Diagnostic utility of caudal vena cava measurements in dogs with cavitary effusions or heart failure

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Iowa State University

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Diagnostic utility of caudal vena cava measurements in dogs with cavitory effusions or heart failure

by

Yen-Yu Chou

A thesis submitted to the graduate faculty
in partial fulfillment of the requirements for the degree of

MASTER OF SCIENCE

Major: Veterinary Clinical Science (Veterinary Medicine)

Program of Study Committee:
Jessica Ward, Co-major Professor
Melissa Tropf, Co-major Professor
Albert Jergens
Jonathan Mochel

The student author, whose presentation of the scholarship herein was approved by the program of study committee, is solely responsible for the content of this thesis. The Graduate College will ensure this thesis is globally accessible and will not permit alterations after a degree is conferred.

Iowa State University
Ames, Iowa
2020

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Thoracic ultrasound has proven effective for the diagnosis of left-sided congestive heart failure (L-CHF) dogs and cats with respiratory distress. The objective of this study was to determine whether ultrasonographic indices of the caudal vena cava (CVC) could be used to diagnose right-sided CHF (R-CHF) in dogs with cavitary effusions.

Dogs were prospectively enrolled in four groups: R-CHF (n = 34), L-CHF (39), cavitary effusions of noncardiac etiology (NC, 41), and pericardial effusion with tamponade (PCEFF, 17). Ultrasonographic indices included right ventricular to left ventricular ratio (RV:LV) and 2D and M-mode subxiphoid measures of CVC maximal and minimal size (CVCmax and CVCmin), CVCmax indexed to aortic dimension (CVC:Ao), and CVC collapsibility index (CVC-CI). Variables were compared between study groups using Kruskal-Wallis and Dunn’s-Bonferroni testing.

All indices (RV:LV, CVCmax, CVCmin, CVC:Ao, and CVC-CI) were significantly different between R-CHF and NC dogs (p < 0.005). A CVC-CI less than 30% (in either M-mode or 2D) was 97% sensitive and 93% specific for diagnosis of R-CHF versus NC effusion. All CVC indices, but not RV:LV ratio, also differed between PCEFF and NC dogs (p < 0.005). Compared to NC, L-CHF dogs had higher CVC:Ao in both 2D (p = 0.017) and M-mode (p = 0.014); compared to R-CHF, L-CHF dogs had higher CVC-CI in both 2D and M-mode (p < 0.005).

Ultrasonographic indices of CVC size and collapsibility are useful to differentiate R-CHF versus NC disease as causes of cavitary effusions. Dogs with L-CHF demonstrate CVC measurements intermediate between R-CHF and NC dogs.
CHAPTER 1. GENERAL INTRODUCTION

Point-of-care ultrasound (POCUS) is an emerging ultrasonographic imaging tool utilized in emergency departments to improve diagnosing and operational efficiency.\(^1\) This modality has been shown to be a fast, non-invasive, cost-effective, and repeatable extension of the clinical examination, and enables non-specialist physicians to perform real-time bedside assessments with minimal patient discomfort.\(^1\) In veterinary medicine, three major POCUS protocols have been described: thoracic or abdominal focused assessment with sonography for trauma (AFAST/TFAST),\(^2\) lung ultrasound (Vet BLUE),\(^3,4\) and focused cardiac ultrasound.\(^5,6\) These POCUS protocols have been utilized for rapid detection of cavitary effusions, pulmonary and pleural space pathology, and severe cardiac disease, respectively,\(^2,4,5,7\) and LUS in particular has proven effective in diagnosing left-sided congestive heart failure (L-CHF) in canine and feline patients presenting with respiratory distress.\(^4,5\)

Cavitary effusions (abdominal, pleural, or pericardial effusions) are common in canine emergency medicine and occur secondary to a wide variety of diseases, including right-sided congestive heart failure (R-CHF). While the POCUS protocol AFAST/TFAST allows rapid detection of cavitary effusions,\(^2\) identifying the etiology of these effusions at triage is more challenging. Dogs that present for cavitary effusions often have nonspecific findings on physical examination.\(^2\) Diagnosis traditionally involves laboratory analysis of cavitary fluid, which may not provide timely or definitive results,\(^8\) as well as advanced imaging techniques (abdominal ultrasonography, echocardiography, and computed tomography), which require additional equipment and specialist expertise. The limitations of existing diagnostic tools to identify etiology of cavitary effusion heightens the need for a first-line screening test in the emergency setting. In particular, a point-of-care test to differentiate R-CHF from noncardiac causes of
cavitary effusion would help emergency clinicians prioritize a patient’s subsequent diagnostic workup.

