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## Abstract

**Background** The diagnosis of congestive heart failure (CHF) in cats is challenging. Point-of-care (POC) thoracic ultrasound and NT-proBNP testing are emerging tools that may aid in diagnosis.

**Hypothesis/Objectives** To assess the diagnostic accuracy of POC lung ultrasound (LUS), focused cardiac ultrasound (FCU), and NT-proBNP in predicting a final diagnosis of CHF.

**Animals** Fifty-one cats in respiratory distress.

**Methods** Blood NT-proBNP, LUS, and FCU evaluating left atrial (LA) size and presence of pericardial effusion (PCEFF) were performed in all cats. Lung ultrasound findings including pleural effusion (PLEFF), number of B-lines, and sub-pleural abnormalities were noted. Medical records were evaluated for final diagnosis.

**Results** Thirty-three of 51 (65%) cats were diagnosed with CHF. Lung ultrasound and blood NT-proBNP were significant predictors of CHF in a multivariate model. The LUS criterion that maximized accuracy for CHF diagnosis was presence of >1 site strongly positive for B-lines (>3 B-lines per site), resulting in sensitivity of 78.8%, specificity of 83.3%, and area under the curve (AUC) of 0.833. Subjective LA enlargement was 97.0% sensitive and 100% specific for CHF (AUC 0.985). Presence of PCEFF also was 100% specific, but only 60.6% sensitive, for CHF (AUC 0.803). A positive blood NT-proBNP test was 93.9% sensitive and 72.2% specific for the diagnosis of CHF (AUC 0.831).

**Conclusions and Clinical Importance** Point-of-care diagnostic techniques of LUS, FCU, and NT-proBNP are useful to diagnose CHF in cats with respiratory distress.

## Keywords

B-lines, biomarker, cardiac, feline, lung, point-of-care, respiratory

## Disciplines

Small or Companion Animal Medicine | Veterinary Preventive Medicine, Epidemiology, and Public Health

## Comments

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## STANDARD ARTICLE

# Evaluation of point-of-care thoracic ultrasound and NT-proBNP for the diagnosis of congestive heart failure in cats with respiratory distress

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**Hypothesis/Objectives:** To assess the diagnostic accuracy of POC lung ultrasound (LUS), focused cardiac ultrasound (FCU), and NT-proBNP in predicting a final diagnosis of CHF.

**Animals:** Fifty-one cats in respiratory distress.

**Methods:** Blood NT-proBNP, LUS, and FCU evaluating left atrial (LA) size and presence of pericardial effusion (PCEFF) were performed in all cats. Lung ultrasound findings including pleural effusion (PLEFF), number of B-lines, and sub-pleural abnormalities were noted. Medical records were evaluated for final diagnosis.

**Results:** Thirty-three of 51 (65%) cats were diagnosed with CHF. Lung ultrasound and blood NT-proBNP were significant predictors of CHF in a multivariate model. The LUS criterion that maximized accuracy for CHF diagnosis was presence of >1 site strongly positive for B-lines (>3 B-lines per site), resulting in sensitivity of 78.8%, specificity of 83.3%, and area under the curve (AUC) of 0.833. Subjective LA enlargement was 97.0% sensitive and 100% specific for CHF (AUC 0.985). Presence of PCEFF also was 100% specific, but only 60.6% sensitive, for CHF (AUC 0.803). A positive blood NT-proBNP test was 93.9% sensitive and 72.2% specific for the diagnosis of CHF (AUC 0.831).

**Conclusions and Clinical Importance:** Point-of-care diagnostic techniques of LUS, FCU, and NT-proBNP are useful to diagnose CHF in cats with respiratory distress.

## KEYWORDS

B-lines, biomarker, cardiac, feline, lung, point-of-care, respiratory

**Abbreviations:** AUC, area under the receiver operating characteristic curve; CHF, congestive heart failure; FCU, focused cardiac ultrasound; LA, left atrium; LA : Ao, left atrium to aorta ratio; LUS, lung ultrasound; NC, noncardiac; PCEFF, pericardial effusion; PLEFF, pleural effusion; POC, point of care; SD, standard deviation; TXR, thoracic radiographs; Vet BLUE, veterinary bedside lung ultrasound examination.

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## 1 | INTRODUCTION

Congestive heart failure (CHF) is a common cause of respiratory distress in cats. The diagnosis of CHF in cats is especially challenging, not only because the fragility of cats in respiratory distress limits the diagnostic evaluation, but also because physical examination and radiographic findings in cats often are nonspecific. Up to 40% of cats in CHF may not have a heart murmur upon initial examination for respiratory distress.<sup>1-3</sup> Moreover, radiographic evidence of pulmonary

edema, left atrial (LA) enlargement, and pulmonary venous distention are notoriously variable in cats with CHF, further complicating the diagnosis.<sup>4,5</sup>

Other diagnostic modalities, such as point-of-care (POC) biomarker testing and ultrasound imaging, are emerging to facilitate a more timely diagnosis and directed treatment of CHF in cats. The POC N-terminal pro-B-type natriuretic peptide (NT-proBNP) test (SNAP Feline proBNP; SNAP Feline proBNP test, IDEXX Laboratories, Inc, Westbrook, Maine) has been helpful in facilitating a rapid and accurate diagnosis of CHF in cats presenting with respiratory distress and pleural effusion (PLEFF).<sup>6,7</sup> However, noncardiac (NC) diseases, such as severe respiratory or kidney disease, can increase NT-proBNP concentrations and increase the likelihood of false positive results.<sup>8</sup> Point-of-care lung ultrasound (LUS) and focused cardiac ultrasound (FCU) also have shown promise in accelerating the emergency diagnosis of CHF in cats.<sup>7,9-11</sup> Lung ultrasound can suggest a diagnosis of cardiogenic pulmonary edema by demonstrating the presence of ultrasonographic artifacts called B-lines. These B-lines, also called "lung rockets," are linear, hyperechoic, laser-like artifacts that extend from the pleural-pulmonary interface to the far aspect of the ultrasound screen without fading and that move synchronously with respiration.<sup>12-14</sup> Many studies in humans<sup>12,15-17</sup> and a few veterinary studies<sup>9,10,13,18,19</sup> have shown that the presence of numerous B-lines in patients presenting with respiratory distress is suggestive of CHF. Conversely, the absence of B-lines strongly refutes the diagnosis of CHF.<sup>11</sup> However, although B-lines are suggestive of CHF, these artifacts also can be present in patients with other causes of fluid accumulation in the alveolar-interstitial lung spaces.<sup>12,15</sup> The finding of LA enlargement on FCU performed by trained clinicians improves the accuracy of CHF diagnosis compared to physical examination alone in cats with respiratory distress.<sup>2,7</sup> However, obtaining an optimal left atrium-to-aorta ratio (LA : Ao) view can be difficult in animals experiencing respiratory distress, especially cats.

To our knowledge, no study has evaluated the relative diagnostic utility of POC LUS, FCU, and NT-proBNP for diagnosis of CHF in a cohort of cats with respiratory distress. Our primary goal was to compare the diagnostic accuracy of each of these diagnostic tests in predicting a final diagnosis of CHF. Additionally, we sought to determine if any combination of clinical variables or findings on these diagnostic tests yielded optimal diagnostic accuracy. We hypothesized that POC ultrasound findings (LUS and FCU) would have equal or higher diagnostic accuracy compared to POC NT-proBNP alone, and that a combination of all diagnostic tests would offer superior diagnostic accuracy compared with any single test.

