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Blood and peritoneal lactate in equine colic: application in emergency care and construction of a decision tree

[*Lactato sanguíneo e peritoneal na cólica equina: aplicação no atendimento de emergência e construção de uma árvore de decisão*]

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ABSTRACT

The objective of this retrospective study was to determine whether blood lactate (BL) and peritoneal lactate (PL) are correlated with heart rate, BL-to-PL ratio and dehydration severity in horses with colic that died within or survived beyond 24 hours of hospital admission, and to construct decision trees aimed at predicting short-term mortality using machine learning algorithms. Medical records (n = 339) from the database of the Veterinary Hospital of the School of Veterinary Medicine and Animal Science, University of São Paulo (FMVZ-USP) of horses admitted with colic were retrieved. Correlations between variables of interest were investigated using the Pearson's or the Spearman's correlation coefficient. The level of significance was set at 5% ($p<0.05$). Algorithms used belong to the WEKA environment and were compared using the paired t test ($p<0.05$). Peritoneal lactate values were strongly and negatively ($p<0.05$) correlated with BL:PL ratio, and moderately and positively ($p<0.05$) correlated with percentage of dehydration. Two decision trees with more than 80% accuracy in predicting mortality were constructed and can be used to inform clinicians about the probability of survival beyond the first 24 hours of hospitalization.

Keywords: lactate metabolism, equine colic, critical care

RESUMO

O objetivo deste estudo retrospectivo é determinar se o lactato sanguíneo (LB) e o lactato peritoneal (PL) estão correlacionados com a frequência cardíaca, a relação BL/PL e a gravidade da desidratação em cavalos com cólica que morreram ou sobreviveram 24 horas após a admissão hospitalar, e construir árvores de decisão destinadas a prever a mortalidade a curto prazo utilizando-se algoritmos de aprendizagem automática. Foram recuperados prontuários (n = 339) do banco de dados do Hospital Veterinário da Faculdade de Medicina Veterinária e Zootecnia da Universidade de São Paulo (FMVZ-USP) de cavalos internados com cólica. As correlações entre variáveis de interesse foram investigadas por meio do coeficiente de correlação de Pearson ou de Spearman. O nível de significância foi estabelecido em 5% (P<0,05). Os algoritmos utilizados pertencem ao ambiente WEKA e foram comparados pelo teste t pareado (P<0,05). Os valores de lactato peritoneal correlacionaram-se forte e negativamente (P<0,05) com a relação BL:PL, e moderada e positivamente (P< 0,05) com o percentual de desidratação. Duas árvores de decisão com mais de 80% de precisão na previsão de mortalidade foram construídas e podem ser usadas para informar os clínicos sobre a probabilidade de sobrevivência além das primeiras 24 horas de hospitalização.

Palavras-chave: metabolismo do lactato, cólica equina, cuidados intensivos

INTRODUCTION

Blood (BL) and peritoneal (PL) lactate are routinely measured in horses with colic. These laboratory parameters reflect tissue hypoperfusion and are often used to determine disease severity. Combined with other clinical variables, BL and PL may help distinguish between clinical and surgical cases (Yamout *et al.*, 2011). In horses with colic, elevated BL and PL concentrations can be attributed to several factors, such as dehydration, hypovolemic shock, endotoxemia and insufficient oxygen delivery to

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the gastrointestinal tract due to ischemia. Intestinal perfusion may also be negatively affected by increased intra-abdominal and intraluminal pressure (Dabareiner *et al*., 2001; Neil, 2008). Plasma lactate is thought to be a marker of mesenteric ischemia in humans and animals. In dogs with gastric dilatation-volvulus, plasma lactate levels are closely related to gastric necrosis and often used as a prognostic indicator (Zacher *et al*., 2010).

In healthy horses, BL is higher than PL (i.e., BL:PL is greater than 1). Poor intestinal perfusion and intestinal ischemia induce anaerobic glycolysis, causing BL and PL to rise. However, this does not happen simultaneously in both compartments. In horses with mild visceral ischemia, PL remains lower than BL at first (Delesalle *et al*., 2007; Tennent-Brown *et al*., 2007). Over time, as ischemia progresses, PL starts to rise faster than BL. At a later stage, when the patient becomes hemodynamically unstable and endotoxemia and hypovolemic shock occur, BL quickly rises and reaches similar levels to PL (Neil, 2008).

Horses with colic requiring surgical intervention and intestinal resection tend to have higher PL levels. Hence, this parameter can be used to distinguish between strangulating and non-strangulating lesions, whereas BL values are more representative of the cardiovascular status of the patient (Shearer *et al*., 2018).

Hemodynamic changes induced by hypoperfusion and/or endotoxemia are common in horses with colic and are reflected in BL and PL values. This retrospective study was designed to determine whether BL and LP levels measured at the time of hospital admission were correlated with heart rate (HR), percentage of dehydration and BL:PL ratio in patients who died within or survived beyond 24 hours of admission.

For a more detailed analysis, data were also analyzed using data mining algorithms (J48, Hoeffding Tree Random Forest, Random Tree and REPTree). Algorithms were used to build decision trees aimed at assisting clinicians in the initial assessment of horses with colic, to predict mortality within 24 hours of hospital admission.

