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Assessment of plasma lactate and core-peripheral temperature gradient in association with stages of naturally occurring myxomatous mitral valve disease in dogs

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Abstract

Objective – To evaluate plasma lactate concentrations and core-peripheral temperature gradients as perfusion parameters in dogs with heart failure caused by myxomatous mitral valve disease (MMVD) and to determine whether the above perfusion parameters are correlated with disease stages.
Design – Prospective observational study.
Setting – University teaching hospital.
Animals – After excluding 129 dogs because of exclusion criteria, 7 dogs with heart failure classified as stage B2 and 10 dogs classified as stage C according to the American Heart Association (AHA)/American College of Cardiology (ACC) were included in the study. Six dogs without MMVD were evaluated as the control group.
Interventions – None.
Measurements and Main Results – Among the evaluated parameters, the plasma lactate concentrations were increased in stage C (median 3.70 mmol/L [33.3 mg/dL], interquartile range (IQR) 0.72 mmol/L [6.5 mg/dL]) compared with those in the control (median 2.80 mmol/L [25.2 mg/dL], IQR 0.8 mmol/L [7.2 mg/dL]; $P = 0.024$) and stage B2 groups (median 2.70 mmol/L [24.3 mg/dL], IQR 1.8 mmol/L [16.2 mg/dL]; $P = 0.045$). Significant differences were not observed in the core-peripheral temperature gradients among the control, stage B2, and stage C dogs.
Conclusions – Dogs with structural heart disease as a result of MMVD may have occult tissue hypoperfusion in stage C that is demonstrated by hyperlactatemia.

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Keywords: cryptic shock, heart failure, hyperlactatemia, lactate, temperature gradients

Abbreviations

BP	blood pressure
HF	heart failure
HR	heart rate
IQR	interquartile range
LA	left atrium
MMVD	myxomatous mitral valve disease

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Introduction

Myxomatous mitral valve disease (MMVD) is the most commonly acquired heart disease in dogs, and it is characterized by collagen destruction associated with mucopolysaccharide deposition in the valve spongiosa and fibrosa layers.[1] This process promotes thickening and irregular formation on the valve surface, which increases the difficulty of congruent coaptation and may lead to heart failure (HF) with mitral regurgitation.[2,3] Intense regurgitation has been suggested as the primary cause of HF in small dogs with MMVD.[4]

Dogs with HF have increased serum aldosterone and plasma renin concentrations, which confirm the activation of the renin, angiotensin, and aldosterone system. This activation leads to increased plasma volume because of sodium and water retention, and it also

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causes decreased venous capacitance because of vasoconstriction. An increase in venous pressure and pulmonary or systemic congestion subsequently occurs, which impairs tissue perfusion in more severe disease stages.[5]

During HF, if the cardiac output decreases, then the blood pressure (BP) can be maintained by peripheral vasoconstriction induced by compensatory mechanisms and Renin Angiotensin Aldosterone System (RAAS) activation.[6] The peripheral tissues are subjected to low flow and hypoxia with normal BP, heart rate (HR), mentation, and ordinary core temperatures. This state is referred to as occult hypoperfusion or cryptic shock.[7–13]

This occult stage is characterized by persistent hyperlactatemia.[10] All nonvital (or terminal) organs, such as the kidney and the gut, will be less perfused because of blood flow diversion to the central organs. Impairment of tissue perfusion may be diagnosed at an earlier period, even before the onset of HF clinical manifestations, by measuring tissue perfusion indicators that are easily used in clinical practice, such as temperature gradients and plasma lactate concentrations.[14,15]

Peripheral vasoconstriction induces decreases in skin temperature because of the reduced blood flow to this vascular bed. This cooling represents how other organs (eg, the gut and kidneys) respond at early stages of hypoperfusion before the central parameters (eg, arterial BP, mental status, and rectal temperature) decompensate.[15,16] Accordingly a patient with occult hypoperfusion can manifest an increase in the core-peripheral temperature gradient.