## 2 | MATERIALS AND METHODS

Procedures were approved by the Institutional Animal Care and Use Committee at both study sites (North Carolina State University and Iowa State University). Informed owner consent was obtained for each study participant.

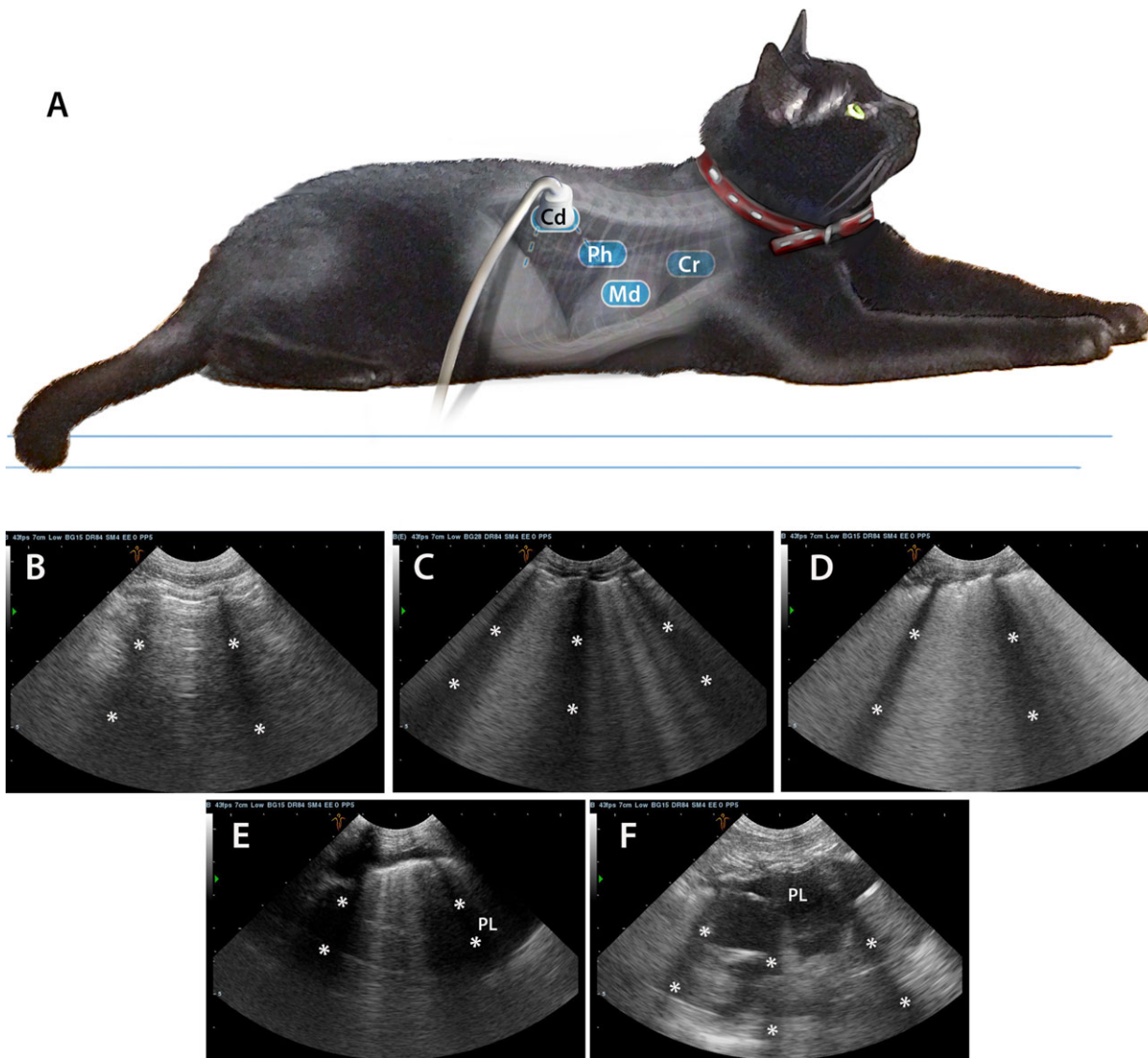
Cats presented to the Small Animal Emergency and Critical Care Services or Cardiology Services at each study site were prospectively enrolled. Inclusion criteria were: (1) cats exhibiting increased respiratory

rate (>40 breaths per minute) and increased respiratory effort on physical examination; (2) a trained examiner was available to perform POC ultrasound; and (3) blood was obtained for the POC NT-proBNP test within 2 hours of POC ultrasound (either before or after ultrasound). Cats with PLEFF regardless of severity were included in our study. If thoracocentesis was performed, the NT-proBNP test also was performed on the pleural fluid. Exclusion criteria were: (1) the cat had a respiratory disturbance suspected to be a pain response (ie, obvious nonrespiratory and noncardiac cause of an abnormal breathing pattern); or (2) the cat had a recent history of trauma. Empirical treatment with furosemide before POC ultrasound was not an exclusion criterion.

Cats were stabilized with oxygen, sedation and other therapeutic maneuvers at the discretion of the emergency or cardiology clinician. Participating POC ultrasound examiners were cardiology and emergency clinicians who had completed a 4-hours training session with an experienced lung ultrasonographer and echocardiographer (T.C. DeFrancesco and J.L. Ward). The trainee had to demonstrate proficiency during 3-5 supervised examinations. All LUS examinations were performed using compact portable ultrasound machines at each center (ISU; CX50 CompactXtreme Ultrasound [model 101855], Philips Healthcare, Andover, Massachusetts; C8-5 Transducer (part # FUS5124), Philips Healthcare, Andover, Massachusetts; NCSU; Fukuda Denshi Ultrasound (model UF-760AG, Version 02), Tokyo, Japan; Fukuda Denshi Transducer [model FUT-CA144-9P], Tokyo, Japan) using a curvilinear probe with standardized settings (ultrasound frequency, 5-8 MHz; depth, 4-6 cm).

The LUS examinations were performed on all cats using the previously described Vet BLUE protocol for LUS.<sup>9,12,13</sup> Cats were scanned in sternal recumbency. Starting on the right hemithorax, a 3-second ultrasound cine loop was obtained at 4 acoustic windows on each side of the patient's thorax at standardized locations, for a total of 8 sites (see Figure 1). After the 4 right-sided views were obtained and before scanning the left hemithorax, a single FCU cine loop was obtained and recorded by the POC ultrasound examiner. This FCU view was a 2-dimensional short axis right parasternal view of the heart base optimized for measurement of the LA : Ao ratio (see Figure 2). The operator recorded his or her real-time subjective assessment of LA size as normal (LA : Ao of approximately 1 : 1) or enlarged (LA : Ao > 1.5) at the time of the examination. Additionally, the 2-dimensional LA : Ao ratio was measured at a later time by a board-certified cardiologist (T.C. DeFrancesco and J.L. Ward) using standard methods, from the first diastolic frame after aortic valve closure.<sup>20,21</sup> Presence or absence of pericardial effusion (PCEFF) also was noted from the LA : Ao view and confirmed by later review by a board-certified cardiologist (T.C. DeFrancesco and J.L. Ward).