The use of POCUS to identify right heart disease has been investigated previously in human medicine. Reference ranges for right heart echocardiographic indices, including inferior vena cava size and collapsibility and presence of hepatic venous distension, have been standardized in people and proven useful to predict R-CHF and elevated central venous pressure.\textsuperscript{9–13} In veterinary medicine, previous studies have reported reference ranges for maximum caudal vena cava diameter (CVC\textsubscript{max}), CVC\textsubscript{max} to aortic ratio (CVC\textsubscript{max} : Ao), CVC collapsibility index (CVC-CI), hepatic vein diameter, and GBW edema in normal dogs.\textsuperscript{14–16} These indices have been evaluated in dogs as potential markers of hypovolemia and systemic or pulmonary hypertension.\textsuperscript{17–20} However, no previous veterinary studies have demonstrated whether these ultrasonographic indices are abnormal in patients with R-CHF, and whether these indices can be used to differentiate R-CHF from noncardiac (NC) causes of cavitary effusions.

The primary objective of this study was to determine whether POCUS right-sided cardiac markers, particularly CVC indices, could be used to differentiate between dogs diagnosed with R-CHF compared to noncardiac causes of cavitary effusions or L-CHF. The secondary objective was to determine the combination of ultrasonographic indices or clinical examination findings that would optimize diagnostic accuracy for R-CHF. We hypothesized that POCUS right-sided cardiac indices would have diagnostic utility in identifying dogs with R-CHF.
CHAPTER 2. MATERIALS AND METHODS

Procedures were approved by the Institutional Animal Care and Use Committee at Iowa State University and North Carolina State University (IACUC protocol 1-18-8688-K). Informed owner consent was obtained for each participating patient.

Client-owned dogs presented to the Iowa State University Lloyd Veterinary Medical Center or North Carolina State Veterinary Hospital were prospectively recruited for this study between October 27, 2018, and December 31, 2019. To be included in this study, patients were required to have at least moderate amount of cavitary effusion (ascites, pleural effusion, and/or pericardial effusion) or cardiogenic pulmonary edema. Exclusion criteria included lack of owner consent or instability of patient.

The following data were collected from the patient’s physical examination on hospital presentation: patient signalment, body weight, temperature, heart rate, respiratory rate, presence and description of heart murmur, presence and description of any arrhythmias, systolic blood pressure, and sedation protocol if applicable. Fluid location (pulmonary edema, pleural effusion, ascites, pericardial effusion), presence or absence of cardiac tamponade, and centesis information (whether centesis was performed, cavity for which centesis was performed, amount of effusion obtained, and effusion characteristics) were also recorded.

POCUS examinations were performed by ACVIM-boarded cardiologists or cardiology residents using platform ultrasound units (EPIQ7, Philips Healthcare, Andover, Massachusetts) coupled to phased-array transducers (S5-1, S8-3, or S12-4; Philips Healthcare, Andover, Massachusetts). Images were obtained in all dogs according to a standard protocol. Dogs were scanned in right lateral recumbency. Starting at the right parasternal location, ultrasound cine-loops of the long-axis 4-chamber view and the short-axis 4-chamber view were obtained using 2-
dimensional (2D) echocardiography for measurement of the RV : LV ratio in long-axis and short-axis.\textsuperscript{21} 2D right parasternal short-axis images of the heart base was obtained for measurement of LA : Ao ratio.\textsuperscript{22} Subcostal views were used to obtain 2D and M-mode images of the CVC in long-axis as it crossed the diaphragm.\textsuperscript{14,17} Images of the liver optimized for the hepatic veins and of the gallbladder in cross-section were also obtained. For cardiac images, cine-loops were recorded to include least 5 cardiac cycles; for CVC images, 6-second cine-loops were obtained to capture the CVC during maximum inspiration and expiration. Image acquisition took approximately 30 seconds per site, for a total imaging time of approximately 2.5 minutes.