Several metabolic pathways produce lactate, and 1 major pathway is anaerobic glycolysis during hypoxia. Cells become dependent on cytosolic glycolysis, which leads to ATP production in the absence of oxygen. The reduction of pyruvate produces lactate, which commonly results in hyperlactatemia.[17] The use of plasma lactate measurements has been widely documented in both human and veterinary medicine to detect systemic or local hypoperfusion, and it has also been used to guide goal-directed therapies.[8,11,12,14,18–30]

Compared with inflammatory factors or other variables calculated to assess tissue oxygenation, such as DO_2 and VO_2, plasma lactate appears to be a superior prognostic predictor.[7,31–34] In the emergency room, different conditions, such as hypoxia, sepsis, catecholamine continuous infusion, thiamine deficiency, alkalosis, liver dysfunction, and nitroprusside intoxication, may contribute to hyperlactatemia. Therefore, hyperlactatemia does not necessarily indicate tissue hypoxia, although persistent hyperlactatemia appears to predict worse outcomes in nearly all disease types independent of its source (type A or B).[25,29,30,35,36] Occult tissue hypoperfusion associated with hyperlactatemia has been studied in human patients with HF; however, we are unaware of any prospective studies that have evaluated its occurrence in stable, treated HF patients under previous therapeutic control at home.[37,38]

The primary objective of this prospective observational study was to evaluate the clinical parameters of perfusion in dogs with heart structural disease caused by MMVD and to determine whether changes follow a pattern according to the illness stage progression.[39] We hypothesize that dogs with HF may experience hyperlactatemia and increased core-peripheral temperature gradients despite the maintenance of other hemodynamic parameters (eg, BP, HR, mentation, core temperature, pulse, mucous membrane color, and capillary refill time), thus indicating occult hypoperfusion.

Materials and methods

Animals and experimental groups

This prospective study was conducted from August to November 2014. The study design was approved by the Bioethics Committee of our institution (UnBDOC No. 45831/2013), and the animals were included after obtaining client consent.

We performed a prospective selection of healthy control dogs and dogs with MMVD that were treated by the Cardiology Service at the veterinary university teaching hospital. The following exclusion criteria were established: (1) presence of concomitant disease, such as chronic kidney disease (using IRIS classification), liver disease (using bilirubin, alkaline phosphatase [ALP], alanine aminotransferase [ALT], and aspartate aminotransferase [AST] as markers), diabetes mellitus, skin lesions, respiratory disease, orthopedic disease, trauma within the past 30 days, sepsis, anemia, cancer, and epilepsy; (2) pregnant bitches or females in estrus according to the owner's account; (3) use of corticosteroid therapy at the time of evaluation; and (4) absence of signed consent by the owner.

Exclusion criteria were used to avoid any causes for compensatory sympathetic activation or hyperlactatemia that was not generated by the ongoing heart disease.[17,40–44] The dogs were divided into the following 3 groups according to the presence or absence of MMVD and the heart structural disease clinical stage based on the modified American Heart Association (AHA)/American College of Cardiology (ACC) system: (1) control, (2) stage B2, and (3) stage C (Table 1).[39]

A single operator performed the clinical evaluations and sample collection for the laboratory tests on the study animals. Thoracic radiographs were performed for all dogs to exclude pulmonary edema as a potential cause of hyperlactatemia and peripheral vasoconstriction.

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Table 1: Classification system for canine chronic valvular heart disease

Stage	Description
A	Patients at high risk for developing heart disease but without currently identifiable structural cardiac disorder (eg, predisposed breed without a heart murmur).
B1	Patients with structural heart disease (eg, presence of heart murmur) but without clinical signs of HF or radiographic or echocardiographic evidence of cardiac remodeling in response to valvular degeneration (eg, increased diameter of left cardiac chambers).
B2	Patients without clinical signs of HF but with structural heart disease (eg, presence of heart murmur) and radiographic or echocardiographic evidence of cardiac remodeling in response to valvular degeneration (eg, increased diameter of left cardiac chambers).
C	Patients with past or current clinical signs of HF associated with structural heart disease (eg, presence of heart murmur) and radiographic or echocardiographic evidence of cardiac remodeling in response to valvular degeneration (eg, increased diameter of left cardiac chambers).
D	Patients with end-stage disease with clinical signs of HF caused by valvular degeneration and radiographic or echocardiographic evidence of cardiac remodeling in response to HF; these patients are refractory to "standard therapy."

