

# Plasma lactate concentrations in septic peritonitis: A retrospective study of 83 dogs (2007–2012)

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## Abstract

**Objective** – To determine if absolute plasma lactate concentration or lactate clearance in dogs with septic peritonitis is associated with morbidity or mortality.

**Design** – Retrospective cohort study from 2007 to 2012.

**Setting** – University teaching hospital.

**Animals** – Eighty-three dogs with septic peritonitis were included. Patients had at least 1 plasma lactate measurement during the course of the hospitalization.

**Results** – Sixty-four percent of the patients survived to discharge, 22% were euthanized, and 14% died during hospitalization. Plasma lactate concentration >2.5 mmol/L on admission (29% of the patients) was associated with mortality ( $P = 0.001$ ). Median admission plasma lactate concentration ( $n = 81$ ) was significantly different between nonsurvivors (2.5 mmol/L, range 0.5–8.4) and survivors (1.4 mmol/L, range 0.5–9.7;  $P = 0.007$ ). Admission plasma lactate concentration >4 mmol/L yielded a sensitivity of 36% and a specificity of 92% for nonsurvival. The inability to normalize plasma lactate concentration within 6 hours of admission ( $n = 10/24$ ) yielded a sensitivity of 76% and specificity of 100% for nonsurvival. Postoperative hyperlactatemia (plasma lactate concentration >2 mmol/L;  $n = 18/76$ ) had a sensitivity of 46% and specificity of 88% for nonsurvival. Persistent postoperative hyperlactatemia ( $n = 11/18$ ) had a sensitivity of 92% and a specificity of 100% for nonsurvival. Lactate clearance less than 21% at 6 hours ( $n = 20$ ) had a sensitivity of 54% and specificity of 91% for nonsurvival. Lactate clearance less than 42% at 12 hours ( $n = 18$ ) had a sensitivity of 82% and a specificity of 100% for nonsurvival.

**Conclusions** – Admission plasma lactate concentration and lactate clearance were good prognostic indicators in dogs with septic peritonitis.

(*J Vet Emerg Crit Care* 2014; 00(0): 1–8) doi: 10.1111/vec.12234

**Keywords:** canine, lactime, outcome, sepsis, shock, survival

## Abbreviations

APPLE	acute patient physiological laboratory evaluation
AUC	area under the curve
BE	base excess
IMHA	immune-mediated hemolytic anemia

lactate <sub>adm</sub>	plasma lactate on admission to the hospital
lactate <sub>hour</sub>	plasma lactate concentration at a specific hour
Lactime	time (hours) until the normalization of plasma lactate concentration
MODS	multiple organ dysfunction syndrome
ROC	receiver operating characteristic

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Offprints will not be provided by the authors.

The authors declare no conflict of interest.

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Submitted October 21, 2013; Accepted May 17, 2014.

## Introduction

Septic peritonitis occurs secondary to microbial contamination of the peritoneal cavity.<sup>1</sup> It has been associated with a high mortality, with a reported survival in dogs ranging from 29% to 71%.<sup>1–3</sup>

Septic peritonitis can be either primary or secondary to intra-abdominal organ leakage and can lead, even with

early surgical treatment, to septic shock.<sup>2,3</sup> The pathophysiology of the condition is intimately related to the complexity of sepsis, including systemic inflammation and its repercussions on major organ systems, cardiovascular instability, and decreased tissue oxygen delivery, and the underlying disease process responsible for the peritonitis.<sup>4</sup> It is therefore difficult to identify a specific and reliable prognostic factor. There has been growing interest toward identification of biomarkers that can serve as prognostic indicators and also as clinical indicators to guide therapy.<sup>5,6</sup>

Many studies, both in human and veterinary medicine, have examined plasma lactate concentration in the clinical context for its diagnostic and prognostic value.<sup>7,8</sup> Lactate is an end product of anaerobic metabolism and its circulating concentrations are increased under conditions of tissue hypoxia.<sup>9,10</sup> Therefore, plasma lactate concentration is not only relevant in assessing the degree of overt or occult hypoperfusion but also in assessing tissue oxygen delivery.<sup>11,12</sup>