Archived cine-loop and still images of sonographic right-sided cardiac markers were evaluated off-line by one investigator at each study location blinded to patient diagnosis. Five cardiac cycles in sinus rhythm for each measured cardiac parameter were averaged and used for further analysis. Maximal right ventricular end-diastolic dimension and maximal left ventricular end-diastolic dimension were obtained at the level of the right and left ventricular papillary muscles in long-axis 4-chamber view and short-axis 4-chamber view, respectively, and RV : LV ratio was calculated in both long-axis and short-axis.\textsuperscript{21} Maximum and minimum CVC diameters were measured in both 2D and M-mode by identifying the maximum and minimum visible diameters of the CVC.\textsuperscript{14,17} Gallbladder wall thickness was measured from cross-sectional view from leading edge to leading edge; presence of gallbladder wall edema was defined as a hypoechoic layer within the hyperechoic gallbladder wall.\textsuperscript{16} Hepatic venous distension was noted by subjective recognition of distended hepatic veins with a “tree-trunk” appearance.\textsuperscript{23,24}

Final clinical diagnosis for the cause of cavitary effusions was determined by retrospective review of each patient's entire medical record by a different investigator at each study location who was blinded to POCUS results. The final diagnosis incorporated physical
examination findings and diagnostic test results other than POCUS, including clinicopathologic and cytologic analysis of cavitary effusions, labwork (complete blood count, chemistry panel, urinalysis), advanced imaging (radiography, complete echocardiography, abdominal ultrasonography, computed tomography), as well as response to therapy. Dogs were assigned to one of four study groups based on the location and etiology of their cavitary effusions. The R-CHF group was defined as dogs with cavitary effusions and severe right heart disease identified on echocardiogram. Dogs with pericardial effusion and cardiac tamponade were analyzed as a separate group (PCEFF). The L-CHF group was defined as dogs with radiographic evidence of cardiogenic pulmonary edema and severe left heart disease identified on echocardiogram. Dogs with cavitary effusions of non-cardiac etiology were categorized as the non-cardiac (NC) group. Dogs with severe cardiac disease who manifested both pulmonary edema and cavitary effusions (biventricular CHF) were categorized as R-CHF or L-CHF based on the predominant fluid location, considering clinical severity of each fluid accumulation and need for therapeutic centesis. Dyspneic dogs with pulmonary edema that also had trace to mild cavitary effusions not requiring centesis were categorized as L-CHF. Dogs requiring therapeutic abdominocentesis or thoracocentesis were classified as R-CHF, even if they also had mild pulmonary edema.

Statistical analyses were performed by use of commercial software. Normality of data was determined by the Shapiro-Wilk test. Variables were compared between study groups using Kruskal-Wallis and Dunn’s-Bonferroni testing. Quantitative data were summarized as mean ± standard deviation (SD) for normally-distributed data, and as median (interquartile range [IQR]) for non-normally distributed data. Sensitivity and specificity were calculated for the ability of POCUS indices at certain cutoffs to differentiate the R-CHF group from the NC group.
CHAPTER 3. RESULTS

The final study population of 122 dogs comprised 97 dogs from Iowa State University and 25 dogs from North Carolina State University, and included 4 intact females, 55 spayed females, 15 intact males, and 48 castrated males. Various breeds were represented (47 breeds in total), with the most common breeds being mixed breed (n = 27), Yorkshire Terrier (9), Labrador Retriever (5), Cavalier King Charles Spaniel (5), Chihuahua (5), and German Shepherd (5). Other clinical variables describing the study population are shown in Table 1.

