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Doppler-derived echocardiographic evidence of pulmonary hypertension in cats with left-sided congestive heart failure☆

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KEYWORDS
Tricuspid regurgitation;
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Abstract *Introduction:* Pulmonary hypertension (PH) caused by left-sided congestive heart failure (L-CHF) is common in dogs and contributes to clinical signs and outcome. The aim of this study was to evaluate the prevalence of Doppler echocardiography—derived PH in a population of cats with L-CHF.
Animals: The study involved 131 cats with L-CHF and 56 control cats.
Methods: The study design is retrospective, observational study. Tricuspid regurgitation velocity, right atrial dimension, right ventricular (RV) dimension and function, RV wall thickness, pulmonary artery (PA) dimension, Doppler-derived systolic time intervals of PA flow, and presence of septal flattening were evaluated. Pulmonary hypertension was considered if tricuspid regurgitation velocity was $>$2.7 m/s.
Results: Tricuspid regurgitation was present in 57/131 (44%) of cats with L-CHF and 24/56 (43%) in control cats based on color flow Doppler. Doppler-derived of PH was identified in 22/131 cats with L-CHF (17%). In 15/22 cats, PH was associated with cardiomyopathy, in 5/22 cases with congenital heart disease, and in 2/22 cases with other causes. Cats with Doppler-derived PH more often had chronic L-CHF, as opposed to acute L-CHF ($p<0.05$). All cats with Doppler-derived PH had subjectively-assessed right-sided heart enlargement, with larger right atrial and

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RV diameters ($p<0.001$), increased RV wall thickness ($p<0.05$), and higher prevalence of septal flattening (<0.001) and PA enlargement ($p<0.05$).
Conclusions: Pulmonary hypertension identified by Doppler echocardiography is not a common finding in cats with L-CHF. Right-sided heart enlargement, more frequently observed, may raise the suspicion of PH in cats with L-CHF.

Abbreviations

Ao	aorta
AT	acceleration time
CV	coefficient of variation
ET	ejection time
HCM	hypertrophic cardiomyopathy
L-CHF	left-sided congestive heart failure
LV	left ventricle
PA	pulmonary artery
PH	pulmonary hypertension
PI	pulmonary insufficiency
PT	pulmonary trunk
RA	right atrium
RAD	right atrial diameter
RV	right ventricle
RVDd	right ventricular dimension at end-diastole
RVFWd	right ventricular free wall thickness at end-diastole
TAPSE	tricuspid annular plane systolic excursion
TR	tricuspid regurgitation

Introduction

Pulmonary hypertension (PH) refers to the elevation of pulmonary arterial pressure and is conceptually classified as precapillary or postcapillary [1]. Precapillary PH is caused by increased flow, elevated blood viscosity, and more commonly pulmonary vascular diseases affecting pulmonary arterioles, parenchymal lung diseases, and pulmonary thromboembolic disorders, all increasing pulmonary vascular resistance. In cats, precapillary PH has been described in association with Eisenmenger's syndrome in congenital heart disease [2—10], pulmonary thromboembolism [11,12], pulmonary fibrosis [13], chronic upper airway obstruction [14], heartworm disease [15,16], and lungworm infection [17].

Postcapillary PH is primarily caused by left-sided heart disease with or without congestive heart failure and is the consequence of passive back transmission of increased left atrial pressure to the pulmonary vascular beds, reactive pulmonary arteriolar vasoconstriction, and pulmonary vascular remodeling. Left-sided congestive heart failure (L-CHF) is characterized by increased hydrostatic pressure with the development of pulmonary edema and/or pleural effusion secondary to severe left heart disease, such as congenital heart disease and cardiomyopathy.

Owing to ease, low expense, and reasonable accuracy, PH is identified and quantified in clinical practice using two-dimensional, M-mode, and Doppler-echocardiographic methods. Right heart catheterization-derived methods, the gold standard in the diagnosis of PH in people, are rarely considered. Pulmonary hypertension caused by L-CHF is common in dogs, with more than 70% of cases affected, and contributes to clinical signs and outcome [18—21]. In contrast, only few reports describe PH in cats with L-CHF [3,4]. In most large-scale studies on feline cardiomyopathy, presence or absence of PH was not reported [22—26]. Hence, the aim of the study was to investigate the Doppler-derived prevalence of PH in a population of cats with L-CHF. The general hypothesis was that Doppler-derived PH secondary to L-CHF is rare in cats.

Animals, materials, and methods

This was a retrospective observational study; therefore, no institutional animal care and use approval or client consent was sought.