Classification algorithms belong to the realm of Artificial Intelligence, a method that allows computer programs to use data inputs to predict outcomes (Sugumaran *et al*., 2007). Two decision tree models were developed in this study. Models were constructed using the J48 and REPTree algorithms. These algorithms were able to select the best variables to support clinicians in the initial evaluation of horses with colic out of a wide range of existing data.

MATERIALS AND METHODS

This is a retrospective study based on data extracted from medical records of equine colic patients seen at the Veterinary Hospital of FMVZ-USP between October 2007 and December 2021.

The following pieces of data were extracted: HR, BL, PL, BL:PL ratio, percentage of dehydration, and death within or survival beyond 24 hours of hospital admission (survivors and non-survivors respectively).

Data were analyzed and tested for normality of residuals and homogeneity of variance using commercial software (SAS System for Windows (SAS Institute Inc., NC, E.U.A.); SAS Guided Data Analysis). Variables that did not meet these assumptions were log transformed (log base 10). Non-parametric analysis was used whenever log-transformation was not sufficient. Groups were analyzed using the Student's t test. Variables were expressed as mean and standard deviation. The level of significance was set at 5% ($p < 0.05$). Correlations between variables were investigated using the Pearson's or the Spearman's correlation coefficient (parametric and non-parametric data respectively). The level of significance was set at 5% ($p < 0.05$). Correlation coefficients less than 0.3, between 0.3 and 0.6 and greater than 0.6 indicated weak, moderate, and strong correlation respectively.

The performance of machine learning algorithms (Hoeffding Tree, J48, Random Forest, Random Tree and REPTree) was assessed using the following metrics: number of correctly classified instances, misclassified instances, kappa coefficient (agreement of predictions), Mean Absolute Error (average magnitude of errors in a set of predictions), RMSE (differences between predicted actual values), Root Relative Squared Error (takes the total squared error and normalizes it by dividing by the total squared error of the mean of the actual values), and Relative Absolute Error (takes the total absolute error and normalizes it by dividing by the total absolute error of the simple predictor).

Other metrics evaluated were True Positive (TP) and False Positive (FP) rates (number of outcomes within a certain class, that actually belong or do not belong to that class respectively), Precision (positive predictive value), Recall (fraction of true positives among predicted positives), F-measure (weighted harmonic mean of precision), and AUROC (comparison between predicted and actual outcomes to assess the discriminating ability of the prognostic model).

Selected algorithms belong to the WEKA machine learning environment (Waikato Environment of Knowledge Analysis (WEKA). Version 3.8.6. © 1999 – 2022. The University of Waikato, Hamilton, New Zealand.) and were elected due to their ability to handle numerical and nominal values simultaneously (Frank *et al*., 2016). Algorithms were configured using default settings. Algorithm performance was evaluated using 10-fold cross-validation and the paired t test, with $p < 0.05$.

RESULTS

Of 339 medical records analyzed, only those including blood and/or peritoneal lactate measurements were used. The final sample comprised 198 records. Thirty-five horses (17.67%) died within and 154 (77.77%) survived beyond 24 hours of admission. Diagnoses attributed to survivors and non-survivors are listed in Table 1 part 1 and Table 1 part 2). Survival data were missing in nine medical records (4.54%). Therefore, data from 189 patients were used in statistical analysis.

Table 1. Diagnoses assigned to horses that died or survived the first 24 hours of hospitalization (non-survivors and survivors respectively). Part 1

Condition	Non-survivors	Survivors
Incarcerated inguinal hernia	1	5
Post-ovulation hemoperitoneum	-	1
Mesodiverticular band entrapment	1	-
Atropine poisoning	-	1
Amitraz poisoning	-	1
Jejunal abscess	-	1
Pelvic flexure adhesion	-	1
Mesenteric root abscess	1	-
Sand impaction	-	1
Large colon or cecal tympanism	-	2
Large colon torsion	-	2
Colitis	-	3
Enterolithiasis	1	8
Gastric dilatation	-	5
Gastritis/stomach ulcer	-	7
Proximal enteritis	-	7
Nephrosplenic entrapment	-	5
Idiopathic episode of colic	-	8
Mesenteric tear with small colon entrapment	1	-
Mesenteric volvulus	1	-

Table 1. Diagnoses assigned to horses that died or survived the first 24 hours of hospitalization (non-survivors and survivors respectively). Part 2

Condition	Non-survivors	Survivors
Pedunculated lipoma	1	-
Liver lobe torsion	1	-
Intussusception	2	2
Small intestinal impaction	2	10
Large colon displacement	2	46
Enterocolitis	2	-
Small intestinal volvulus	2	1
Epiploic foramen entrapment	3	1
Mesenteric tear with small bowel entrapment	3	2
Large colon impaction	4	35
Large colon volvulus	4	-
Peritonitis	4	2
Intestinal or gastric rupture	5	-

Variables of interest measured in survivors and non-survivors are shown in Table 2. Correlations between variables are shown in Tables 3 and 4. Blood lactate-to-peritoneal lactate ratio was the only variable that did not differ significantly ($p = 0.3404$) between groups (Table 2).

Peritoneal lactate values were strongly and negatively correlated with BL:PL ratio, and moderately and positively correlated with percentage of dehydration in both groups. In horses who survived the first 24 hours of hospitalization, BL and PL lactate were positively and strongly correlated with BL:PL ratio and HR, while percentage of dehydration was positively and moderately correlated with HR and negatively and strongly correlated with BL:PL ratio (Table 3 and Table 4).