Studies in different critically ill populations suggest that serial plasma lactate measurements and the change in plasma lactate concentration in response to therapy are a more significant prognostic indicator than a single lactate measurement at admission.<sup>12–14</sup> Lactate clearance, expressed as the percentage change over time of plasma lactate concentration, is a sensitive prognostic indicator, but interest has also grown toward “lactime,” defined as the time lapsed from admission to normalization of plasma lactate concentration.<sup>12,14,15</sup>

The objective of this study was to assess if the plasma lactate concentration at admission or lactate clearance in the hours following hospital admission was able to predict survival in dogs with septic peritonitis. Additional study aims were to evaluate the association between plasma lactate concentration and morbidity, defined as the duration of ICU stay or the requirement for blood product transfusion or vasopressor support.

## Materials and Methods

The electronic medical records database of the Queen Mother Hospital for Animals at the Royal Veterinary College was searched for cases of septic peritonitis in dogs. The inclusion criterion was a diagnosis of septic peritonitis, either at presentation to the hospital or at any point during hospitalization. The criteria for diagnosis of septic peritonitis were the identification of intracellular bacteria or fungal agents on cytologic evaluation of abdominal fluid, or a positive bacterial or fungal culture from this fluid. Dogs with intraoperative evidence of macroscopic leakage of the gastrointestinal tract or intra-abdominal rupture of an abscess or pyometra were

also included. In addition, at least 1 plasma lactate measurement during the course of the hospitalization was necessary for inclusion. Patients with missing or incomplete records, an unconfirmed diagnosis, or those who underwent euthanasia without attempted surgical treatment were excluded from analysis.

Medical records of enrolled cases were reviewed by a single author. Data including signalment, relevant history, admission cardiorespiratory parameters, available plasma lactate concentration measurements, intraoperative findings, postoperative requirements for vasopressors, blood product transfusions and synthetic colloids, and outcome were recorded. Hypotension was defined as a blood pressure measured using a Doppler ultrasonic flow probe <90 mm Hg or a mean arterial blood pressure less than 60 mm Hg when oscillometric or direct measurement was used. Multiple organ dysfunction syndrome (MODS) was identified based on the criteria defined by Kenney *et al.*<sup>16</sup> Acute patient physiologic laboratory scores (APPLE) scores, in full and fast form, were retrospectively calculated where suitable data were available and were expressed as the mortality prediction probability (score 0–1).<sup>17</sup>

Plasma lactate concentration was measured with a bench-top blood gas analyzer<sup>a</sup> using heparinized venous or arterial blood samples. Hyperlactatemia was defined as a plasma lactate concentration >2.5 mmol/L.<sup>18</sup> Where available, serial plasma lactate and base excess (BE) concentrations were recorded, together with their time relative to presentation and surgery.

Lactate clearance, defined as the percentage change in lactate, was calculated for each dog that had hyperlactatemia on admission to the hospital at 3, 6, 12, and 24 hours as  $([\text{lactate}_{\text{adm}} - \text{lactate}_{\text{hour } x}]/\text{lactate}_{\text{adm}}) \times 100$  (where  $\text{lactate}_{\text{adm}}$  is plasma lactate on admission to the hospital,  $\text{lactate}_{\text{hour}}$  is plasma lactate concentration at a specific hour). The plasma lactate concentration at each of these time intervals was extracted from the medical records with a tolerance of 2 hours before or after the actual time point, except for the 3-hour time point, which was given a tolerance of 30 minutes.

Lactime was defined as the time (hours) lapsed from admission until the normalization of plasma lactate (defined as plasma lactate within the reference interval, 0–2.5 mmol/L) from admission was achieved.

