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Caudal vena cava point-of-care ultrasound in dogs with degenerative mitral valve disease without clinically important right heart disease☆,☆☆

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KEYWORDS
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Abstract *Objectives:* Caudal vena cava (CVC) diameter and collapsibility index (CVC_D and CVC_{CI}) have been used to assess intravascular volume status (IVS). Maladaptations with progressive degenerative mitral valve disease (DMVD) lead to hypervolemia. We hypothesised that stages of DMVD will affect ultrasonographic CVC variables in dogs without clinically important right heart disease.
Animals, materials and methods: This retrospective study included 79 dogs with DMVD presented to the cardiology department between January 2017 and 2019. Subxiphoid views were used to obtain CVC cineloops. By visual inspection, CVC was subjectively scored as flat, normal or fat. Maximal and minimal CVC_D were

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☆☆ A unique aspect of the Journal of Veterinary Cardiology is the emphasis of additional web-based materials permitting the detailing of procedures and diagnostics. These materials can be viewed (by those readers with subscription access) by going to http://www.sciencedirect.com/science/journal/17602734. The issue to be viewed is clicked and the available PDF and image downloading is available via the Summary Plus link. The supplementary material for a given article appears at the end of the page. To view the material is to go to http://www.doi.org and enter the doi number unique to this paper which is indicated at the end of the manuscript.

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measured and indexed to aortic diameter ($CVC_{D\text{-}max/Ao}$ and $CVC_{D\text{-}min/Ao}$); CVC_{CI} was calculated as ($CVC_{D\text{-}max}$-$CVC_{D\text{-}min}$)/$CVC_{D\text{-}max}$. Fisher's exact and Kruskal–Wallis tests were used to compare CVC variables.
Results: Subjective assessment was associated with American College of Veterinary Internal Medicine (ACVIM) stages ($P < 0.001$). The proportion of fat CVC was greater in stages C and D. In stage D, $CVC_{D\text{-}max/Ao}$ was larger compared with stages B1, B2 and C ($P = 0.002$, $P = 0.002$ and $P = 0.035$, respectively). In stages C and D, $CVC_{D\text{-}min/Ao}$ was larger compared with B1 ($P = 0.016$ and $P = 0.001$) and B2 ($P = 0.002$ and $P < 0.001$. In stages C and D, CVC_{CI} was less than stage B1 ($P = 0.016$ and $P = 0.044$) and B2 ($P = 0.001$ and $P = 0.010$).
Conclusions: In dogs with DMVD without clinically important right heart disease, CVC variables differ across ACVIM stage. Subjective and objective CVC variables may be used to predict hypervolemia.

Abbreviations

ACEI	angiotensin-converting enzyme inhibitor
ACVIM	American College of Veterinary Internal Medicine
ADHF	acute decompensated heart failure
CVC	caudal vena cava
CVCD	caudal vena cava diameter
$CVC_{D\text{-}min}$	minimal caudal vena cava diameter
$CVC_{D\text{-}max}$	maximal caudal vena cava diameter
$CVC_{D\text{-}min/Ao}$	minimal caudal vena cava diameter indexed to aortic diameter
$CVC_{D\text{-}max/Ao}$	maximal caudal vena cava diameter indexed to aortic diameter
CVC_{CI}	caudal vena cava collapsibility index
DMV_D	degenerative mitral valve disease
IVC	inferior vena cava
IVC_D	inferior vena cava diameter
IVC_{CI}	inferior vena cava collapsibility index
IVS	intravascular volume status
PH	pulmonary hypertension

Introduction

Degenerative mitral valve disease (DMVD) is the most common cause of congestive heart failure in dogs and occurs in up to 80% of acquired canine cardiac disease patients [1]. Disease progression is associated with compensatory mechanisms, such as activation of the renin-angiotensin-aldosterone system and arginine-vasopressin release, causing water retention and hypervolemia [1]. Over time, compensatory mechanisms occur, leading to maladaptive cardiac remodelling and fluid retention, sometimes culminating in left-sided congestive heart failure [1]. Considering that hypervolemia is indicative of maladaptation and treatment is specifically targeted at reducing intravascular volume, markers of intravascular volume status (IVS), and specifically of hypervolemia, might help in the assessment and management of dogs with DMVD [1].

Central venous pressure has been suggested to represent IVS in veterinary patients [2]. In the absence of vascular obstruction and with normal right ventricular function, central venous pressure has been considered a surrogate for right ventricular preload [3]. However, the correlation of central venous pressure to global IVS is questionable [4]. Moreover, placement of an indwelling central access line is impractical for routine and emergency cardiac consultations.