Performance analysis of data mining algorithms revealed a similar ability to predict the probability of mortality within 24 hours of admission (Table 5).

Table 2. Variables of interest measured in horses that died or survived the first 24 hours of Hospitalization (non-survivors and survivors respectively). Correlation coefficients less than 0.3, between 0.3 and 0.6 and greater than 0.6 indicated weak, moderate and strong correlation respectively

Variable	Survivors	Non-survivors	P-value
Blood lactate (mmol/L)	4.07 ± 2.88	6.78 ± 4.89	0.0089
Peritoneal lactate (mmol/L)	5.31 ± 2.88	11.44 ± 6.93	<.0001
BL:PL	1.03 ± 0.55	1.11 ± 1.26	0.3404
Dehydration (%)	4.95 ± 1.91	7.02 ± 1.70	<.0001
Heart rate	61.56 ± 18.58	77.31 ± 23.42	<.0001

Abbreviation: BL:PL = blood lactate-to-peritoneal lactate ratio

Table 3. Correlations between selected clinical variables in horses that survived the first 24 hours of hospitalization. Table 2. Variables of interest measured in horses that died or survived the first 24 hours of Hospitalization (non-survivors and survivors respectively). Correlation coefficients less than 0.3, between 0.3 and 0.6 and greater than 0.6 indicated weak, moderate and strong correlation respectively

Variable	Blood lactate	Peritoneal lactate	BL:PL	Dehydration	Heart rate
Blood lactate	-	r = 0.69 p <.0001	r = 0.02 p = 0,8571	r = 0.20 p = 0.067	r = 0.36 p= 0.0012
Peritoneal lactate	-	-	r = -0.69 p <.0001	r = 0.37 p <.0001	r = 0.40 p < .0001
BL:PL	-	-	-	r = -0.60 p < .0001	r = 0.44 p < 0.0020
Dehydration	-	-	-	-	R = 0.36 p < .0001

Abbreviations: BL:PL = blood lactate-to-peritoneal lactate ratio.

Table 4. Correlations between selected clinical variables in horses that did not survive the first 24 hours of hospitalization. Table 2. Variables of interest measured in horses that died or survived the first 24 hours of Hospitalization (non-survivors and survivors respectively). Correlation coefficients less than 0.3, between 0.3 and 0.6 and greater than 0.6 indicated weak, moderate, and strong correlation respectively

Variable	Blood lactate	Peritoneal lactate	BL:PL	Dehydration	Heart rate
Blood lactate	-	r = 0.29 p = 0.2534	r = 0.25 p = 0.2534	r = 0.35 p = 0.1378	r = 0.01 p = 0.9532
Peritoneal lactate	-	-	r = -0.71 p = 0.0012	r = 0.55 p = 0.0010	r = 0.16 p = 0.34
BL:PL	-	-	-	r = -0.08 p = 0.7341	r = 0.31 p = 0.2457
Dehydration	-	-	-	-	r = 0.16 p = 0.3752

Abbreviation: BL:PL = blood lactate-to-peritoneal lactate ratio

Table 5. Performance analysis of data mining algorithms. J48, Random Forest and REPTree perform better

J48	Hoeffding Tree	Random Forest	Random Tree	REPTree
83.16	79.73	83.76	76.25	83.39
(v/ /*)	(0/1/0)	(0/1/0)	(0/1/0)	(0/1/0)

Decision trees could not be constructed using the Random Forest or the Hoeffding Tree algorithms in this paper. The decision tree constructed using the Random algorithm was difficult to understand and interpret.

The decision tree constructed using the REPTree algorithm (Fig. 1) had only two nodes (peritoneal lactate and percentage of dehydration) and was more straightforward relative to the tree obtained using the J48 algorithm. The REPTree algorithm starts with the PL value. Values lower than 12.05mmol/L (108.55mg/dL) indicate survival. Whenever PL values exceed this threshold, the tree leads the clinician to the next component (percentage of dehydration). Dehydration less than 6.5% indicates survival, while higher dehydration percentages indicate death. The REPTree algorithm was able to correctly analyze 83.59% of instances. The remaining instances (16.41%) were misclassified.

The decision tree derived from the J48 algorithm is shown in Fig. 2. This tree was constructed using HR, percentage of dehydration, and BL and PL values. The proportion of correctly classified and misclassified instances was similar to the REPTree algorithm (83.59% and 16.41% respectively).

Other metrics used to assess algorithm performance in this study are given below (Table 6 and Table 7).

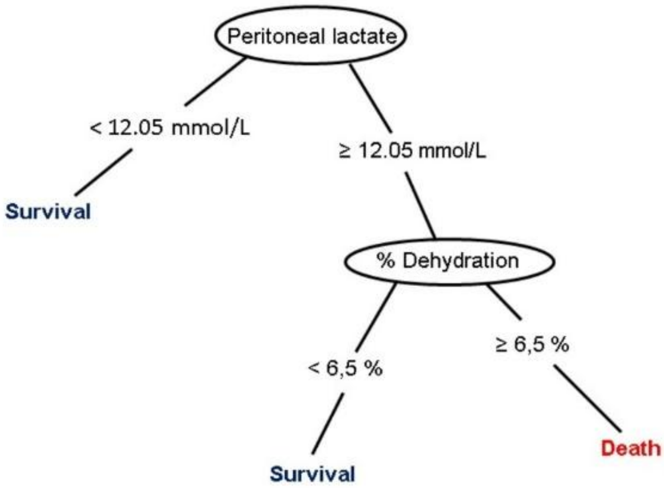

Figure 1. Decision tree constructed using the REPTree algorithm. After data mining from the data collected in the medical records, the respective algorithm was able to identify the parameters related to the patient's death or discharge. It is worth remembering that the parameters collected were heart rate, blood lactate (BL), peritoneal lactate (PL) and BL:PL ratio.