## Statistical Analyses

Data were recorded in an electronic spreadsheet<sup>b</sup> and were analyzed using commercial statistical software.<sup>c</sup> Each dataset was analyzed for distribution using the Shapiro–Wilk test and expressed as mean ( $\pm$ SD) or median (range) depending on the presence or absence of a normal distribution. Continuous variables were

compared with the Student's *t*-test for parametric data and Mann Whitney U-test for nonparametric data. Discrete variables were analyzed for difference using analysis of variance (ANOVA) for parametric data and Kruskal–Wallis test for nonparametric data. Categorical variables were analyzed using chi-square or Fisher's exact test if the contingency table contained an expected value <4. For lactate clearance and absolute plasma lactate concentration, a receiver operating characteristic (ROC) curve was generated and an optimal cutoff visually defined for each time point. For all statistical analyses, a *P*-value less than 0.05 was considered significant

## Results

The medical records search identified 363 dogs. After application of the inclusion and exclusion criteria, 83 dogs with septic peritonitis were included in the study. The median age was 60 months (range 4–142 months) and the median weight was 25.7 kg (range 1.7–46.1 kg). There were a variety of breeds represented in this study, with the most common being Labradors (13), Springer Spaniels (8), and mixed breeds (5). There were 53 male dogs (64%; 36 neutered [68%] and 17 [32%] intact) and 30 female dogs (36%; 20 neutered [67%] and 10 intact [33%]) studied.

Seventy-seven dogs (93%) were referred from another veterinary practice whereas 6/83 (7%) were seen as primary emergency patients. Sixty-one (74%) of the patients received IV fluids at another clinic prior to presentation, while 22 (26%) did not. Forty-four dogs (53%) had undergone surgery within the 10 days prior to presentation.

In 73 dogs (89%), the gastrointestinal system was the focus of the sepsis, in 5 dogs (6%) there was a urogenital focus, 3 dogs (4%) had hepatobiliary disease, and 1 (1%) had a primary (idiopathic) peritonitis. Thirty-eight dogs (46%) had a gastrointestinal foreign body, 11 (13%) had gastrointestinal ulceration leading to perforation, 6 (7%) were diagnosed with gastrointestinal neoplasia, 7 (8%) had intestinal biopsies, 4 (6%) had a gastric dilation-volvulus. Three (4%) had an intussusception, 2 (2.4%) each were diagnosed with hepatic disease, pyometra, abscessation, mesenteric volvulus, and trauma, and 1 (1%) each had a primary diagnosis of dystocia, a mesenteric thrombus, retention of a surgical swab (gossypiboma), and idiopathic peritonitis. Sixty patients (72%) had a positive bacterial culture from the abdominal fluid, 3 patients had *Candida albicans* isolated, 7 patients had a negative culture, and 13 patients did not have a culture performed.

Fifty-three (64%) of the patients survived to discharge, 18 (22%) were euthanized, and 12 (14%) died during hospitalization. Median hospitalization time was 7 days

(range 0–21 d) and the median time spent in the ICU was 3 days (range 0–17 d). MODS was identified in 15 (18%) of the patients. Median APPLE full score was 0.06 (range 0.00–0.95) and median APPLE fast score was 0.21 (range 0.01–0.99). APPLE full and fast scores were calculated in 46 patients (Table 1).

On admission, the mean ( $\pm$ SD) heart rate was  $126 \pm 34$ /min, the median (minimum–maximum value) respiratory rate was 32/min (14–100/min) and the median temperature was 38.6°C (36°C–40.4°C). The mean admission blood pressure using a Doppler ultrasonic flow probe was performed in 37 cases and was  $140 \pm 35$  mm Hg, with 4 of these dogs (5%) being hypotensive. Oscillometric blood pressure was recorded in 6 dogs on admission and the mean of the mean arterial blood pressure was  $85 \pm 13$  mm Hg. Median blood glucose was 5.8 mmol/L [104.5 mg/dL] (1.8–10.4 mmol/L [32.4–187.4 mg/dL]). Plasma lactate concentration on admission was available for 81 cases with a median of 1.7 mmol/L (0.5–9.7 mmol/L) and median BE for 78 dogs was  $-4.9$  mmol/L ( $-17.1 \pm 5.3$ ) (Table 2). Because of the retrospective nature of the study, plasma lactate measurements were not available for all the dogs at the different time points; serial plasma lactate concentration for all time points was available for 17 patients (Table 2).

