ABSTRACT

Acute abdominal emergencies in calves due to abomasal disorders, gastrointestinal ileus, or peritonitis are characterized by a rapid disease progression and usually require immediate surgical intervention. Those conditions are associated with a guarded prognosis, and the aim of the present study was to assess the prognostic relevance of preoperatively measured plasma L-lactate concentrations (L-LAC) in a large study population of calves with a broad spectrum of acute abdominal emergencies. For the purpose of this study, the medical records of 587 calves admitted to a veterinary teaching hospital over a 10-yr period were analyzed retrospectively. Plasma L-LAC was measured as part of a routinely performed biochemistry panel before initiation of surgical intervention. Hyper-L-lactatemia (plasma L-LAC >2.2 mmol/L) was evident in 75% of calves, and the overall survival rate until hospital discharge was 31%. Calves with a negative outcome were younger (median: 3.4 vs. 6 wk) and had higher plasma L-LAC (median: 4.96 vs. 3.09 mmol/L) than calves with a positive outcome. At the individual diagnosis level, L-LAC was associated with mortality in calves with a diagnosis of mesenteric torsion, right-sided dilated abomasum, small intestinal volvulus, or paralytic ileus, but not in calves suffering from peritonitis, malformations, abomasal volvulus, bloat, or small intestinal intussusceptions. Considering the whole study population, the area under the receiver operating characteristic (ROC) curve for plasma L-LAC was 0.66 [95% confidence interval (CI): 0.61–0.70]. A classification tree analysis indicated that L-LAC >8.84 mmol/L and age categories of <3 wk and <1 wk were independent predictors of mortality. The area under the ROC curve of this model was 0.75 (95% CI: 0.71–0.79) and the resulting sensitivity and specificity for the prediction of nonsurvival at the optimal probability cut-point of 0.62 were 67.7 and 76.6%, respectively. In conclusion, hyper-L-lactatemia is common in calves suffering from acute abdominal emergencies. Markedly increased plasma L-LAC is associated with an increased mortality risk, but it is not possible to reliably predict the outcome of affected calves based on a single, preoperative measurement. However, a clinically important finding of this study was that the ability to predict a negative outcome is improved when the age of the calf is considered in addition to plasma L-LAC. 

Key words: calf, gastrointestinal ileus, peritonitis, hyper-L-lactatemia, mortality

INTRODUCTION

Acute abdominal emergencies in calves due to abomasal disorders, gastrointestinal ileus, or peritonitis are characterized by abdominal distension and circulatory or peristaltic abnormalities, as well as variable degrees of colic and other signs of abdominal pain (Mulan and Desrochers, 2005; Rademacher and Lorch, 2005). These conditions are characterized by a rapid disease progression and usually require immediate surgical intervention to save the animal and confirm the suspected diagnosis. Previous retrospective analyses from veterinary teaching hospitals indicate that acute abdominal emergencies in calves are associated with a guarded prognosis with reported mortality rates ranging from 49 to 76% (Naylor and Bailey, 1987; Iselin et al., 1997; Mulon and Desrochers, 2005). For that reason, there is interest in objective preoperative parameters that reliably predict the outcome of therapy in affected animals.

L-Lactate is a well-established biomarker of tissue hypoxia, sepsis, disease severity, and mortality in critically ill humans and domestic animals (Kraut and Madias, 2016; Rosenstein et al., 2018a). Hyper-L-lactatemia can arise from systemic or peripheral hypo-perfusion due to hypovolemia or shock but also from regional hypo-perfusion such as in ischemic mesenteric conditions (Pang and Boysen, 2007; Rosenstein et al., 2018a). The association between hyper-L-lactatemia and poor
outcome is well documented in patients with acute abdominal emergencies such as in dogs with gastric dilatation-volvulus (Zacher et al., 2010; Green et al., 2011), horses with colitis or intestinal ileus (Johnston et al., 2007; Tennent-Brown et al., 2010; Petersen et al., 2016), and humans suffering from acute mesenteric ischemia or peritonitis (Lange and Jäckel, 1994; Leone et al., 2015). Measurement of blood L-lactate concentrations (L-LAC) has attracted increasing attention in bovine medicine due to the availability and validation of cheap and portable L-lactate analyzers (Karapinar et al., 2013; Buczinski et al., 2014). Recently, increased preoperative blood L-LAC were reported to be reliable prognostic indicators in dairy cows with right-sided displacement of the abomasum or abomasal volvulus (Boulay et al., 2014; Buczinski et al., 2015), making L-LAC a potentially useful predictor of negative outcome for other abdominal disorders in cattle as well.