The inferior vena cava (IVC) in humans, or the caudal vena cava (CVC) in companion animals, is a collapsible major vein. Its size varies with intravascular pressure and volume changes, and its diameter is minimally affected by vasoconstriction [5]. The collapsibility of the abdominal portion of

this vessel is influenced by intrathoracic pressure changes during the respiratory cycle. During spontaneous inspiration, negative intrathoracic pressure tends to collapse the vessel, with a concurrent increased venous return. Conversely, blood flow to the thorax is impeded during expiration, increasing in the size of IVC or CVC. In human medicine, changes in inferior vena cava diameter (IVC_D) and calculated inferior vena cava collapsibility index (IVC_{CI}) are used as predictors of fluid responsiveness. Specifically, a higher collapsibility index suggests a greater likelihood that fluid administration will lead to increased cardiac output and improved tissue perfusion [6–9]. IVS refers to the blood volume contained in the vascular bed (arteries, arterioles, capillaries, venules and veins) while fluid responsiveness is defined as an increase in stroke volume upon fluid challenge [10]. Inferior vena cava variables are considered to be superior to other non-invasive markers, such as non-invasively measured blood pressure, heart rate and aortic diameter, to assess IVS in human critical care [11].

In cardiac patients, IVC_D has been correlated with right atrial pressure, central venous pressure, as well as pulmonary capillary wedge pressure and N-terminal pro-B-type natriuretic peptide measurements [12,13]. Specifically, a wider IVC has been associated with higher right atrial pressure, higher pulmonary capillary wedge pressure and higher N-terminal pro-B-type natriuretic peptide values. In dyspnoeic patients, IVC alone or in combination with lung ultrasound was able to diagnose acute decompensated heart failure (ADHF) [14,15].

In dogs, reference values for CVC diameter (CVC_D) have been established and identified as reliable static markers of IVS [3,16,17]. Nevertheless, to the author's knowledge, CVC variables have never been extensively studied in dogs with different stages of DMVD. We hypothesized that CVC variables are associated with the American College of Veterinary Internal Medicine (ACVIM) stages in DMVD.

Animals, materials and methods

Animals

All dogs presented to the cardiology department and diagnosed with DMVD between January 2017 and January 2019 were retrospectively identified. Dogs were presented for new consultation, recheck consultation or after initial presentation and stabilization via the emergency department. For each dog, history, clinical signs and cardiac treatments received at the time of examination were recorded. Dogs were allocated to one of three groups based on their disease status: dogs in stage B1 and B2 were included in Group 1; dogs in stage C and D with controlled, chronic, left-sided congestive heart failure were included in Group 2, and dogs in stage C and D with left-sided ADHF were included in Group 3. Compensation status for dogs in groups 2 and 3 was determined by the cardiologist based on history, clinical examination and echocardiography as a minimum. Exclusion criteria included evidence of any degree of pulmonary hypertension (PH) in dogs with ACVIM stage B1 and B2 disease, to avoid potential bias as post-capillary PH is less common in these dogs [18,19]. Dogs with ACVIM stage C and D disease and severe PH (pressure gradient estimated >80 mmHg) were also excluded. Moreover, dogs with pericardial effusion, evidence of congenital right heart disease or severe degenerative tricuspid valve disease (defined as including severe tricuspid regurgitation with a colour Doppler regurgitant jet greater than 70% of the right atrial area) were excluded from further analysis. Finally, dogs with important right-sided cardiac remodelling not thought to be related to the underlying left-sided heart disease as assessed by the cardiologist were also excluded from the study. Important right-sided cardiac remodelling was defined as right atrial or right ventricular dilation, right ventricular free wall hypertrophy, flattening of interventricular septum and/or main pulmonary artery enlargement.

Ultrasound examination

Simultaneous echocardiographic and electrocardiographic recordings were obtained using a commercially available ultrasound machine[d], equipped with 2.2–3.5 MHz and 5.5–7.5 MHz phased-array transducers. Echocardiography was performed by a board-certified cardiologist (A-C.M.). Echocardiography was performed with dogs in lateral recumbency. If deemed necessary, butorphanol was administered (0.2–0.3 mg/kg intramuscularly) for mild sedation. Disease severity was determined by identifying ACVIM stage according to published guidelines [20]. Right heart chambers were subjectively assessed for dilation.

[d] Vivid I, General Electric Medical System, 3000 N Grandview Blvd, Waukesha, WI 53188, USA.

Left atrial size was assessed using the ratio of the left atrial dimension to the aortic annulus dimension on right parasternal short-axis view at the level of the aorta. It was also assessed on right parasternal long-axis view using left atrial diameter as previously described [21]. Left ventricular dimensions were assessed in M-mode and normalized using allometric scaling [22]. Ratios of the left atrial dimension to the aortic annulus dimension greater than or equal to 1.6 were considered enlarged. Normalized end-diastolic left ventricular internal diameters greater than or equal to 1.7 for dogs weighing less than 15 kg, and greater than or equal to 1.85 for those weighing more than 15 kg were considered enlarged.