Of all the enrolled patients, 34 (28%) dogs were categorized as having R-CHF, 30 (25%) as L-CHF, 41 (34%) as NC causes of effusion, and 17 (14%) had PCEFF. Causes of R-CHF included pulmonary hypertension (n = 10), congenital heart diseases including pulmonic stenosis or tricuspid valve dysplasia (6), dilated cardiomyopathy (DCM) (4), degenerative mitral valve disease (DMVD) or degenerative tricuspid valve disease (DTVD) (4), bradyarrhythmia (4), inflow obstruction due to compressive neoplasia (3), arrhythmogenic right ventricular cardiomyopathy (2), and transfusion associated circulatory overload (1). Causes of L-CHF were DMVD (n = 22), DCM (6), patent ductus arteriosus (1), and bradyarrhythmia (1). Causes of PCEFF were right atrial or auricular mass (n = 7), heart base tumor (3), idiopathic pericarditis (3), left atrial rupture (2), mesothelioma (1), and septic pericarditis (1). Neoplasia was the most common cause of NC effusion (n = 12), with lymphoma and hepatic masses being diagnosed most frequently (n = 3 each). Other diagnosed NC diseases included hypoalbuminemia (n = 9), chylothorax (3), pancreatitis (2), pyothorax (2), hemoabdomen secondary to trauma or coagulopathy (2), hemothorax (2), hepatopathy (2), septic abdomen (1), uroabdomen (1), and intra-abdominal cysts (1). Cause of effusion was ultimately unknown in 4 cases with incomplete
diagnostic workup; these cases were assigned to the NC group based on complete echocardiography showing no evidence of structural cardiac disease.

No significant differences were detected between the four study groups in terms of age, sex, body weight, rectal temperature, presence of arrhythmia, or incidence of sedation (see Table 1). Heart rate differed between the L-CHF and NC group, with L-CHF dogs having higher heart rate compared to dogs with NC disease (P = .0063). Additionally, respiratory rate was significantly higher in the L-CHF group compared to NC, R-CHF, and PCEFF groups (P < .0001, P = .0005, and P = .0014, respectively). Murmur incidence was higher in L-CHF dogs compared to NC (P < .0001) or PCEFF (P = .0012) dogs, as well as in R-CHF dogs compared to NC (P < .0001) or PCEFF (P = .0012) dogs. Systolic blood pressure was lower in L-CHF dogs compared to dogs with NC effusion (P = .0081).

Table 1. Clinical data for 122 dogs diagnosed with R-CHF, L-CHF, NC disease, or PCEFF. Continuous normally-distributed data are presented as mean ± SD, continuous non-normally distributed data are presented as median (IQR), and categorical data are presented as number and percentage of dogs with each finding. Different superscript letters indicate significantly different values between study groups (P < 0.05, with Bonferroni correction). When multiple letters are listed, the value for the indicated group is significantly different from more than one other group. Abbreviations: L-CHF, left-sided congestive heart failure; NC, non-cardiac; PCEFF, pericardial effusion; R-CHF, right-sided congestive heart failure.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All dogs</th>
<th>R-CHF</th>
<th>PCEFF</th>
<th>L-CHF</th>
<th>NC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of dogs</td>
<td>122</td>
<td>34</td>
<td>17</td>
<td>30</td>
<td>41</td>
</tr>
<tr>
<td>Age (years)</td>
<td>8.7 ± 3.9</td>
<td>8.7 ± 3.7a</td>
<td>9.5 ± 3.6a</td>
<td>9.9 ± 3.2a</td>
<td>7.5 ± 4.3a</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>63/122 (52)</td>
<td>18/34 (53)</td>
<td>9/17 (53)</td>
<td>14/30 (47)</td>
<td>22/41 (54)</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>18.4 ± 13.4</td>
<td>16.6 ± 11.4a</td>
<td>23.9 ± 14.6a</td>
<td>13.8 ± 21.0 ±</td>
<td>13.8 ± 21.0 ±</td>
</tr>
<tr>
<td>Rectal temperature (°C)</td>
<td>38.4 ± 0.78</td>
<td>38.2 ± 0.81a</td>
<td>38.4 ± 0.74a</td>
<td>38.4 ± 0.60a</td>
<td>38.5 ± 0.88a</td>
</tr>
<tr>
<td>Heart rate (per minute)</td>
<td>139 ± 42</td>
<td>135 ± 53ab</td>
<td>138 ± 36ab</td>
<td>155 ± 39ab</td>
<td>131 ± 32b</td>
</tr>
<tr>
<td>Respiratory rate (per minute)</td>
<td>45 ± 18</td>
<td>41 ± 16ab</td>
<td>41 ± 14ab</td>
<td>59 ± 19b</td>
<td>37 ± 13a</td>
</tr>
<tr>
<td>Murmur present, n (%)</td>
<td>69/122 (57)</td>
<td>28/34 (82)ab</td>
<td>4/17 (24)bc</td>
<td>28/30 (93)ab</td>
<td>9/41 (22)b</td>
</tr>
<tr>
<td>Arrhythmia present, n (%)</td>
<td>29/122 (24)</td>
<td>12/34 (35)ab</td>
<td>2/17 (12)ab</td>
<td>10/30 (33)ab</td>
<td>5/41 (12)a</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>126 ± 27</td>
<td>127 ± 24ab</td>
<td>131 ± 26ab</td>
<td>116 ± 26a</td>
<td>135 ± 27b</td>
</tr>
<tr>
<td>Sedation, n (%)</td>
<td>25/122 (21)</td>
<td>11/34 (32)ab</td>
<td>4/17 (24)ab</td>
<td>3/30 (10)ab</td>
<td>7/41 (17)a</td>
</tr>
</tbody>
</table>
Performance of POCUS was technically feasible in all dogs. Right-sided POCUS indices obtained from the four groups of patients are summarized in Table 2. Significant differences were found between groups for all POCUS indices. CVC-CI measurements in both 2D and M-mode were significantly lower in the R-CHF group compared to NC or L-CHF groups, and were also lower in PCEFF dogs compared to NC dogs (P < .005 for all group comparisons). The CVC : Ao ratio in 2D was significantly higher in the R-CHF, PCEFF, and L-CHF groups compared to the NC group (P = .017, P = .004, and P < .005, respectively). Likewise, CVC : Ao ratio in M-mode was significantly higher in the R-CHF, PCEFF, and L-CHF groups compared to the NC group (P = .014, P = .001, and P < .005, respectively). Long axis RV : LV ratio was significantly higher in the R-CHF group compared to PCEFF, NC, and L-CHF groups (P = .018, P = .003, and P < .005, respectively), and lower in the L-CHF group compared to NC (P = .013) or PCEFF (P < .005) groups. Figure 1 displays differences between groups for select POCUS indices.