For each Vet BLUE site, the examiner was asked to determine the presence or absence of PLEFF, B-lines, and other sub-pleural abnormalities (Nodule [Nd], Shred [Sh], or Tissue [Ti] signs).<sup>14</sup> A Nd sign was defined as a small, well-marginated hypoechoic circular or ellipsoid structure, with or without a hyperechoic distal border, and with or without acoustic enhancement appearing as a B-line extending from its distal border through the far field of the ultrasound screen.<sup>14,22-24</sup> A Sh sign was an irregular discontinuity of the expected linear pulmonary-pleural interface with hyperechoic foci within the consolidation, representing lung consolidation with aeration analogous to a



**FIGURE 1** Stylized photographic depiction of the VetBLUE technique for LUS (A) and representative LUS images (B-F). A, The ultrasound probe is held horizontally at 4 sites on each hemithorax to record images. The LA : Ao focused cardiac ultrasound image is obtained from the right hemithorax at approximately the Md site. Corresponding lung locations as viewed on a lateral thoracic radiograph are also shown. Cd, caudodorsal; Cr, cranial; Md, middle; Ph, perihilar. B-F, Still B-mode image of LUS findings from cats, with rib shadows identified (\*). B, LUS image from a normal cat, showing presence of horizontal A-lines. C, LUS image from cat in respiratory distress, showing multiple B-lines. The B-lines are visible as multiple linear hyperechoic artifacts extending from the pleural-pulmonary interface to the far edge of the screen. The cranial ICS contains infinite B-lines (the artifacts coalesce and individual B-lines can no longer be discerned), while the caudal ICS contains >3 B-lines that can still be recognized individually. D, LUS image with infinite B-lines at all ICSS. E, LUS image from a cat with large volume PLEFF; B-line artifacts are seen within the PLEFF. F, LUS images from a cat with large volume PLEFF. ICS, intercostal space; LUS, lung ultrasound; PL, pleural effusion. Illustration by Alice MacGregor Harvey, permission to print courtesy of North Carolina State University

radiographic air bronchogram.<sup>14,22,23</sup> A Ti sign appeared as linear to triangular discontinuity or deviation from the expected pulmonary-pleural interface, void of hyperechoic foci within the consolidation, representing consolidation without aeration described as hepatization of lung.<sup>14,22,23,25</sup> Combinations of PLEFF, B-lines, and sub-pleural abnormalities could be noted within a single Vet BLUE site (eg, a site could contain both PLEFF and B-lines, or a combination of Sh sign and B-lines).

In sites where B-lines were present, the maximum number of B-lines within an intercostal space was recorded as 0, 1, 2, 3, >3 or infinite.<sup>9</sup> Infinite refers to the situation where B-lines are so numerous that they are no longer discernable as individual B-lines (see Figure 1D). An

individual Vet BLUE site where either >3 or infinite B-lines were recorded was scored as a “strong positive” site. A diagnosis of suspected cardiogenic pulmonary edema on LUS was defined according to the method established by a consensus panel for LUS in humans (the so-called “Volpicelli method”)<sup>9,15</sup> as a LUS examination that contained at least 2 strong positive sites on each hemithorax. The total number of B-lines in all 8 individual Vet BLUE sites then was summed to create a “B-line score” for the overall LUS examination. For purposes of total B-line score, >3 B-lines per ICS were counted as 4 B-lines for that site, and infinite B-lines per ICS were counted as 10 B-lines for that site, consistent with protocols used in humans.<sup>26</sup> For example, a cat that had 3 Vet BLUE sites each containing 2 B-lines, 3 Vet BLUE sites





**FIGURE 2** Still B-mode focused cardiac ultrasound short axis images of the base of the heart showing a normal left atrium (A), and a subjectively enlarged left atrium (B,C). The normal ratio of the diameter of the LA to the diameter of the Ao should be  $\sim 1 : 1$ . In addition to an enlarged LA : Ao ratio, a scant amount of PCE is visualized in C

devoid of B-lines, and 2 Vet BLUE sites with infinite B-lines would have a total B-line score of  $2 + 2 + 2 + 0 + 0 + 0 + 10 + 10 = 26$ .

The POC NT-proBNP tests (SNAP Feline proBNP test, IDEXX Laboratories, Inc, Westbrook, Maine) were performed according to manufacturer's instructions using serum (and if available, PLEFF) within 24 hours of venipuncture, by an individual blinded to final diagnosis. After a 10-minute incubation time, the relative color density of the sample (patient) spot was compared with the reference spot by visual inspection. Results were recorded as either positive (abnormal) when the color of the sample spot was equal to or darker than the reference spot or negative (normal) when the color of the sample spot was lighter than the reference spot.

Final clinical diagnosis for cause of respiratory distress was determined by retrospective review of each patient's medical record by a board-certified cardiologist (T.C. DeFrancesco and J.L. Ward) who was blinded to the cat's NT-proBNP test results. The final diagnosis incorporated all other diagnostic test results, including thoracic radiographs (TXR), echocardiography, airway sampling (tracheal wash or bronchoalveolar lavage), PLEFF cytology, and necropsy findings, as well as response to treatment.

Statistical analyses were performed using commercial software (MedCalc Version 17.6, MedCalc Software, Seoul, South Korea; NCSS Version 10, NCSS LLC, Laysville, Utah). A prospective sample size calculation extrapolated from the previous study of LUS in dogs and cats with respiratory distress<sup>8</sup> showed that 36 cats (18 with CHF, 18 with NC disease) would be required to estimate diagnostic accuracy of LUS within 10% with 95% confidence.<sup>8</sup> Normality was assessed by the Shapiro-Wilk test. Categorical data were summarized as frequencies and proportions; quantitative data were summarized as mean  $\pm$  standard deviation (SD) if normally distributed, and as median (range) if non-normally distributed. Student's *t*-tests (continuous normally distributed data), Mann-Whitney log-rank tests (continuous non-normally distributed data), or Fisher's exact or Chi-square analyses (categorical data) were used to compare clinical data between cats with a final diagnosis of CHF versus NC disease. Sensitivity and specificity were calculated for the association of LUS, FCU, and NT-proBNP with final diagnosis of CHF. Univariate logistic regression analysis was performed initially to assess continuous and categorical variables for their utility in diagnosing CHF. Variables significant in the univariate logistic regression analysis subsequently were entered into a multivariate stepwise logistic regression analysis. Variables demonstrating quasi-complete or complete separation in the univariate

logistic regression analysis were not entered into the multivariate logistic regression analysis, but subsequently were evaluated by chi-square analysis. Receiver operator curve analysis was performed on all significant variables to identify diagnostic thresholds with optimal sensitivity and specificity using the Youden index. Statistical significance was set at  $P < .05$  for all analyses.

### 3 | RESULTS

#### 3.1 | Study population and clinical findings

Fifty-two cats initially met inclusion criteria for the study, but 1 cat was not enrolled because it was too fractious to permit ultrasound examination. The final study population of 51 cats comprised 35 cats from North Carolina State University and 16 cats from Iowa State University. Thirty-six cats were castrated males, whereas 15 were spayed females. Domestic shorthair cats were most common ( $n = 34$ ). Other cat breeds represented included domestic longhair cats ( $n = 8$ ), Siamese ( $n = 3$ ), Himalayan ( $n = 3$ ), Maine Coon ( $n = 1$ ), Norwegian Forest Cat ( $n = 1$ ), and Bengal ( $n = 1$ ). Other clinical variables describing the study population are listed in Table 1. Point-of-care ultrasound was performed by a board-certified cardiologist in 21 cases (41%), cardiology resident in 20 cases (39%), and emergency clinician in 10 cases (20%). Study diagnostics (POC ultrasound and NT-proBNP) were performed before any treatment in 40/51 (78%) cats. Seven cats (14%) had furosemide administered before diagnostic tests, whereas 4/51 (8%) cats had emergency thoracocentesis performed before study diagnostic tests (all of which had residual PLEFF identified on POC ultrasound). Subsequent diagnostic tests performed to obtain a final diagnosis in study cats included TXR (47/51 cats, 92%), complete echocardiography (32/51 cats, 63%), and thoracocentesis with PLEFF analysis (23/51 cats, 45%). One cat each underwent endotracheal wash, fine needle aspirate of a lung mass, and necropsy.