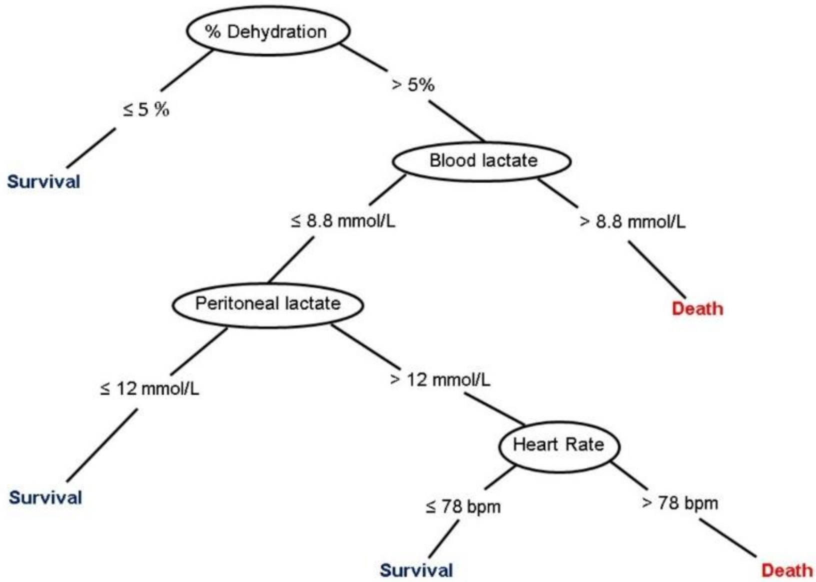

Figure 2. Decision tree constructed using the J48 algorithm. After data mining from the data collected in the medical records, the respective algorithm was able to identify the parameters related to the patient's death or discharge. It is worth remembering that the parameters collected were heart rate, blood lactate (BL), peritoneal lactate (PL) and BL:PL ratio.

Table 6. Metrics for evaluating data mining algorithms according to the occurrence of survival or death. Attention to AUROC (comparison between predicted and actual outcomes to assess the discriminating ability of the prognostic model). Note that J48 and REPTree Algorithms used to construct the decision trees in this work present AROUC indicative of good performance

Algorithm	Class	TP Rate	FP Rate	Precision	Recall	F-Measure	AUROC
J48	Death	0.257	0.032	0.643	0.257	0.367	0.760
J48	Survival	0.968	0.743	0.851	0.968	0.906	0.706
Hoeffding Tree	Death	0.257	0.071	0.450	0.257	0.327	0.665
Hoeffding Tree	Survival	0.929	0.743	0.846	0.929	0.885	0.630
Random Forest	Death	0.286	0.039	0.625	0.286	0.392	0.789
Random Forest	Survival	0.961	0.714	0.855	0.961	0.905	0.713
Random Tree	Death	0.314	0,104	0.407	0.314	0.355	0.680
Random Tree	Survival	0.896	0.686	0.852	0.896	0.873	0.641
REPTree	Death	0.286	0.039	0.625	0.286	0.392	0.714
REPTree	Survival	0.961	0.714	0.855	0.961	0.905	0.682

Abbreviation: AUROC = Area Under Receiver Operating Characteristic Curve.

Table 7. Metrics for evaluating data mining algorithms. Pay attention to the percentage of instances classified as correctly or incorrectly by the J48 and REPTree algorithms

Algorithm	Correctly Classified Instances	Incorrectly Classified Instances	Kappa statistic	MAE	RMSE	RAE	RRSE
J48	158 (83.59%)	31 (16.40%)	0.2925	0.2355	0.3484	77.42 %	89.64 %
Hoeffding Tree	152 (80.42 %)	37 (19.57%)	0.2226	0.2741	0.4046	90.11 %	104.10 %
Random Forest	158 (83.59 %)	31 (16.40 %)	0.3122	0.2158	0.3488	70.93 %	89.74 %
Random Tree	149 (78.83%)	40 (21.16 %)	0.2308	0.2329	0.4224	76.56 %	108.68 %
REPTree	158 (83.59 %)	31 (16.40 %)	0.3122	0.2516	0.3636	82.69 %	93.55 %

Abbreviations: MAE = Mean Absolute Error; RMSE = Root Mean Squared Error; RAE = Relative Absolute Error; RRSE = Root Relative Squared Error

In the tree constructed using the J48 algorithm, percentage of dehydration is the root node. Dehydration less than or equal to 5% indicates survival, while dehydration percentages higher than 5% lead the clinician to BL measurements. Blood lactate values greater than 8.8mmol/L (79.27mg/dL) are associated with an increased risk of mortality. Whenever BL values are equal to or lower than 8.8mmol/L (79.29mg/dL), the next step is to check PL values. Peritoneal lactate values higher than 12mmol/L (108.10mg/dL) lead the clinician to heart rate measurements. Heart rate higher than 78 bpm is also a predictor of mortality (i.e., horses with lower HR are more likely to survive). Likewise, horses with PL values less than or equal to 12 mmol/L (108.10 mg/dL) have a greater chance of survival.