Diagnosis of valve disease and staging of HF

All of the dogs in each group received a cardiac evaluation that included the clinical history, a physical examination, and echocardiography to diagnose valve disease and classify the patients in all different HF stages. The control group was asymptomatic and did not have heart murmurs, mitral valve thickening, or any regurgitant flow in the left atrium (LA) according to color Doppler and continuous Doppler evaluations during echocardiography. The stage B2 and C animals that were asymptomatic and symptomatic for HF underwent echocardiographic examinations after the auscultation of a mitral systolic heart murmur. During this study, thickening of the mitral valve leaflets and regurgitant flow into the LA were observed. The animals included in these groups had a LA/Aorta ratio greater than 1.5, and in certain cases, they had an increase in the internal diameter of the left ventricle during diastole and systole.[45] To obtain images in different echocardiographic modalities, an echocardiograph[a] with a sector transducer was used.

Evaluation of clinical and laboratory parameters

All of the dogs were evaluated at a single time after the confirmatory diagnosis or exclusion of MMVD. Noninvasive BP was measured using a vascular Doppler[b] and a sphygmomanometer[c] according to the literature.[46] Sequentially, the temperatures of the room, the rectum, and the interdigital space in the left hind limb (peripheral) were recorded to calculate the core-peripheral temperature gradient (ΔT_{cp}) and the room-peripheral temperature gradient (ΔT_{rp}). The rectal temperature was measured in the mid-portion of the rectum as an indicator of the actual body temperature because the proximal portion (influenced by the iliacal and hypogastric veins) and the distal portion (influenced by the hemorrhoidal veins) may be altered by peripheral vasoconstriction.[47] The peripheral temperature was the mean of 3 measurements recorded in the interdigital space of the left hind limb using an infrared thermometer (0.98 emissivity).[d]

Finally, blood samples were obtained from the external jugular vein to measure plasma lactate, CBC, and biochemistry profile. During venipuncture, the occlusive pressure was released for blood collection to minimize potential interference on the plasma lactate concentration. Immediately after collection, the plasma lactate concentrations were measured with a hand-held lactometer.[e]

Statistical analysis

The distribution of data from the continuous variables was analyzed using the Shapiro–Wilk test, and a normal distribution was not observed according to the medians and interquartile ranges (IQRs). The Kruskal–Wallis test for nonparametric data was then used to perform comparisons between the groups. The two-tailed Mann–Whitney *U*-test was used as a post hoc test for the precise determination of previously verified significant differences between the groups. The tests that showed P values < 0.05 were considered statistically significant.[f]

Results

Study population characteristics

Among the 146 dogs with MMVD evaluated throughout the study period, 129 were excluded for the reasons explained in Figure 1. As a matter of resource rationalization, animals classified as stage B1 were removed from the study. These dogs had a lower probability of showing occult hypoperfusion (as stated in the hypothesis) than the animals classified as stage B2 or C. The stage B2 group contained 7 dogs, and the stage C Group contained 10 dogs. Six dogs without MMVD were included in the control group.

The study animals were adults and primarily male, and they were older than 6 years and weighed <20 kg.[48] A significant difference was observed in the age