Synthetic colloids (hydroxyethyl starches) were used in 46 (55%) of the patients, human albumin in 9 (11%), blood products (packed red blood cells or plasma) in 30 (36%), and vasopressors (dopamine or norepinephrine) in 16 (19%) of the patients.

Admission plasma lactate concentration was not predictive of administration of synthetic colloids ( $P = 0.14$ ) or albumin ( $P = 0.53$ ), although it was predictive of the use of blood products ( $P < 0.01$ ) and vasopressors ( $P < 0.01$ ). Dogs with hyperlactatemia on admission had a significantly shorter ICU stay (median 2 days, range 0–11) compared to patients that were normolactatemic at admission (median 4, range 0–17) ( $P = 0.03$ ). When comparing only patients that survived, normolactatemic patients did not have significantly higher median total stay in the hospital (8.3 days, range 5–21) compared to the hyperlactatemic patients (8.2 days, range 4–13;  $P = 0.72$ ) or have a shorter ICU stay (4 days, range 1–17) compared to the hyperlactatemic patients (4.5 days, range 1–11;  $P = 0.73$ ). Twenty-four (29%) patients had hyperlactatemia on admission and 14 of these dogs did not survive. Hyperlactatemia on admission was associated with mortality ( $P = 0.01$ ) (Figure 1).

Admission plasma lactate concentration  $>4$  mmol/L (81 total patients) was significantly associated with mortality (odds ratio 7.1, 95%CI 2–25,  $P = 0.002$ ). Fifteen patients (19%) had admission plasma lactate  $>4$  mmol/L. Of these, 11 (73%) of the patients died versus 19 (28%) of the patients with a lactate  $<4$  mmol/L (68 total patients).

**Table 1:** Various parameters in dogs with septic peritonitis compared between survivors and nonsurvivors

	Survivors	Nonsurvivors	P value
Heart rate (per min)	117 ( $\pm$ 32)	141 ( $\pm$ 30)	0.001
Respiratory rate (per min)	32 (14–100)	32 (20–100)	0.6
Temperature ( $^{\circ}$ C)	38.6 (36.3–40.3)	38.4 (36–40.1)	0.52
Doppler systolic pressure (mm Hg)	145 ( $\pm$ 26)	121 ( $\pm$ 42)	0.04
Blood glucose (mmol/L); [mg/dL]	5.7 [102.7](2.9–10.9 [52.3–196.4])	6.3 [113.5] (1.8–9.6 [32.4–173.0])	0.16
Ionized calcium (mmol/L)	1.16 (0.99–1.42)	1.1 (0.87–1.34)	0.013
Plasma lactate on admission to hospital (mmol/L)	1.4 (0.5–9.7)	2.5 (0.5–8.4)	0.007
Base excess adm. (mmol/L)	–4.8 (–15 to –0.2)	–6.2 (–17.1 to 5.3)	0.17
ICU stay (days)	4 (1–17)	3 (0–11)	0.039
Hospital stay (days)	7 (4–21)	3 (0–12)	0.001
Time of administration of antimicrobial medication from admission (hours)	3 (0–48)	3 (1–56)	0.72
Time from admission to surgery (hours)	3 (1–48)	3 (1–56)	0.83
APPLE full	0.03 (0–0.38)	0.2 (0.01–0.95)	0.001
APPLE fast	0.13 (0.01–0.77)	0.55 (0.05–0.99)	0.001

Adm, admission. APPLE, acute patient physiologic laboratory evaluation. Data presented as mean ( $\pm$ SD) or median (range). A *P* value of  $<0.05$  was considered statistically significant.