To the best of our knowledge, little information is available about the relevance and prognostic utility of increased plasma L-LAC in calves with acute abdominal emergencies. The aim of the present study was therefore to determine the prevalence and prognostic utility of increased preoperative plasma L-LAC in calves with acute abdominal emergencies. The goal of this retrospective case series was to determine the prevalence and prognostic utility of increased preoperative plasma L-LAC in a large population of hospitalized calves with a broad spectrum of acute abdominal emergencies, and to assess whether the extent and prognostic accuracy of hyper-L-lactatemia depends on the underlying disorder. Based on the results of previous studies, we hypothesized that increased plasma L-LAC in affected animals are associated with a higher mortality but that the prognostic utility depends on the respective diagnosis.

**MATERIALS AND METHODS**

**Calves**

For the purpose of this retrospective case series, we analyzed the medical records of 587 calves up to 6 mo of age admitted to the Clinic for Ruminants with Ambulatory and Herd Health Services, LMU Munich (Oberschleissheim, Germany) between May 2005 and August 2015. Medical records were identified using log-books and the clinic’s electronic database. Calves were selected for the study if plasma L-LAC, as part of a routine biochemistry panel, was measured on admission and a subsequent surgical intervention was performed during the first hours of hospitalization for reason of an acute abdominal emergency (including all cases of abomasal disorders, suspected gastrointestinal ileus, malformations, or peritonitis) was planned or carried out. Furthermore, calves were eligible for inclusion if they experienced an acute abdominal emergency during the hospital stay and plasma L-LAC was measured immediately before surgery.

**Review of Medical Records**

Information retrieved from the medical records included age, sex, breed, surgical procedures, intraoperative diagnoses, outcome, and the results of biochemical analyses. Grouping of calves was carried out by the location of the underlying problem (abomasum, small intestine, large intestine, multiple parts of the gastrointestinal tract, or abdominal cavity) as well as by the major clinical diagnosis. The latter was determined based on the documented clinical and intraoperative findings and was considered to be the single most detrimental diagnosis that was responsible for the clinical picture and the condition of the calf, even if other contributing problems were present.

**Laboratory Analyses**

Plasma L-LAC was determined using lithium heparinized blood samples containing potassium fluoride as glycostatic agent. Samples were collected from the jugular vein and analyzed by means of automatic systems [Hitachi 911 (from 2005–2012) and Cobas c311 (from 2012–2015) analyzers; Roche Diagnostics, Basel, Switzerland] using the same enzymatic test reaction (Shimojo et al., 1989), with a minimum limit of quantification of 0.17 mmol/L. Hyper-L-lactatemia was defined as a plasma L-LAC >2.2 mmol/L (Rosenberger, 1990).

**Treatment of Calves**

Perioperative treatment of calves included intravenous fluid therapy with constant drip infusions consisting of saline and glucose, as well as administration of antibiotics and nonsteroidal drugs. In 534 calves (91%), surgical intervention was carried out by means of a right flank laparotomy, whereas an umbilical incision was performed in the remaining 53 calves (9%). In most calves (n = 563, 95.9%), anesthesia was induced by administration of ketamine and xylazine and maintained by inhalation of isoflurane. In the remaining 24 calves (4.1%), combined anesthesia was carried out by means of injections of xylazine and ketamine and local infiltration of the surgical site with procaine hydrochloride. Postoperative treatment consisted of continuation of intravenous fluid therapy, administration of antibiotics and nonsteroidal drugs, and intraruminal administration of sodium sulfate. Neostigmine as a pro-kinetic agent was administered at the discretion of the respon-
Outcome of Therapy

A positive outcome (survival) was defined as discharge from the hospital. The group of animals with a negative outcome (nonsurvival) consisted of calves that died or were euthanized during hospitalization because of fatal intraoperative findings, massive deterioration in general condition, ongoing signs of gastrointestinal ileus, or animal welfare reasons.

Statistical Analyses

Statistical analyses were performed using SPSS for Windows (version 24.0, IBM Corp., Armonk, NY), GraphPad Prism (version 7.01, GraphPad Software, San Diego, CA), and the partykit (version 1.1–1) package in R (version 3.4.4, R Core Team; Hothorn et al., 2006; Hothorn and Zeileis, 2015). Values of \( P < 0.05 \) were considered statistically significant. Because most of the data were not normally distributed, as indicated by the Shapiro-Wilk test and visual examination of Q-Q (quantile-quantile) plots, data are presented as medians and interquartile ranges \((Q_1–Q_3)\). Mann-Whitney U-tests were used to compare continuous parameters between groups. Survival rates in relation to deciles of age and plasma \( l\)-LAC were evaluated. In case of plasma \( l\)-LAC, a chi-squared test was used to compare survival rates of each decile to the survival rate of calves of the decile that best lay within the reference range (Trefz et al., 2017). The level of significance for the comparison of the 9 deciles to the reference decile was adjusted using the Bonferroni method \((P < 0.006)\). The predictive ability of those variables was assessed by means of a receiver operating characteristic (ROC) analysis. This included the calculation of the area under the ROC curve \((AUC)\) and the associated 95% CI, as well as identification of cut-off values that optimized the resulting sensitivity and specificity for the prediction of a negative outcome based on the Youden Index.