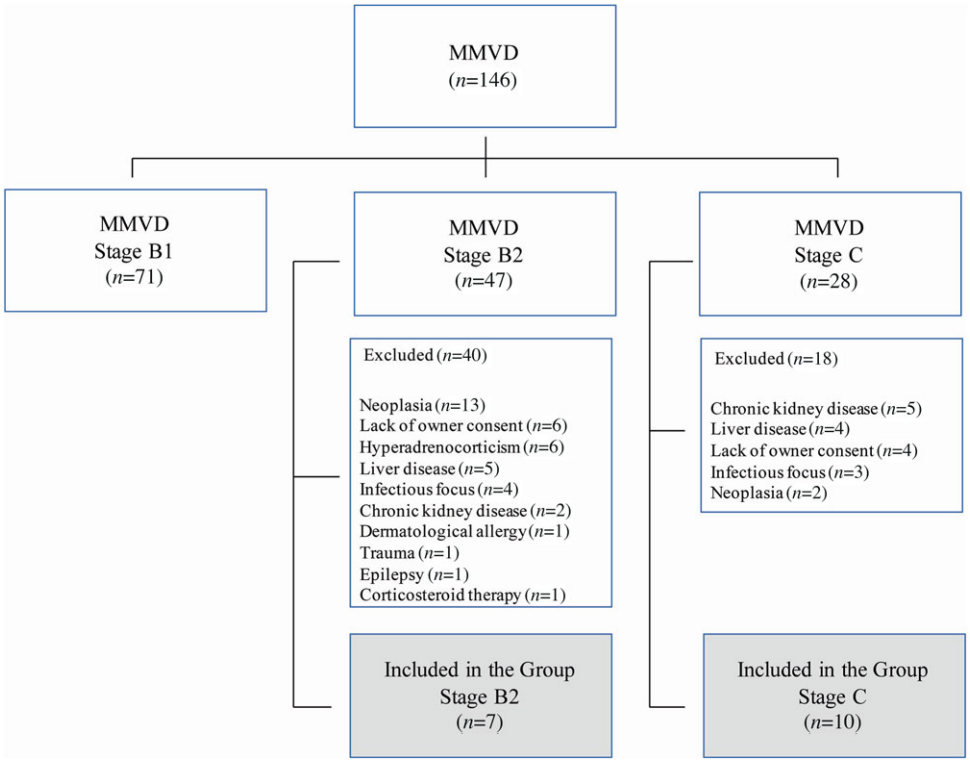


Figure 1: Case selection flowchart for dogs with MMVD and exclusion criteria.

Table 2: Patient demographics for the control and study groups

Features	Control ($n = 6$)	Stage B2 ($n = 7$)	Stage C ($n = 10$)
Sex			
Male (%)	67 (4)	57 (4)	80 (8)
Female (%)	33 (2)	43 (3)	20 (2)
Age (years; mean ± SD; range)	9 ± 2; 6–11	11.29 ± 1.79; 9–14	13.50 ± 1.84; 10–16
Weight (kg; mean ± SD; range)	7.62 ± 2.32; 3.25–10.2	11.84 ± 4.21; 6.8–18.4	6.00 ± 3.02; 1.9–10
Breed			
Poodle	2	2	3
Mongrel	2	2	3
Dachshund	1	–	–
Yorkshire	1	–	1
Cocker spaniel	–	2	–
Brazilian terrier	–	1	–
Miniature pinscher	–	–	3

between the control and the stage C group ($P = 0.001$) and between the stage B2 and C groups ($P = 0.039$), with the stage C group including older dogs than the other groups. This information as well as the breed distribution pattern can be found in Table 2.

The animals included in the control group were not under any therapeutic interventions at the time of evaluation. The distribution of all medications received by the animals in the stage B2 and C groups is depicted in Table 3. The median treatment time was 6 months (IQR = 8) and 7 months (IQR = 11.8) for the stage B2 and C groups, respectively ($P = 0.721$).

Physical examination, perfusion, and hematological parameters

The animals in the stage C group had a history of cough (100%), exercise intolerance (40%), choking (40%), syncope (30%), cyanosis (30%), limb edema (10%), and lethargy (10%). Upon physical examination, none of the animals had clinical evidence of dehydration or hypovolemia, and all the animals had normal vesicular breathing sounds during pulmonary auscultation. The dogs in the stage B2 and C groups displayed systolic heart murmurs of various grades, which are specified in Table 4.

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Table 3: Medications administered to stage B2 and stage C groups

	Treatment *n* (%)						
Groups (*n*)	**ACEi**	**Spironolactone**	**Furosemide**	**Pimobendan**	**Sildenafil**	**Codeine**	**Digoxin**
Stage B2 (7)	7 (100)	7 (100)	1 (14)	0	0	0	0
Stage C (10)	10 (100)	8 (80)	10 (100)	6 (60)	2 (20)	2 (20)	1 (10)

ACEi, angiotensin converting enzyme inhibitor.

Table 4: Description of the heart murmur grades present in the animals in stage B2 and stage C groups

Heart murmur grade *n* (%)	**Stage B2 ($n = 7$)**	**Stage C ($n = 10$)**
Mitral focus		
II/VI	1 (14.28)	0
III/VI	6 (85.71)	1 (10)
IV/VI	0	6 (60)
V/VI	0	3 (30)
Tricuspid focus		
No auscultable murmur	2 (28.57)	0
II/VI	2 (28.57)	1 (10)
III/VI	3 (42.85)	3 (30)
IV/VI	0	4 (40)
V/VI	0	2 (20)