**Table 2:** Median plasma lactate concentration (minimum-maximum value) in survivors and nonsurvivors

	Survivors	Nonsurvivors	P value
Plasma lactate (mmol/L) on admission	1.4 (0.5–9.7) ( <i>n</i> = 52)	2.5 (0.4–8.4) ( <i>n</i> = 29)	0.007
Plasma lactate (mmol/L) 3 hours after admission	1 (0.5–7.2) ( <i>n</i> = 15)	2.3 (0.7–4.1) ( <i>n</i> = 8)	0.4
Plasma lactate (mmol/L) 6 hours after admission	1 (0.2–5) ( <i>n</i> = 36)	3.8 (0.7–11.8) ( <i>n</i> = 19)	$<0.001$
Plasma lactate (mmol/L) 12 hours after admission	0.7 (0.2–2) ( <i>n</i> = 32)	2.9 (0.6–10.4) ( <i>n</i> = 22)	0.017
Plasma lactate (mmol/L) 24 hours after admission	0.7 (0.2–5.4) ( <i>n</i> = 33)	1.5 (0.3–6.8) ( <i>n</i> = 11)	0.014

An admission plasma lactate concentration  $> 4$  mmol/L yielded a sensitivity of 36% and specificity of 92% for nonsurvival.

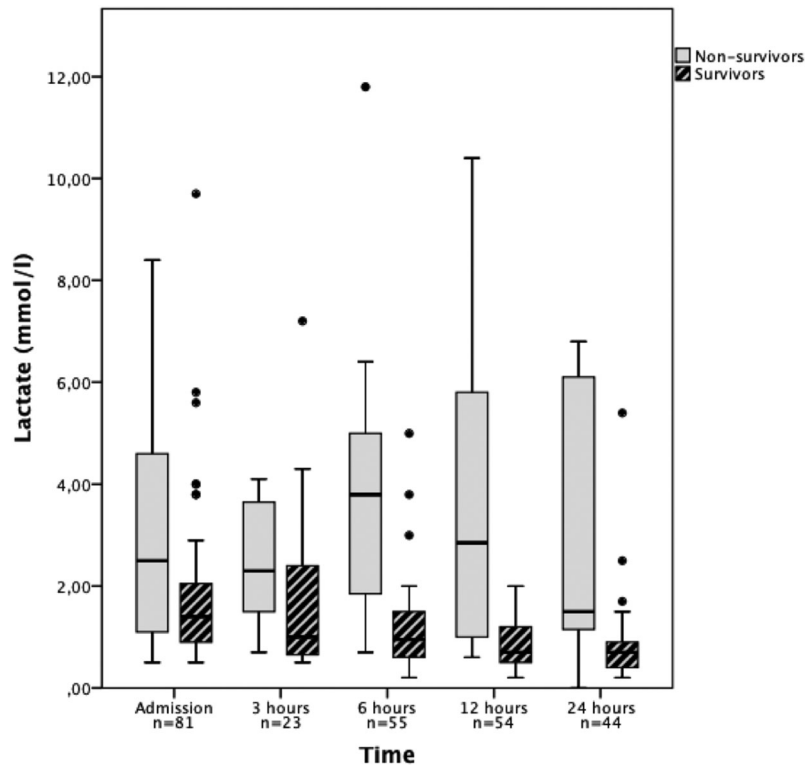
Lactime could be calculated for 24 dogs, of which 13 patients died and 11 survived. Among the 24 dogs, 10 failed to resolve hyperlactatemia prior to death (ranging from 1 hour to 24 hours), and none of these patients survived. Of the 14 patients that did have resolution of hyperlactatemia, 11 survived and 3 did not. A ROC curve of the lactime yielded poor sensitivity and specificity for survival with an area under the curve (AUC) of 0.66.

Twenty-four dogs had measurements of plasma lactate performed at 6 hours from admission. All 10 of the patients that did not have resolution of hyperlactatemia within 6 hours died. Among the 14 dogs that had resolution of hyperlactatemia within 6 hours from admission, 11 (79%) survived and 3 (21%) died. The inability to resolve hyperlactatemia within 6 hours yielded a sensitivity of 76% and specificity of 100% for nonsurvival.