Case selection

Consecutive cats with L-CHF were identified by searching the medical record database of the Veterinary Medical Center at The Ohio State University from 2004 to 2016. Patient identification and data collection was carried out at The Ohio State University. Inclusion criteria were unequivocal diagnosis of acute or chronic L-CHF based on the presence of clinical signs, left atrial enlargement, and radiographic or ultrasonographic

evidence of pleural effusion or radiographic evidence of pulmonary edema. The same database was also used for identification of an age-matched and body weight—matched control group, including healthy cats with no clinical signs, no echocardiographic structural or functional abnormalities, and no systemic disease. Data on signalment, day of examination, ongoing diuretic medications (yes/no), timing of L-CHF (acute/chronic), evidence of pleural effusion (yes/no), pulmonary edema (yes/no), pericardial effusion (yes/no), echocardiographic diagnosis, and 'other' observations were retrieved. Timing of L-CHF was established based on chronicity/acuteness of clinical L-CHF from medical history. Cats already on treatment with diuretic medications because of a previous episode of documented L-CHF were deemed as 'chronic'. Differently, cats with rapid onset of clinical signs, who had never previously exhibited L-CHF, were classified as 'acute'.

Echocardiography

Transthoracic echocardiographic examination had been carried out by board-certified cardiologists or supervised residents in cardiology with ultrasound machines[c] equipped with phased-array transducers and nominal frequencies ranging from 6 to 12 MHz and a simultaneous single-lead electrocardiogram. Cats were imaged from right and left parasternal positions, and standard echocardiographic two-dimensional, M-mode, and Doppler images were acquired [27].

A single trained observer with several years of experience in the field of feline echocardiography (T.V.) reviewed each study, selected the images to be analyzed, remeasured all variables, and reported the results as the average of 3—5.

Measurements

Heart rate was determined as the average of three randomly selected RR intervals. For measurements of atrial diameters, ventricular chamber dimensions, and thickness of the interventricular septum, the distance from blood—tissue interface to blood—tissue interface was used [28]. For measurement of the left ventricular posterior wall thickness at end-diastole and the right ventricular free wall thickness at end-diastole (RVFWd), the leading edge to trailing edge method was applied. The maximum left atrial diameter and right atrial diameter (RAD) were measured from a right parasternal long-axis 4-chamber view [28,29]. The right ventricular dimension in diastole (RVDd) and the RVFWd were each measured from a right parasternal long-axis 4-chamber view [29].

The left ventricular internal dimension at end-diastole, RVFWd, and the interventricular septum thickness at end-diastole were each measured from a right parasternal long-axis 4-chamber view [30] using two-dimensional images. Left ventricular (LV) fractional shortening was calculated from M-mode recordings, acquired from the right parasternal short-axis view, and measured at the level of the chordae tendineae.

Right-heart enlargement was also subjectively assessed as per the visual impression of right atrial (RA) and/or right ventricular (RV) size compared with other internal cardiac reference structures and classified as either present (yes) or absent (no). The presence of interventricular septal flattening was subjectively assessed from standard right-parasternal short-axis views and classified as either present (yes) or absent (no) independent of the phase of the cardiac cycle.

From the right parasternal short-axis heart base view, measurements of the early diastolic internal dimensions of both the pulmonary artery (PA) at the level of the pulmonary valve and the pulmonary trunk (PT) in long axis and the aortic valve dimension (Ao) in short axis measured from the blood—tissue to the blood—tissue interface were obtained. The ratios PA:Ao and PT:Ao were calculated [18]. The PT measurement was obtained approximately midway between the pulmonary valve and PA bifurcation [31].

Right ventricular systolic function was evaluated through the peak tricuspid annular plane systolic excursion (TAPSE) and measured from anatomical M-mode recordings of the lateral tricuspid valve annulus from a left apical four-chamber view, as previously described [32].

Whenever tricuspid regurgitation (TR) or pulmonary insufficiency (PI) were present, peak velocities were measured. Pulmonary hypertension was defined as a peak TR velocity $>$ 2.7 m/s and/or peak PI velocity $\geq$ 2.2 m/s from whatever echocardiographic view permitting best alignment of flow with the Doppler cursor was available [3,33]. For the sake of simplicity, the terms 'echocardiographically-derived PH' and 'PH' are used synonymously in the paragraphs that follow. Tricuspid regurgitation severity (mild, moderate, or severe) was evaluated qualitatively, using color flow Doppler mapping of the TR jet size and continuous wave Doppler flow envelope characteristics, as described elsewhere [34]. The TR signal

[c] GE Vivid 7 and GE E9 with XDclear, General Electric, Waukesha, WI, USA.

quality on continuous wave Doppler was subjectively classified into poor, equivocal, and good categories.