PH was assessed by evaluating tricuspid regurgitation and/or pulmonic insufficiency and calculating the associated pressure gradient using the modified Bernoulli equation. Tricuspid regurgitation was interrogated in right parasternal long-axis and left caudal parasternal views to get the best alignment possible and avoid underestimation. PH was defined as a corresponding pressure gradient greater than or equal to 30 mmHg for tricuspid regurgitation (degree of PH was identified based on pressure gradient: mild, 30—50 mmHg; moderate, 50—80 mmHg and severe, >80 mmHg) and above 13 mmHg for peak pulmonic insufficiency. When neither tricuspid nor pulmonic insufficiency were present, indirect markers for the presence of PH were subjectively assessed, including the presence of right ventricular free wall and/or papillary muscle hypertrophy, interventricular septal flattening, altered pulsed-wave Doppler systolic pulmonary flow profile and/or dilation of the main pulmonary artery compared with the aorta.

CVC ultrasound was performed through a subxiphoid view with dogs in right lateral recumbency as previously described [23].

Additional testing

Additional workup was requested in selected cases at the discretion of the cardiologist. In some cases, three-view thoracic radiographs were performed to identify signs of ADHF (such as venous congestion and signs of pulmonary oedema) or to screen for comorbidities. Other tests, including Doppler blood pressure measurements and clinicopathological testing, were performed if deemed necessary. For dogs that presented via the emergency department, additional testing was performed at the discretion of the primary clinician to determine the origin of the dog's symptoms.

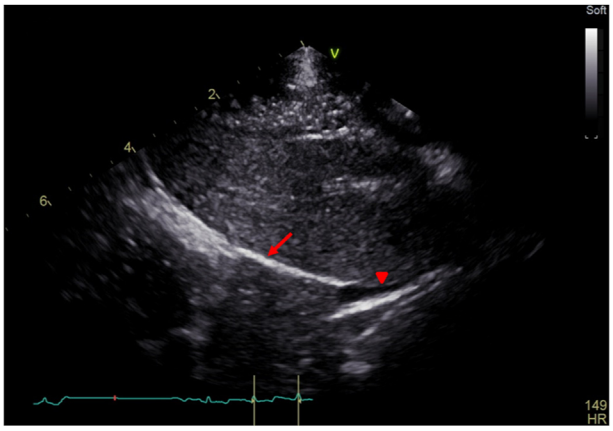

Figure 1 Subxyphoid view of the caudal vena cava (CVC) (B-mode): example of a flat CVC (arrow: diaphragm; ar: CVC).

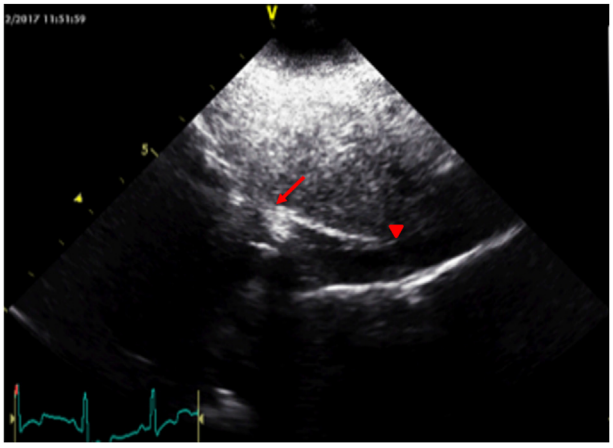

Figure 2 Subxyphoid view of the caudal vena cava (CVC) (B-mode): example of a fat CVC (arrow: diaphragm; ar: CVC).

Caudal vena cava measurements

One single investigator (L.G.), blinded to history, clinical signs, ACVIM stage and treatment, assessed CVC cineloops retrospectively. The investigator subjectively scored the CVC (Figs. 1 and 2) as flat (small size, with diameter changing more than approximately 50% during respiration), normal (medium size, changing approximately 25—50% during respiration) or fat (large size, changing less than approximately 25% during respiration).

Following subjective assessment, measurements were obtained. Maximal ($CVC_{D\text{-}max}$) and minimal ($CVC_{D\text{-}min}$) CVC_D were measured when the CVC was at its widest and narrowest diameter, respectively. Maximal CVC diameter and $CVC_{D\text{-}min}$ were measured perpendicular to the walls of the CVC by identifying the dorsal and ventral walls of the CVC using an inner edge to inner edge method (Figs. I and II available in Supplemental Material online). To correct for body weight, $CVC_{D\text{-}max}$ and $CVC_{D\text{-}min}$ were indexed to aortic diameter ($CVC_{D\text{-}max/Ao}$ and $CVC_{D\text{-}min/Ao}$, respectively), which was obtained through the right parasternal short-axis view and measured at end-systole when the aortic valve closes. Caudal vena cava collapsibility index (CVC_{CI}) was calculated via the following formula ($CVC_{D\text{-}max}$-$CVC_{D\text{-}min}$)/$CVC_{D\text{-}max}$ in 2D-mode.