All 83 dogs underwent surgery. Plasma lactate immediately following surgery was recorded in 76 dogs.

Postoperative hyperlactatemia was present in 18 dogs, 12 of which (67%) died. Of the 58 dogs that were not hyperlactatemic postoperatively, 14 died (24%) and 44 survived (76%). The difference in survival between animals with and without postoperative hyperlactatemia was significant ( $P = 0.002$ ). Postoperative hyperlactatemia had a sensitivity of 46% and specificity of 88% for nonsurvival. Persistent postoperative hyperlactatemia was significantly associated with mortality ( $P < 0.001$ ). Of 18 dogs that were hyperlactatemic postoperatively, 11 failed to regain a normal plasma lactate concentration. Of these 11 dogs, 4 had normal lactate concentration on admission but none survived to discharge. Of the remaining 7 dogs with postoperative hyperlactatemia that resolved, 6 survived and 1 did not survive. Persistent postoperative hyperlactatemia had a sensitivity of 92% and a specificity of 100% for nonsurvival.

A ROC curve was generated for lactate concentration at 6 hours following admission (calculated from 55 of 83 dogs), which had an AUC of 0.87 and a cutoff of a plasma lactate of 2.3 mmol/L yielding a sensitivity of 68% and



**Figure 1:** Box and whisker plot representing median plasma lactate concentration (mmol/L) and interquartile range (box) at different time points from admission in survivors and nonsurvivors from a group of 83 dogs with septic peritonitis. The black line within the box indicates the median and the black dots represent outliers. Significance was set at a  $P$  value  $<0.05$ . A significant difference between the 2 groups was detected at admission and 6, 12, and 24 hours following admission.

specificity of 92% for nonsurvival. Lactate clearance at 6 hours could be calculated for 20 patients, and ROC curve analysis produced an AUC of 0.81 and a sensitivity of 54% and specificity of 91% for nonsurvival with a cutoff value of 21% clearance.

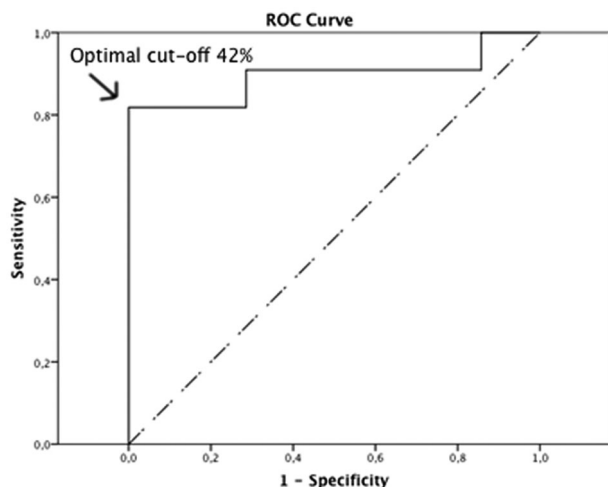
Analysis of absolute plasma lactate concentration at 12 hours following admission ( $n = 54$ ) produced a ROC curve with an AUC of 0.86 and a cutoff of 2.4 mmol/L resulting in a sensitivity of 54% and a specificity of 100% for nonsurvival. Lactate clearance at 12 hours following admission could be calculated for 18 patients and ROC curve analysis produced a curve with an AUC of 0.90 and a cutoff of 42% resulted in a sensitivity of 82% and specificity of 100% for nonsurvival (Figure 2). Lactate clearance at 3 hours post admission was not significantly different between survivors and nonsurvivors ( $n = 9$ ,  $P = 0.25$ ).