Systolic time intervals of pulmonary flow (i.e. acceleration time [AT], ejection time [ET], and AT/ET ratio) were acquired from the right parasternal short-axis view at the level of the heart base using pulse-wave Doppler flow signals and small sample volume size (2—3 mm). The pulmonary systolic flow profile was defined as type I (normal flow profile, symmetric envelope, and similar acceleration and deceleration times), type II (abnormal flow profile, asymmetric envelope, and peak velocity occurring early in systole with a longer deceleration time), and type III (abnormal flow profile, asymmetric envelope, and rapid acceleration with notching during deceleration) [35].

Left ventricular diastolic function was assessed by Doppler echocardiography using transmitral flow patterns, pulmonary venous flow profiles, and tissue Doppler recordings when available. Left ventricular diastolic function was divided into groups: group-1, normal-to-mild dysfunction (normal or impaired relaxation inflow pattern); group-2, moderate-to-severe dysfunction (pseudonormal or restrictive inflow pattern); and group-3, summation of E and A waves [36].

Observer measurement variability was evaluated by repeated analysis of six randomly selected echocardiographic studies. These studies were measured three times within one month by one observer (T.V.) for determination of intraobserver measurement variability and once by a second observer (K.E.S) for quantification of interobserver measurement variability, with the results unknown to each other.

Statistical analysis

Analyses were performed with commercially available software (Graph Pad Prism, version 5; San Diego, CA, USA). The normality of data distribution was tested using the Shapiro—Wilk test. Continuous variables were reported as mean and standard deviation or median and range (minimum—maximum). Categorical data were reported as absolute (number) and frequency (percent).

Clinical and echocardiographic variables were first compared between the control group and the L-CHF group and subsequently between cats in L-CHF with and without Doppler-derived evidence of PH. Continuous variables were compared using an unpaired t-test or the Mann—Whitney U-test, based on data distribution. Chi-squared or Fisher's exact tests were used to compare categorical variables.

The Pearson correlation coefficient was used to study correlation between right heart dimensions (RAD, RVDd, RVFWd) and body weight in the control group.

Intraobserver and interobserver measurement variability for different echocardiographic variables was calculated using the coefficient of variation (CV) and the following formula: CV (%) = (mean difference of the measurements/average of the measurements) × 100 [29]. The degree of variability was classified as previously reported [37]: CV < 5% (excellent); CV 5—15% (good); and CV > 15% (poor).

A value of $p<0.05$ was considered statistically significant.

Results

Overall demographic and clinical data

A summary of clinical data is presented in Table 1. The study included 187 cats: 56 healthy cats (control group) and 131 cats with L-CHF (study group). In the control group, among parameters of right heart size, only RVFWd showed a weak positive correlation with body weight ($r = 0.337$, $p=0.012$). Right atrial diameter ($r = 0.241$, $p=0.085$) and RVDd ($r = 0.216$, $p=0.113$) were not correlated with body weight in healthy cats. Among cats with L-CHF, 80 (61%) had hypertrophic cardiomyopathy (HCM) with normal or increased LV systolic function, 23 (17.6%) had end-stage HCM characterized by LV systolic dysfunction and LV dilatation, 8 (6%) had restrictive cardiomyopathy, 6 (4.6%) had unclassified cardiomyopathy, 5 (3.8%) had dilated cardiomyopathy, 3 (2.3%) had an atrioventricular septal defect, 2 (1.5%) had bradycardia-induced L-CHF secondary to complete atrioventricular block of unknown cause, and one each (0.8%) had mitral valve dysplasia, patent ductus arteriosus, corticosteroid-induced L-CHF, and volume-overload induced L-CHF secondary to anemia and hyperthyroidism.

A summary on the echocardiographic data of the left heart and right side are presented in Tables 2 and 3, respectively. Right ventricular size (RVDd, $p<0.001$) was larger in cats with L-CHF compared with controls. Cats with L-CHF presenting with pleural effusion had larger RA dimension (RAD, $p<0.05$), but similar RV dimension (RVDd, $p=0.062$) and RV wall thickness (RVFW, $p=0.969$) in comparison to cats in L-CHF without pleural effusion. Subjective (visual) enlargement of the right heart was present in 54 (41%) cats with L-CHF.

Table 1 Clinical data of all cats included (n = 187).

