pTRV measurement emphasize the need for alternative or complementary echocardiographic approaches beyond pTRV when evaluating PH severity in clinical practice.

Pulmonary hypertension is well known to induce various forms of right heart remodeling, but relying on a single echocardiographic finding is insufficient to capture the clinical status of PH patients.[37] A study examining 53 dogs with Doppler-derived

evidence of PH found that the extent of anatomic remodeling and hemodynamic changes varied according to PH severity.[1] Findings from several studies indicate that a progressively larger RV or IVS flattening or both are associated with PH severity, with these echocardiographic features appearing more frequently in dogs with severe PH than in those with mild or moderate PH.[6,23,30] In addition, a recent study on dogs with precapillary PH found that an index quantifying the severity of IVS flattening effectively distinguished dogs with moderate and severe PH from those with no or mild PH.[18] Collectively, these studies suggest that more advanced PH is associated with more pronounced remodeling changes, emphasizing the variability in echocardiographic manifestations based on the magnitude of increased PAP. Building upon this concept, a scoring system based on right heart parameters recently was proposed to assess precapillary PH, using a binary classification of remodeling features.[38] In contrast, our study adopted weighted values and semiquantitative severity grading, which may have contributed to the higher correlation observed with pTRV, compared with approaches relying solely on binary categorization of echocardiographic findings. It has been suggested that a comprehensive evaluation incorporating multiple indices is necessary to assess the adaptive remodeling of the right heart under increased load.[2,37] This conclusion supports the advantage of using a tool such as our PH score to integrate various echocardiographic features for assessing the severity of PH in dogs.

The PH score had strong diagnostic ability in assessing and differentiating pTRV categories in dogs without substantial left heart remodeling. Misclassifications were observed when using the cut-off of 4 to distinguish dogs with pTRV < 3.4 m/s and those ≥ 3.4 m/s, whereas no misclassifications occurred with the higher cut-off of 9 for differentiating dogs with pTRV < 4.3 m/s and those ≥ 4.3 m/s. The 5-fold cross-validation results indicate consistent internal performance and support the generalizability of the PH score. The minor variation in cut-off performance at pTRV ≥ 3.4 m/s likely reflects variability in the echocardiographic findings during early-stage PH, whereas the stable cut-off of 9 for pTRV ≥ 4.3 m/s supports the scoring system's robustness in identifying more advanced disease. These findings are consistent with previous studies that evaluated alternative echocardiographic indices and emphasized the inherent difficulty in reliably diagnosing less advanced PH using echocardiography.[15–18] Clinicians therefore should exercise caution when applying indirect methods such as the PH score in early-stage disease.

Notably, the PH score accuracy was lower in cases with postcapillary PH, in particular with LA-to-aorta ratio ≥ 2. This limitation primarily arises because the scoring for RV and RA remodeling is based on comparisons with left heart structures rather than direct quantitative measurements of the right heart. In group 2 PH, despite evident right heart remodeling secondary to increased PAP, the proportional comparison with an enlarged left heart becomes less reliable.[2,39] Altered left heart dimensions distort the expected relationship, thereby decreasing the diagnostic accuracy of our PH score. Nevertheless, using left heart comparisons provides a convenient and straightforward approach for readily available echocardiographic assessments, whereas direct measurements of right heart structures often require normalization to body weight using allometric scaling or nonlinear regression.[39,40] Alternatively, indexing right heart

ratios to a different structure, such as the aorta, may allow for more accurate assessment of right heart remodeling, independent of left heart enlargement.[39] Consequently, modified scoring variables and adjusted cut-off values established from dogs with postcapillary PH may be necessary for dogs with left heart remodeling. A different semiquantitative scoring system specifically designed for dogs with severe LA enlargement could offer a more reliable tool for evaluating postcapillary PH in the future.

