

# Survival analysis of hypotensive cats admitted to an intensive care unit with or without hyperlactatemia: 39 cases (2005–2011)

Emily K. Shea BA

Stefan C. Dombrowski PhD

Deborah C. Silverstein DVM

From the Department of Clinical Studies, School of Veterinary Medicine, University of Pennsylvania, Philadelphia, PA 19104 (Shea, Silverstein); and the Department of Graduate Education, Leadership and Counseling, Rider University, Lawrenceville, NJ 08648 (Dombrowski).

Address correspondence to Dr. Silverstein (dcsilver@vet.upenn.edu).

## OBJECTIVE

To examine the association between blood lactate concentration and survival to hospital discharge in critically ill hypotensive cats.

## DESIGN

Retrospective case series.

## ANIMALS

39 cats admitted to an intensive care unit of a university veterinary hospital between January 2005 and December 2011 for which blood lactate concentration was recorded  $\leq$  1 hour before or after a Doppler-derived arterial blood pressure measurement  $\leq$  90 mm Hg (ie, hypotension) was obtained.

## PROCEDURES

Medical records of each cat were reviewed to assess survival to hospital discharge, illness severity, duration of hospitalization, age, body weight, and PCV. Results were compared between hypotensive cats with and without hyperlactatemia (blood lactate concentration  $\geq$  2.5 mmol/L).

## RESULTS

6 of 39 (15%) hypotensive cats survived to hospital discharge. Twelve (31%) cats were normolactatemic (blood lactate concentration  $<$  2.5 mmol/L), and 27 (69%) were hyperlactatemic. Hypotensive cats with normolactatemia had a higher blood pressure and higher survival rate than hypotensive cats with hyperlactatemia. Five-day Kaplan-Meier survival rates were 57% for normolactatemic cats and 17% for hyperlactatemic cats. Age, body weight, duration of hospitalization, PCV, and illness severity did not differ significantly between hypotensive cats with and without hyperlactatemia.

## CONCLUSIONS AND CLINICAL RELEVANCE

Hypotensive, normolactatemic cats in an intensive care unit had a significantly greater chance of survival to hospital discharge than their hyperlactatemic counterparts. Blood lactate concentration may be a useful prognostic indicator for this patient population when used in conjunction with other clinical and laboratory findings. (*J Am Vet Med Assoc* 2017;250:887–893)

Lactate is produced in anaerobic conditions when hypoxia prevents pyruvate from entering the Krebs cycle, resulting in the conversion of pyruvate to lactate and release of hydrogen as a byproduct. In healthy individuals, lactate is produced primarily by erythrocytes, skeletal muscle, the renal medulla, skin, and brain tissue and is metabolized by the liver, kidneys, and heart.<sup>1-3</sup> The liver plays the most important role in lactate clearance and homeostasis.<sup>1-3</sup> However, in conditions of severe hypoxia, the liver and kidneys also switch to anaerobic metabolism and produce lactate, contributing to hyperlactatemia.<sup>2,3</sup>

Hyperlactatemia develops when the mechanisms for lactate clearance fail or are saturated and cannot compensate for overproduction of lactate. When marked increases in lactate production occur, the increased number of hydrogen ions released into the blood can overwhelm body buffering systems, resulting in lactic acidosis.<sup>1,3</sup> Hyperlactatemia may also exist without systemic acidosis if the buffering capacity of the blood is adequate.

Tissue hypoxia resulting in anaerobic metabolism is the most common cause of lactate accumulation and is classified as type A lactic acidosis.<sup>1-5</sup> Causes of tissue hypoxia include systemic or local hypoperfusion, severe hypoxemia, severe anemia, impaired hemoglobin oxygen-carrying capacity, and substantial increases in oxygen demand (eg, during seizures).<sup>1-5</sup> Type B lactic acidosis is characterized by normal blood and tissue oxygenation, and causes include diseases (eg, liver disease, renal failure, or neo-

## ABBREVIATIONS

DBP	Doppler-derived arterial blood pressure
ICU	Intensive care unit
SPI2	Survival prediction index 2 value
SpO <sub>2</sub>	Oxygen saturation as measured by pulse oximetry

plasia) that cause a decrease in lactate clearance or increase in lactate production; drugs or toxicants that interfere with oxidative phosphorylation thereby preventing metabolism of pyruvate via the Krebs cycle; mitochondrial disease, which also prevents oxidative phosphorylation and leads to an increase in lactate production via anaerobic metabolism; or D-lactic acidosis due to bacterial lactate production in the gastrointestinal tract.<sup>1-5</sup>