Variable	Control (n = 56)	L-CHF (n = 131)	p	L-CHF w/o PH (n = 109)	L-CHF with PH (n = 22)	p
Age (yrs)	6.25 (3.00–14.30)	9.00 (1.50–16.40)	0.110	9.00 (1.50–16.50)	10.00 (0.32–16.85)	0.858
Male, n (%)	33 (59%)	102 (78%)	<0.001	88 (81%)	14 (64%)	0.094
Pure-bred: n (%)	18 (32%)	21 (16%)	0.018	15 (14%)	6 (27%)	0.122
BW (kg)	4.60 (2.78–7.74)	5.10 (2.52–7.34)	0.059	5.24 ± 1.28	4.65 ± 2.07	0.080
HR (bpm)	186 ± 27	188 ± 38	0.676	188 ± 38	192 ± 44	0.627
L-CHF (Acute/Chronic)	0/0	62/29[a]	<0.001	56/19	6/10	0.007
Pulmonary edema: n (%)	0 (0%)	98 (96%)[b]	<0.001	82 (96%)	16 (94%)	0.523
Pleural effusion: n (%)	0 (0%)	66 (50%)	<0.001	52 (48%)	14 (64%)	0.242
Pericardial effusion: n (%)	0 (0%)	46 (35%)	<0.001	40 (37%)	6 (27%)	0.469
Furosemide: n (%)	0 (0%)	55 (45%)[c]	<0.001	44 (46%)	11 (58%)	0.452

L-CHF, left-sided congestive heart failure; PH, pulmonary hypertension; BW, body weight; HR, heart rate; n, number of cats; SD, standard deviation.
Results presented as mean ± SD or median (5th and 95th percentiles) according to data distribution.
[a] Chart information only available in 91/131 cases.
[b] Chart information only available in 102/131 cases.
[c] Chart information only available in 121/131 cases.

Table 2 Left-sided echocardiographic variables of the study population (n = 187).

Variable	Control (n = 56)	L-CHF (n = 131)	p value	L-CHF w/o PH (n = 109)	L-CHF with PH (n = 22)	p value
LAD (mm)	14.19 (11.74–17.19)	20.94 (16.16–27.70)	<0.001	20.98 (15.79–28.11)	20.44 (16.60–23.79)	0.503
LVIDd (mm)	13.52 (10.50–18.17)	14.71 (10.25–19.83)	0.014	14.59 (9.93–19.73)	16.07 (10.78–28.04)	0.064
LVPWd (mm)	4.31 (3.24–5.34)	6.59 (3.25–9.04)	<0.001	6.77 (3.88–9.04)	5.11 (2.53–10.80)	0.006
IVSd (mm)	4.82 ± 0.62	5.80 ± 1.40	<0.001	5.92 ± 1.36	5.27 ± 1.51	0.047
Fractional shortening (%)	51 ± 10	45 ± 16	0.010	45 ± 16	44 ± 16	0.852
LV diastolic function (group 1/2/3)	42/0/14	7/56/51[a]	<0.001	7/43/48	0/15/3	0.188

n, number of cats; L-CHF, left-sided congestive heart failure; PH, pulmonary hypertension; LAD, left atrial diameter; LVIDd, left ventricular internal dimension at end-diastole; LVPWd, left ventricular posterior wall thickness at end-diastole; IVSd, thickness of the interventricular septum at end-diastole; LV diastolic function group 1 – normal to mild dysfunction, group 2 – moderate to severe dysfunction, group 3 – cannot be evaluated due to summation of filling waves.
Results presented as mean ± SD or median (5th and 95th percentiles) according to data distribution.
[a] Chart information only available in 114/131 cases.

Table 3 Right-sided echocardiographic variables of the study population (n = 187).