Sensitivity and specificity of POCUS indices for diagnosis of R-CHF versus NC effusion are summarized in Table 3. Of the POCUS indices measured, CVC:CI < 30% in either 2D or M-mode provided maximal sensitivity and specificity for prediction of R-CHF.
Table 2. POCUS indices in dogs from the R-CHF, L-CHF, NC, and PCEFF groups. Continuous normally-distributed data are presented as mean ± SD, continuous non-normally distributed data are presented as median (IQR), and categorical data are presented as number and percentage of dogs with each finding. Different superscript letters indicate significantly different values between study groups (P < 0.05, with Bonferroni correction). When multiple letters are listed, the value for the indicated group is significantly different from more than one other group. Abbreviations: 2D, two-dimensional; CVC : Ao ratio, caudal vena cava to aortic diameter ratio; CVC-CI, caudal vena cava collapsibility index; CVC Max, maximal caudal vena cava diameter; CVC Min, minimal caudal vena cava diameter; L-CHF, left-sided congestive heart failure; M-mode, motion mode ultrasound; NC, non-cardiac; PCEFF, pericardial effusion; R-CHF, right-sided congestive heart failure; RV : LV ratio, right-to-left ventricular end-diastolic dimension ratio.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Unit</th>
<th>Median (interquartile range)</th>
<th>R-CHF (n = 34)</th>
<th>PCEFF (n = 17)</th>
<th>L-CHF (n = 30)</th>
<th>NC (n = 41)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RV : LV ratio, long axis</td>
<td></td>
<td></td>
<td>0.79 (0.39)a</td>
<td>0.55 (0.19)c</td>
<td>0.37 (0.11)b</td>
<td>0.55 (0.10)c</td>
</tr>
<tr>
<td>RV : LV ratio, short axis</td>
<td></td>
<td></td>
<td>0.67 (0.61)a</td>
<td>0.45 (0.26)ab</td>
<td>0.29 (0.16)b</td>
<td>0.46 (0.16)a</td>
</tr>
<tr>
<td>CVC Max (2D)</td>
<td>mm</td>
<td></td>
<td>12.1 (4.8)a</td>
<td>13.0 (8.0)a</td>
<td>9.2 (8.1)ab</td>
<td>9.3 (6.0)b</td>
</tr>
<tr>
<td>CVC Max (M-mode)</td>
<td>mm</td>
<td></td>
<td>12.1 (4.7)a</td>
<td>13.5 (7.3)a</td>
<td>9.9 (7.8)b</td>
<td>9.3 (5.0)b</td>
</tr>
<tr>
<td>CVC Min (M-mode)</td>
<td>mm</td>
<td></td>
<td>10.6 (5.2)a</td>
<td>10.8 (6.7)a</td>
<td>4.2 (7.8)b</td>
<td>4.4 (3.8)b</td>
</tr>
<tr>
<td>CVC-CI (2D)</td>
<td>%</td>
<td></td>
<td>16.8 (10.7)a</td>
<td>20.5 (7.5)ab</td>
<td>38.0 (34.6)b</td>
<td>49.6 (15.3)b</td>
</tr>
<tr>
<td>CVC-CI (M-mode)</td>
<td>%</td>
<td></td>
<td>17.1 (11.2)a</td>
<td>21.5 (9.1)ab</td>
<td>37.2 (42.0)b</td>
<td>50.8 (19.0)b</td>
</tr>
<tr>
<td>CVC : Ao ratio (2D)</td>
<td></td>
<td></td>
<td>0.76 (0.24)a</td>
<td>0.68 (0.26)a</td>
<td>0.66 (0.43)a</td>
<td>0.49 (0.20)b</td>
</tr>
<tr>
<td>CVC : Ao ratio (M-mode)</td>
<td></td>
<td></td>
<td>0.77 (0.25)a</td>
<td>0.75 (0.24)a</td>
<td>0.62 (0.44)a</td>
<td>0.48 (0.17)b</td>
</tr>
</tbody>
</table>