DISCUSSION

In this study, BL:PL ratio was the only variable that did not differ significantly between groups. Non-survivors had higher BL, PL, percentage of dehydration and HR compared to survivors. These findings were not unexpected and reflect disease severity in some of the horses that died within 24 hours of admission. These patients were more likely to develop septic shock and consequent hemodynamic changes, such as increased lactate levels and HR[6]. In one case, the horse was diagnosed with ceco-colic intussusception and euthanized intraoperatively 4 hours after admission. Postmortem examination revealed a dark cecum with swollen mucosa. Endotoxin-induced bacterial translocation, a potential cause of septic shock, was suspected (Vinther *et al*., 2015).

In cases of sepsis, hyperlactatemia and lactic acidosis may occur for different reasons (Tennent-Brown *et al*., 2014). Approximately 80% of the glucose metabolized by leukocytes is thought to be converted to lactate. Higher *ex vivo* lactate production by lipopolysaccharide-stimulated leukocytes isolated from human Intensive Care Unit patients relative to healthy individuals has also been reported (Haji-Michael *et al*., 1999).

This study revealed strong negative correlations between PL values and BL:PL ratio, and moderate positive correlations between PL values and percentage of dehydration in both groups (i.e., the higher the PL level, the lower BL:PL ratio and the more severe the dehydration). It has been suggested that peritoneal lactate may be a better indicator of intestinal ischemia than BL (Neil, 2008). Intestinal necrosis is closely related to increased PL levels but poorly related to increased BL levels. The fact that BL may be impacted by other pathological conditions, such as hemoconcentration and endotoxemia, may explain this discrepancy.

Interestingly, both groups in this study included horses admitted with strangulating and non-strangulating lesions, such as large colon and ileal impactions, which do not compromise intestinal perfusion in the short term. Hence, increased PL concentrations cannot be explained by ischemia alone. Prior studies in horses with colic failed to reveal positive correlations between PL levels and length of ischemic bowel resected, suggesting that ischemic bowel is not the only source of lactate production Delesalle *et al*., 2007; Latson *et al*., 2015; Shearer *et al*., 2018).

Distention proximal to the site of intestinal obstruction increases intraluminal pressure and reduces blood flow (Snyder *et al*., 1990; Dabareiner *et al*., 2001), inducing a shift to anaerobic metabolism due to insufficient oxygen delivery to affected segments. In these cases, impaired venous drainage, and increased lactate production cause lactate to accumulate and diffuse into the peritoneal cavity. This hypothesis is supported by findings of different studies. Critical levels of intraluminal pressure have been shown to compromise tissue perfusion (Moore *et al*., 1977; Dabareiner *et al*., 1993, 2001). Increasing PL levels from hospital admission to a second clinical assessment 1 to 6 hours later have been reported in cases of ileal and large colon impaction (Peloso and Cohen, 2012).

Enhanced endotoxin absorption due to impaired intestinal mucosal barrier function further compromises blood flow to the gastrointestinal tract, leading to progressive lactate accumulation (Moore and Barton, 2003). These mechanisms may explain elevated PL levels in horses with non-strangulating injuries (Shearer *et al*., 2018). Disease progression was not described in medical records in our study. Information on time spans from initial clinical manifestations to referral would contribute to our understanding of potential associations between intestinal abnormalities and increased PL values.

Dehydration severity varies according to the cause and duration of colic episodes. Hence the positive correlation between PL values and percentage of dehydration. Packed cell volume (PCV) can be easily measured and is widely used to estimate the percentage of dehydration. As in other studies, increased PCV at the time of admission was associated with mortality in horses with large colon volvulus (Van Hoogmoed *et al*., 2000; Kelleher *et al*., 2013; Hackett *et al*., 2015).

Packed cell volume reflects the degree of systemic compromise in cases of colic and can be used as a marker of systemic inflammatory response syndrome, pain and increased sympathetic tone. As PCV increases, tissue perfusion decreases and cells are starved of oxygen, leading to a shift from aerobic to anaerobic metabolism and lactic acidosis (Latson *et al*., 2015). Associations between high PCV (> 45%) and poor prognosis have been reported in horses (Proudman *et al*., 2002, 2006).

In this study, PCV in particular, but also capillary refill time and the dryness of the oral mucosa were used to estimate the percentage of dehydration. Thirty-one horses (15.65%) with strangulating or non-strangulating lesions were severely dehydrated (more than 8%). In both cases, PL tends to go up in response to impaired intestinal perfusion. In some types of colic, intestinal secretion increases while absorption is reduced. Affected patients may also lose fluids and electrolytes through sweat and urine, which, combined with lower water intake, leads to dehydration (Schusser *et al*., 2007). Correlations between LP and percentage of dehydration in both groups in this study were therefore unexpected.