Sepsis involves a complex and incompletely understood combination of mechanisms that can lead to hyperlactatemia and lactic acidosis. In humans with sepsis, mitochondrial dysfunction (cytopathic hypoxia) or an increase in pyruvate production may be more important contributors to hyperlactatemia than tissue hypoxia.<sup>6,7</sup> However, normolactatemic humans with septic shock reportedly have a lower mortality rate (7.7%) than hyperlactatemic humans with septic shock (42%).<sup>8</sup> Together with the finding that normolactatemic humans with septic shock have significantly higher platelet counts and more preserved blood flow than their hyperlactatemic counterparts, these data suggest that blood lactate concentration is in fact related to microcirculatory function and remains an important prognostic indicator in septic patients.<sup>8,9</sup>

When clinical history and diagnostic testing rule out sepsis and type B lactic acidosis, plasma lactate concentration is a good clinical indicator of the degree of tissue perfusion. The usefulness of lactate clearance rate and serial lactate measurements as markers of perfusion and predictors of mortality rate has been well reviewed in the human literature.<sup>10-17</sup> In the 2012 international guidelines for management of severe sepsis and septic shock in humans,<sup>16</sup> restoration of blood lactate concentration to below the upper reference interval or clearance of lactate from the bloodstream over time is recommended as an endpoint target for resuscitation in septic patients. Several clinical studies<sup>18-27</sup> have also shown the value of blood lactate concentration as a prognostic indicator in dogs and horses. In a study<sup>18</sup> involving dogs admitted to the ICU of a veterinary teaching hospital, normolactatemic hypotensive dogs had a significantly lower mortality rate and better prognosis than hyperlactatemic hypotensive dogs.

Few studies have been conducted to investigate blood lactate concentrations in cats and their usefulness as a prognostic indicator in this species. Although hypotension when considered alone has been correlated with a higher mortality rate in critically ill cats, no prognostic indicators have been established for hypotensive cats in the ICU.<sup>28</sup> Establishment of a prognostic indicator for this particular patient population would allow earlier institution of aggressive treatment and enable clinicians to better inform owners about the severity of disease and prognosis for their cats.

The primary goal of the study reported here was to examine the relationship between blood lactate

concentration and survival to hospital discharge in hypotensive cats admitted to an ICU. We hypothesized that hyperlactatemia (blood lactate concentration  $\geq 2.5$  mmol/L) would be associated with hypotension, more severe illness, and a higher mortality rate, and therefore that hyperlactatemia would indicate a poor prognosis in hypotensive cats.<sup>29,30</sup>

## Materials and Methods

### Case selection criteria

The medical record database of the University of Pennsylvania veterinary teaching hospital was searched to identify cats that had been admitted to the ICU and whose owners had been charged for a blood lactate measurement from 2005 through 2011. To be included in the study, cats were required to have had an arterial blood pressure  $\leq 90$  mm Hg measured via Doppler ultrasonic flow detector  $\leq 1$  hour before or after lactate measurement. Cats with a definitive or strongly suspected diagnosis of neoplasia were excluded.

### Medical records review

Medical records for cats that met these criteria were further reviewed, and data were extracted regarding cat signalment, service of entry (medicine or surgery), body weight, primary diagnosis, comorbidities, duration of hospitalization, and outcome (survival to hospital discharge or death or euthanasia before hospital discharge). Disease processes known to cause lactic acidosis, including liver dysfunction, renal failure, thromboembolism, carbon monoxide toxicosis, asthma, seizure activity, diabetes mellitus, and thiamine deficiency were also recorded when noted at any time during hospitalization.<sup>2,4</sup> Administration or ingestion during or within 1 week before or after hospitalization of medications or substances known to cause type B lactic acidosis including corticosteroid drugs, ethylene glycol, xylitol, cyanide, strychnine, ethanol, salicylates, high-dose epinephrine ( $> 0.1$  mg/kg [0.045 mg/lb]), high-dose norepinephrine ( $> 0.3$   $\mu$ g/kg/min [0.14  $\mu$ g/lb/min]), nitroprusside, bicarbonate, halothane, acetaminophen, terbutaline, total parenteral nutrition, and activated charcoal was also recorded.<sup>2,4</sup> Other variables including PCV, SpO<sub>2</sub>, Pao<sub>2</sub>, and respiratory effort were recorded if they had been measured  $\leq 2$  hours before or after blood lactate measurement. In addition, DBP, respiratory rate, serum creatinine and albumin concentrations, and PCV were recorded if measured within the first 24 hours after hospital admission, and these variables were used to retrospectively calculate a survival prediction index (SPI2).<sup>31</sup> The SPI2 was subsequently used to assess illness severity.