For multivariable modeling of plasma \( l\)-LAC and age, data were analyzed using classification tree analysis to identify additional cut-points as potential mortality predictors for subsequent evaluation using binary logistic regression analysis. Variables identified as statistically significant predictors during classification tree analysis were subsequently entered as categorized outcome variables into multivariable regression models using a stepwise backward procedure with Wald \( P < 0.05 \) as selection criterion. The fit of the final logistic regression models was evaluated by means of the Hosmer-Lemeshow goodness-of-fit test. The predictive abilities of the models were compared by calculating the AUC and sensitivity and specificity at the optimal cut-point identified using the Youden index.

RESULTS

General Conditions

A total of 587 calves fulfilled the inclusion criteria. Most of the calves \((n = 523; 89\%)\) were Simmental (German Fleckvieh), which is the most common dairy breed in Bavaria. The proportion of male and female calves was 47.7\% \((n = 280)\) and 52.3\% \((n = 307)\), respectively. The median age (and interquartile range) was 4.9 \((1.6–9.1)\) wk, and neonatal calves \((age <3 wk)\) represented 36.8\% of the study population \((n = 216)\).

Diagnoses and Outcome of Therapy

The overall survival rate until hospital discharge was 31.3\% \((n = 184)\). As shown in Figure 1, 14 calves \((2.4\%)\) died or had to be euthanized due to massive deterioration in general condition or agonal state before surgical intervention. In those calves, the underlying disorder was diagnosed by an in-house necropsy examination. A total of 264 calves \((45\%)\) had a negative outcome during surgery, whereas 125 calves \((21.3\%)\) died or were euthanized after surgery (Figure 1). The median length of hospitalization (and interquartile range) for calves with a positive outcome was 5 \((4–8)\) d.

Individual diagnoses and respective survival rates of calves are listed in Table 1. A total of 100 calves \((17.0\%)\) were suffering from an abomasal disorder, 131 calves \((22.3\%)\) had a problem located in the small intestine, and 92 calves \((15.7\%)\) had a problem in the large intestine. Multiple parts of the gastrointestinal tract were affected in 116 calves \((19.8\%)\), and 148 calves \((25.2\%)\) had a diagnosis of peritonitis. The latter was the most frequent finding in calves of this study population and was classified as generalized in 107 and as local in 41 cases. Peritonitis was considered related to perforated abomasal ulcers \((n = 39; of which 30 calves had an omental bursitis)\), intestinal contusion or perforation \((n = 35)\), infection of intra-abdominal umbilical structures \((n = 28)\), necrosis of the intestinal wall \((n = 22)\), septicemia \((n = 21)\), rupture of the abomasum \((n = 2)\), and wound dehiscence after previous laparotomy \((n = 1)\).

Intestinal malformations were seen in 47 calves of our study population, which included 38 cases of partial atresia of the colon. In neonatal calves aged <3 wk, malformations and peritonitis accounted for 21.3\% \(n\)
Association Between Age and Outcome of Therapy

Calves with a negative outcome of therapy were younger (median: 3.4 wk) than calves with a positive outcome (median: 6 wk) of therapy \((P < 0.001)\). The proportion of calves with non-survival in deciles of age is shown in Figure 2. Survival rates of calves in deciles 1 (<0.6 wk) and 2 (0.6 to 1.2 wk) were only 3.4 and 8.6%, respectively. The AUC for age as a prognostic indicator was 0.65 (95% CI: 0.60–0.69; \(P < 0.001\)) and a cut-point of 3.7 wk maximized the sensitivity (51.1%) and specificity (78.8%) for the prediction of non-survival.

Association Between \(L\)-Lactate and Outcome of Therapy

Hyper-\(L\)-lactatemia, defined as plasma \(L\)-LAC >2.2 mmol/L, was present in 441 calves (75%). Plasma \(L\)-LAC was higher in nonsurvivors than in survivors \((P < 0.001)\), although a considerable overlap in values was observed (Figure 3). The proportion of calves with non-survival in deciles of plasma \(L\)-LAC is shown in Figure 4. Only the survival rates of calves in the 9th and 10th deciles were significantly different from those of calves in the reference decile. The ROC curve displaying the general characteristic of plasma \(L\)-LAC as a prognostic indicator is shown in Figure 5. The AUC of the ROC curve was 0.66 (95% CI: 0.61–0.70; \(P < 0.001\)) and an identified cut-point for plasma \(L\)-LAC of 4.56 mmol/L had a sensitivity and specificity for the prediction of nonsurvival of 54.1 and 69.0%, respectively.

