Preoperative cow-side lactatemia measurement predicts negative outcome in Holstein dairy cattle with right abomasal disorders

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ABSTRACT

The objectives of the current study were (1) to determine the gain in prognostic accuracy of preoperative L-lactate concentration (LAC) measured on farm on cows with right displaced abomasum (RDA) or abomasal volvulus (AV) for predicting negative outcome; and (2) to suggest clinically relevant thresholds for such use. A cohort of 102 cows with on-farm surgical diagnostic of RDA or AV was obtained from June 2009 through December 2011. Blood was drawn from coccygeal vessels before surgery and plasma LAC was immediately measured by using a portable clinical analyzer. Dairy producers were interviewed by phone 30 d following surgery and the outcome was determined: a positive outcome if the owner was satisfied of the overall evolution 30 d postoperatively, and a negative outcome if the cow was culled, died, or if the owner reported being unsatisfied 30 d postoperatively. The area under the curve of the receiver operating characteristic curve for LAC was 0.92 and was significantly greater than the area under the curve of the receiver operating characteristic curve of heart rate (HR; 0.77), indicating that LAC, in general, performed better than HR to predict a negative outcome. Furthermore, the ability to predict a negative outcome was significantly improved when LAC measurement was considered in addition to the already available HR data (area under the curve: 0.93 and 95% confidence interval: 0.87, 0.99). Important inflection points of the misclassification cost term function were noted at thresholds of 2 and 6 mmol/L, suggesting the potential utility of these cut-points. The 2 and 6 mmol/L thresholds had a sensitivity, specificity, positive predictive value, and negative predictive value for predicting a negative outcome of 76.2, 82.7, 53.3, and 93.1%, and of 28.6, 97.5, 75, and 84%, respectively. In terms of clinical interpretation, LAC ≤ 2 mmol/L appeared to be a good indicator of positive outcome and

could be used to support a surgical treatment decision. The treatment decision for cows with LAC between 2 and 6 mmol/L, however, would depend on the economic context and the owner's attitude to risk in regard to potential return on its investment. Finally, performing a surgical correction on commercial cows with RDA or AV and a LAC ≥ 6 mmol/L appeared to be unjustified and these animals should be culled based on their high probability of negative outcome.

Key words: dairy cow, abomasal disorder, lactate, prognosis

INTRODUCTION

Abomasal displacement is among the most commonly encountered surgical disorders in modern dairy herds (Shaver, 1997) and the associated treatments and milk losses can have a substantial economic impact (Detilleux et al., 1997; Cameron et al., 1998; Gröhn et al., 1998). Unlike left displaced abomasum (LDA) and right displaced abomasum (RDA), abomasal volvulus (AV) is a life-threatening condition and may lead to a negative outcome due to ischemic lesions to the abomasum, peritonitis, or vagal nerve damage (Sattler et al., 2000). To control the economic losses associated with abomasal disorders, early identification and culling of animals that are at higher risk of developing a negative outcome would be of interest. Negative outcome has been reported to range from 12 to 17% of cases for LDA (Figueiredo et al., 2006; Roy et al., 2008; Sterner et al., 2008), 8.7 to 14.7% for RDA (Fubini et al., 1991; Kümper, 1995; Figueiredo et al., 2006), and 26.3 to 65.0% for AV (Constable et al., 1991a; Fubini et al., 1991; Figueiredo et al., 2006). Due to the abnormal position of the abomasum against the left abdominal wall, clinical diagnosis of LDA is relatively straightforward. For right-sided abomasal disorders, however, it is almost impossible to differentiate, with absolute certainty, RDA from AV with a routine physical examination, and, most of the time, final diagnosis must be established through surgical exploration (Smith et al., 1982; Smith, 1987; Trent, 1990). Because the prognoses of these disorders differ, it would be very helpful to

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have presurgical indicators that could assist the veterinary practitioner in predicting outcome for these cows.