Skilled veterinary nurses measured blood pressure indirectly by use of a Doppler ultrasonic flow detector<sup>a</sup> with a 9.5-MHz probe and an appropriate cuff size (40% of limb width). Three measurements were obtained per cat, and the mean of the 3 measurements was recorded. Location of blood pressure measurement was not standardized across cats. Hypotension was defined as DBP  $\leq 90$  mm Hg. In cats with multiple low DBP measure-

ments, the lowest value with a concurrent blood lactate measurement was used for analysis.

A lactate analyzer<sup>b</sup> was used to measure lactate concentrations in venous blood samples within 30 seconds after collection into heparinized syringes. Hyperlactatemia was defined as a blood lactate concentration  $\geq 2.5$  mmol/L and normolactatemia as a blood lactate concentration  $< 2.5$  mmol/L.<sup>28-30</sup> Anemia was defined as PCV  $< 25\%$ , severe anemia was defined as PCV  $< 15\%$ , and hypoxemia was defined as a Pao<sub>2</sub>  $< 80$  mm Hg or Spo<sub>2</sub>  $< 95\%$ .<sup>32,33</sup>

## Statistical analysis

The main outcome of interest was whether (yes or no) a cat survived to hospital discharge. Data distributions for all variables were assessed for normality via the Shapiro-Wilk test and by assessment of skewness and kurtosis. Relationships between blood lactate concentration ( $< 2.5$  or  $\geq 2.5$  mmol/L) and normally distributed variables (age, body weight, DBP, SPI2, and PCV) were assessed by use of the Student *t* test. Relationships between blood lactate concentration and nonnormally distributed variables (survival to hospital discharge and duration of hospitalization) were assessed by use of the Mann-Whitney *U* test.

Kaplan-Meier survival analysis was performed to further explore the relationship between blood lactate concentration and the probability of survival. All analyses were conducted with standard statistical software,<sup>c</sup> and values of *P*  $< 0.05$  were considered significant.

## Results

### Cats

Thirty-nine hypotensive cats were included in the study. Mean  $\pm$  SD age was  $8.8 \pm 5.1$  years, and mean  $\pm$  SD body weight was  $4.2 \pm 1.4$  kg ( $9.2 \pm 3.1$  lb). Cats included 19 females (18 spayed and 1 sexually intact) and 20 males (19 castrated and 1 sexually intact). Twelve (31%) cats were normolactatemic (blood lactate concentration  $< 2.5$  mmol/L), and 27 (69%) were hyperlactatemic.

The primary critical illnesses were renal or urinary disease (*n* = 8 [21%]), gastrointestinal disease (5 [13%]), respiratory disease (4 [10%]), cardiac disease (3 [8%]), sepsis (2 [5%]), and other conditions not otherwise listed (17 [44%]). Seven (18%) cats had renal failure, 4 (10%) had diabetes mellitus, 2 (5%) had asthma, and 2 (5%) had a history of seizures. Four (10%) cats had masses that were not definitively diagnosed, but noncancerous disease processes were considered most likely; these 4 cats were therefore retained in the study. Seventeen (44%) cats had high liver enzyme activities or liver abnormalities detected via ultrasonography or necropsy, but none had liver failure or cirrhosis. Six (15%) cats had a history of corticosteroid treatment prior to hospitalization, and 1 (3%) cat was treated with corticosteroid drugs during hospitalization. Fourteen (36%) cats received total parenteral nutrition, 13 (33%) cats received a vasopressor (norepinephrine) at traditionally recommended doses (0.05 to 0.2  $\mu$ g/

kg/min [0.023 to 0.09  $\mu$ g/kg/lb]), and 1 (3%) cat was treated with activated charcoal during hospitalization.

Fifteen (38%) cats were anemic (PCV  $< 25\%$ ), and 2 (5%) cats were severely anemic (PCV  $< 15\%$ ). Data regarding Spo<sub>2</sub> were available for only 15 (38%) cats, yielding a mean Spo<sub>2</sub> of 96.7%; 4 of these cats had an Spo<sub>2</sub>  $< 95\%$ , and none had an Spo<sub>2</sub>  $< 90\%$ . Data regarding Pao<sub>2</sub> were recorded for only 1 cat (101.9 mm Hg without oxygen supplementation).

Isotonic crystalloid fluid<sup>d</sup> was administered IV to cats with clinical evidence of hypovolemia as judged via physical examination (pale mucous membranes, prolonged capillary refill time, poor pulse quality, and cold extremities). Measurements of DBP and blood lactate concentration were obtained during or after IV fluid resuscitation in 2 (5%) and 27 (69%) cats, respectively. Blood sample collection for measurement of lactate concentration and measurement of DBP were performed concurrently in 31 (79%) cats, within 1 hour of each other in 5 (13%) cats, and within 2 hours of each other in 3 (8%) cats.