Statistics

All statistical analyses were performed with standard software[e]. Normal distribution of values was proved by the Shapiro—Wilk test. Continuous data were reported as median and range. The Fisher's Exact Test was used to evaluate associations between subjective assessment of CVC and ACVIM stages. The objective (i.e. measured) CVC variables $CVC_{D\text{-}min/Ao}$, $CVC_{D\text{-}max/Ao}$ and CVC_{CI} were compared across ACVIM stages using the Kruskal—Wallis analysis of variance on ranks, with pairwise comparisons by Dunn's test performing post hoc. Prior to perform ANCOVA to assess the effect of ACVIM stage and diuretic dosage on CVC variables, data that were not normally distributed were modified using Johnson transformation. Assumptions of normal residual distribution and homoscedasticity were met before fitting the model. Torasemide doses were converted to furosemide doses (the dose of torasemide was multiplied by 10 if the dog received $<$0.2 mg/kg/day to obtain the furosemide equivalent, while it was multiplied by 20 if the dog received $>$0.2 mg/kg/day) for the purpose of statistical analysis [24]. The level of significance was set at 0.05.

Results

Eighty-six dogs with DMVD met the inclusion criteria, of which seven dogs were subsequently excluded. Three dogs were excluded due to pericardial effusion (suspected to be secondary to left atrial rupture in one dog, a heart base mass in another and resulting from bilateral congestive heart failure in the third). Two dogs were excluded due to concomitant important right-sided heart disease (degenerative tricuspid valve disease). Two dogs with mild to moderate PH and ACVIM B1 or B2 DMVD were excluded. Remaining dogs were classified as ACVIM stage B1 (23 dogs), B2 (22 dogs), C (27 dogs) and D (seven dogs). Of the dogs included, none had severe PH, while 10 had moderate and four had mild PH. Forty-five dogs were categorized into Group 1; 9 dogs were categorized into Group 2 (eight stage C dogs and one stage D dog); 25 dogs were categorized into Group 3 (19 stage C dogs and six stage D dogs).

Demographic data

Of the 79 dogs included in the study, breeds represented included the following: Chihuahua (n = 13), mixed breed (n = 11), Maltese (n = 10), Jack Russel Terrier (n = 9), Cavalier King Charles Spaniel (n = 7), Dachshund (n = 5), Yorkshire Terrier (n = 3), Shih-tzu (n = 3), Havanese (n = 2), Miniature Pinscher (n = 2), Airedale Terrier (n = 2), English Cocker Spaniel (n = 2) and one each of 10 other breeds (Briard, Cairn Terrier, Beagle, Long-Haired Pyrenean Sheepdog, Italian Sighthound, American Cocker Spaniel, Lhasa Apso, Chinese Crested Dog, Parson Russell Terrier, Whippet). Forty-five (55%) were male, and thirty-six (45%) were female. Median age was 11 years old (range 6—17 years old). Median weight was 7 kg (range 1.8—32.4 kg).

Five of 23 stage B1 dogs, 12/22 stage B2 dogs, 26/27 stage C and 7/7 stage D dogs were receiving various cardiac treatments. Data regarding cardiac treatments and loop diuretic dosages at the time of inclusion can be found in Tables 1 and 2, respectively. Overall, 35.4% (28/79) of dogs were receiving loop diuretics, 40.5% (32/79) were receiving angiotensin-converting enzyme inhibitors and 39.2% (31/79) were receiving pimobendan at the time of enrolment.

Subjective caudal vena cava assessment

CVCs were subjectively assessed as flat, normal and fat in 12, 42 and 27 dogs, respectively. Distribution of CVC categories according to ACVIM stage can be found in Fig. 3. Flat CVC were found in 26% (6/23) of stage B1 dogs, 12.5% (3/24) of stage B2 dogs and 11.1% (3/27) of stage C dogs. CVCs were considered normal in 69.5% (16/23) of stage B1 dogs, 75% (18/24) of stage B2 dogs, and 29.6% (8/27) of stage C dogs. Fat CVCs were seen in 4.5% (1/23) of stage B1 dogs, 12.5% (3/24) of stage

[e] Xlstat 2014.6.01, Addinsoft, 40 rue Damrémont, 75018 Paris, France.

Table 1 Cardiac medications administered in study dogs at the time of enrolment.

	B1	B2	C	D	Total number (and proportion) of dogs for each treatment
Furosemide	1	2	14	5	22 (27.8%)
Torasemide	0	1	3	2	6 (7.6%)
Pimobendan	1	8	16	6	31 (39.2%)
Ramipiril	0	3	0	2	5 (6.3%)
Benazepril	5	4	14	3	26 (32.9%)
Enalapril	0	0	0	1	3 (3.8%)
ACEI (not specified)	0	0	1	0	1 (1.2%)
Spironolactone	2	3	8	4	17 (21.5%)
Sildenafil	0	0	0	1	1 (1.2%)
Amlodipine	0	0	1	1	2 (2.5%)
Digoxine	0	0	1	0	1 (1.2%)
Diltiazem	0	0	2	1	3 (3.8%)

Table 2 Loop diuretic dosages administered to study dogs at the time of enrolment.