Chronicity also plays an important role in the consideration of remodeling changes in right heart structures. Chronic PH in human patients often featured obvious RV hypertrophy, whereas marked RV hypertrophy almost never was observed in acute PH, with RV dilatation being more common.[41] The key distinction between these manifestations is that the myocardium can adapt and remodel to compensate under chronic pressure overload, but in acute pressure overload it has only limited time to respond, leading predominantly to RV dilatation.[42] A recent study using an experimentally induced model of PH in dogs found RV wall thickening in the early stages that gradually increased over time.[43] Notably, RV dilatation occurred in the later stages of this PH model, reflecting maladaptive remodeling. Although chronicity or disease onset affects the right heart remodeling process,[1,43] additional factors such as genetic and epigenetic influences also contribute to the adaptive response.[44] Moreover, even though the chronic phase was defined as systolic PAP remaining above 50 mmHg for 4 weeks in an experimental model in dogs,[43] no clear definition currently exists for chronic vs acute PH in naturally occurring cases. Therefore, it was not possible to confidently classify each case as acute or chronic PH in our study without long-term monitoring before the day of PH diagnosis by echocardiography. Despite the difficulty in precisely classifying acute vs chronic PH in clinical dogs at the present time, the potential influence of chronicity on the echocardiographic manifestations evaluated in the PH score should be carefully considered.

Our study had some limitations. First, the severity definition of PH was determined based on pTRV, which has some flaws and may not always accurately correspond to the true severity of PH. Accordingly, the PH score is not intended to replace invasive measurements and is not a tool for definitive classification, which should be based on right heart catheterization. Rather, it is designed to assist clinical decision-making when such diagnostic testing is not feasible. A second limitation was that the PH score was developed for and intended to be applied to routinely acquired echocardiographic images, but image acquisition can influence the perception of observations, because right heart chamber size may vary depending on the imaging view.[39] In addition, because the PH score relies on visual comparisons between right and left heart structures, inclusion of dogs with left heart disease and mild remodeling but without severe LA enlargement may introduce confounding that could affect the interpretation of right-sided changes. Third, the observer who assessed echocardiographic remodeling severity was not blinded to the pTRV results, which may have introduced observer bias, but this risk was mitigated by review using a blinded experienced cardiologist. Fourth, potential institutional bias cannot be excluded because of the imbalance in case numbers across centers. However, this imbalance alternatively may reflect the actual distribution of PH cases across institutions with variable clinical expertise and referral patterns. Fifth, the proposed PH

score was based only on right parasternal imaging views to allow determination in all dogs, including dogs where left-sided imaging views could be obtained. Comprehensive evaluation of RA and RV remodeling requires a complete echocardiographic examination that includes both right and left standard planes. A scoring system might differ if left apical and cranial views were incorporated into its design. Finally, the PH score was developed using a combination of statistical modeling and clinical interpretation, rather than purely data-driven computation. Although this approach enhances clinical applicability, it may introduce subjectivity and warrants future validation against invasive standards such as right heart catheterization. Future studies may explore the development of multiple alternative models using different variable weighting strategies, followed by statistical comparison to identify the model with the best fit.

In conclusion, we demonstrated that a semiquantitative scoring system based on remodeling and associated echocardiographic features can aid in the assessment of PH in dogs. The PH score showed a positive correlation with pTRV and effectively predicted pTRV categories, particularly in cases without clinically relevant left heart disease. Our findings support the PH score as a valuable complementary or alternative tool for evaluating PH in dogs. This scoring system may be especially useful when TR is absent or poorly documented, and it can also facilitate comparisons of PH severity across studies that utilize different indices beyond pTRV.

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Author contributions

Wei-Tao Chang (Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Writing—original draft, Writing—review & editing), Laín García-Guasch (Data curation, Investigation, Methodology, Project administration, Supervision, Validation, Writing—original draft), I-Ping Chan (Data curation, Investigation, Methodology, Project administration, Supervision, Validation), José Alberto Montoya-Alonso (Investigation, Project administration, Resources, Supervision), Jorge I. Matos (Data curation, Investigation, Methodology, Writing—original draft), Pei-Ying Lo (Conceptualization, Methodology, Resources, Supervision), Man-Cham Lam (Data curation, Investigation), Hui-Wen Chen (Project administration, Resources), Chinhao Chang (Formal analysis, Methodology, Writing—review & editing), and Chung-Hui Lin (Conceptualization, Investigation, Methodology, Project administration, Supervision, Validation, Writing—original draft, Writing—review & editing)

Conflicts of interest

The authors declare no conflicts of interest.

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Off-label antimicrobial declaration

The authors declare no off-label use of antimicrobials.

Institutional animal care and use committee or other approval declaration

The study involved only stored images from routine echocardiography and did not affect any medical decisions regarding the dogs. Therefore, no institutional animal care and use approval or client consent was required at each center.

Human ethics approval declaration

The authors declare human ethics approval was not needed.

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