## Comparisons between hypotensive cats with and without hyperlactatemia

The distribution of data for blood lactate concentration was positively skewed. Median (interquartile range) blood lactate concentration for hypotensive cats with hyperlactatemia was 4.8 mmol/L (3.3 to 6.3 mmol/L), whereas that for hypotensive cats without hyperlactatemia was 1.8 mmol/L (1.1 to 2.1 mmol/L).

No significant difference was identified between cats with and without hyperlactatemia in mean age, body weight, SPI2, PCV, or median duration of hospitalization (**Table 1**). Administration of vasopressors, total parenteral nutrition, or activated charcoal was not significantly (*P* = 0.49) related to hyperlactatemia. Mean DBP was significantly (*P* = 0.04) lower in cats with hyperlactatemia than in cats with normolactatemia, and the effect size (Cohen *d* = 0.69) for this analysis suggested a medium-to-large strength of association.

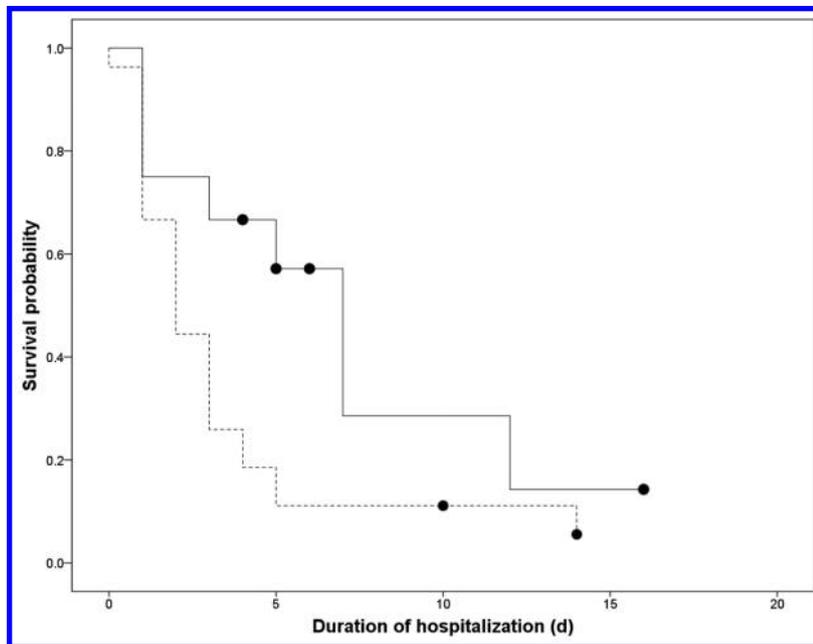
**Table 1**—Descriptive statistics for critically ill hypotensive (DBP  $\leq 90$  mm Hg) cats with (*n* = 27) or without (12) hyperlactatemia (blood lactate concentration  $\geq 2.5$  mmol/L) admitted to an ICU between 2005 and 2011.

Variable	With hyperlactatemia	Without hyperlactatemia	<i>P</i> value
Age (y)	8.3 $\pm$ 5.0	9.6 $\pm$ 5.6	0.52
Body weight (kg)	4.1 $\pm$ 1.8	4.4 $\pm$ 1.7	0.47
DBP (mm Hg)	70.0 $\pm$ 14.2	79.5 $\pm$ 9.4	0.04
SPI2*	0.83 $\pm$ 0.82	0.85 $\pm$ 0.91	0.93
Duration of hospitalization (d)	1 (0–2)	2 (1–4)	0.06
PCV (%)	26.7 $\pm$ 8.9	28.3 $\pm$ 8.7	0.88

Values reported are median (interquartile range) for duration of hospitalization (nonnormally distributed data) and mean  $\pm$  SD for all other variables (normally distributed data).

\*The SPI2 could be calculated for only 38 cats (26 with hyperlactatemia and 12 without hyperlactatemia).

To convert kilograms to pounds, multiply by 2.2.



**Figure 1**—Kaplan-Meier survival curves for critically ill hypotensive (DBP  $\leq$  90 mm Hg) cats with (n = 27; dashed line) and without (12; solid line) hyperlactatemia (blood lactate concentration  $\geq$  2.5 mmol/L). Steps on each curve denote cat nonsurvival (death or euthanasia), whereas circles represent censorship (survival to hospital discharge).

Of the 39 hypotensive cats included in the study, 6 (15%) survived to hospital discharge. Of the 33 nonsurvivors, 29 (88%) were euthanized and 4 (12%) died naturally. Median (interquartile range) blood lactate concentration for cats that survived to hospital discharge was 2.3 mmol/L (1.1 to 2.6 mmol/L), and that for cats that did not survive was 4.5 mmol/L (2.4 to 6.1 mmol/L). Cats with a high blood lactate concentration were significantly ( $P = 0.01$ ) less likely to survive to hospital discharge than were cats with a lower blood lactate concentration. The effect size (0.41) suggested a medium-to-large strength of association between blood lactate concentration and survival to hospital discharge.