Overall, 33 (65%) cats had a final diagnosis of CHF, whereas 18 (35%) were diagnosed with NC causes of respiratory distress. Causes of CHF were hypertrophic cardiomyopathy ( $n = 23$ ), hyperthyroid heart disease ( $n = 5$ ), unclassified cardiomyopathy ( $n = 3$ ), restrictive cardiomyopathy ( $n = 1$ ), and unspecified cardiomyopathy ( $n = 1$ ).<sup>27</sup> Five cats with CHF (5/33, 15%) had recently received IV fluid treatment, and the etiology of CHF in these cases was suspected to include a component of acute fluid overload. The most commonly

**TABLE 1** Clinical data for 51 cats in respiratory distress diagnosed with either congestive heart failure (CHF) or NC disease

Parameter	All cats	CHF	NC	P-value
Number of cats	51	33	18	–
Age (years)	10.3 +/- 3.7	10.5 +/- 3.6	10.0 +/- 4.1	.65
Male, n (%)	36/51 (70.6)	25/33 (75.8)	11/18 (61.1)	.34
Body weight (kg)	5.3 +/- 1.5	5.0 +/- 1.1	5.8 +/- 1.9	.089
Body condition score	5.6 +/- 1.7	5.0 +/- 1.6	6.1 +/- 1.9	.17
Rectal temperature (°F)	100.3 +/- 1.6	100.3 +/- 1.6	100.4 +/- 1.6	.82
Heart rate (per minute)	198.7 +/- 31.3	193.9 +/- 32.9	207 +/- 26.9	.14
Respiratory rate (per minute)	68 +/- 23	63 +/- 16	78 +/- 30	.024*
Murmur present, n (%)	15/51 (29.4)	13/33 (39.4)	2/18 (11.1)	.052
Arrhythmia present, n (%)	6/51 (11.8)	5/33 (15.2)	1/18 (5.6)	.41
S4 gallop present, n (%)	13/51 (25.5)	13/33 (39.4)	0/18 (0)	.0017*

Continuous data are presented as mean +/- SD, whereas categorical data are presented as number and percentage of cats with each finding. Significant *P*-values (*P* < .05) are denoted with an asterisk (\*).

diagnosed NC disease was neoplasia (9/18, 50%), including primary lung tumor (n = 5) and metastatic neoplasia (n = 4). Other NC diseases were idiopathic chylothorax (n = 4), feline asthma (n = 3), fungal disease (n = 1, disseminated cryptococcosis), and suspected aerosolized toxin exposure (n = 1).

No significant differences were detected between CHF and NC groups in terms of age, sex, weight, rectal temperature, heart rate, or presence of arrhythmia (see Table 1). Overall, 15/51 cats (29%) were diagnosed with a heart murmur on auscultation, including 13/33 (39%) cats diagnosed with CHF and 2/18 (11%) cats diagnosed with NC disease. The difference in murmur incidence between CHF and NC cats was not statistically significant (*P* = .052). Thirteen cats (25%) had an S4 gallop noted on auscultation, all of which were diagnosed with CHF; cats with CHF were more likely to have an S4 gallop than cats with NC disease (*P* = .0017). The only other clinical finding that differed between groups was respiratory rate, with NC cats having higher respiratory rates

on presentation compared to cats with CHF (78 +/- 30 breaths/minutes versus 63 +/- 16 breaths/minutes, *P* = .024).

### 3.2 | Point-of-care thoracic imaging

Except for the single cat excluded from the study, performance of LUS and FCU was technically feasible (all images obtained at all described sites) in all cats. Lung ultrasound and FCU were completed without difficulty in <5 minutes in 48/51 (94%) cats. In 3 cats, examiners recorded that examination time was prolonged (5–10 minutes) because of patient instability (n = 2) or behavioral noncompliance (n = 1).

Overall, 44/51 (86%) of cats had at least 1 B-line identified on LUS, including 32/33 (97%) cats with CHF and 12/18 (67%) cats with NC disease (see Table 2). Cats with CHF were more likely to have any B-lines compared with cats with NC causes of respiratory distress (*P* = .0056)

**TABLE 2** Thoracic ultrasound and POC cardiac biomarker testing in 51 cats with respiratory distress diagnosed with congestive heart failure or NC disease

Parameter	All cats	CHF	NC	P-value
Number of cats	51	33	18	–
B-lines present, n (%)	44/51 (86.3)	32/33 (97.0)	12/18 (66.7)	.0056*
Vet BLUE sites containing B-lines (#)	5 (0–8)	6 (0–8)	1 (0–8)	.0026*
Strong positive Vet BLUE sites (#)	2 (0–8)	4 (0–8)	0.5 (0–7)	<.001*
Volpicelli positive exam, n (%)	18/51 (35.3)	16/33 (48.5)	2/18 (11.1)	.013*
Total B-line score (sum of 8 sites, #)	20 (0–74)	26 (0–74)	3.5 (0–34)	<.001*
PLEFF present, n (%)	36/51 (70.6)	26/33 (78.8)	10/18 (55.6)	.11
Vet BLUE sites containing PLEFF (#)	0 (0–8)	0 (0–8)	1.5 (0–8)	.61
PCEFF present, n (%)	20/51 (39.2)	20/33 (60.6)	0/18 (0)	<.001*
LA : Ao subjectively enlarged, n (%)	32/51 (62.7)	32/33 (97.0)	0/18 (0)	<.001*
LA : Ao	1.8 +/- 0.6	2.1 +/- 0.5	1.2 +/- 0.2	<.001*
Blood NT-proBNP positive, n (%)	36/51 (70.6)	31/33 (93.9)	5/18 (27.8)	<.001*
PLEFF NT-proBNP positive, n (%)	14/19 (73.7)	11/12 (91.7)	3/7 (42.9)	.034*

Continuous data are presented as mean +/- SD if normally distributed, and as median (range) if non-normally distributed. Categorical data are presented as number and percent of cats with each finding. See text for definitions of strong positive vet BLUE sites and total B-line score.

**Abbreviations:** #, number; CHF, congestive heart failure; NC, noncardiac disease; LA : Ao, ratio of left atrial to aortic diameter; PLEFF, pleural effusion; PCEFF, pericardial effusion; NT-proBNP, N-terminal pro-B-type natriuretic peptide; vet BLUE, veterinary bedside lung ultrasound examination. Significant *p*-values (*p* < .05) are denoted with an asterisk (\*).



and had a higher number of Vet BLUE sites containing any B-lines (median, 6; range, 0–8) compared with NC cats (median, 1; range, 0–8;  $P = .0026$ ). Cats with CHF had a higher total B-line scores (median, 26; range, 0–74) compared with NC cats (median, 3.5; range, 0–34;  $P < .001$ ) as well as a higher number of strong positive Vet BLUE sites (sites with >3 or infinite B-lines) compared with NC cats (median, 4 versus 0.5;  $P < .001$ ). Using previously established criterion<sup>9,15</sup> that at least 2 strong positive sites on each hemithorax defines a positive LUS examination, Volpicelli positive examinations were more common in CHF cats (16/33, 48.5%) compared with NC cats (2/18, 11.1%;  $P = .013$ ).