This analysis also revealed strong positive correlations between BL and PL, along with moderate positive correlations between BL:PL ratio and HR, and percentage of dehydration and HR in horses that survived the first 24 hours of hospitalization. In contrast, correlations between BL:PL ratio and percentage of dehydration were strong and negative.

Once released into the abdominal cavity, lactate is rapidly absorbed by the peritoneum and may cause BL concentrations to rise (Van den Boom *et al*., 2010). This may explain correlations between BL and probability of survival. The fact that BL concentrations reflect lactate production by other organs (primarily muscle tissues) and severity of dehydration may account for the weakness of these correlation relative to PL.

Positive correlations between BL and PL in this study may be explained by compromised bowel integrity. Peritoneal lactate is thought to increase in response to intestinal ischemia. Lactate absorption by the peritoneum, along with other systemic changes, then causes BL to rise. Blood lactate levels reflect the balance between lactate production and clearance. Accumulated lactate diffuses out of cells and is transported to other tissues to be used as fuel (Neil, 2008).

In this study, BL:PL ratio and percentage of dehydration were positively correlated with HR in horses who survived the first 24 hours of hospitalization (i.e., the higher the BL:PL ratio and the percentage of dehydration, the higher the RH). Horses with colic are often hypovolemic and must rely on compensatory mechanisms to maintain cardiac output and tissue perfusion. In these patients, BL levels tend to rise in response to poor tissue perfusion. Hence the positive correlation between BL:PL ratio and percentage of dehydration.

Endotoxemia is another common complication of acute abdomen in adult horses, with significant impacts on the cardiovascular status of the patient (Grulke *et al*., 2001). Bacterial endotoxins induce the release of several pro-inflammatory mediators with direct or indirect negative effects on systemic vascular resistance and cardiac output (Corley, 2004; Boyd and Walley, 2009). Sympathetic stimulation, release of endogenous substances such as catecholamines and vasopressin, and activation of the renin-angiotensin-aldosterone system also trigger compensatory vasoconstriction, causing HR to increase (Borde *et al*., 2011).

Appropriate interpretation of persistent tachycardia in the context of equine colic requires a comprehensive understanding of cardiac function and its relationships with other body organs and systems. Tachycardia is a physiological response to hypovolemia, fever, pain, and anemia. However, persistent tachycardia after intravascular volume and core temperature normalization, pain control or correction of anemia is pathological and potentially harmful (McConachie, 2015).

Positive correlations in this study were non-significant in horses that died within 24 hours of admission. A plausible explanation for this finding is that, in severe cases of colic, the hyperdynamic status of the patient only allows for a transient increase in cardiac output. In these cases, cardiac output and systemic vascular resistance decrease and progressive hypotension develops despite persistent tachycardia. Lack of vascular response to catecholamines and myocardial depression then lead to hypodynamic shock (Rudiger and Singer, 2007; Casserley *et al*., 2009). Therefore, even when dehydration is severe and BL values exceed the upper limit of the reference range, HR may not increase due to impaired myocardial function and hypodynamic shock (Chiew *et al*., 2019).

Interestingly, negative correlations between BL:PL ratio and percentage of dehydration were significant in survivors and non-significant in non-survivors. Isolated analysis of percentage of dehydration as a precursor of hypovolemia and resultant hypoperfusion revealed that dehydration alone cannot account for increased BL values and higher BL:PL ratio.

In the decision tree constructed using the J48 algorithm, percentage of dehydration is the starting point for estimating the probability of survival. In cases of moderate to severe dehydration (> 5%), BL values should be checked. Blood lactate values higher than 8.8 mmol/L (79.27 mg/dL) indicate a high risk of mortality. This threshold value is supported by clinical observation. Blood lactate concentrations above 6 to 8 mmol/L (54.05 and 79.27 mg/dL respectively) are associated with considerably poorer prognosis and horses with BL concentrations higher than 8 to 10 mmol/L (79.27 mg/dL and 90.09 mg/dL respectively) are unlikely to survive (Vinther *et al*., 2015).

In patients with BL values less than or equal to 8.8 mmol/L (79.27 mg/dL), LP should be checked. Whenever PL lactate values exceed 12 mmol/L (108.10 mg/dL), the next step is to check the HR. Heart rate higher than 78 bpm indicates mortality, while HR lower than or equal to 78 bpm indicates survival. Peritoneal lactate values less than 12 mmol/L (108.10 mg/dL) also indicate survival. Horses with BL levels higher than 16 mmol/L (144.14 mg/dL) have lower chances of survival (Neil, 2008). Associations between PL values higher than 9.4 mmol/L (84.68 mg/dL) and mortality have been reported (Van den Boom *et al*., 2010).

Peritoneal lactate values are thought to reflect the degree of intestinal ischemia. Peritoneal lactate and HR are directly related and increase in response to hemodynamic changes resulting from dehydration and endotoxemia.

As with the J48 algorithm, the decision tree constructed using the REPTree algorithm yielded threshold values of 12.05mmol/L (108.55 mg/dL) and 6.5% for PL and percentage of dehydration respectively. This tree comprises only two variables. However, it was considered equally accurate and may expedite patient assessment.

Decision trees constructed in this study achieved an accuracy score of 83.59% and enabled consistent interpretation of clinical data. However, outcomes could be improved by equivalence between the number of survivors and non-survivors and severe and less severe cases. To accurately determine which variables are related to survival and/or death, algorithms must be able to identify characteristics of both survivors and non-survivors. Large differences between these groups will be reflected in outcomes. Of the 198 horses in this sample, 35 (17.67%) died and 154 (77.77%) survived the first 24 hours of hospitalization. Findings of this study reflect this discrepancy.