		B1	B2	C	D
Furosemide	<2 mg/kg/day	0	1	3	0
	2–4 mg/kg/day	0	0	6	0
	>4 mg/kg/day	1	1	3	4
	Dose not recorded	0	0	2	1
Torasemide	<0.2 mg/kg/day	0	0	1	1
	>0.2 mg/kg/day	0	1	2	0
	Dose not recorded	0	0	0	1
Total (% of dogs in each stage)		1 (4%)	3 (13.6%)	17 (62.9%)	7 (100%)

B2 dogs, 59.3% of stage C dogs (16/27) and 100% of stage D dogs (7/7). Statistical analysis revealed a significant association ($P < 0.001$) between subjective assessment of CVC and ACVIM stage.

Objective caudal vena cava variables

Data were normally distributed within each ACVIM class for $CVC_{D\text{-}max/Ao}$ and CVC_{CI}, while $CVC_{D\text{-}min/Ao}$ results were not normally distributed. Median $CVC_{D\text{-}max}$ was 5 mm (range 1.9–14.4 mm) while median $CVC_{D\text{-}min}$ was 2.3 mm (range 1.1–9.9 mm). Dogs in stage D had significantly larger $CVC_{D\text{-}max/Ao}$ compared with dogs in stages B1, B2 and C (Fig. 4). Dogs in stages C and D had significantly larger $CVC_{D\text{-}min/Ao}$ compared with dogs in stages B1 and B2 (Fig. 5). Median CVC_{CI} was 0.43 (range 0.01–0.81). In dogs with stages C and D disease, CVC_{CI} was significantly reduced compared with dogs with ACVIM stage B1 and B2 disease (Fig. 6). When comparing according to compensation status, there was a significant difference between Groups 1 and 3 for $CVC_{D\text{-}max/Ao}$, $CVC_{D\text{-}min/Ao}$ and CVC_{CI} (Table 3). CVC variables in Group 2 were not significantly different from Groups 1 and 3. Analysis of covariance revealed that ACVIM stages, but not loop diuretic dosage, influenced CVC variables.

Discussion

This study demonstrated that ACVIM stages of DMVD affected static ($CVC_{D\text{-}max/Ao}$ and $CVC_{D\text{-}min/Ao}$)

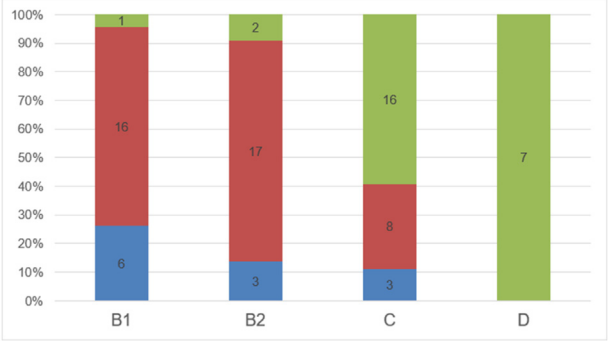

Figure 3 Histogram showing the number of dogs in each category of subjective assessment of the caudal vena cava (CVC) according to ACVIM stage (blue: flat; red: normal; green: fat; B1: ACVIM stage B1 disease; B2: ACVIM stage B2 disease; C: ACVIM stage C disease; D: ACVIM stage D disease).