## Discussion

Septic peritonitis is a complex and severe inflammatory process caused by the presence of infectious agents in the peritoneal cavity. Interactions between the host inflammatory response, the coagulation and vascular

endothelial systems may lead to abnormalities in the macro- and microcirculation, multiorgan failure, and ultimately death. Hypoperfusion may occur through various pathophysiologic pathways, including hypovolemia, cardiogenic shock, vasoplegia, and splanchnic microthrombi.<sup>19</sup>

Hyperlactatemia results from either an imbalance between tissue oxygen supply and demand (type A) or altered cellular metabolism (type B). In patients with sepsis, hyperlactatemia may occur due to hypoperfusion, mitochondrial dysfunction, increased leukocyte activity, organ dysfunction, decreased lactate clearance,  $\text{Na}^+$ - $\text{K}^+$  ATPase activation, hypoglycemia, or dysregulation of pyruvate dehydrogenase.<sup>9,20–22</sup> Recent veterinary studies have found neoplasia to be a cause of increased lactate but typically this is not clinically significant and was unlikely to be a significant confounder in our study as a neoplastic process was only identified in 6 (7%) of the enrolled patients.<sup>23,24</sup> Similarly, the presence of a primary liver disease (2 patients, 2%), steroid administration (documented in 4 patients, 5%), or the use of catecholamines (16 patients, 19%) could have increased the plasma lactate concentrations and should be considered possible confounders of our study.<sup>10,24</sup>



**Figure 2:** Receiver operating characteristic (ROC) analysis of lactate clearance at 12 hours following admission stratified for survival or nonsurvival in a group of hyperlactatemic dogs with septic peritonitis. The area under the curve is 0.90 and the arrow indicates the optimal cutoff point of 42% for lactate clearance to predict survival.

In our study, plasma lactate on admission was significantly higher in nonsurvivors compared to survivors, although median lactate for nonsurvivors (2.5 mmol/L) was only the upper reference limit of plasma lactate described by a previous study.<sup>18</sup> This suggests that even moderate increases in lactate should be concerning and warrant immediate attention. In previous veterinary studies, admission plasma lactate was proposed to offer varying degrees of prognostic value. In a study on a heterogeneous population of systemically ill dogs, admission plasma lactate was not found to be significantly associated with mortality;<sup>12</sup> in patients with immune-mediated hemolytic anemia (IMHA), survivors had a lower plasma lactate on admission (median 2.9 mmol/L) compared to nonsurvivors (4.8 mmol/L).<sup>14</sup> In dogs with babesiosis, the difference in plasma lactate concentration between survivors and nonsurvivors was more marked (2.6 mmol/L in survivors versus 8.5 mmol/L in nonsurvivors).<sup>15</sup> These findings suggest that perhaps plasma lactate values should be interpreted differently according to the underlying pathophysiologic process, and therefore should always be considered within a disease-related context.

Severe hyperlactatemia on admission was defined as plasma lactate >4 mmol/L, and was associated with a higher mortality. These results are in accordance with studies in human patients in whom hyperlactatemia was associated with a higher mortality, independent of organ failure or shock, and an admission plasma lactate concentration >4 mmol/L was associated with a 6-fold higher probability for death within 3 days.<sup>25,26</sup> A retrospec-

tive study on dogs with IMHA showed that an admission plasma lactate concentration cutoff of 4.4 mmol/L was a good predictor of survival.<sup>14</sup> In dogs with gastric dilation-volvulus, an admission plasma lactate concentration <4.1 mmol/L was the best cutoff for predicting survival based on a ROC analysis.<sup>27</sup>

Interestingly, and in contrast to a veterinary study in trauma patients, admission BE was not significantly associated with survival in this study ( $P = 0.17$ ), highlighting that BE can vary in septic patients for reasons unrelated to lactate accumulation.<sup>6</sup> A reduction in standard BE and consequent metabolic acidosis is likely multifactorial in sepsis, and the contribution of lactate can be less than 10%.<sup>28</sup> Other contributing factors to acidosis include hyperchloremia, accumulation of inorganic unmeasured ions (eg, keto acids or sulfate), or hypoalbuminemia.<sup>29</sup>

Admission plasma lactate concentration was associated with patient morbidity in this study, with a higher median lactate reported for dogs that required transfusions or vasopressors. Anemia and hypotension induce tissue hypoxia due to reduced tissue oxygen delivery. It is assumed that patients that received transfusions or vasopressors had higher plasma lactate concentrations due to anemia or hypotension but due to the retrospective nature of the study we cannot exclude that high lactate was an actual indication for blood transfusion administration or vasopressor therapy. Hyperlactatemia was associated with a shorter ICU stay in this patient population. This finding is likely explained by the early euthanasia or death of this population.