Although CHF cats had more B-lines than NC cats by all measures, distribution of B-lines among individual Vet BLUE sites was relatively uniform for both groups. For CHF cats, the Vet BLUE site where B-lines were most commonly noted was the RPh site (81.8% of CHF cats had B-line at this site), whereas the site least commonly containing B-lines was the RCr site (B-lines present in 51.5% of CHF cats). For NC cats, the Vet BLUE site where B-lines were most commonly noted was the RCr site (55.6% of NC cats had B-lines at this site), whereas the site least commonly containing B-lines was the RPh site (B-lines present in 22.2% of NC cats). In both groups, occurrence of B-lines among Vet BLUE sites was not statistically different from an equal distribution ( $P = .896$  for CHF,  $P = .617$  for NC).

Subpleural LUS abnormalities (other than B-lines) were noted in 13 cats (25%). Seven cats had Sh, including 6 cats with CHF and 1 cat with feline asthma. Four cats had Ti, including 2 cats with CHF, 1 cat with feline asthma (and suspected mucus plugging of the airways), and 1 cat with pulmonary metastasis. Sh and Ti always occurred in conjunction with B-lines at the same Vet BLUE site; presence of Sh was associated with strong positive sites in 5/7 cats, and presence of Ti was associated with strong positive sites in 3/4 cats. Three cats had Nd, including 1 cat each diagnosed with disseminated fungal disease, pulmonary metastasis, and primary lung tumor. Cats with NC disease were more likely to have Nd compared to cats with CHF ( $P = .015$ ).

A total of 36/51 (71%) cats had PLEFF identified on LUS, including 26/33 (79%) cats with CHF and 10/18 (56%) cats with NC disease (see Table 2). Of 8 possible Vet BLUE sites, PLEFF was noted in an average of 2.7 +/- 3.2 sites per cat. Incidence of PLEFF ( $P = .11$ ) and number of sites containing PLEFF ( $P = .48$ ) did not

differ between cats with CHF and NC disease. Nineteen cats (37%) had at least 1 site that contained both PLEFF and B-lines, with an average of 1.0 +/- 1.5 such sites per cat. Coexistence of PLEFF and B-lines was not more common in CHF cats compared with NC cats ( $P = .37$ ).

Pericardial effusion was noted on FCU in 20/51 cats (39%), all of which were diagnosed with CHF (see Table 2). Cats with CHF were significantly more likely to have PCEFF (20/33, 61%) compared with NC cats (0/18, 0%;  $P < .0001$ ). Volume of PCEFF was described as trace (<3 mm) in 14 cats and mild (3–6 mm) in 6 cats. Subjective LA enlargement was noted in 32/51 (62.7%) cats, including 32/33 (97%) cats diagnosed with CHF and 0/18 (0%) cats diagnosed with NC disease ( $P < .0001$ ). Average quantitative LA : Ao was significantly higher in cats with CHF (2.1 +/- 0.49) compared with NC cats (1.2 +/- 0.21;  $P < .0001$ ).

### 3.3 | Biomarker testing

Point-of-care NT-proBNP testing was performed on blood samples from all cats. The SNAP test was visually positive in 36/51 (71%) cats, including 31/33 (94%) cats diagnosed with CHF and 5/18 (28%) cats diagnosed with NC disease. Point-of-care NT-proBNP testing also was performed using samples of PLEFF in 19 cats. The SNAP test was visually positive in 14/19 (74%) PLEFF samples, including 11/12 (92%) from CHF cats and 3/7 (43%) from cats with NC disease. Compared to cats with NC disease, cats diagnosed with CHF were more likely to have positive NT-proBNP tests performed on both blood ( $P < .0001$ ) and PLEFF ( $P = .034$ ; Table 2).

### 3.4 | Diagnostic accuracy

Univariate logistical regression was performed to evaluate clinical, LUS, FCU, and biomarker variables for association with a final diagnosis of CHF. Results for variables found to be significant in univariate analysis are shown in Table 3. Two variables (subjective LA : Ao enlargement and presence of PCEFF) showed quasi-complete separation on univariate regression, and Chi-square analyses were performed to evaluate their association with CHF diagnosis and obtain

**TABLE 3** Diagnostic accuracy of variables associated with final diagnosis of congestive heart failure (CHF) in univariate analysis

Parameter	AUC	Optimal cutoff to predict CHF	Sensitivity (%)	Specificity (%)	P-Value
Respiratory rate	0.711 (0.567-0.830)	<68	66.7 (48.2–82.0)	77.8 (52.4–93.6)	.014
Vet BLUE sites containing B-lines	0.749 (0.608-0.860)	>2	84.9 (68.1–94.9)	66.7 (41.0–86.7)	.0016
Strong positive Vet BLUE sites	0.833 (0.703-0.923)	>1	78.8 (61.1–91.0)	83.3 (58.6–96.4)	<.001
Volpicelli positive exam	0.687 (0.542-0.809)	–	48.5 (30.8–66.5)	88.9 (65.3–98.6)	.0048
Total B-line score	0.822 (0.690-0.915)	>4	87.9 (71.8–96.6)	66.7 (41.0–86.7)	<.001
PCEFF present	0.803** (0.668-0.901)	–	60.6 (42.1–77.1)	100 (81.5–100)	<.001
LA : Ao subjectively enlarged	0.985** (0.903-1.00)	–	97.0 (84.2–99.9)	100 (81.5–100)	<.001
LA : Ao	0.981 (0.896-1.00)	>1.5	93.9 (79.8–99.3)	94.4 (72.7–99.9)	<.001
Blood NT-proBNP positive	0.831 (0.700-0.921)	–	93.9 (79.8–99.3)	72.2 (46.5–90.3)	<.001

Optimal cutoffs for prediction of CHF are listed for continuous variables; 95% confidence intervals for each result are listed in parentheses.

**Abbreviations:** AUC, area under the receiver operating characteristic curve; LA : Ao, ratio of left atrial to aortic diameter; PCEFF, pericardial effusion; NT-proBNP, N-terminal pro-B-type natriuretic peptide; vet BLUE, veterinary bedside lung ultrasound examination.

\*\*Indicates variables that displayed quasi-complete separation on univariate regression.

ROC curves. The following variables were not significantly associated with final diagnosis of CHF in univariate analysis ( $P > .05$ ): age, sex, body weight, body condition score, rectal temperature, heart rate, presence of arrhythmia, presence of PLEFF, and number of sites positive for PLEFF. Although 2 variables (presence of heart murmur and PLEFF NT-proBNP) were significant in a univariate analysis, the ROC curves developed for these variables did not differ significantly from the diagonal line (area under the curve [AUC] = 0.5).