Variable	Healthy (n = 56)	L-CHF (n = 131)	p	L-CHF w/o PH (n = 109)	L-CHF with PH (n = 22)	p
RAD (mm)	12.19 (9.57–15.41)	12.24 (8.52–19.72)	0.631	11.51 (8.42–18.34)	17.06 (10.66–26.57)	<0.001
RVDd (mm)	5.56 (3.42–8.60)	7.48 (4.28–11.93)	<0.001	7.04 (4.28–10.73)	10.45 (4.31–20.24)	<0.001
RVFWd (mm)	2.62 (1.87–3.89)	2.84 (1.96–4.52)	0.037	2.76 (1.99–4.29)	3.47 (1.84–5.56)	0.011
Right-sided enlargement: n (%)	2 (4%)	54 (41%)	<0.001	33 (30%)	22 (100%)	<0.001
Septal flattening: n (%)	0 (0%)	8 (6%)[a]	0.014	2 (2%)	6 (27%)	<0.001
PA/Ao	0.90 (0.81–1.08)	0.85[b] (0.66–1.12)	<0.001	0.83 ± 0.10	0.95 ± 0.17	<0.001
PT/Ao (mm)	1.07[c] (0.88–1.34)	0.82[d] (0.63–1.53)	<0.001	0.82 (0.63–1.08)	0.87 (0.78–1.53)	0.025
TAPSE (mm)	7.87[f] (5.59–10.83)	6.00[g] (3.30–11.62)	<0.001	6.08 (3.27–10.85)	5.84 (4.83–11.62)	0.454
TR presence: n (%)	24 (43%)	57 (44%)	1.000	17 (16%)	22 (100%)	<0.001
TR (m/s)	2.25 (0.88–2.71)	2.99 (1.21–4.13)	0.003	2.10 (1.21–2.65)	3.43 (2.71–4.13)	<0.001
PI presence: n (%)	3 (5%)	5 (4%)	0.694	2 (2%)	3 (14%)	0.033
AT (ms)	59 ± 9	59 ± 15[e]	0.802	60 ± 15	54 ± 15	0.117
AT/ET	0.41 ± 0.06	0.43 ± 0.10[e]	0.145	0.45 (0.30–0.59)	0.41 (0.12–0.51)	0.047
PA flow profile (type 1/2/3)	52/4/0	90/7/0[e]	0.767	75/4/0	15/3/0	0.012

n, number of cats; L-CHF, left-sided congestive heart failure; PH, pulmonary hypertension; RAD, maximum right atrial diameter; RVDd, right ventricular dimension at end-diastole; RVFWd, right ventricular free wall thickness at end-diastole; PA, pulmonary artery measured at the level of the pulmonary valve; Ao, aorta; PT, pulmonary trunk; TAPSE, tricuspid annular plane systolic excursion; TR, tricuspid regurgitation; PI, pulmonary insufficiency; AT, acceleration time; ET, ejection time.

[a] Chart information only available in 122/131 cases.
[b] Chart information only available in 94/131 cases.
[c] Chart information only available in 45/56 cases.
[d] Chart information only available in 47/131 cases.
[e] Chart information only available in 90/131 cases.
[f] Chart information only available in 46/56 cases.
[g] Chart information only available in 59/131 cases. For all other variables, 100% (131 observations) per variable were available.

Table 4 Proportion (n [%]) of cats with pulmonary hypertension in cats with left-sided congestive heart failure secondary to congenital heart disease and cardiomyopathy.

Etiology	Pulmonary hypertension
Congenital heart disease	5/5 (100%)
Restrictive cardiomyopathy	3/8 (37.5%)
Unclassified cardiomyopathy	2/6 (33%)
Dilated cardiomyopathy	1/5 (20%)
End-stage hypertrophic cardiomyopathy	3/23 (13%)
Hypertrophic cardiomyopathy	6/80 (7.5%)

CHF, congestive heart failure; PH, pulmonary hypertension. In the remaining 2 cases, PH was associated with bradycardia-induced CHF due to idiopathic complete atrioventricular block in one cat and volume-overload CHF secondary to anemia and hyperthyroidism in another cat.

Tricuspid regurgitation was present in 24 (43%) control cats and in 57 (44%) cats with L-CHF ($p=1.000$). Quality of the TR signal was good, equivocal, or poor in 20%, 40%, and 40% of control cats, and 39%, 49%, and 12% of cats with L-CHF, respectively ($p<0.05$). In all control cats presenting with TR, the severity of regurgitation was mild. In cats with L-CHF presenting with TR, severity of TR assessed subjectively was mild in 37 (65%) cats, moderate in 15 (26%) cats, and severe in 5 (9%) cats. Severity of TR was higher in cats with right-sided enlargement compared with cats without right-sided enlargement ($p<0.001$). As per TR and PI peak velocity, PH was present in 22 (17%) of cats with L-CHF. Measurable PI was present in only 5/131 (4%) cats with L-CHF, with a median value of 2.46 m/s (range, 1.58—4.50 m/s). Among cats with PI, 2 cats had PH based on both TR (3.14 m/s and 3.72 m/s) and PI (2.46 m/s and 2.86 m/s), 1 cat had PH only based on PI (4.50 m/s), and the remaining 2 cats did not have echocardiographic signs of PH.

Cats with TR-based PH

A summary on the clinical data of cats with PH is presented in Table 1. Cats with PH more often had chronic CHF (as opposed to acute CHF) compared with cats without PH ($p<0.05$). Underlying heart diseases associated with PH are presented in Table 4. Among cardiomyopathies, the proportion of cats with HCM in the group with PH (6/22, 27%) was significantly lower in comparison to cats without PH (74/109, 68%; $p<0.001$).