Multivariable Analyses

A classification tree analysis based on age and plasma \(L\)-LAC indicated that non-survival was associated with plasma \(L\)-LAC >8.84 mmol/L and age categories of <1 wk and <3 wk, respectively (Figure 6). The results of subsequent logistic regression with those categories of plasma \(L\)-LAC and age is shown in Table 2. The AUC of this model was 0.75 (95% CI: 0.71–0.79; \(P < 0.001\)), and the resulting sensitivity and specificity for the prediction of nonsurvival at the optimal probability cut-point of 0.62 was 67.7 and 76.6%, respectively.

Prognostic Value of Plasma \(L\)-Lactate Stratified by Intraoperative Diagnoses

Plasma \(L\)-LAC stratified by major clinical diagnoses and respective values of calves with positive and negative outcomes are presented in Table 1. The highest values for plasma \(L\)-LAC were seen in calves with an abomasal volvulus and calves with a diagnosis of mesenteric torsion.

A statistically significant difference in plasma \(L\)-LAC between calves with a positive and a negative outcome was only found for calves with right-sided dilatation of the abomasum, small intestinal volvulus, mesenteric torsion, and paralytic ileus. Results of a ROC analysis assessing the diagnostic accuracy of plasma \(L\)-LAC for the prediction of nonsurvival in those groups of calves are presented in Table 3.

DISCUSSION

This study demonstrated that increased plasma \(L\)-LAC is common and associated with an increased mor-
Table 1. Diagnoses, survival rates, total plasma l-lactate concentrations, and plasma l-lactate concentrations stratified by the outcome of therapy in 587 hospitalized calves with acute abdominal emergencies

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>n</th>
<th>Survival rate (%)</th>
<th>l-Lactate (mmol/L)</th>
<th>Calves with a positive outcome</th>
<th>Calves with a negative outcome</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td></td>
<td></td>
<td>n</td>
<td>l-Lactate (mmol/L)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>n</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abomasum</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right-sided dilatation²</td>
<td>54</td>
<td>72</td>
<td>3.60 (1.94–6.62)</td>
<td>39</td>
<td>2.64 (1.80–5.03)</td>
<td>0.001</td>
</tr>
<tr>
<td>Abomasal volvulus³</td>
<td>40</td>
<td>35</td>
<td>8.34 (3.94–11.18)</td>
<td>14</td>
<td>6.09 (2.71–8.95)</td>
<td>0.067</td>
</tr>
<tr>
<td>Miscellaneous⁴</td>
<td>6</td>
<td>83</td>
<td>4.36 (1.34–9.91)</td>
<td>5</td>
<td>4.01 (1.16–5.16)</td>
<td>0.33</td>
</tr>
<tr>
<td>Small intestine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Volvulus</td>
<td>48</td>
<td>44</td>
<td>5.34 (3.07–8.06)</td>
<td>21</td>
<td>3.68 (2.27–5.34)</td>
<td>0.01</td>
</tr>
<tr>
<td>Hernial incarceration</td>
<td>21</td>
<td>67</td>
<td>1.83 (1.33–4.16)</td>
<td>14</td>
<td>1.75 (1.18–3.98)</td>
<td>0.44</td>
</tr>
<tr>
<td>Congestion</td>
<td>21</td>
<td>33</td>
<td>2.28 (1.72–4.74)</td>
<td>7</td>
<td>1.91 (1.10–4.94)</td>
<td>0.22</td>
</tr>
<tr>
<td>Intussusception</td>
<td>18</td>
<td>22</td>
<td>3.47 (1.82–7.15)</td>
<td>4</td>
<td>4.55 (1.49–10.93)</td>
<td>0.96</td>
</tr>
<tr>
<td>Malformations</td>
<td>8</td>
<td>0</td>
<td>4.65 (3.25–6.51)</td>
<td>0</td>
<td>NA</td>
<td>0.67</td>
</tr>
<tr>
<td>Malformation</td>
<td>8</td>
<td>0</td>
<td>7.95 (2.3–14.49)</td>
<td>3</td>
<td>2.53 (NA)</td>
<td>0.40</td>
</tr>
<tr>
<td>Small intestine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malformations</td>
<td>39</td>
<td>0</td>
<td>3.06 (1.89–4.03)</td>
<td>0</td>
<td>NA</td>
<td>0.06</td>
</tr>
<tr>
<td>Intussusception</td>
<td>21</td>
<td>24</td>
<td>1.99 (1.27–4.58)</td>
<td>5</td>
<td>1.83 (0.93–5.66)</td>
<td>0.78</td>
</tr>
<tr>
<td>Torsio ceci or coli</td>
<td>16</td>
<td>19</td>
<td>3.09 (1.86–9.62)</td>
<td>3</td>
<td>2.69 (NA)</td>
<td>0.80</td>
</tr>
<tr>
<td>Dilatatio ceci</td>
<td>10</td>
<td>40</td>
<td>2.17 (1.14–5.52)</td>
<td>4</td>
<td>1.59 (1.17–10.25)</td>
<td>0.91</td>
</tr>
<tr>
<td>Congestion</td>
<td>6</td>
<td>50</td>
<td>2.81 (1.67–6.51)</td>
<td>3</td>
<td>2.54 (NA)</td>
<td>1.00</td>
</tr>
<tr>
<td>Multiple parts</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mesenteric torsion</td>
<td>73</td>
<td>33</td>
<td>8.93 (4.82–16.64)</td>
<td>24</td>
<td>4.40 (2.16–6.83)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Bloat/gas colic⁷</td>
<td>32</td>
<td>84</td>
<td>3.84 (1.68–5.86)</td>
<td>27</td>
<td>3.57 (1.53–5.17)</td>
<td>0.087</td>
</tr>
<tr>
<td>Paralytic ileus</td>
<td>11</td>
<td>46</td>
<td>3.88 (1.81–9.78)</td>
<td>5</td>
<td>1.81 (1.16–3.43)</td>
<td>0.017</td>
</tr>
<tr>
<td>Abdominal cavity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peritonitis</td>
<td>148</td>
<td>3</td>
<td>4.53 (2.75–7.34)</td>
<td>5</td>
<td>3.42 (1.44–6.59)</td>
<td>0.35</td>
</tr>
</tbody>
</table>