This analysis revealed AUROCs of 0.760 and 0.714 for death within 24 hours of admission, and 0.706 and 0.682 for survival beyond this time span (J48 and REPTree respectively). The fact that AUROCs were smaller than 1 but above the lower limit of 0.5 suggests correlations between variables of interest and survival did not result from random chance. However, the ability of algorithms to predict outcomes based on certain metrics was limited.

Root Mean Squared Errors of 0.3484 and 0.3636, and kappa values of 0.2925 and 0.3122 (J48 and REPTree respectively) are in keeping with a prior study and indicate less than excellent performance. In that study, the perception multilayer classifier was evaluated using 10-folds cross validation, and RMSE and kappa values of 0.2646 and 0.04 have been reported (Kumar and Sahoo, 2012). Ideally, minimum RMSE values of 0.15 should be obtained and kappa should be close to 1.

The smaller the RMSE value, the more accurate the model. Root-mean-square error values obtained in this study suggest the accuracy of decision trees constructed can be improved. In cross-validation, the database is divided into a training and a test set. In this analysis, Kappa values indicated low agreement between predicted and actual instances when test and training subsets were paired. Although Kappa values higher than zero indicate greater agreement than the expected chance agreement, Kappa values were lower than the cut-offs for moderate (0.40 to 0.49) or excellent (1) agreement. Data collection should be refined by inclusion of prospective data and a larger number of patients for construction of decision trees with close to 100% accuracy in predicting short term survival.

CONCLUSIONS

Findings of this study suggest selected clinical variables can be used to predict mortality within 24 hours of hospitalization. Decision trees constructed using the J48 and the REPTree algorithms were not perfect models. Still, they may assist clinicians in emergency care of horses with colic. The tree constructed with the J48 algorithm includes more nodes and allows for a more comprehensive clinical interpretation. That tree revealed correlations between HR, BL, PL, and percentage of dehydration, as intended this study. The tree derived from the REPTree algorithm is more straightforward and user-friendly, and has good predictive ability. Combined analysis of BL, PL and other variables contributes to appropriate patient assessment in emergency cases of colic and may help clinicians to predict imminent death or survival. Equine colic is a potentially fatal multifactorial disease and comprehensive analysis of clinical parameters is crucial for accurate diagnosis and treatment selection. Decision trees are valuable tools for decision making and risk analysis in clinical practice. Optimal decision trees should be able to predict mortality with close to 100% accuracy. Future studies with a larger set of prospectively collected data are warranted to refine outcomes and improve the predictive ability of algorithms presented in this study.

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REFERENCES

BORDE, L.; AMORY, H.; LEROUX, A.A. *et al*. Echocardiographic assessment of left ventricular systolic function in colic horses. *J. Equine Vet. Sci.*, v.31, p.481-487, 2011.

BOYD, J.H.; WALLEY, K.R. The role of echocardiography in hemodynamic monitoring. *Curr. Opin. Crit. Care*, v.15, p.239-243, 2009.

CASSERLY, B.; READ, R.; LEVY, M.M. Hemodynamic monitoring in sepsis. *Crit. Care Clin.*, v.25, p.803-823, 2009.

CHIEW, C.J.; LIU, N.; TAGAMI, T. *et al*. Heart rate variability based machine learning models for risk prediction of suspected sepsis patients in the emergency department. *Medicine*, v.98, p.1-6, 2019.

CORLEY, K.T.T. Inotropes and vasopressors in adults and foals. *Vet. Clin. N. Am., Equine Pract*., v.20, p.77-106, 2004.

DABAREINER, R.M.; SULLINS, K.E.; SNYDER, J.R. *et al*. Evaluation of the microcirculation of the equine small intestine after intraluminal distention and subsequent decompression. *Am. J. Vet. Res.*, v.50, p.1673-1682, 1993.

DABAREINER, R.M.; WHITE, N.A.; DONALDSON, L.L. Effects of intraluminal distention and decompression on microvascular permeability and hemodynamics of the equine jejunum. *Am. J. Vet. Res.*, v.62, p.225-236, 2001.

DELESALLE, C.; DEWULF, J.; LEFEBVRE, R.A. *et al*. Determination of lactate concentrations in blood plasma and peritoneal fluid in horses with colic by an Accusport analyzer. *J. Vet. Intern. Med.*, v.21, p.293-301, 2007.

FRANK, E.; HALL, M.A.; WITTEN, I.H. *The WEKA workbench*. Online appendix for “data mining: practical machine learning tools and techniques.” 4.ed. MA: Morgan Kaufmann; 2016. 633p.

GRULKE, S.; OLLE, E.; DETILLEUX, J. Determination of a gravity and shock score for prognosis in equine surgical colic. *J. Vet. Med. Ser. A*, v.48, p.465-473, 2001.

HAJI-MICHAEL, P.G.; LADRIERE, L.; SENER, A. *et al*. Leukocyte glycolysis and lactate output in animal sepsis and ex vivo human blood. *Metabolism*, v.48, p.779-785,1999.