Table 3. Diagnostic accuracy of POCUS variables for the differentiation of R-CHF from NC causes of effusion. Abbreviations: 2D, two-dimensional ultrasound; CVC : Ao ratio, caudal vena cava to aortic diameter ratio; CVC-CI, caudal vena cava collapsibility index; M-mode, motion mode ultrasound; NC, non-cardiac; R-CHF, right-sided congestive heart failure; RV : LV ratio, right-to-left ventricular end-diastolic dimension ratio.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Threshold value</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>CVC-CI (2D or MM)</td>
<td>&lt; 30%</td>
<td>97.1%</td>
<td>92.7%</td>
</tr>
<tr>
<td>CVC : Ao ratio (2D)</td>
<td>≥ 0.65</td>
<td>82.3%</td>
<td>80.4%</td>
</tr>
<tr>
<td>CVC : Ao ratio (MM)</td>
<td>≥ 0.65</td>
<td>85.2%</td>
<td>85.4%</td>
</tr>
<tr>
<td>RV : LV ratio, long axis</td>
<td>&gt; 0.6</td>
<td>82.3%</td>
<td>82.9%</td>
</tr>
<tr>
<td>RV : LV ratio, short axis</td>
<td>&gt; 0.5</td>
<td>64.7%</td>
<td>65.8%</td>
</tr>
<tr>
<td>Hepatic venous distension</td>
<td>Presence</td>
<td>97.1%</td>
<td>85.3%</td>
</tr>
<tr>
<td>Heart murmur</td>
<td>Presence</td>
<td>82.3%</td>
<td>78.0%</td>
</tr>
</tbody>
</table>
Figure 1. Box and whisker plot of data of select POCUS indices obtained from the four study groups (left-sided CHF, right-sided CHF, pericardial effusion, and noncardiac effusion): CVC-CI in 2D (A), CVC-CI in M-mode (B), CVC : Ao ratio in 2D (C), CVCmax : Ao ratio in M-mode (D), RV : LV ratio in long axis (E). The horizontal line in each box represents the median. The boxes represent the interquartile range. Whiskers represent the 5th and 95th percentiles, and the outliers are plotted as dots. Abbreviations: 2D, two-dimensional ultrasound; CVC : Ao ratio, caudal vena cava to aortic diameter ratio; CVC-CI, caudal vena cava collapsibility index; M-mode, motion mode ultrasound; CHF, congestive heart failure; RV : LV ratio, right-to-left ventricular end-diastolic dimension ratio.
Figure 1. (continued)
CHAPTER 4. DISCUSSION

As hypothesized, the POCUS right-sided cardiac markers investigated in this study differed between disease groups and were diagnostically useful for prediction of R-CHF as a cause of cavitary effusions in dogs. Findings of the current study confirmed that CVC-CI, incidence of hepatic venous distension, and CVC : Ao ratio in M-mode were the POCUS indices with the highest sensitivity and specificity for the detection of R-CHF versus NC disease, with CVC-CI having sensitivity and specificity both greater than 90%. These findings are logical since elevated central venous hydrostatic pressure in patients with R-CHF will be transmitted to the CVC and result in greater CVCmax, decreased CVC-CI, and hepatic venous distension.