Lactate was recorded at 3 hours and at 6, 12, and 24  $\pm$  2 hours after admission when available. The best area under ROC curves for absolute plasma concentration were obtained at 6 and 12 hours post admission; lactate concentrations >2.3 mmol/L at 6 hours or >2.4 mmol/L at 12 hours were good predictors of mortality (specificity 92% and 100%, respectively). These levels are only mildly increased or within the reference range, suggesting that any single value should be critically interpreted in consideration of the underlying disease. In addition, patients with plasma lactate concentrations within the normal limits established in healthy dogs could still be experiencing inadequate tissue oxygen delivery. The low sensitivity for mortality of the chosen ROC cutoffs at 6 and 12 hours after admission suggests that plasma lactate concentrations below these points should not decrease the clinician's concern for these patients.

The plasma lactate clearance at 6 and 12 hours after admission was also a good predictor of mortality in this study. This is in accordance with the findings of Stevenson *et al*,<sup>12</sup> who examined systemically ill dogs with a variety of diseases and found that lactate clearance <50% at 6 hours after admission was associated with mortality.<sup>12</sup> Similarly, Nel *et al*<sup>15</sup> found

that a lactate clearance <50% at 8 and 16 hours after admission was a poor prognostic indicator in canine babesiosis.<sup>15</sup> Additionally, failure to normalize plasma lactate within 6 hours of admission has been associated with mortality in dogs with IMHA.<sup>14</sup> Similar results have been found in people with septic peritonitis; lactate clearance at 6 hours was prognostically superior to a change in central venous saturation of oxygen (ScvO<sub>2</sub>), and a 24-hour window for plasma lactate clearance was also a good predictor of survival in this population.<sup>30,31</sup>

There are several limitations to this study, most of which are intrinsic to its retrospective design. The majority of the patients (93%) included in the study were referred from another veterinary clinic and may have received treatment and in some cases even had surgery prior to referral. As a result, lactate measurements taken at the time of admission or subsequent points may not represent the same stage of disease in different patients. The plasma lactate concentrations were extracted from records rather than being prospectively timed and this likely led to more data points being available in the sickest patients. It is assumed that stable patients with normal lactate recorded continued to have normal lactate but in patients with hyperlactatemia on admission, samples were serially measured to look for normalization.

The number of patients for which lactate was available at our predetermined time points was low and therefore the power of the study when looking at lactate at time points other than hospital admission is reduced. Also, the 2-hour tolerance window for the time points might actually have influenced the results; a further prospective study with sampling performed at specific times could overcome this limitation. The fact that some patients were euthanized is another limitation inherent to many veterinary studies. Given that the majority of patients were referred from another center, financial constraints and owner factors may have been less of a confounding factor in this population. The difference in APPLE scoring between the survivors and nonsurvivors supports the notion that mortality in this population was associated with disease severity rather than financial factors. Still, the results regarding the hospitalization and ICU time or discharge time should be interpreted with caution in this retrospective study, as these times can often be clinician and finance-based.

This study demonstrated that plasma lactate concentration was associated with mortality and morbidity in dogs with septic peritonitis. In particular, the results suggest that lactate normalization within a 6–12 hour window is associated with survival and that persistent postoperative hyperlactatemia should raise particular concerns. Further prospective studies are needed in order to assess the potential role of lactate-guided therapy in sepsis.

## Footnotes

- <sup>a</sup> Critical Care Xpress and Phox Ultra, Nova Biomedical, Waltham, MA.
- <sup>b</sup> Microsoft Excel, version 2008, Microsoft Inc, Redmond, WA.
- <sup>c</sup> SPSS, version 20, SPSS Inc, Chicago, IL.

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