HACKETT, E.S.; EMBERTSON, R.M.; HOPPER, S.A. *et al*. Duration of disease influences survival to discharge of Thoroughbred mares with surgically treated large colon volvulus. *Equine Vet. J.*, v.47, p.650-654, 2015.

KELLEHER, M.E.; BROSNAN, J.R.; KASS, P.H. *et al*. Use of physiologic and arterial blood gas variables to predict short-term survival in horses with large colon volvulus. *Vet. Surg.*, v.42, p.107-113, 2013.

KUMAR, Y.; SAHOO, G. Analysis of parametric & non-parametric classifiers for classification technique using WEKA. *Int. J. Inf. Technol. Comput. Sci*, v.7, p.43-49, 2012.

LATSON, K.M.; NIETO, J.E.; BELDOMENICO, P.M. *et al*. Evaluation of peritoneal fluid lactate as a marker of intestinal ischaemia in equine colic. *Equine Vet. J.,* v.37, p.342-346, 2005.

MCCONACHIE, E.L. *Cardiovascular system assessment and multiple organ dysfunction in horses with acute gastrointestinal disease*. 2015. 200f. Dissertation (Doctoral) - University of Georgia, USA.

MOORE, J.N.; BARTON, M.H. Treatment of endotoxemia. *Vet. Clin. North Am. Equine Pract*., v.19, p.681-695, 2003.

MOORE, J.N.; TRAVER, D.S.; TURNER, M.F. *et al*. Lactic acid concentration in peritoneal fluid of normal and diseased horses. *Res. Vet. Sci.*, v.23, p.117-118, 1977.

NEIL, K. How to use lactate in equine practice. *Austr. Equine Vet.*, v.27, p.34-48, 2008.

PELOSO, J.G.; COHEN, N.D. Use of serial measurements of peritoneal fluid lactate concentration to identify strangulating intestinal lesions in referred horses with signs of colic. *J. Am. Vet. Med. Assoc.*, v.240, p.1208-1217, 2012.

PROUDMAN, C.J.; DUGDALE, A.H.; SENIOR, J.M. *et al*. Pre-operative and anaesthesia-related risk factors for mortality in equine colic cases. *Vet. J.*, v.171, p.89-97, 2006.

PROUDMAN, C.J.; SMITH, J.E.; EDWARDS, G.B. *et al*. Long-term survival of equine surgical colic cases. Part 1: patterns of mortality and morbidity. *Equine Vet. J*., v.34, p.432-437, 2002.

RUDIGER, A.; SINGER, M. Mechanisms of sepsis-induced cardiac dysfunction. *Crit. Care Med.*, v.35, p.1599-1608, 2007.

SHEARER, T.R.; NORBY, B.; CARR, E.A. Peritoneal fluid lactate evaluation in horses with nonstrangulating versus strangulating small intestinal disease. *J. Equine Vet. Sci.*, v.61, p.18-21, 2018.

SCHUSSER, G.F.; RIECKHOFF, K.; UNGEMACH, F.R. Effect of hydroxyethyl starch solution in normal horses and horses with colic or acute colitis. *J. Vet. Med. Ser. A*, v.54, p.592-598, 2007.

SNYDER, J.R.; PASCOE, J.R.; HARVEY, J.O. *et al*. Vascular injury associated with naturally occurring strangulating obstructions of the equine large colon. *Vet.* Surg., v.19, p.446-455, 1990.

SUGUMARAN, V.; MURALIDHARAN, V.; RAMACHANDRAN, K.I. Feature selection using tree and classification through proximal support vector machine for fault diagnostics of roller bearing. *Mech. Syst. Signal Proc.*, v.21, p.930-942, 2007.

TENNENT-BROWN, B.S.; WILKINS, P.A.; LINDBORG, S. *et al*. Assessment of a point-of-care lactate monitor in emergency admissions of adult horses to a referral hospital. *J. Vet. Intern. Med.*, v.21, p.1090-1098, 2007.

TENNENT-BROWN, B. Blood lactate measurement and interpretation in critically ill equine adults and neonates. *Vet. Clin. North Am. Equine Pract.*, v.30, p.399-413, 2014.

VAN DEN BOOM, R.; BUTLER, C.M.; SLOET VAN OLDRUITENBORGH-OOSTERBAAN, M.M. The usability of peritoneal lactate concentration as a prognostic marker in horses with severe colic admitted to a veterinary teaching hospital. *Equine Vet. Educ.*, v.22, p.420-425, 2010.

VAN HOOGMOED, L.; SNYDER, J.R.; PASCOE, J.R. *et al*. Use of pelvic flexure biopsies to predict survival after large colon torsion in horses. *Vet. Surg.*, v.29, p.572-577, 2000.

VINTHER, A.M.L.; SKOVGAARD, K.; HEEGAARD, P.M.H. *et al*. Dynamic expression of leukocyte innate immune genes in whole blood from horses with lipopolysaccharide-induced acute systemic inflammation. *BMC Vet. Res.*, v.11, p.1-11, 2015.

YAMOUT, S.Z.; NIETO, J.E.; BELDOMENICO, P.M. *et al*. Peritoneal and plasma D-lactate concentrations in horses with colic. *Vet. Surg.*, v.40, p.817-824, 2011.

ZACHER, L.A.; BERG, J.; SHAW, S.P. *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.*, v.236, p.892-897, 2010.