Kaplan-Meier survival curve analysis revealed a significantly ( $P = 0.03$ ) different predicted survival time for critically ill hypotensive cats with (n = 27) and without (12) hyperlactatemia (**Figure 1**). These results suggested that hypotensive cats with hyperlactatemia were more likely to die or be euthanized the longer they were hospitalized, compared with hypotensive cats without hyperlactatemia. Median survival times during hospitalization were 2 days for hypotensive hyperlactatemic cats and 7 days for hypotensive normolactatemic cats; Kaplan-Meier estimated 5-day survival rates were 17% and 57%, respectively.

## Discussion

Results of the study reported here indicated that hypotensive (DBP  $\leq$  90 mm Hg) cats in an ICU with a blood lactate concentration  $<$  2.5 mmol/L (ie, normo-

lactatemia) had a significantly greater chance of survival to hospital discharge than similar cats with a blood lactate concentration  $\geq$  2.5 mmol/L (ie, hyperlactatemia). These findings are consistent with those of a study<sup>18</sup> involving dogs, which showed that hypotensive dogs with a blood lactate concentration  $<$  2.0 mmol/L had a better outcome than hypotensive dogs with hyperlactatemia. In another study,<sup>28</sup> hypotensive cats admitted to an ICU had a significantly higher mortality rate than normotensive cats, suggesting that all cats with hypotension should receive close monitoring. The present study further showed that among the hypotensive cats, concurrent hyperlactatemia suggested a more guarded prognosis and the need for aggressive, timely intensive care.

Normolactatemia in hypotensive patients may represent an early stage in disease progression during which peripheral blood pressure is low but organ perfusion is maintained. Early intervention with fluid therapy during this stage may be a reason for the higher survival rates in this group of patients. Type B causes of high lactate production or low lactate clearance may have also contributed to lower survival rate of hyperlactatemic cats in the present study, independently of perfusion status.

In a study<sup>34</sup> involving cats brought to the emergency service of a referral hospital (n = 111), cats with white mucous membranes, abnormal pulses, and hypothermia had a significantly higher initial blood lactate concentration than cats with unremarkable clinical perfusion findings, suggesting a negative correlation between degree of perfusion and blood lactate concentration. However, no significant association was identified in that study<sup>34</sup> between initial blood lactate concentration or change in blood lactate concentration and outcome (survival to discharge vs euthanasia). One potential explanation for this discrepancy in results between that study and the present study is the difference in patient populations. Cats brought to an emergency service represent a highly heterogeneous group in terms of disease severity, whereas most cats in the present study had already undergone triage and admission to the ICU at the time blood lactate concentration had been measured and were therefore more likely to be severely ill and refractory to stabilization efforts. Another notable difference between the 2 studies is that 65% of cats in the previous study<sup>34</sup> were euthanized  $\leq$  12 hours after initial evaluation and none of the cats died naturally. Consequently, those cats may not have had time to develop a detectable increase in blood lactate concentration prior to euthanasia. The fairly small sample size in

both studies may have also contributed to the disparate results, and larger prospective studies focused on specific patient populations are needed.

In the present study, hyperlactatemic cats had a significantly lower mean DBP than normolactatemic cats (70.0 mm Hg vs 79.5 mm Hg, respectively). This finding was consistent with the negative correlation identified between blood lactate concentration and DBP in both dogs and cats<sup>18,34</sup> and supports the hypothesis that low blood pressure and resultant organ hypoperfusion are important causes of anaerobic metabolism and increased lactate production.<sup>20,35</sup> It may also suggest that the cutoff for anaerobic metabolism is closer to a Doppler blood pressure value of 80 mm Hg, although the mortality rate increases in critically ill cats with a DBP < 90 mm Hg.<sup>28</sup> However, because cats in the present study had other potential causes of hyperlactatemia, it remains unknown whether this value is the cutoff for anaerobic metabolism.

In addition to hypotension, 38% of cats in the study reported here had anemia (PCV < 25%) and 5% of cats had severe anemia (PCV < 15%). Oxygenation status was unknown for most cats, but among the 15 cats with a recorded SpO<sub>2</sub>, 4 were mildly hypoxemic (SpO<sub>2</sub> < 95% but > 90%). Unless hypoxemia or anemia is very severe or a patient has concurrent cardiovascular dysfunction, increases in cardiac output can compensate for mild decreases in blood oxygen content so that normal tissue oxygenation is maintained.<sup>5</sup> In the hypotensive, cardiovascularly compromised cats of the present study, anemia or blood oxygenation status may have contributed to hyperlactatemia, although no significant relationship was detected between hyperlactatemia and PCV.