A summary of left-sided echocardiographic data in cats with PH are presented in Table 2. In cats with PH, left atrial size (maximum left atrial diameter, $p=0.50$), LV size (left ventricular internal dimension at end-diastole, $p=0.06$), and LV systolic function (fractional shortening, $p=0.85$) were not different in comparison to cats without PH. Conversely, cats with PH had thinner LV walls (interventricular septum thickness at end-diastole and left ventricular posterior wall thickness at end-diastole, both $p<0.05$).

A summary of right-sided echocardiographic data in cats with PH is presented in Table 3. Right atrial size (RAD, $p<0.001$) and RV size (RVDd, $p<0.001$) were larger in cats with PH than in cats without PH. Similarly, the RV wall (RVFWd, $p<0.05$) was thicker in cats with PH than in cats without PH. All cats with PH (22/22, 100%) had subjectively assessed right-sided enlargement (Fig. 1), dissimilar from cats without PH in which it was present in 33/109 (30%) cats ($p<0.001$). The point prevalence of septal flattening at the time of examination was higher in cats with PH (6/22, 27%) in comparison to cats without PH (2/109, 2%, $p<0.001$). Pulmonary artery dimension measured at the pulmonary valve (PA/Ao, $p<0.001$) and PT size (PT/Ao, $p<0.05$) were larger in cats with PH in comparison to cats without PH. In cats with PH, TR was mild in 5/21 (24%) cats, moderate in 11/21 (52%) cats, and severe in 5/21 (24%) cats. Regarding pulmonary blood flow profile, type 2 was more frequent in cats with PH in comparison to cats without PH ($p<0.05$). Concerning Doppler-derived systolic time intervals, AT/ET ($p<0.05$), but not AT ($p=0.117$), was lower in cats with PH in comparison to cats without PH.

Results on evaluation of observer measurement variability are reported in Table 5.

Discussion

The major findings of this retrospective study are that (1) PH as determined by transthoracic echocardiographic methods is not a common finding in cats with L-CHF but, if present, appears more frequent with congenital heart disease and chronic L-CHF, (2) Doppler-derived PH in cats is often associated with right-sided heart enlargement, and (3) septal flattening and PA enlargement are additional echocardiographic findings suggestive of PH in cats.

Doppler-derived evidence of PH in cats with L-CHF

In our study, Doppler-derived PH was present in 17% of cats with L-CHF. In a recent study in humans

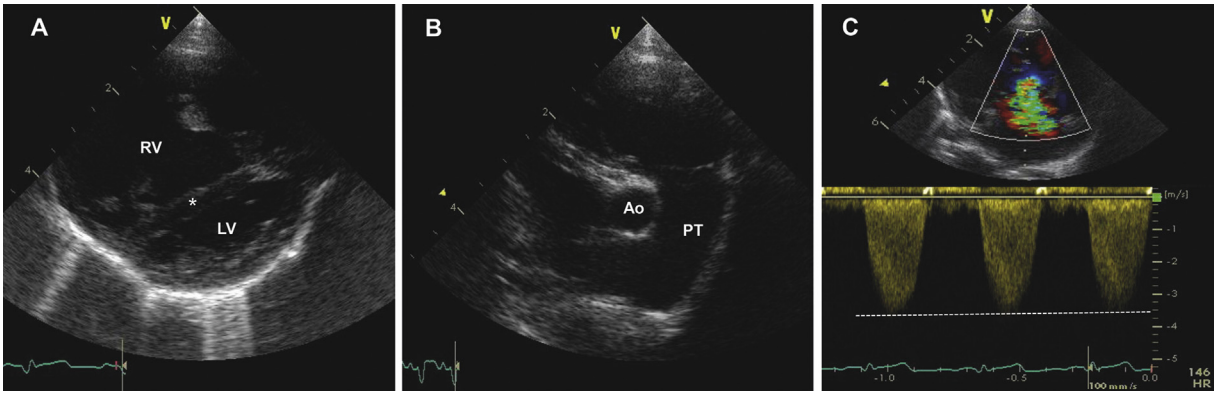

Fig 1 Two dimensional and Doppler images of a cat with echocardiographic signs of pulmonary hypertension: Panel A: Right ventricular dilation with septal flattening (*). Panel B: Enlargement of the pulmonary trunk. Panel C: High velocity tricuspid regurgitation (peak velocity = 3.63 m/s). RV, right ventricle; LV, left ventricle; Ao, aorta; PT, pulmonary trunk.