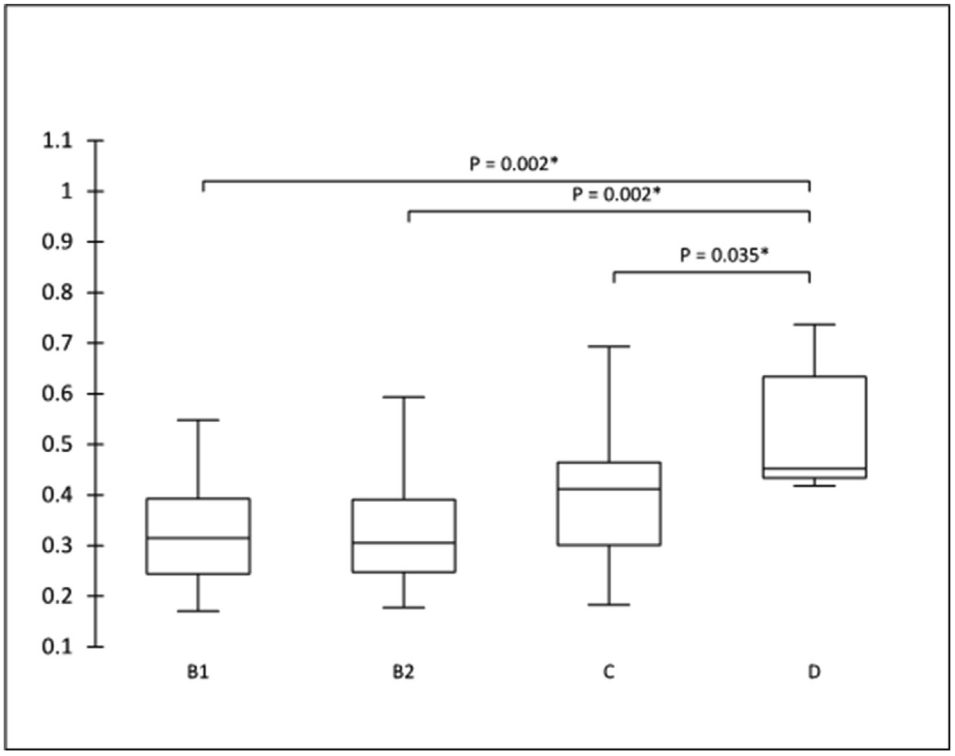

Figure 4 Box and whiskers plot representing maximal caudal vena cava diameter indexed to aortic diameter ($CVC_{D\text{-}max/Ao}$) according to ACVIM stage). (*) represents significant differences from ACVIM stage D disease. (B1: ACVIM stage B1 disease; B2: ACVIM stage B2 disease; C: ACVIM stage C disease; D: ACVIM stage D disease). In the figure, the whiskers of the box plots extend to the most extreme observation which is within 1.5 times the IQR.

and dynamic (CVC_{CI}) CVC variables in dogs without clinically important right heart disease. Subjective and objective CVC variables were associated with ACVIM stages. These results are in accordance with human studies in critically ill patients without severe tricuspid regurgitation, which showed that IVC_D is directly correlated with right atrial pressure, pulmonary capillary wedge pressure and left ventricular filling pressure [12]. In our study, dogs with left-sided ADHF (Group 3) had wider and less collapsible CVC compared with dogs with earlier disease stages that had never experienced cardiac decompensation (Group 1). In dogs with controlled, chronic left-sided congestive heart failure (Group 2), CVC variables were not significantly different from dogs in groups 1 and 3. This might be because dogs with chronic left-sided congestive heart failure display less severe hypervolemia and venous congestion than dogs with left-sided ADHF. Hence, CVC variables in Group 2 would be expected to fall somewhere in between those for Groups 1 and 3, which might explain the lack of statistical significance. Assessment of the CVC in dogs with DMVD might add information regarding left ventricular filling pressure and may help to discriminate compensated and decompensated stages.

When DMVD progresses, compensatory mechanisms, such as renin-angiotensin-aldosterone system activation, induce hypervolemia. Hypervolemia causes the CVC to become bigger and less collapsible [3]. When the combination of hypervolemia and cardiac remodelling cause signs of left-sided congestive heart failure, loop diuretic therapy is typically implemented to alleviate symptoms. In human medicine, IVC_D has been shown to decrease by an average of 0.21 cm after a single dose of furosemide in patients with ADHF [25]. One veterinary study found a correlation between volume depletion and CVC_D after furosemide administration in healthy Beagle dogs [17]. These findings suggest CVC variables can be used to assess IVS in healthy dogs. In our study, diuretic administration and dosage did not affect CVC variables. This might be explained by several factors. Firstly, loop diuretic dosages were not standardized in our study, which may have affected results. Secondly, duration of administration was not recorded, and in clinical patients, contrary to an acute and experimental setting, chronic activation of the renin-angiotensin-aldosterone system may override the effect of diuretics on IVS. Finally, the low proportion of dogs receiving diuretics (28/79) may have led to non-