To date, few presurgical clinical variables have been identified as potential prognostic tools in cases of RDA or AV. Among these, heart rate (HR; Smith, 1978; Hjortkjaer and Svendsen, 1979; Constable et al., 1991a) and hydration status (Hjortkjaer and Svendsen, 1979; Constable et al., 1991a) have been suggested as the most valuable. Hydration status is, however, a subjective measure and, despite the presence of guidelines to estimate dehydration percentage, evaluation of this clinical sign can yield variable results between practitioners (Radostits et al., 2007). Heart rate, on the other hand, is usually considered the most objective and best prognostic indicator that can be obtained before surgery. Increased HR is associated with decreased chance of recovery under referral hospital conditions (Gröhn et al., 1990; Constable et al., 1991a). In fact, 56% of AV with HR ≥ 100 beats/min were salvaged, euthanized, or died in course of hospitalization compared with only 12 to 25% for AV with HR < 100 beats/min (Smith, 1978; Constable et al., 1991a). The determination of HR is routinely done during examination of a sick animal by the practitioner, so its inclusion as a prognostic factor can easily be applied on a farm setting. Nevertheless, HR can be modulated by many factors and this variable has been shown to be less specific in its intermediate range of values (between 90 and 120 beats/min; Radostits et al., 2007). For these reasons, the development of an ancillary test that could help veterinary practitioners to establish more precisely a presurgical prognosis in case of RDA or AV would be of value.

Various blood markers have been linked with prognosis in cows with RDA or AV. These variables are indicators of the severity of metabolic acidosis or hypoperfusion [anion gap, L-lactate concentration (LAC), bicarbonate, pH, and creatinine], or the importance of abomasal stasis (chloride). Most of these markers except LAC cannot be assessed rapidly or at low cost on the farm. L-Lactate is produced under normal stages of anaerobic metabolism such as exercise, trembling, and excessive muscular activity, but its concentration can increase under pathologic conditions due to poor systemic tissue perfusion, reduced peripheral perfusion (Weil and Afifi, 1970; Bakker et al., 1996; Bernardin et al., 1996), as well as local hypoperfusion (Liao et al., 1995; Wittek et al., 2004). Higher LAC has been associated with poor outcome in dogs with gastric dilatation and volvulus (de Papp et al., 1999; Zacher et al., 2010) and in horses with colic (Moore et al., 1976; Delesalle et al., 2007; Johnston et al., 2007). A recent study on cows with RDA and AV conducted in hospital settings has shown substantial prognostic potential for this metabolite (Figueiredo et al., 2006) and, thus, LAC could be

used to establish a prognosis for RDA or AV. With the recent availability of L-lactate portable clinical analyzers, LAC can now be measured on farm with results available in 1 min and at low cost (less than US\$3.00).

Currently, no field study has evaluated the potential of L-lactate as a complementary diagnostic tool for on-farm use to establish a presurgical prognosis for RDA or AV. We hypothesized that L-lactate measurement could be a valuable tool to establish on-farm presurgical prognosis for RDA or AV. The objectives of this study were, therefore, to (1) determine the test characteristics and prognostic gain (i.e., beyond the already available routine physical examination) for L-lactate measurement when used on farm with a portable clinical analyzer as a prognostic indicator for cows with RDA or AV; and (2) to suggest potential LAC thresholds and corresponding clinical interpretations.

MATERIALS AND METHODS

Study Population

From June 2009 through December 2011, all cows (first lactation and greater) that presented to the bovine field service of the Faculté de médecine vétérinaire of the Université de Montréal and for which a diagnosis of RDA or AV was suspected based on presence of a typical right-sided tympanic resonance were recruited in this cohort study. This study was approved by the Comité d'éthique sur l'utilisation des animaux de la Faculté de médecine vétérinaire, Université de Montréal. The cows were enrolled in the study if the diagnosis of RDA or AV was confirmed by exploratory laparotomy and excluded if another diagnosis (ileus, duodenal sigmoid flexure volvulus, cecal dilatation) was found during surgery. Cows were also excluded from this study if they had been treated for another digestive medical condition < 7 d before developing the RDA or AV. Information on participating cows was collected by veterinary practitioners during farm visits and recorded on data sheets. Collected data included cow identification, parity, stage of lactation, and general physical examination findings.