with HCM and advanced heart failure, PH was observed in more than half of the patients; however, 25% of cases with PH also had comorbidities possibly contributing to PH [38]. Pulmonary hypertension caused by L-CHF is common in dogs, with more than 70% of cases affected [18—21]. Only few reports describe PH in cats with L-CHF [3,4]. In a study on radiographic findings in cats with L-CHF, 68% of cases had PA enlargement on thoracic radiographs [26]. However, no echocardiographic data on right heart chamber size and TR velocity were reported. A possible reason for lower Doppler-derived prevalence of PH in cats in comparison to humans and dogs could be the infrequent presence of echocardiographically detectable TR in cats with L-CHF. In our study, only 44% of cats with L-CHF presented with TR and a similar proportion was found in normal cats. In contrast, TR can be identified in 86%—92% of dogs with L-CHF [19]. Another possible reason for the low Doppler-derived prevalence of PH in our study of cats with L-CHF may be linked to the quality of the Doppler flow signal and Doppler alignment with TR flow. The combination of high heart rate and low-volume TR, often found in cats, may lead to weak and possibly abbreviated Doppler signals difficult to quantify. In our study, TR was mild in 65% of cases and the quality of the TR signal was equivocal-to-poor in 61%. This can influence echocardiographic estimation of systolic PA pressure, possibly leading to underestimation of TR velocity and thus PH evidence and severity. Finally, species variation in pulmonary vascular reactivity has been documented [39]. There is evidence that cats affected by heartworm or lungworm disease rarely develop PH, even if presenting significant pulmonary parenchymal and arterial damage [40,41]. Therefore, a different pulmonary arterial response pattern to pulmonary venous hypertension cannot be excluded in cats with L-CHF compared with dogs and humans. Because right heart catheterization was not performed in this study, it was not possible to differentiate isolated postcapillary PH due to 'pure' pulmonary venous hypertension from combined precapillary and postcapillary PH due to a left-heart and pulmonary vascular disease (reactive vasoconstriction or pulmonary vascular remodeling with obliteration). However, these terms are poorly defined in dogs and cats, thus given the low number of cats with PH and the different etiologies separation of cats into isolated postcapillary (previously called 'passive') and combined

Table 5 Intraobserver and interobserver measurement variability of selected echocardiographic variables from 12 randomly selected cats (6 from control group and 6 from L-CHF group).

Variable	Intraobserver CV		Interobserver CV	
	mean	(%)	mean	(%)
LAD (mm)	22.78	1	22.68	5
LVIDd (mm)	14.48	3	15.21	5
LVPWd (mm)	7.99	4	7.74	10
IVSd (mm)	6.63	4	6.46	9
RAD (mm)	18.76	2	19.21	5
RVDd (mm)	9.55	3	10.65	11
RVPWd (mm)	4.11	5	4.79	17
PT/Ao	0.87	6	0.92	9
AT (ms)	55.56	4	52.50	9
AT/ET	0.39	4	0.37	9
TAPSE (mm)	6.25	9	6.04	9
TR (m/s)	3.12	2	3.16	2

CV, coefficient of variation. *See* Tables 2 and 3 for remainder of key.

precapillary and postcapillary PH (previously called 'reactive') would have led to speculative conclusions rather that evidence-based facts. Finally, it is possible that cats develop intrapulmonary arteriovenous anastomoses preventing or attenuating the development of PH.

Clinical data in cats with L-CHF and PH

In our study, PH was more prevalent in cats with L-CHF secondary to congenital heart disease. Only few reports describe PH in cats with L-CHF and congenital heart disease [3,4] where patent ductus arteriosus and mitral valve stenosis were the underlying causes of PH. In dogs, PH is more often observed with acquired left heart disease [18—20].

To the authors' knowledge, this is the first study reporting on echocardiographically derived PH in cats with L-CHF secondary to cardiomyopathy. In our sample population, among acquired cardiac diseases, the main causes of PH were restrictive cardiomyopathy, unclassified cardiomyopathy, and dilated cardiomyopathy. Hypertrophic cardiomyopathy was a less common etiology. Recent studies on feline HCM demonstrated significant RV hypertrophy in addition to LV disease in a relevant number of cats, with RVFWd increasing with disease severity [29,32]. Right ventricular hypertrophy could limit the development of TR in cats with HCM, making it difficult to echocardiographically detect PH and thus leading to underestimation of PH prevalence. Whether or not differences in heart failure pathophysiology (diastolic heart failure in cats with HCM versus systolic heart failure in cats with dilated cardiomyopathy and end-stage HCM) lead to different pulmonary vascular response patterns is currently unknown but deserves further study.