Although the probability of survival to hospital discharge was associated with whether a cat was hyperlactatemic or normolactatemic, mean disease severity, as measured by SPI2, did not differ significantly between the hyperlactatemic and normolactatemic groups in the present study. This lack of significance may have been attributable to the severity of illness of all included cats, as suggested by the overall survival rate of only 15%. Alternatively, SPI2 may not be an accurate indicator of disease severity in the population from which the study cats originated. The feline acute patient physiologic and laboratory evaluation (APPLE) scoring system may be a more accurate measure of disease severity in that population.<sup>36</sup> However, because that scoring system includes blood lactate concentration in score calculation, comparison of disease severity scores between 2 groups with different blood lactate concentrations would not have been possible had that system been used in the present study.

Two studies have involved examination of the effects of stress on blood lactate concentration in healthy cats. In the first,<sup>35</sup> a 5-minute spray bath led to a significant increase in blood lactate and glucose concentrations in 20 healthy cats, and this increase was correlated with the extent of struggling behav-

ior observed. However, in the second study,<sup>30</sup> which more closely replicated the situation of cats admitted to a veterinary ICU, no correlation was identified between blood lactate concentration and struggling scores.<sup>30</sup> In the authors' experience, because of the severity of their illness, most cats admitted to veterinary ICUs do not struggle much when handled. In addition, an IV sample collection line had been placed in all cats in the present study to enable retrieval of blood samples without restraint or occlusion of blood vessels, so it was unlikely that a high blood lactate concentration was attributable to distress, struggling, or vessel occlusion during blood sample collection.

The present study had several limitations. Its retrospective nature had many consequences, including the inability to use serial lactate measurements or lactate clearance data and the lack of standardization of treatment protocols. Additionally, DBP and lactate measurements were recorded concurrently for only 79% of included cats.

Another important limitation was that 30 (77%) cats had a disease or were given a drug with the potential to cause type B hyperlactatemia. In addition, necropsy results were only available for a limited number of cats, so undiagnosed neoplasia could not be ruled out as a cause of hyperlactatemia in most affected cats. The extent to which these diseases and drugs may have contributed to high blood lactate concentrations was impossible to determine. However, no relationship was found between the administration of vasopressors, total parenteral nutrition, or activated charcoal and hyperlactatemia. Furthermore, norepinephrine was by far the most commonly used vasopressor, and because this drug has little  $\beta_2$ -adrenoceptor activity, it causes little change in blood lactate concentration.<sup>37-39</sup> Given that 14 cats received total parenteral nutrition and 13 required vasopressor treatment, it would have been impossible to exclude these cats without drastically decreasing the sample size, which was already small. Moreover, because vasopressor administration is the treatment of choice for animals with persistent hypotension refractory to fluid therapy, it can be challenging to attribute hyperlactatemia when it exists to persistent hypotension, vasopressor therapy, or a combination of both. A prospective study involving serial lactate measurements is needed to determine the exact cause of the hyperlactatemia.

Finally, as is the situation in many retrospective veterinary studies, nonsurvival included cats that were euthanized ( $n = 29$ ) and those that died naturally (4). For most owners, the decision to euthanize an animal involves not only the clinical severity of illness, but also the financial and personal burdens of continuing treatment. Some cats with a high lactate concentration that were euthanized may have survived if treatment had been continued. Similarly, some cats with a poor prognosis may have been euthanized before additional complications developed.

The results of the present study supported the hypothesis that hypotensive, normolactatemic cats

have a better prognosis than hypotensive, hyperlactemic cats. Blood lactate concentration and, probably more importantly, temporal changes in this variable, should be used together with other clinical findings to direct treatment of critically ill hypotensive cats and advise owners of their prognosis. Results of several studies<sup>4,5,12,23</sup> in human medicine suggest that serial lactate measurements are a more accurate means of assessing perfusion status and disease progression in critically ill patients than more commonly used variables, such as physical examination findings, arterial blood pressure, and central venous oxygen saturation. Prospective studies involving consistent protocols are necessary to determine the value of serial blood lactate measurements in critically ill cats and other veterinary patients.

## Acknowledgments

The authors declare that there were no conflicts of interest.

The authors thank Drs. Laura Ateca and Annie Wayne for their technical and intellectual support of this project.

## Footnotes

- Parks Medical Electronics Inc, Aloha, Ore.
- Accutrend Plus lactate analyzer, Heska Corp, Loveland, Colo.
- IBM SPSS Statistics, version 22, IBM Corp, Armonk, NY.
- Plasmalyte A, Abbott Labs, North Chicago, Ill.