¹Values for plasma l-lactate concentrations are given as median and interquartile ranges.
²Defined as an enlargement and displacement of the abomasum attributable to gas or fluid with the pylorus located caudally, and the absence of any palpable twisting of the omentum on the axial surface of the abomasum.
³Defined as an enlargement and displacement of the abomasum attributable to gas or fluid with the pylorus located cranially, the presence of palpable twisting on the axial surface of the abomasum, and the requirement of a clockwise or anticlockwise rotation of the abomasum during surgical correction when viewed from the right side of the abdomen.
⁴Including 3 calves with abomasal impaction and 3 calves with an incarceration of the abomasum in an umbilical hernia.
⁵Not applicable.
⁶Intestinal strangulations through intra-abdominal adhesions, navel structures, or mesenteric defects.
⁷Characterized by gaseous distension of multiple parts of the gastrointestinal tract.
tality risk in calves with acute abdominal emergencies, as indicated by the first branch of the classification tree and the identified cut-point for plasma L-LAC of 8.84 mmol/L. However, findings of this study also indicate that a single, preoperative measurement of plasma L-LAC has limited clinical utility because the ability to predict a negative outcome requires knowledge of a definite intraoperative diagnosis. These findings are in line with the results of a recent review (Rosenstein et al., 2018b), which indicated that the predictive power of L-LAC in terms of mortality is usually moderate in critically ill humans and animals, but can vary from poor to excellent depending on the target population.

One explanation for the limited prognostic accuracy of plasma L-LAC in the present study was obviously the high number of calves with fatal intraoperative findings such as peritonitis and malformations that were not necessarily accompanied by markedly increased plasma L-LAC (Table 1). This high proportion of fatal intraoperative findings also partly explains the observed survival rate of 31%, although this was similar to previous studies reporting survival rates of hospitalized calves with surgical abdominal emergencies of 24 and 26%, respectively (Naylor and Bailey, 1987; Iselin et al., 1997).
Another possible explanation for the limited applicability of a single, preoperative measurement of plasma \( \text{l-LAC} \) to predict a negative outcome is the variety of pathophysiological events that potentially contributed to hyper-\( \text{l-lactatemia} \) in calves of the present study population but might have affected the outcome in a different manner. Hyper-\( \text{l-lactatemia} \) could be the result of systemic or peripheral hypo-perfusion due to hypovolemia, the presence and extent of hypovolemic shock, or the extent of mesenteric ischemia, as all of these are proposed mechanisms for hyper-\( \text{l-lactatemia} \) due to insufficient tissue oxygen supply (Pang and Boysen, 2007; Rosenstein et al., 2018a). A further contributing factor to hyper-\( \text{l-lactatemia} \) in calves of the present study population might be endotoxemia, which has been reported to occur in horses as a result of disruption of the blood–gut barrier following intestinal strangulations (Moore et al., 1981). Furthermore, hyperlactatemia has been a prominent feature of experimental intravenous endotoxin challenges in calves and humans (Tennant et al., 1973; Gerros et al., 1995; Michaëli et al., 2012), and it was recently demonstrated that plasma \( \text{l-LAC} \) and LPS concentrations are positively correlated in neonatal diarrheic calves (Gomez et al., 2019). Endotoxemia can lead to microcirculatory dysfunction (Ince, 2005), sequestration of leukocytes (Haji-Michael et al., 1999), and altered cellular respiration (cytopathic hypoxia) (Fink, 2002; Rosenstein et al., 2018a), which contribute to an increase in \( \text{l-lactate} \) production.