Another clinical finding of our study is that Doppler-derived PH was more prevalent in cats with chronic L-CHF. This is in line with the human literature, where PH secondary to left-sided heart disease is related to chronicity of heart failure [42].

Finally, in our study, the frequency of pulmonary edema, pleural effusion, and pericardial effusion was not different between cats with and without PH. However, RA size was significantly larger in cats with L-CHF and pleural effusion in comparison to cats without pleural effusion. This finding is in accordance with previous studies in cats with L-CHF, in which pleural effusion was associated with larger RA size, RV dimensions, and poorer left atrial function [32,43,44]. A theoretical explanation is that significant RA enlargement could be a marker of more severe TR, stronger neurohormonal activation and fluid retention, or possibly indicating the presence of significant PH echocardiographically not detectable but contributing to right-sided CHF.

Echocardiographic data in cats with L-CHF and PH

Left atrial and ventricular chamber size was not different in cats with and without echocardiography-determined PH. Left ventricular wall thickness was lower in cats with PH because of the higher proportion of cats with HCM in the group without PH.

Regarding right heart evaluation, all cats with PH presented with right heart enlargement, determined by both objective and subjective evaluation. This is in line with previous observations in cats with PH [2,3,5,7,9,10]. In addition, similar to dogs [18,31,33] and horses [45], our cats with L-CHF and PH had a significantly larger PA size and a higher prevalence of septal flattening. This observation suggests that the presence of right heart enlargement, PA enlargement, and/or septal flattening should raise suspicion of PH in cats with L-CHF if TR-based Doppler estimates of systolic PA pressure are not readily available and relevant TR is absent.

In dogs, the PA flow profile and systolic time intervals (AT and AT/ET) are echocardiographic predictors of PH [18,46]. In our study, AT was not different between cats with and without PH but AT/ET was lower in cats with PH and the pulmonary flow profile had a higher prevalence of the type 2 in cats with PH. However, the differences were small and thus are probably not clinically important. Therefore, we do not recommend suspecting PH only based on pulmonary flow profile and systolic time intervals in cats with L-CHF.

Right ventricular systolic function is affected by afterload and thus would be expected to be low normal or decreased with moderate and severe PH if other variables such as heart rate, preload, and contractility were unchanged. In our study, TAPSE was reduced in cats with L-CHF cats in comparison to controls, and this finding is in accordance with previous studies in cats with HCM [32,47]. However, TAPSE was not reduced in our subset of cats with PH. Reduced TAPSE in dogs with moderate-to-severe PH is a controversial finding and probably depends on the underlying cause of PH [21,31,48]. In our population, most cats presented with mild PH as per the TR peak velocity. Therefore, PH not severe enough to affect RV systolic function could be a possible explanation for normal TAPSE in our

cats with PH. However, TAPSE was not available in all cats, thus limiting the statistical power to detect differences between groups.

This study has certain strengths and weaknesses. Strengths include the total number of cats enrolled, the presence of an age-matched and body weight—matched control group, the measurement of all data in a consistent manner, and, finally, the consideration of both functional and structural variables. Limitations of our study include its retrospective nature, missing of a gold standard in the evaluation of PH (right heart catheterization was not performed), possible underestimation of Doppler-derived evidence of PH due to weak TR signals and eccentric TR jets, and the lack of information on heartworm status in some cats. It would have been desirable to include only cats with TR and/or PI for which more definitive statements regarding presence or absence of PH could have been made in this study. However, due to the high frequency of only mild regurgitation (65%) and weak Doppler signals (61%) in cats with L-CHF, eliminating all cats without TR would have led to relevant selection bias and acceptance cats with suboptimal images to be included in the reference population. This would have led to clear deviation from the aims of the study, namely echocardiographically investigating the frequency of PH in cats with L-CHF. More data, including information from prospective studies and the use of right-heart catheterization as the gold standard in the evaluation of pulmonary arterial pressures and pulmonary capillary wedge pressures, are needed to better understand the prevalence and physiopathologic characteristics of PH in cats with L-CHF.

Conclusions

Compared with historical data in dogs, PH determined by Doppler echocardiography is not a common finding in cats with L-CHF. Right-sided heart enlargement is commonly observed in cats with L-CHF and Doppler-derived evidence of PH. Further studies are needed to identify reasons and mechanisms for the obvious differences between dogs and cats.

Conflicts of Interest Statement

The authors do not have any conflicts of interest to disclose.

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