## References

- Allen SE, Holm JL. Lactate: physiology and clinical utility. *J Vet Emerg Crit Care* 2008;18:123-132.
- Karagiannis MH, Reniker AN, Kerl ME, et al. Lactate measurement as an indicator of perfusion. *Compend Contin Educ Vet* 2006;28:287-298.
- Pang DS, Boysen S. Lactate in veterinary critical care: pathophysiology and management. *J Am Anim Hosp Assoc* 2007;43:270-279.
- Lagutchnik MS, Ogilvie GK, Wingfield WE, et al. Lactate kinetics in veterinary critical care: a review. *J Vet Emerg Crit Care* 1996;6:81-95.
- Mizock BA, Falk JL. Lactic acidosis in critical illness. *Crit Care Med* 1992;20:80-93.
- Fink MP. Cytopathic hypoxia. Mitochondrial dysfunction as mechanism contributing to organ dysfunction in sepsis. *Crit Care Clin* 2001;17:219-237.
- Gore DC, Jahoor F, Hibbert JM, et al. Lactic acidosis during sepsis is related to increased pyruvate production, not deficits in tissue oxygen availability. *Ann Surg* 1996;224:97-102.
- Hernandez G, Castro R, Romero C, et al. Persistent sepsis-induced hypotension without hyperlactatemia: is it really septic shock? *J Crit Care* 2011;26:435.e9-435.e14.
- Hernandez G, Bruhn A, Castro R, et al. Persistent sepsis-induced hypotension without hyperlactatemia: a distinct clinical and physiological profile within the spectrum of septic shock. *Crit Care Res Pract* 2012;2012:536852.
- Rivers E, Nguyen B, Havstad S, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med* 2001;345:1368-1377.
- Mikkelsen ME, Miltiades AN, Gaijeski DF, et al. Serum lactate is associated with mortality in severe sepsis independent of organ failure and shock. *Crit Care Med* 2009;37:1670-1677.
- Nguyen HB, Rivers EP, Knoblich BP, et al. Early lactate clearance is associated with improved outcome in severe sepsis and septic shock. *Crit Care Med* 2004;32:1637-1642.
- Bernardin G, Pradier C, Tiger F, et al. Blood pressure and arterial lactate level are early indicators of short-term survival in human septic shock. *Intensive Care Med* 1996;22:17-25.
- Cerović O, Golubovic V, Spec-Marn A, et al. Relationship between injury severity and lactate levels in severely injured patients. *Intensive Care Med* 2003;29:1300-1305.
- Meregalli A, Oliveira RP, Friedman G. Occult hypoperfusion is associated with increased mortality in hemodynamically stable, high-risk, surgical patients. *Crit Care* 2004;8:R60-R65.
- Dellinger RP, Levy MM, Rhodes A, et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock, 2012. *Intensive Care Med* 2013;39:165-228.
- Jansen TC, van Bommel J, Schoonderbeek FJ, et al. Early lactate-guided therapy in intensive care unit patients: a multicenter, open-label, randomized controlled trial. *Am J Respir Crit Care Med* 2010;182:752-761.
- Ateca LB, Dombrowski SC, Silverstein DC. Survival analysis of critically ill dogs with hypotension with or without hyperlactatemia: 67 cases (2006-2011). *J Am Vet Med Assoc* 2015;246:100-104.
- Castagnetti C, Pirrone A, Mariella J, et al. Venous blood lactate evaluation in equine neonatal intensive care. *Theriogenology* 2010;73:343-357.
- Corley KT, Donaldson LL, Furr MO. Arterial lactate concentration, hospital survival, sepsis and SIRS in critically ill neonatal foals. *Equine Vet J* 2005;37:53-59.
- de Papp E, Drobatz KJ, Hughes D. Plasma lactate concentration as a predictor of gastric necrosis and survival among dogs with gastric dilatation-volvulus: 102 cases (1995-1998). *J Am Vet Med Assoc* 1999;215:49-52.
- Holahan ML, Brown AJ, Drobatz KJ. The association of blood lactate concentration with outcome in dogs with idiopathic immune-mediated hemolytic anemia: 173 cases (2003-2006). *J Vet Emerg Crit Care (San Antonio)* 2010;20:413-420.
- Lagutchnik MS, Ogilvie GK, Hackett TB, et al. Increased lactate concentrations in ill and injured dogs. *J Vet Emerg Crit Care* 1998;8:117-127.
- Nel M, Lobetti RG, Keller N, et al. Prognostic value of blood lactate, blood glucose, and hematocrit in canine babesiosis. *J Vet Intern Med* 2004;18:471-476.
- Stevenson CK, Kidney BA, Duke T, et al. Serial blood lactate concentrations in systemically ill dogs. *Vet Clin Pathol* 2007;36:234-239.
- Tennent-Brown BS, Wilkins PA, Lindborg S, et al. Sequential plasma lactate concentrations as prognostic indicators in adult equine emergencies. *J Vet Intern Med* 2010;24:198-205.
- Zacher LA, Berg J, Shaw SP, et al. Association between outcome and changes in plasma lactate concentration during presurgical treatment in dogs with gastric dilatation-volvulus: 64 cases (2002-2008). *J Am Vet Med Assoc* 2010;236:892-897.
- Silverstein DC, Wininger FA, Shofer FS, et al. Relationship between Doppler blood pressure and survival or response to treatment in critically ill cats: 83 cases (2003-2004). *J Am Vet Med Assoc* 2008;232:893-897.
- Christopher MM, O'Neill S. Effect of specimen collection and storage on blood glucose and lactate concentrations in healthy, hyperthyroid and diabetic cats. *Vet Clin Pathol* 2000;29:22-28.
- Redavid LA, Sharp CR, Mitchell MA, et al. Plasma lactate measurements in healthy cats. *J Vet Emerg Crit Care (San Antonio)* 2012;22:580-587.
- King LG, Wohl JS, Manning AM, et al. Evaluation of the survival prediction index as a model of risk stratification for clinical research in dogs admitted to intensive care units at four locations. *Am J Vet Res* 2001;62:948-954.
- Hopper K, Powell LL. Basics of mechanical ventilation for dogs and cats. *Vet Clin North Am Small Anim Pract* 2013;43:955-969.
- Ramsey I, Gould S. Feline anaemia 1. Clinical signs and investigation. *In Pract* 1999;21:411-415.
- Reineke EL, Rees C, Drobatz KJ. Association of blood lactate concentration with physical perfusion variables, blood pressure, and outcome for cats treated at an emergency service. *J Am Vet Med Assoc* 2015;247:79-84.
- Rand JS, Kinnaird E, Baglioni A, et al. Acute stress hyper-