It is also known that increased muscular activity and stress can lead to increased blood \( \text{l-LAC} \) in cattle (Upadhay and Madan, 1985; Mitchell et al., 1988). Therefore, stress due to abdominal pain and transportation, as well as increased muscular activity due to profound signs of colic, as is typically the case in the acute phase of abomasal volvulus or cases of mesenteric torsion in calves (Rademacher and Lorch, 2005; Van Metre et al., 2005), might represent additional contributing factors. The relative importance of those potential mechanisms can unfortunately not be clarified by means of the present study design, and further studies are required to gain insights into pathophysiological events that lead to hyper-\( \text{l-lactatemia} \) in calves with

![Figure 6. Classification tree illustrating the association between mortality and categories of age and plasma \( \text{l-lactate} \) concentrations of 587 calves with acute abdominal emergencies. Each oval identifies a subset of the population, the probability of mortality for the subset, and the number of calves in the subset. Lines leaving the ovals identify a study variable and its cut-point value that is a significant predictor for a negative outcome of therapy. Branches to the left indicate subgroups with a better outcome (lower mortality), whereas branches to the right indicate subgroups with a poorer outcome (higher mortality). Classification tree analysis indicated that hospital mortality was associated with plasma \( \text{l-lactate} \) concentrations >8.84 mmol/L and age categories of <3 wk and <1 wk, respectively.](image)

Another possible explanation for the limited applicability of a single, preoperative measurement of plasma \( \text{l-LAC} \) to predict a negative outcome is the variety of pathophysiological events that potentially contributed to hyper-\( \text{l-lactatemia} \) in calves of the present study population but might have affected the outcome in a different manner. Hyper-\( \text{l-lactatemia} \) could be the result of systemic or peripheral hypo-perfusion due to hypovolemia, the presence and extent of hypovolemic shock, or the extent of mesenteric ischemia, as all of these are proposed mechanisms for hyper-\( \text{l-lactatemia} \) due to insufficient tissue oxygen supply (Pang and Boysen, 2007; Rosenstein et al., 2018a). A further contributing factor to hyper-\( \text{l-lactatemia} \) in calves of the present study population might be endotoxemia, which has been reported to occur in horses as a result of disruption of the blood–gut barrier following intestinal strangulations (Moore et al., 1981). Furthermore, hyperlactatemia has been a prominent feature of experimental intravenous endotoxin challenges in calves and humans (Tennant et al., 1973; Gerros et al., 1995; Michaëli et al., 2012), and it was recently demonstrated that plasma \( \text{l-LAC} \) and LPS concentrations are positively correlated in neonatal diarrheic calves (Gomez et al., 2019). Endotoxemia can lead to microcirculatory dysfunction (Ince, 2005), sequestration of leukocytes (Haji-Michael et al., 1999), and altered cellular respiration (cytopathic hypoxia) (Fink, 2002; Rosenstein et al., 2018a), which contribute to an increase in \( \text{l-lactate} \) production.

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### Table 2. Multivariable logistic regression model for identifying associations between categories of plasma \( \text{l-lactate} \) concentrations and age with nonsurvival in 587 hospitalized calves with acute abdominal emergencies

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient</th>
<th>SE</th>
<th>Odds ratio</th>
<th>95% CI for odds ratio</th>
<th>( P )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>-0.08</td>
<td>0.12</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1 wk</td>
<td>3.34</td>
<td>0.60</td>
<td>28.2</td>
<td>8.7–91.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1 to 2.9 wk</td>
<td>1.20</td>
<td>0.25</td>
<td>3.3</td>
<td>2.0–5.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥3 wk</td>
<td>Referent</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>( \text{l-Lactate} )</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;8.84 mmol/L</td>
<td>2.03</td>
<td>0.32</td>
<td>7.61</td>
<td>4.08–14.17</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≤8.84 mmol/L</td>
<td>Referent</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\( ^1 \)Hosmer-Lemeshow goodness of fit \( \chi^2 = 0.093, \text{df} = 2, \ P = 0.96 \). Entered predictors were identified by means of classification tree analysis.
acute abdominal emergencies to better understand the prognostic implications that can be drawn from plasma t-LAC measurements.