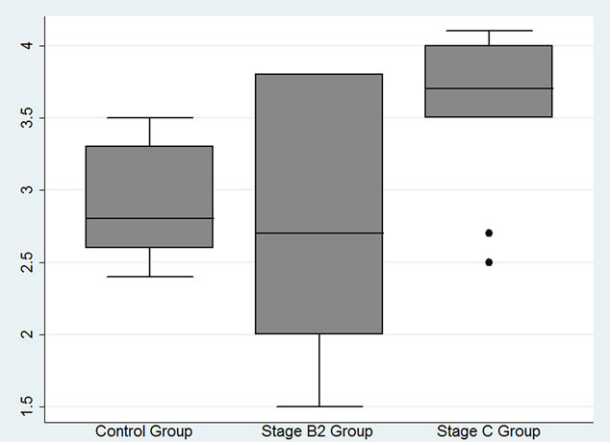


Figure 2: Box-plot graph depicting the lactate levels (mmol/L) in the different experimental groups.

All the animals presented strong and synchronous femoral pulses at palpation. In the stage C group, 1 animal had jugular distension (10%) and another one had positive hepatojugular reflex (10%). Significant differences were not observed between the HR values, rectal temperatures, or Doppler BP among the groups. Significant differences were not observed between the respiratory rates or the room temperatures between the groups (Table 5).

During the peripheral clinical parameters assessment, all the animals were alert, had pink mucous membranes, and had a capillary refill time of less than 2 seconds. Significant differences were not observed between the groups for the ΔT_{cp} or ΔT_{rp}. The only statistically significant difference between the groups was observed for plasma lactate concentrations (Table 5). The stage C group (median 3.70 mmol/L [33.3 mg/dL], IQR 0.72 mmol/L [6.5 mg/dL]) had higher plasma lactate concentrations than both the control (median 2.80 mmol/L [25.2 mg/dL], IQR 0.8 mmol/L [7.2 mg/dL]; $P = 0.024$) and stage B2 groups (median 2.70 mmol/L [24.3 mg/dL], IQR 1.8 mmol/L [16.2 mg/dL]; $P = 0.045$), whereas statistically significant differences in lactate levels were not observed between the control and B2 groups (Figure 2).

The groups did not show statistically significant differences between the packed cell volumes, RBC count, or hemoglobin. The only hematological parameter that showed a statistically significant difference between the groups was the platelet count, in which the control group presented a significant difference from the stage C group ($P = 0.011$), with the stage C group presenting a higher platelet count than the control group (Table 5).

Discussion

Plasma lactate measurements are widely used as an indicator of tissue perfusion because it represents anaerobic metabolism during tissue hypoxia.[49] Furthermore, evidence supports its use as an occult hypoperfusion marker.[50,51] In situations with decreased cardiac output, hyperlactatemia most likely results from anaerobic metabolism.[28,52] Plasma lactate is easily measured in comparison to other perfusion assessment variables, such as CO_2 gap, mixed venous oxygen saturation, and central venous oxygen saturation, which needs arterial puncture (oxygen delivery [DO_2], oxygen uptake [VO_2], oxygen extraction ratio [O_2ER]).[10,50,53]

However, measuring lactate has limitations because several conditions may increase its plasma concentrations, such as those resulting in type B hyperlactatemia. In this study, the focus was on type A hyperlactatemia caused by poor perfusion.[50,54] The exclusion criteria developed for this study were meant to eliminate potential generators of type B hyperlactatemia that