- glycemia in cats is associated with struggling and increased concentrations of lactate and norepinephrine. *J Vet Intern Med* 2002;16:123-132.
36. Hayes G, Mathews K, Doig G, et al. The feline acute patient physiologic and laboratory evaluation (feline APPLE) score: a severity of illness stratification system for hospitalized cats. *J Vet Intern Med* 2011;25:26-38.
  37. Myburgh JA, Higgins A, Jovanovska A, et al. A comparison of epinephrine and norepinephrine in critically ill patients. *Intensive Care Med* 2008;34:2226-2234.
  38. Masoli M, Walley KR. Lactic acidosis in sepsis: it's not all anaerobic. Implications for diagnosis and management. *Chest* 2015;148:843-844.
  39. Totaro RJ, Raper RF. Epinephrine-induced lactic acidosis following cardiopulmonary bypass. *Crit Care Med* 1997;25:1693-1699.



#### From this month's AJVR

### Description and comparison of excretory urography performed during radiography and computed tomography for evaluation of the urinary system in healthy New Zealand White rabbits (*Oryctolagus cuniculus*)

Laura Vilalta et al

#### OBJECTIVE

To evaluate the usefulness of excretory urography performed during radiography (REU) and CT (CTEU) in healthy rabbits, determine timings of urogram phases, and compare sensitivities of REU and CTEU for detection of these phases.

#### ANIMALS

13 New Zealand White rabbits (*Oryctolagus cuniculus*).

#### PROCEDURES

Rabbits were screened for signs of systemic and urinary tract disease. An REU examination of each was performed, followed  $\geq 5$  days later by a CTEU examination. Contrast images from each modality were evaluated for quality of opacification and intervals between initiation of contrast medium administration and detection of various urogram phases.

#### RESULTS

Excretory urograms of excellent diagnostic quality were achieved with both imaging modalities. For all rabbits, the nephrographic phase of the urogram appeared in the first postcontrast REU image (obtained between 34 and 40 seconds after initiation of contrast medium administration) and at a median interval of 20 seconds in CTEU images. The pyelographic phase began at a median interval of 1.63 minutes with both imaging modalities. Contrast medium was visible within the urinary bladder at a median interval of 2.20 minutes. Median interval to the point at which the nephrogram and pyelogram were no longer visible in REU images was 8 hours and 2.67 hours, respectively. The CTEU technique was better than the REU technique for evaluating renal parenchyma.

#### CONCLUSIONS AND CLINICAL RELEVANCE

Findings suggested that REU and, particularly, CTEU may be valuable tools for the diagnosis of renal and urinary tract disease in rabbits; however, additional evaluation in diseased rabbits is required. (*Am J Vet Res* 2017;78:472-481)



See the midmonth issues of *JAVMA* for the expanded table of contents for the *AJVR* or log on to [avmajournals.avma.org](http://avmajournals.avma.org) for access to all the abstracts.