In the present study, the highest values for plasma t-LAC were observed in calves with a diagnosis of mesenteric torsion (median 8.93 mmol/L). This finding suggests that the extent of intestinal ischemia was indeed an important contributor to hyper-t-lactatemia as the rotation of the mesenteric root affects the vascularization of almost the entire intestine. However, sequestration of massive amounts of fluids in the intestines and the development of mesenteric edema can also result in severe dehydration and concomitant hypovolemic shock in affected animals (Rademacher et al., 1995; Anderson, 2008), with shock being considered the most common cause of pathologic hyperlactatemia in veterinary emergency and critical care practice (Rosenstein et al., 2018a). Similar mechanisms likely contributed to hyper-t-lactatemia in the group of calves with small intestinal volvulus, but the lower observed values of plasma t-LAC (median 5.34 mmol/L) compared with calves with a diagnosis of mesenteric torsion might indicate a lower extent of intestinal strangulation.

An interesting finding of this study was that plasma t-LAC differed significantly between survivors and nonsurvivors in calves with right-sided dilatation of the abomasum, but not in calves with a diagnosis of abomasal volvulus. This finding is in marked contrast to results of a recent study by Boulay et al. (2014), where blood t-LAC was associated with a negative outcome in adult dairy cows with abomasal volvulus but not in cows with a right displaced abomasum. However, tympany and torsions of the abomasum in calves are characterized by a more rapid disease progression and potential pathogenetic differences compared with adult dairy cows. Alterations of abomasal motility due to metabolic disorders or concomitant diseases such as endometritis, mastitis, and claw disorders are considered to play a key role in the pathogenesis of displacements of the abomasum in adult dairy cows (Doll et al., 2009). In contrast, as described by Doll (1991) and Rademacher and Lorch (1999), the occurrence of right abomasal disorders in calves is usually associated with dietary changes during the weaning period, when those animals still consume considerable quantities of milk or milk replacer in addition to solid feed. In those calves, fermentation of milk components may lead to excessive production of gas, resulting in rapid and extreme distention of the abomasum. Therefore, our finding concerning the prognostic utility of t-LAC could be explained by the resulting intraluminal pressure in calves suffering from abomasal tympany, which can be as high as or even more pronounced than in calves with an abomasal volvulus (Doll, 1991). Wittek et al. (2004) have shown that the abomasal luminal gas pressure is positively correlated with plasma t-LAC and negatively correlated with abomasal O$_2$ saturation in cows with abomasal volvulus, indicating that abomasal perfusion decreases with increasing luminal pressure. This corresponds with our clinical experience that rapid and extreme gaseous distention of the abomasum can lead to profound ischemic lesions and damage of the abomasal wall. Such lesions can also result in spontaneous rupture of the abomasum, even in the absence of a torsion of the organ (Rademacher and Lorch, 1999). Profound gaseous distention of the abomasum can occur in calves with abomasal volvulus but there are cases of acute torsions in calves where the abomasum is predominantly filled with fluid (Doll, 1991). In such cases, hyper-t-lactatemia can probably arise from circulatory failure due to sequestration of fluid in the abomasum, which probably has a more favorable impact on the outcome than hyper-t-lactatemia that is almost exclusively the result of hypo-perfusion and therefore extensive damage of the abomasal wall.

A clinically useful finding of this study is that survival rates of affected calves aged <3 wk and especially <1 wk were markedly low and that the predictive accuracy of plasma t-LAC was improved when the age of the calf was considered, as indicated by the results of the classification tree analysis (Figure 6). One explanation for the low survival rate in the group of neonatal calves was the high proportion of animals with peritonitis and malformations, which accounted for 56.9% of diagnoses.

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**Table 3.** Results of a receiver operating characteristic (ROC) analysis assessing the diagnostic accuracy of plasma t-lactate concentrations for the prediction of nonsurvival in calves with a diagnosis of mesenteric torsion, right-sided dilatation of the abomasum (RDA), small intestinal volvulus, or paralytic ileus

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>n</th>
<th>AUC$^1$</th>
<th>95% CI for AUC</th>
<th>P-value</th>
<th>Cut-off for t-lactate (mmol/L)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mesenteric torsion</td>
<td>73</td>
<td>0.82</td>
<td>0.70–0.94</td>
<td>&lt;0.001</td>
<td>5.59</td>
<td>87.8</td>
<td>70.8</td>
</tr>
<tr>
<td>RDA</td>
<td>54</td>
<td>0.80</td>
<td>0.67–0.93</td>
<td>0.001</td>
<td>3.17</td>
<td>93.3</td>
<td>59.0</td>
</tr>
<tr>
<td>Small intestinal volvulus</td>
<td>48</td>
<td>0.79</td>
<td>0.66–0.91</td>
<td>0.001</td>
<td>5.41</td>
<td>70.4</td>
<td>81.0</td>
</tr>
<tr>
<td>Paralytic ileus</td>
<td>11</td>
<td>0.93</td>
<td>0.8–1.1</td>
<td>0.018</td>
<td>2.81</td>
<td>100</td>
<td>80.0</td>
</tr>
</tbody>
</table>