This study represents the first investigation of POCUS parameters for the diagnosis of R-CHF in veterinary patients. Sensitivity and specificity of CVC-CI (97.1% and 92.7%, respectively) reported in our study was similar or higher than IVC-CI accuracy in multiple human studies. In people, IVC-CI with a cutoff of 22% was 78% sensitive and 98% specific for differentiating patients with R-CHF from healthy patients without cardiac or lung disease. In other human studies regarding diagnostic utility of IVC-CI in dyspneic patients, IVC-CI with a cutoff of 15% was 93% sensitive and 84% specific for a diagnosis of CHF versus noncardiac causes of respiratory distress, and IVC-CI with a cutoff of 20% was 52% sensitive and 86% specific for differentiating patients with acute decompensated CHF from those with noncardiac causes of acute dyspnea. Additionally, IVC-CI with a cutoff of 50.5% was 84% sensitive and 91% specific for detecting CHF versus primary pulmonary disease as the cause of dyspnea in elderly patients.

Accuracy of POCUS for detection of R-CHF versus NC disease in our study was higher than in a previous study investigating the utility of POCUS to predict pulmonary hypertension in
dogs, which found only 11% sensitivity and 88% specificity. The difference in POCUS accuracy can be explained by differences in study populations. In the prior study, dogs with mild to severe pulmonary hypertension were included; while these dogs by definition had elevated right ventricular systolic pressure, few would be expected to have elevated right ventricular diastolic (right atrial) pressure. Changes to CVC size and distensibility would only be expected in dogs with right heart disease that had advanced to the point of elevated central venous pressure and R-CHF. In our study, only dogs diagnosed with overt R-CHF (cavitary effusion) secondary to their right heart disease were included in the R-CHF group. Just as elevated pulmonary venous pressure would be a poor screening test for systemic hypertension, looking for evidence of elevated central venous pressure would be an insensitive method to screen for pulmonary arterial hypertension.

Our data demonstrated a much larger variability in CVC-CI for the L-CHF group compared to other disease groups. We speculate that this disparity occurred because the change in the size of the CVC depends on the change in intrathoracic pressure during respiration. Respiratory rate and degree of respiratory distress were higher and more variable within the L-CHF group compared to the other disease groups, wherein most dogs had normal respiratory rate and effort. This increase respiratory effort in a severely dyspneic patient would cause a more significant magnitude of the collapse of the CVC. Thus, we suspect that the significant variance in the respiratory effort in the L-CHF group caused considerable variation in CVC-CI for these dogs. Indeed, the influence of diaphragmatic movement on IVC-CI has been demonstrated in humans. However, it is challenging to quantify the magnitude of the respiratory effort in spontaneous breathing veterinary patients.
There was no significant difference in GBW thickness or incidence of GBW edema between the four study groups, suggesting that presence or absence of GBW edema is a poor screening tests for R-CHF. This is not necessarily surprising, as a wide variety of causes for GBW edema have been identified, including R-CHF, PCEFF, anaphylaxis, hepatitis, hypoproteinemia, volume overload, and cholecystitis. Interestingly, RV : LV ratio in short axis had relatively low sensitivity and specificity (64.7% and 65.8%, respectively) for differentiating the R-CHF and NC groups, while the same ratio in long-axis performed better, with 82.3% sensitivity and 82.9% specificity. We suspect that this occurred because the crescent-shaped geometry of the right ventricle can lead to underestimation of this chamber size in short axis, particularly in patients with concurrent left heart disease.