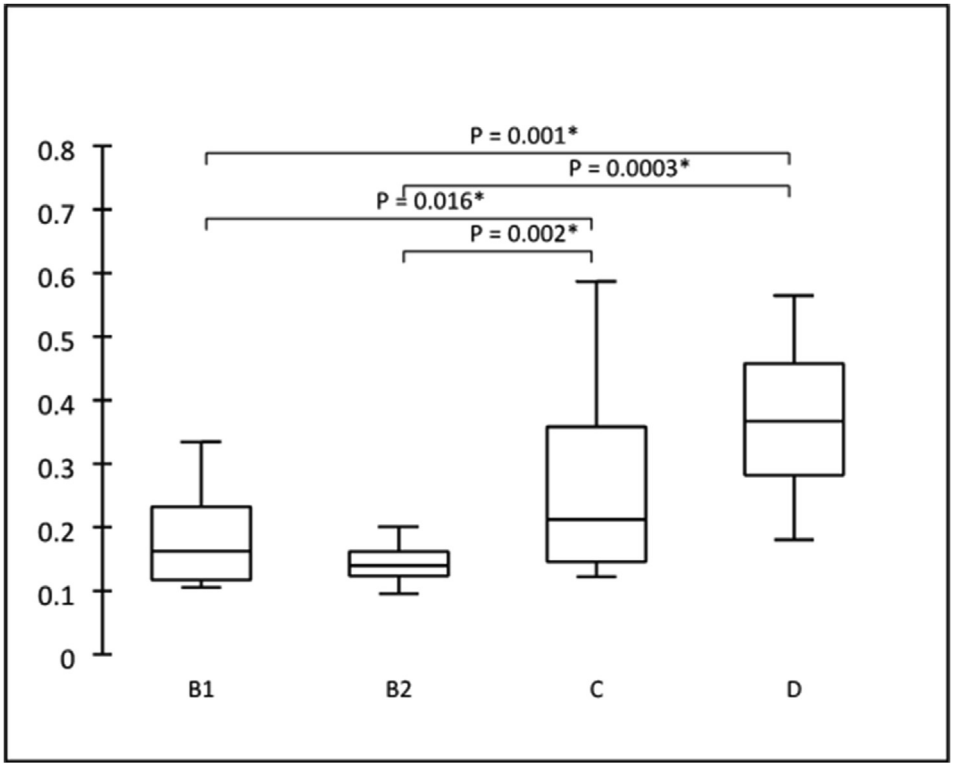

Figure 5 Box and whiskers plot representing minimal caudal vena cava diameter indexed to aortic diameter ($CVC_{D\text{-}min/Ao}$) according to ACVIM stage. (*) represents significant differences from ACVIM stage D disease and from ACVIM stage C disease. (B1: ACVIM stage B1 disease; B2: ACVIM stage B2 disease; C: ACVIM stage C disease; D: ACVIM stage D disease). In the figure, the whiskers of the box plots extend to the most extreme observation which is within 1.5 times the IQR.

significant results due to low statistical power. Further prospective studies are needed to better understand the impact of acute and chronic administration of loop diuretics on CVC variables and IVS.

To our knowledge, this is the first veterinary study demonstrating that subjective assessment of the CVC correlates well with objective measurements, as dogs with increasing disease severity have a greater proportion of fat, wider and less collapsible CVC. This is in agreement with human papers identifying a positive correlation between subjective and objective CVC variables [26—28]. Point-of-care subjective evaluation of the IVC is used in human emergency departments as a rapid, non-invasive variable contributing valuable information to IVS assessment [27,29]. Prospective investigation of the usefulness of point-of-care subjective evaluation of CVC in veterinary patients is warranted.

Several human studies have shown the prognostic utility of IVC variables regarding risk of readmission or mortality in cardiac patients [26,30—32]. In our study, all dogs in stage D, known to be associated with poor prognosis had a wider, less compliant and subjectively fat CVC, which might suggest the fact that heart failure was less well controlled this subset of dogs. Thus, these variables might be useful for identification and prognostication in dogs with advanced DMVD, alongside other reported prognostic indicators such as furosemide dosage and hospitalization requirements [33], though further prospective studies are warranted to study the association between CVC variables and DMVD prognosis.

In the dogs of this study, the CVC became less collapsible with increasing disease severity, as evidenced by a decreasing CVC_{CI}. As we excluded dogs with clinically important right heart disease, this suggests more severe hypervolemia and pronounced venous congestion, as is expected in advanced stages of DMVD. In Group 3, CVC_{CI} was also significantly lower compared with Group 1, indicating that this easily accessible variable could be used to help in the diagnosis of ADHF in veterinary patients. In human cardiology, IVC_D and IVC_{CI} are useful to diagnose ADHF in dyspnoeic patients, alone or in combination with lung ultrasound [15,34,35]. A recent human study demonstrated that nearly 50% of ambulatory patients with chronic heart failure, thought not to be