$^1$Area under the curve.
in calves <3 wk of age. Another explanation for the lower survival rates in neonatal calves might be the low degree of fat deposition in the omentum and mesentery compared with that in older calves or adult animals, which might make neonatal calves more vulnerable to ischemic or necrotizing lesions due to strangulating events.

The most common malformation in neonatal calves was a partial atresia of the colon. The pathogenesis of atresia coli in calves is still unknown but a genetic component (Constable et al., 1997) and an association with amniotic palpation for early pregnancy diagnosis leading to disruption of the embryonic vasculature have been discussed (Ness et al., 1982). In the present study, the fatality rate of affected calves was 100% because all calves were euthanized during exploratory laparotomy despite established surgical procedures that include creation of a colonic anastomosis or a colostomy (anus praeter). Several retrospective studies on cases (22 to 53 calves) of partial atresia coli that underwent surgical therapy revealed short-term survival rates ranging from 38 to 62% (Constable et al., 1989; Smith et al., 1991; Kilic and Sarierler, 2004). However, long-term success rates are reported to be lower than 18% (Constable et al., 1989; Smith et al., 1991; Kilic and Sarierler, 2004), and a retrospective study at our hospital revealed a survival rate of only 12% after surgical intervention (Rademacher et al., 2002). For that reason and requirements of high therapeutic expenditures, the standard protocol in our clinic is to euthanize calves with partial atresia coli after diagnosis confirmation. According to other authors, euthanasia of affected calves is also justified for animal welfare reasons, the high prevalence of concurrent malformations, and the unknown impact of further breeding with affected animals on the persistence of the defect in the population (Meylan, 2008).

Although this study provides valuable information in respect to the prognostic relevance of plasma L-LAC in calves with acute abdominal emergencies, it has several limitations. First, the analysis was based on a university hospital population, which is usually preselected toward more severely affected cases. Additionally, this study was retrospective, which has potential limitations due to the lack of standardized documentation and individual treatment variations, which were not considered in the present analysis. Further potential limitations include small individual time variations between blood sampling and the onset of surgical intervention and, most importantly, the potential impact of euthanasia on the outcome. Although euthanasia appeared to be justified for medical or animal welfare reasons during review of the medical records, we cannot exclude the possibility that some calves would have recovered with intensive and high-cost therapy. An obvious strength of this study is the large sample size and the broad spectrum of acute abdominal emergencies that were used for our analysis.

Previous studies have shown that heart rate is associated with a negative outcome in cows with right-sided abomasal disorders and that a combination of heart rate and L-LAC provides useful prognostic information (Figueiredo et al., 2006; Boulay et al., 2014). In contrast, Naylor and Bailey (1987) did not find an association between heart rate and mortality in calves with acute abdominal emergencies, and heart rate was not included in the present analysis because of the retrospective nature of our study. However, prospective studies could be added to assess whether standardized documented clinical variables could be used as prognostic indicators in addition to L-LAC.

Based on a recent review, sequential L-lactate measurements and calculated relative measures appear to outperform single measurements in terms of prognostic utility (Rosenstein et al., 2018b). In equine medicine, this has been especially documented for critically ill foals (Wotman et al., 2009; Borchers et al., 2013) and horses with colitis and other abdominal disorders (Tennent-Brown et al., 2010; Hashimoto-Hill et al., 2011), where a delayed normalization or persistent lactatemia represented a more reliable indicator of non-survival than L-LAC at admission. Further studies therefore are indicated to assess whether serial measurements of blood or plasma L-LAC in calves with acute abdominal emergencies would provide more reliable prognostic information than a single measurement before the initiation of therapy.

CONCLUSIONS

A single preoperative measurement of plasma L-LAC has limited clinical utility for predicting non-survival in calves with acute abdominal emergencies because the respective prognostic information depends on the intraoperative diagnosis. However, a clinically useful finding of this study is that the ability to predict a negative outcome improves when the age of the calf is considered in addition to plasma L-LAC. A classification tree analysis indicated that survival rates of calves aged <3 wk and especially <1 wk or with a measured plasma L-LAC >8.84 mmol/L are markedly low, which can help clinicians allocate calves with an acute abdominal emergency into higher and lower risk categories for a negative outcome of therapy.

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