In the R-CHF group, ascites was present in 34/34 (100%) dogs, while pleural effusion was only present in 5/34 (15%) of dogs; isolated pleural effusion occurred exclusively in the NC group. In a previous study of dogs with right-sided manifestations of CHF secondary to DCM or DMVD, 40/60 (67%) of dogs with R-CHF had ascites, 26/60 (43%) had pleural effusion, and 13/60 (22%) had PCEFF, and similarly no dogs had pleural effusion only. The higher incidence of ascites and lower incidence of pleural effusion in the present study might reflect the difference in inclusion criteria between studies, since the prior study described dogs with primarily left-sided heart disease who nonetheless had cavitary effusions as part of their manifestation of CHF. Together, these studies suggest that absence of ascites, and particularly the finding of isolated pleural effusion, should significantly decrease suspicion for R-CHF.

One of the limitations of this study was that no healthy control group was recruited for comparison of CVC indices. Bodyweight-normalized reference intervals for maximal CVC diameter in 2D and M-mode have previously been established in dogs from a paralumbar view.
Reference intervals for minimal CVC diameter and CVC-CI were not provided due to poor inter-rater agreement. Although ultrasound images were obtained from a different view in the present study (subxiphoid versus paralumbar), the majority of CVC measurements from the NC group were within the 95% prediction interval for normal dogs (76% for 2D, 85% for M-mode). Not surprisingly, a much smaller percentage of CVC measurements were within normal 95% prediction intervals for dogs with R-CHF (18% in both 2D and M-mode), PCEFF (41% and 35%, respectively), or L-CHF (50% and 57%, respectively). Thus although the present study did not specifically recruit a cohort of control dogs, results suggest that dogs with NC causes of cavitary effusion generally have normal CVC size, while maximal CVC measurements in dogs with L-CHF, R-CHF, and PCEFF are larger than normal.

Our study had several additional limitations. Because the primary study investigators were from the Cardiology Service, the patient population was biased toward including more patients with cardiac disease (R-CHF, L-CHF, or PCEFF) versus NC disease. Investigators were less likely to enroll unstable patients or those requiring emergency surgery; for instance, only one patient with hemoabdomen secondary to splenic hemangiosarcoma was enrolled. Time between hospital presentation and POCUS was not standardized, although the examination typically occurred within 12 hours of presentation; it is possible that the disease status could have changed during that time period, particularly if treatment for CHF (e.g. furosemide) or intravenous fluids had been administered before POCUS was performed. Furthermore, operators were not blinded to the presumptive diagnosis of the patient at the time of the thoracic ultrasound, which may have led to bias during image acquisition.

An additional major limitation is that all of our POCUS examinations were performed by highly trained cardiologists or cardiology residents utilizing a platform cardiac ultrasound...
machine; personnel and equipment would be different in a primary care setting or emergency department. Differences in the operators, ultrasound model, probes, and software can lead to disparities in imaging quality and results. Furthermore, interobserver reliability was not assessed in this study. Previous study suggests that inter-rater agreement of CVC measurements were good to excellent when performed at the hepatic view, paralumbar view, and spleno-renal view, but poor when performed at the subxiphoid view. However, another study of ultrasound measurement at subxiphoid view in 15 healthy Beagle dogs reported that interobserver agreement between non-cardiologists and cardiologists was acceptable in maximum CVC diameter, while non-acceptable in minimum CVC diameter and CVC-CI. Therefore, our results obtained from the subxiphoid view may have been different from other operators or observers. This is important because CVC measurements taken from planes that do not transect the actual middle of the vessel can underestimate the true diameter, and this can occur during the shift of CVC during inspiration and expiration. We intentionally chose to perform POCUS at the subcostal view using the sagittal imaging plane since these are the easiest to obtain reliably, and are the views most commonly used in emergency practice currently.
CHAPTER 5. GENERAL CONCLUSION

In conclusion, the current study showed that POCUS was a feasible and accurate diagnostic test for the detection of R-CHF in dogs with cavitary effusion. Dogs with NC effusion have CVC size and collapsibility similar to normal dogs, while dogs with R-CHF had large indistensible CVC, and dogs with L-CHF had CVC measurements in between these two extremes. CVC-CI in either 2D or M-mode was the best ultrasonographic index to discriminate between study groups, and a cutoff value of <30% was more than 90% sensitive and specific for diagnosis of R-CHF versus NC effusion. POCUS can be used in the emergency setting to increase or decrease index of suspicion for R-CHF as the cause of cavitary effusions, allowing clinicians to prioritize treatment and diagnostic plans.
REFERENCES