Variables found to be significant in univariate analysis were entered into a stepwise multivariate logistic regression model (respiratory rate, total B-line score, number of Vet BLUE sites containing B-lines, number of strong positive Vet BLUE sites, Volpicelli exam positive, and blood NT-proBNP positive). Variables displaying quasi-complete separation on univariate regression could not be entered into the multivariate model. Additionally, LA : Ao was not included in the model because its high discriminatory power in univariate analysis nullified the significance of all other variables in multivariate analysis. Two variables remained significant in the final multivariate regression: number of strong positive Vet BLUE sites ( $P = .036$ ) and blood NT-proBNP ( $P = .001$ ). Relative performance of this multivariate model compared with univariate models for the quasi-separated and highly discriminatory univariate variables in univariate analysis are shown in Table 4.

### 3.5 | False positive and false negative results

Presence of B-lines on LUS incorrectly categorized some cats as having CHF (false positives). Using the criterion of >1 strong positive Vet BLUE site, LUS incorrectly classified 3 cats as having CHF, all of which were diagnosed with neoplasia (primary pulmonary or metastatic). False positives also occurred using the NT-proBNP SNAP test. Five cats were incorrectly classified as having CHF based on a positive NT-proBNP result, including 1 cat with feline asthma (LA : Ao 0.96) and 4 cats with neoplasia (LA : Ao 1.22, 1.30, 1.33, and 1.50). The FCU variables of subjective LA : Ao enlargement and presence of PCEFF were highly specific (100%) indicators of CHF, with no false positives in our patient population.

All diagnostic tests failed to correctly identify at least 1 cat with CHF (false negatives). Using the criterion of >1 strong positive site, LUS missed the diagnosis of CHF in 7 cats. Of these cats, 6/7 had PLEFF, 5/7 had PCEFF, and 6/7 were positive on NT-proBNP SNAP test. The NT-proBNP SNAP test missed the diagnosis of CHF in 2 cats. Both of these cats had severe LA enlargement and PLEFF; 1 cat had PCEFF and

8 strong positive Vet BLUE sites, whereas the other had a total B-line score of 3 with no strong positive Vet BLUE sites. Subjective LA size assessment produced only 1 false negative CHF diagnosis. This cat had an LA : Ao of 1.30 on FCU, but a subsequent complete echocardiogram identified hypertrophic cardiomyopathy with LA : Ao of 1.65, suggesting that the FCU view underestimated true LA size in this cat.

## 4 | DISCUSSION

The POC diagnostic techniques (LUS, FCU, and NT-proBNP) used in our study had good to excellent sensitivity and specificity for the diagnosis of CHF in cats with respiratory distress. Regarding LUS, the presence of > 1 Vet BLUE site scoring “strongly positive” for B-lines (>3 B-lines per site) was the criterion with the best diagnostic accuracy. This finding was 78.8% sensitive and 83.3% specific for a diagnosis of CHF. Accuracy of LUS in our study was lower than in a previous study involving 24 cats, in which the Vet BLUE protocol was 87% sensitive and 89% specific for a diagnosis of CHF.<sup>9</sup> This difference likely reflects differences in exclusion criteria between the 2 studies. In the prior study, cats with moderate to severe PLEFF (fluid accumulation > 1 cm) were deliberately excluded to avoid the possibility that lung atelectasis secondary to effusion might have caused B-lines independent of true pulmonary disease. In our study, cats were included regardless of the presence or volume of PLEFF. Cats can manifest left-sided CHF in a variety of ways, including pulmonary edema, PLEFF, PCEFF, or any combination thereof.<sup>4</sup> Some cats with CHF in our study had cavitory effusion (PLEFF or PCEFF or both) without pulmonary edema, and without B-lines on LUS. Therefore, it is logical that a B-line LUS criterion could have false negatives and lower sensitivity for diagnosis of CHF in cats in which cardiogenic fluid accumulation is primarily PLEFF. However, if lung atelectasis does result in B-lines, PLEFF also could lead to false positive diagnoses of CHF on LUS; additional studies pre- and post-thoracocentesis are needed to determine the effect of large-volume PLEFF on LUS imaging.

Pleural effusion was quite common in our study regardless of underlying diagnosis, occurring in 36/51 (70.6%) cats, including 26/33 (78.8%) CHF cats and 10/18 (55.6%) NC cats. Neither presence, volume, nor distribution of PLEFF was useful in discriminating between CHF and NC disease. In a previous study, PLEFF was identified as a manifestation of fluid accumulation in 51/100 (51%) cats with acute CHF.<sup>4</sup> The higher incidence of PLEFF in our study might reflect a bias

**TABLE 4** Diagnostic accuracy for prediction of congestive heart failure (CHF) of the final multivariate regression model compared to highly discriminatory individual parameters showing quasi-complete separation on univariate analysis

Parameter	AUC	Sensitivity (%)	Specificity (%)	P-value
Multivariate model: >1 Vet BLUE site strongly positive for B-lines and blood NT-proBNP positive	0.895 (0.777-0.963)	75.8 (57.7-88.9)	88.9 (65.3-98.6)	.0016
PCEFF present	0.803 (0.668-0.901)	60.6 (42.1-77.1)	100 (81.5-100)	<.001
LA : Ao subjectively enlarged	0.985 (0.903-1.00)	97.0 (84.2-99.9)	100 (81.5-100)	<.001
LA : Ao	0.981 (0.896-1.00)	93.9 (79.8-99.3)	94.4 (72.7-99.9)	<.001

Ninety-five percent confidence intervals for each result are reported in parentheses.

**Abbreviations:** AUC, area under the receiver operating characteristic curve; LA : Ao, ratio of left atrial to aortic diameter; PCEFF, pericardial effusion; NT-proBNP, N-terminal pro-B-type natriuretic peptide; vet BLUE, veterinary bedside lung ultrasound examination.

in the referred patient population (ie, primary care veterinarians might elect to refer cats with known or suspected PLEFF to a tertiary care center if they lack the equipment or expertise to perform thoracocentesis). The overall frequency of PLEFF in cats with respiratory distress in our study highlights the utility of POC ultrasound to identify PLEFF and expedite therapeutic thoracocentesis.

Pulmonary neoplasia (primary pulmonary or metastatic) was the most common NC cause of false positive LUS results in our study. This finding differs from previous LUS studies in dogs, in which the most common NC diseases associated with numerous B-lines were acute respiratory distress syndrome, pulmonary thromboembolism, and pneumonia.<sup>9,28</sup> This difference likely reflects species differences in the types of NC diseases causing respiratory distress. In the studies of dogs, frequently diagnosed underlying diseases included pulmonary thromboembolism, airway disease, and pneumonia. In our study of cats, neoplasia was the most common NC disease, diagnosed in 9/18 (50%) cats. Because B-lines are caused by presence of alveolar or interstitial infiltrates regardless of etiology, false positive results can occur with any NC disease that causes significant alveolar or interstitial pathology. Lung ultrasound findings therefore must be interpreted in the context of relevant differential diagnoses for the patient population.