Table 5: Physical, perfusion, and hematological examination parameters

	Control		Stage B2		Stage C		
	median (IQR)	N	median (IQR)	n	median (IQR)	n	*P* value[#]
Clinical parameters							
Heart rate (bpm)	119 (55)	6	120 (44)	7	142 (16)	10	0.1436
Rectal temperature (°C)	38.7 (1.1)	6	38.9 (0.3)	7	38.6 (0.7)	10	0.4518
(°F)	101.6 (1.8)		102.0 (0.5)		101.4 (1.3)		
BP (mm Hg)	146.6 (26)	6	145.8 (22.4)	7	143.8 (24.0)	10	0.4982
Core-peripheral ΔT (°C)	5.95 (6.0)	6	8.07 (2.0)	7	5.57 (4.3)	10	0.2750
(°F)	10.7 (10.7)		14.5 (3.6)		10.0 (7.7)		
Peripheral-room ΔT (°C)	9.02 (7.4)	6	6.60 (1.3)	7	7.96 (3.0)	10	0.3629
(°F)	16.2 (13.3)		11.8 (2.3)		14.3 (5.4)		
Lactate (mmol/L)	2.80 (0.8)*	6	2.70 (1.8)*	7	3.70 (0.72)**	10	0.0385
(mg/dL)	25.22 (7.2)		24.32 (16.2)		33.33 (6.5)		
Respiratory rate (bpm)	36 (50)	5	44 (44)	3	44 (22)	6	0.4579
Room temperature (°C)	24.05 (1.43)		24.30 (1.4)		24.5 (2.3)		
(°F)	75.2 (2.6)	6	75.7 (2.5)	7	76.1 (5.9)	10	0.8518
Hematological parameters							
PCV (L/L)	0.51 (0.12)	6	0.41 (0.09)	7	0.45 (0.15)	10	0.1106
(%)	51 (12.5)		41 (9.0)		45.5(15.5)		
RBC (x 10^{12}/L or x $10^6/\mu L$)	7.4 (6.45-8.27)	6	6.46 (5.2-6.56)	7	6.42 (5.15-7.27)	10	0.1064
Hemoglobin (g/L)	163.0 (44.0)	6	146.0 (26)	7	151.5 (49.2)	10	0.2195
(g/dL)	16.30 (4.4)		14.60 (2.6)		15.15 (4.9)		
WBC (x 10^9/L or x $10^3/\mu L$)	5.15 (3.62-7.35)	6	6.1 (4.90-8.70)	7	7.3 (5.65-9.32)	10	0.2219
Platelets (x 10^9/L or x $10^3/\mu L$)	308.5 (271-362)*	6	373 (354-439)*/**	7	416 (362-504)**	10	0.0331
TP (g/L)	67 (9.5)	6	70 (8)	7	70 (10)	10	
(g/dL)	6.7 (0.95)		7.0 (0.8)		7.0 (1.0)		0.5078

IQR, interquartile range; Δ*T*, temperature gradient; BP, blood pressure; PCV, packed cell volume; RBC, red blood cell count; TP, total protein. * and ** indicate no statistically significant differences, and # indicates the Kruskal–Wallis test.

could behave as confounding factors. Hyperlactatemia that occurs with the advancement of HF in the Stage C Group was most likely a result of type A hyperlactatemia.

Reports have indicated that a 3–5 mmol/L (27.0–45.0 mg/dL) plasma lactate concentration corresponds to a mild increase that would represent systemic hypoperfusion in dogs.[14,54] The reference value set for the measurement of plasma lactate in dogs using a whole blood sample in the Accutrend Plus Roche unit is 1.2 to 3.1 mmol/L (10.8–27.9 mg/dL), and only the median of the stage C group was above this upper limit.[55] For animals undergoing urgent treatment independent of primary disease, plasma lactate concentrations below 3.2 mmol/L (28.8 mg/dL) are associated with higher survival.[56]

In this study, the stage C group had higher plasma lactate concentration than the control and stage B2 groups, and these differences were clinically and statistically significant. Our results did not show differences in major physical exam parameters, such as HR, Doppler BP, rectal temperature, or consciousness level, among the groups. These data support the initial hypothesis that dogs with HF may present occult hypoperfusion because dogs classified as stage C showed significant hyperlactatemia despite normal central hemodynamic parameters.[10,37,38,50,57,58]

Goutal et al[59] performed a retrospective study and evaluated dogs and cats that presented to an emergency department with HF. One hundred twelve animals with class II International Small Animal Cardiac Health Council (ISACHC), which corresponds to a stage C classification in the American Heart Association/American College of Cardiology, were subjected to measurement of plasma lactate concentration upon admission. Seventy-two (64%) of these animals had hyperlactatemia according to the institutional reference range, although comorbidities, such as chronic kidney disease and HF resulting from other illnesses, which were subject to the exclusion criteria in our study, could have influenced the diagnosis of hyperlactatemia. This article as well as the previously quoted study showed the prevalence of hyperlactatemia in more advanced HF stages.

In people with HF treated at an emergency department, statistically significant differences were observed in the plasma lactate measurements upon hospital

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admission. The patients had normal HR and BP values in the presence of hyperlactatemia, thus indicating the occurrence of an occult perfusion deficit in patients with HF.[57,60] In our study, patients with more severe HF were more likely to have higher plasma lactate concentrations in the absence of clinical HF.