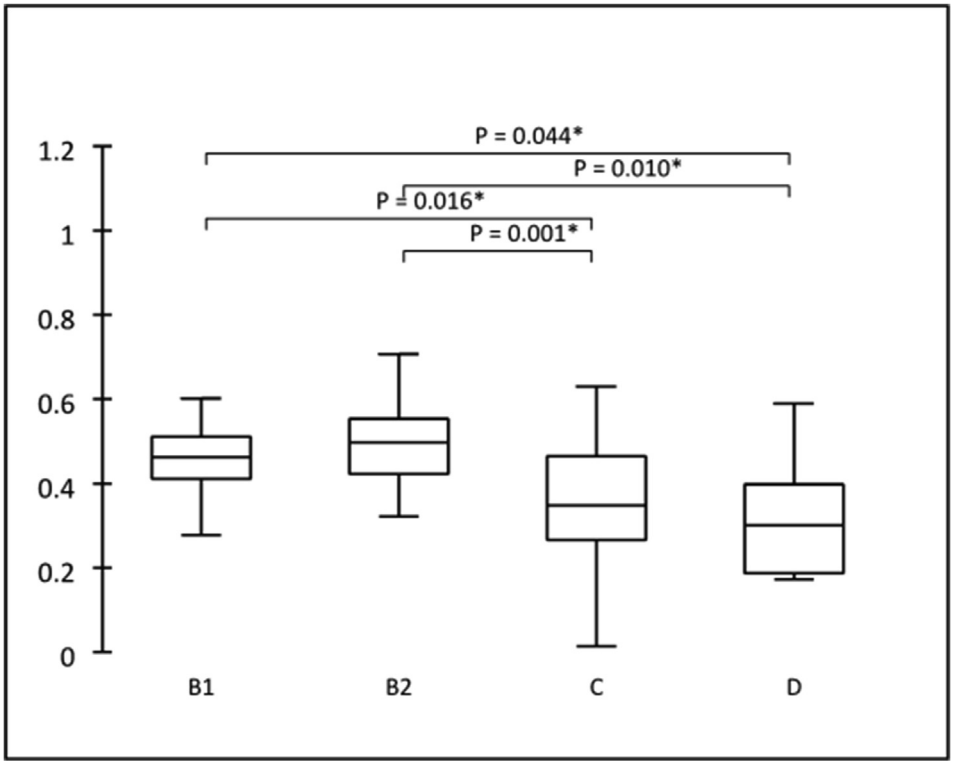

Figure 6 Box and whiskers plot representing caudal vena cava collapsibility index (CVC_{CI}) according to ACVIM stage. (*) represents significant differences from ACVIM stage D disease and from ACVIM stage C disease. (B1: ACVIM stage B1 disease; B2: ACVIM stage B2 disease; C: ACVIM stage C disease; D: ACVIM stage D disease). In the figure, the whiskers of the box plots extend to the most extreme observation, which is within 1.5 times the IQR.

Table 3 Objective caudal vena cava variables according to compensation status.

	Group 1	Group 2	Group 3	P-value
Number of dogs	45	9	25	N/A
$CVC_{D\text{-}max/Ao}$ *(median, [range])*	0.31 [0.17—0.59]*	0.41 [0.18—0.49]	0.44 [0.19—0.73]*	$P = 0.007$*
$CVC_{D\text{-}min/Ao}$ *(median, [range])*	0.14 [0.10—0.48]*	0.20 [0.13—0.43]	0.30 [0.12—0.59]*	$P < 0.001$*
CVC_{CI} *(median, [range])*	0.48 [0.16—0.81]*	0.38 [0.13—0.63]	0.34 [0.01—0.60]*	$P < 0.001$*

Indicated P-values relate to statistical differences between Group 1 and Group 3, as marked by (*) symbol.

clinically congested, had ultrasonographic evidence of congestion (e.g. dilated, non-collapsible IVC and/or B-lines), which was associated with a worse outcome [36]. Whether using such parameters to evaluate congestion could guide management of such cases and improve prognosis has yet to be determined.

Limitations

CVC variables are correlated with right atrial pressure [7], so any disease causing a rise in right atrial pressure might influence these variables. In this study, we excluded dogs in which right atrial pressure could have been modified independently of left-sided heart disease, in an effort to minimize this potential bias. Similarly, dogs with severe PH as assessed by the presence of high-velocity tricuspid regurgitation were excluded from the study population. Nevertheless, some patients with PH do not have identifiable tricuspid regurgitation [37] and although right-sided cardiac chambers were carefully assessed, some cases of severe PH could have been missed. Hence, one could argue that PH, rather than left-sided heart disease, might influence CVC variables. However, a recent study failed to identify an effect of PH on CVC_D in dogs [38]. Moreover, as we excluded dogs with important right-sided cardiac remodelling, including apparent right atrial dilation, any effect directly attributable to severe PH seems unlikely. That being said, right heart chambers were

subjectively assessed in our study. Although this is the case in several studies and is common in clinical practice [18,19], right heart remodelling might be harder to evaluate in dogs with left-sided pathology as proportions are disrupted. Thus, some dogs with mild heart changes corresponding to a degree of right-sided heart disease or PH could have been erroneously included in the study population.

Another limitation of our study is its retrospective nature, so not all information was available for all patients. In particular, cardiac treatments and dosages were not standardized in our population. It is, therefore, possible that treatment could have influenced CVC variables. As discussed, loop diuretics influence IVS and may have biased our results. However, this would be expected to have a negative influence on IVS (e.g. decreasing blood volume), while in our population, dogs in stages C and D receiving higher diuretic dosages had larger and less collapsible CVC. Angiotensin-converting enzyme inhibitors and pimobendan were administered in 40.5% and 39.2% of study dogs, respectively. These medications are known to influence venous diameter and could theoretically have had an independent effect on CVC variables in dogs with DMVD [39,40]. However, any effect of the cardiac medications reported in this study is likely to be small as IVC_D is known to be minimally affected by vasoconstriction [5]. Because doses were not standardized and were inconsistently reported, statistical analysis regarding treatments other than loop diuretic dosage was not performed. Further prospective studies are warranted to assess the potential effect of cardiac medications on CVC variables.

Finally, the subxiphoid view has been reported to have poorer repeatability for CVC variables compared with other views when performed in healthy dogs by non-cardiologists [23,41]. However, it is the only view that allows for assessment of CVC_{CI} and is part of the routine echocardiographic evaluation at our institution. All cineloops were recorded by a single observer, a board-certified cardiologist, preventing repeatability assessment and point-of-care assessment recorded by a non-cardiologist.

Conclusions

This study demonstrates that CVC variables are associated with ACVIM stages in dogs with DMVD. Advanced disease is associated with a wider and less collapsible CVC, which probably reflects volume overload. CVC variables could add valuable information about the patient's IVS and may help to differentiate compensated from decompensated stages.

Conflicts of Interest Statement

None of the authors has any conflict of interest to report.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jvc.2022.01.001.

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