The distribution of B-lines among Vet BLUE sites was relatively uniform in cats with CHF in our study, and did not differ from that of cats with NC disease. This observation is consistent with previous studies of LUS in cats<sup>10,29</sup> in which cats with CHF usually have B-lines in all Vet BLUE sites (diffuse distribution). This finding is also consistent with the typical radiographic appearance of pulmonary edema in cats, often described as patchy, multifocal, or diffuse.<sup>5,29,30</sup> Additional subpleural LUS abnormalities other than B-lines (Sh, Ti, or Nd) were seen in a minority of cats (25%). Shred most commonly were seen in cats with CHF, usually associated with multiple Vet BLUE sites containing infinite B-lines. This finding differs from a previous study of LUS in coughing dogs<sup>28</sup> in which Sh occurred most commonly in dogs with bacterial pneumonia, and only were noted focally in a single, gravity-dependent Vet BLUE site (Cr or Md). Similar to the study of coughing dogs, however, all cats diagnosed with Nd in our study had either fungal or neoplastic disease. Further research with larger sample sizes would be required to determine the diagnostic accuracy of Nd or other subpleural abnormalities for the diagnosis of specific NC diseases. Nonetheless, documentation of all LUS abnormalities at each Vet BLUE site, in addition to B-lines, is recommended when performing POC LUS.<sup>14</sup>

Our study further supports the notion that LA enlargement identified on FCU strongly suggests CHF as the cause of respiratory distress in cats. Subjective LA enlargement was noted in real-time by the examiner in nearly all (32/33) cats diagnosed with CHF and in none of the cats diagnosed with NC disease. Indeed, the criterion of subjective LA enlargement (Yes or No) was 97.0% sensitive and 100% specific for a diagnosis of CHF (AUC of 0.985). Quantitative LA enlargement measured from FCU images also was highly diagnostic; a cutoff of LA : Ao > 1.5 maximized accuracy (AUC 0.981) with a sensitivity of 93.9% and specificity of 94.4% for detection of CHF. Because these 2 indices (subjective and quantitative LA : Ao) both measure the same variable (LA size), it is not surprising that both were highly

discriminatory for the diagnosis of CHF. We chose to measure both indices in our study because we wanted to compare the performance of subjective LA : Ao assessment as performed in "real-time" by the POC ultrasound examiner to quantitative LA : Ao measurement of the same image by a cardiologist. Interestingly, the subjective assessment had slightly higher diagnostic accuracy than the objective measurement in our study. However, these 2 variables showed significant overlap in 95% confidence intervals for AUC, and thus this difference could be because of chance (in fact, both indices had such high discriminatory power that neither was entered into the multivariate analysis). Nonetheless, the LA is a complex 3-dimensional dynamic chamber, whereas quantitative LA : Ao is a single 2-dimensional index performed on a static image. It is possible that real-time LA assessment truly does allow superior visualization of the entire LA and left auricle throughout the cardiac cycle, allowing more accurate detection of LA enlargement.

Previous clinical studies similarly have shown that increased LA size in cats with respiratory signs strongly suggests CHF, especially in cats with PLEFF.<sup>2,7</sup> One study found that a maximal LA size of >16.5 mm measured in B-mode from the right parasternal 4-chamber long axis view had a sensitivity and specificity of 87% for a diagnosis of CHF.<sup>2</sup> In another study, the finding of an enlarged LA during an emergency POC ultrasound increased the confidence and accuracy for the diagnosis of CHF compared with physical examination alone.<sup>7</sup> Our study and previous studies show that conversely, if LA size is normal, NC causes of respiratory distress are more likely.

Ours is the first study to demonstrate that the FCU finding of even a trace amount of PCEFF in a cat with respiratory distress is highly suggestive of CHF. Pericardial effusion was present in 20/33 (61%) cats with CHF in our study and in none of the cats (0/18, 0%) with NC disease. A previous study of cats with acute CHF reported that 23/100 (23%) cats had mild PCEFF on echocardiography.<sup>4</sup> The higher proportion of CHF cats with PCEFF in our study could be explained by differences in ultrasound timing. In the prior study, echocardiography was performed after 43% of cats had received diuretic treatment,<sup>4</sup> whereas only 14% of cats in our study received furosemide before POC ultrasound. Conversely, the largest retrospective case series of cats with PCEFF reported that CHF was the most commonly diagnosed underlying cause of PCEFF, accounting for 113/146 (77%) cases; the remaining 23% of cats were diagnosed with NC diseases including neoplasia or idiopathic PCEFF.<sup>31</sup> In our study, no cat with NC disease had PCEFF. This finding suggests that PCEFF is highly specific for CHF in cats with respiratory distress, but the absence of PCEFF does not rule out CHF. However, the amount of PCEFF can be minimal, and PCEFF might be difficult to distinguish from PLEFF, especially for a novice sonographer.

Point-of-care LUS and FCU had favorable diagnostic utility for evaluating cats with respiratory distress in our study. The main advantage of these POC thoracic ultrasound techniques is that they can be performed quickly (while administering oxygen treatment, if needed) with minimal additional distress to the cat and without the need for clipping hair. For the majority of cats in our study (48/51), both US examinations were completed in <5 minutes with no complications. Three cats with extreme respiratory distress had more prolonged (5–10 minutes) ultrasound examinations, with intermittent breaks to

minimize stress. Another potential advantage is that these POC techniques are cost efficient and can be performed by personnel with minimal training, thereby increasing the timeliness and accuracy of diagnosis in these fragile patients. A study of veterinary interns and (noncardiology) residents showed improved and acceptable diagnostic accuracy for sonographic identification of atrial enlargement, PCEFF, and PLEFF after 6 hours of training.<sup>32</sup> In human medicine, the combination of FCU and LUS by emergency physicians has high and improved diagnostic accuracy compared to conventional diagnostic techniques.<sup>33,34</sup> These POC ultrasound techniques, however, should not replace more detailed evaluations with TXR or a comprehensive echocardiogram by a cardiologist or other qualified specialist to confirm the initial POC assessment once the patient is more stable. However, POC imaging can allow a more accurate working diagnosis to keep patients alive until more comprehensive testing can be performed. One of the main drawbacks of POC ultrasound is that image acquisition, more so than image interpretation, can be challenging in certain cases, especially for a novice sonographer. Imaging difficulties caused by inexperience or low-quality ultrasound equipment could lead to misdiagnosis.

Our supports findings of previous studies regarding the usefulness of the biomarker NT-proBNP for the diagnosis of CHF in cats presenting with respiratory distress. A positive POC NT-proBNP test performed on a blood sample was 93.9% sensitive and 72.2% specific for the diagnosis of CHF in our study. Previous studies have reported high sensitivity (90%-93%) and specificity (80%-87%) of NT-pro-BNP for diagnosis of CHF in cats with respiratory distress, depending on what cut-off values and specific assays were used.<sup>35,36</sup> However, these initial studies employed a quantitative NT-proBNP assay, which is available as a send-out test to commercial laboratories, hindering its application in an emergency setting. A feline-specific POC NT-proBNP ELISA assay (SNAP Feline proBNP test, IDEXX Laboratories, Inc, Westbrook, Maine) has since been marketed and studied in both symptomatic and asymptomatic cats. In a recent study of 33 cats with respiratory distress, this POC NT-proBNP test demonstrated 100% sensitivity and 86.7% specificity for the diagnosis of CHF.<sup>7</sup> In cats with PLEFF, the POC NT-proBNP test performed on plasma samples also had good to excellent sensitivity (95.2%) and specificity (87.5%) for differentiating CHF from NC causes of effusion. In comparison, when using PLEFF (rather than plasma) as the test sample, the POC test had excellent sensitivity (100%) but low specificity (64.7%).<sup>6</sup> We also evaluated the use of PLEFF samples for POC NT-proBNP testing in 19 cats. The pleural fluid POC NT-proBNP results were positive in 11/12 (91.7%) cats with CHF and in 3/7 (42.9%) cats with NC causes of PLEFF. The moderate to high rate of false positives in the pleural fluid tests suggests that blood samples are preferred over pleural fluid samples for POC NT-proBNP testing, and corroborates previous studies suggesting that the POC NT-proBNP test appears to be most helpful in ruling out (rather than ruling in) CHF in cats with respiratory distress.<sup>6</sup> However, diluting pleural fluid 1 : 1 with saline may increase the specificity of POC NT-proBNP performed on PLEFF samples<sup>37</sup> but this dilution technique was not used in our study. The advantage of the POC NT-proBNP is its relatively low cost (as compared with an ultrasound unit), as well as the speed and ease of performing the test and interpreting results.