Significant local hypoperfusion of certain organs, such as the skin and the gut, can occur before systemic hypoperfusion manifests clinically, for example, in the form of hypotension.[14,58,61,62] In circulatory failure, blood flow is decreased to the peripheral tissue (such as skin) and maintained to the critical organs (such as the brain and heart). Thus, monitoring perfusion in peripheral organs may be an early hypoperfusion marker.[15,16,63] It is essential to control the room temperature in all studies that assess temperature gradients as performed in this study, where the room temperature was maintained in the thermoneutral range of approximately 24°C (75.2°F), to eliminate its influence on the peripheral temperature.[64,65]

Sympathetic neurohumoral responses predominate in the skin and cause a decrease in skin temperature during circulatory failure.[15] Consequently, this redistribution increases the core-peripheral temperature gradient, which is an indicator of peripheral perfusion compared with the reference interval of 3–7°C (5.4–12.6°F).[16,66] The stage B2 group had the highest core-peripheral temperature gradient, although this result was not significant. However, significant results may be achieved with a larger sample size.

In this study, the animals in the stage C group did not show an increase in the core-peripheral temperature gradient as expected, and increases in plasma lactate concentrations were observed, which indicated hypoperfusion. Pimobendan administration in certain patients from this group may have inhibited cutaneous vasoconstriction and consequently increased the core-peripheral temperature gradient. Pimobendan promotes vasodilation by inhibiting phosphodiesterase-III in vascular smooth muscle cells, and this action is maintained even in dogs with severe HF.[67] Furthermore, elderly human patients may present physical difficulties responding with sympathetic efficiency in cases of serious flow deviation between vascular beds, which is most likely a result of the sympathetic aging process.[68] Although this process has not been studied in dogs, patients in the stage C group were statistically older than the patients in the stage B2 group.

A statistically significant difference was observed in the platelet count between the stage C and control groups. Although these values were within the species reference range, an increasing trend was observed in the stage C group platelet count.[69] HF is known to cause a sustained increase in the concentration of serum proinflammatory cytokines, including IL-1, IL-6, IL-18, and TNF-α, which can lead to an increase in platelet count.[70,71] The study patients also had normal RBC counts, hemoglobin, or packed cell volumes, thus eliminating anemia as a cause for hyperlactatemia.[43]

The limitations of this study include the lack of treatment standardization because the therapeutic approaches had to meet the clinical needs of each patient. No other perfusion evaluation methods, such as side stream darkfield microscopy, tissue oxygen saturation, sublingual or gastric tonometry, mixed venous oxygen saturation, central venous oxygen saturation, base deficit, pH, or CO_2 gap, were used that could assist in confirming hyperlactatemia as a result of hypoperfusion (type A).[10] Because certain animals were not seen at the emergency room and most of the animals were held by the owners, it was difficult to obtain more invasive data. Stage B1 patients were not included in this study due to budgetary matters, although that would help to rule out possible inconsistences in plasma lactate measurements among groups. This study was completed at a single center with a small number of animals; thus, the results cannot be extrapolated to all dogs with HF as a result of MMVD. However, these observational data may be useful for the clinical treatment of patients with HF resulting from MMVD. Hyperlactatemia can be a predictor of decompensation and hypoperfusion, thus indicating the need for therapeutic adjustments for such patient.

We believe that the hyperlactatemia found in group C is a clinically important indicator of an early physiological response to a low flow state that may be related to worsening heart disease (low cardiac output).

Future directions may include plasma lactate monitoring on a long-term basis to determine whether there is a relationship between lactate and peripheral perfusion during disease decompensation.

Finally, our results indicate that dogs with HF resulting from MMVD may have occult hypoperfusion in stage C, which was demonstrated by hyperlactatemia. HF must be considered as a differential for hyperlactatemia in patients with MMVD when other causes of the disease have been excluded.

Footnotes

[a] DC3-Vet, Mindray, Shenzhen, China.
[b] DV 610, Medmega, Franca, Brazil.
[c] Gamma G5, Heine, Herrsching, Germany.
[d] ST-700, Incoterm, Porto Alegre, Brazil.
[e] Accutrend Plus, Roche, Basel, Switzerland.
[f] GraphPad Prism 6 software, version 6.05, GraphPad Software Inc., San Diego, CA.

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