The only clinical variable that was independently associated with a final diagnosis of CHF in our study was respiratory rate on presentation. Interestingly, cats with CHF had a lower average respiratory rate than cats with NC disease (63 versus 78 breaths per minute). The explanation for this finding is unclear. Cats with NC diseases (most commonly neoplasia, idiopathic chylothorax, and feline asthma) may have simply had more severe pulmonary or pleural space compromise compared with cats with CHF. Alternatively, cats with CHF might have displayed other nonrespiratory clinical signs (lethargy, inappetence) that prompted owners to seek veterinary care at an earlier stage of disease. Emergency treatment is unlikely to have played a role, because respiratory rate was recorded on each cat's triage intake form as part of an initial physical examination before any treatment. Although the difference in respiratory rate between CHF and NC cats was statistically significant, this finding is not likely to be clinically important or useful in a triage setting. Degree of tachypnea should not be used to stratify suspicion of CHF in cats. Indeed, respiratory rate was not a significant variable in multivariate analysis and its addition did not improve diagnostic accuracy of the primary POC tests (LUS, FCU, and NT-proBNP). No other clinical variables, including heart rate, rectal temperature, and presence of a heart murmur, were associated with a final diagnosis of CHF. These findings are somewhat surprising. Given the pathophysiologic nature of heart disease, cats with CHF might be expected to have higher heart rates, lower rectal temperatures, and a higher incidence of heart murmurs compared with cats with NC disease. These findings might be attributable to variable presence of heart murmurs in cats with cardiomyopathy,<sup>3,38</sup> spectrum of disease severity in cats with CHF (with only a subset having evidence of low cardiac output), low statistical power or some combination of these factors. Our results are similar to those of a previous study of LUS in 76 dogs and 24 cats, in which no clinical variables at presentation improved the diagnostic accuracy of LUS for detection of CHF.<sup>9</sup>

With a variety of POC diagnostic modalities available, practitioners naturally will seek the test (or combination of tests) that maximizes sensitivity and specificity for a diagnosis of CHF. The results of our study suggest that the finding of subjective LA enlargement on FCU by an experienced operator is the single best predictor of CHF in a cat with respiratory distress. This finding is not surprising because establishing the presence of clinically relevant structural heart disease (as evidenced by LA enlargement) approximates the gold standard of echocardiography in a triage setting. The finding of PCEFF, if present, further confirms a diagnosis of CHF (100% specific in our study). However, the 2 findings with the highest diagnostic utility (LA enlargement and PCEFF) also are among most technically challenging for inexperienced ultrasonographers. Positioning and optimization of the LA : Ao view can be particularly problematic in a compromised patient. Similarly, identification of trace to mild PCEFF can be difficult, particularly in views also containing PLEFF or an enlarged LA. In contrast, LUS is less technically demanding to perform, and blood sampling for NT-proBNP requires no special expertise. Therefore, when evaluating a cat for possible CHF, novice ultrasonographers may focus less on FCU findings, and instead rely more on the presence of numerous B-lines on LUS combined with NT-proBNP results. This approach is consistent with POC emergency management



procedures in humans, where LUS and NT-proBNP are used together to increase diagnostic accuracy with combined sensitivity and specificity approaching 100% in clinical trials.<sup>17,39</sup> As with any diagnosis in veterinary medicine, test results must be considered in the context of the patient's signalment, history, and physical examination findings. In patients in which clinical presentation is compatible with CHF, the suite of POC diagnostic tests evaluated in our study can provide useful information to increase or decrease the index of suspicion for CHF.

Our study had several limitations. First, the number of study subjects was limited (n = 51), and only 18 cats were diagnosed with NC disease. This sample size naturally limits our statistical power, and makes it particularly difficult to draw conclusions about patterns of diagnostic findings in individual NC conditions. Second, patients were enrolled as a convenience sample of cats presenting for respiratory distress at referral teaching hospitals. Conducting our study at referral institutions may have introduced bias in patient selection. Cats with the most severe respiratory distress may have been underrepresented (potentially being unstable or unsuitable for transport), and cats with PLEFF may have been overrepresented (because of the previously discussed referral bias). Enrollment practices also may have led to exclusion of some cats that presented after-hours when none of the investigators was available to facilitate study enrollment. Third, the majority of LUS and FCU examinations was performed by cardiologists or cardiology residents. Although our subjective impression was that the required didactic training and supervised practice in LUS and FCU increased proficiency of inexperienced examiners in performing these techniques, the overall high level of operator experience may have played a role in high diagnostic accuracy of LUS and FCU in our study. Furthermore, ultrasound images were reviewed by only 1 blinded observer experienced in performing and interpreting POC ultrasound. Previous work suggests that interobserver agreement in LUS is high, even when comparing novice and experienced individuals<sup>9</sup> but interobserver agreement has not been assessed for FCU, especially subjective assessment of LA size. Therefore, our results may have been different with other operators or observers. Further work is needed to determine intraobserver and interobserver observer agreement of FCU and to evaluate the accuracy of POC imaging modalities by less experienced ultrasonographers. Additionally, only the LA : Ao view on FCU was used to evaluate presence of PCEFF in our study. It is possible that the sensitivity of PCEFF for diagnosis of CHF would have been higher had other views been obtained. A general limitation to LUS and FCU is the requirement for a POC ultrasound machine. Disparities in ultrasound model, probes, and software can lead to substantial differences in image quality. We intentionally chose to use small, portable, moderately priced laptop ultrasound units for our study to most closely approximate the equipment available in a primary care or emergency setting. In-house ultrasound units are becoming more common in veterinary practices, and clinicians will benefit from training and experience in POC techniques such as LUS and FCU.

In our study, the POC diagnostic techniques of LUS, FCU, and NT-proBNP were useful to diagnose CHF in a population of cats with respiratory distress. The presence of subjective LA enlargement, PCEFF, >1 site strongly positive for B-lines, and positive blood NT-

proBNP all were highly associated with a diagnosis of CHF. Point-of-care ultrasound is a useful modality in the emergency setting and can provide rapid triage information, particularly for cats in which respiratory distress limits other diagnostic evaluation.

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## CONFLICT OF INTEREST DECLARATION

Dr Lisciandro is the owner of FASTVet.com, a private corporation that provides veterinary ultrasound training to practicing veterinarians. He teaches ultrasound courses for Sound, SonoSite, EI Medical, and scil animal care, and has licensed education materials to EI Medical. He has also received ultrasound equipment on loan from SonoSite, Sound, EI Medical, and scil animal care.

## OFF-LABEL ANTIMICROBIAL DECLARATION

Authors declare no off-label use of antimicrobials.

## INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVED DECLARATION

Procedures were approved by the IACUC at both study sites (North Carolina State University). Informed consent was obtained for each study participant.

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