Lactate Measurements

Blood was drawn from coccygeal vessels before surgery and before any treatment. Plasma LAC was immediately measured with a portable clinical analyzer (Lactate Pro, Arkray KDK, Kyoto, Japan). This portable clinical analyzer has been found accurate and reliable compared with the reference method in bovine species (Buczinski et al., 2013). L-Lactate measurement with this portable clinical analyzer requires the

transformation of lactate in the sample. Lactate reacts with potassium ferricyanide and lactate oxidase to form potassium ferrocyanide and pyruvate. Upon application of a given voltage, ferrocyanide is oxidized, releasing electrons and creating a current. This current is measured amperometrically and is directly proportional to the lactate concentration of the sample (Tanner et al., 2010). Sample analysis time is 60 s, and the analyzer displays lactate concentrations from 0.8 to 23.3 mmol/L. Values out of that range are reported as "HI" if >23.3 mmol/L or "LO" if <0.8 mmol/L. Lactate concentration was recorded by the owner or a veterinary student, and the veterinary practitioners were blinded to the L-lactate measurement to avoid any effect on case management. Surgery was then performed and the type of surgical technique used and treatments administered during the farm visit were recorded.

Surgical Findings

Laparotomy in the right paralumbar fossa under regional anesthesia was performed on all cows. Differentiation between RDA, AV, and other conditions was established by direct visualization or palpation of the stomach compartment at the time of surgery. An RDA was defined as abnormal enlargement of the abomasum attributable to gas or gas and fluid, such that the greater curvature of the body of the abomasum had become displaced dorsally and the lesser curvature was positioned ventrally (Fubini et al., 1991). Furthermore, cows with obstruction of the cranial part of the duodenum (Fubini et al., 1991) or for which a clockwise rotation of the abomasum during gas decompression was observed (Constable et al., 1991b) were not considered as having a RDA. An AV was diagnosed whenever a distinct twist of the abomasoduodenal loop, with or without a variable degree of omasal involvement, was identified, when the cranial part of the duodenum coursed between the rumino-omasal or the omaso-abomasal junction (Fubini et al., 1991), or when surgical correction required a clockwise rotation of the abomasum (when viewed from the right side of the animal; Constable et al., 1991b). Diagnosis and surgical corrections were made by 10 different surgeons, who had between 2 and 12 yr of clinical experience. In all but 2 cows that died during surgery, abomasal position was corrected and stabilized by omentopexy with or without pyloropexy, depending on the surgeon's preference and omental integrity. In all instances, surgeries were conducted as suggested in the literature (Fubini and Ducharme, 2004).

Pre- and Postsurgical Treatments

Decisions regarding supportive medical treatments were left to the surgeon's discretion. Treatments could

be given during the preoperative period, the postoperative period, or both. Supportive medical treatments most often consisted of the administration of antimicrobial therapy, a nonsteroidal antiinflammatory drug, intravenous calcium fluids, intravenous dextrose fluids, and, on a few occasions, intravenous hypertonic fluids.

Follow-Up

Dairy producers were interviewed by phone by the first author (GB) 30 d following surgery. Owners were asked to provide the following information: whether the cow was alive or dead; whether she was still in the herd; and whether the owner was satisfied or not with the animal's postsurgical progress. If the cow was culled from the herd, the owner was asked when she was culled, the reason for culling, and whether culling was related to the initial digestive problem.

Statistical Analysis

In all the following analyses, the outcome was classified as positive or negative. The outcome was defined as positive if the owner was satisfied with the overall progress 30 d postoperatively and as negative if the cow was culled, died, or if the owner reported to be unsatisfied 30 d postoperatively. Such a case definition was chosen based on the assumption that the dairy producer would likely have decided not to have the surgery performed if he had known that he would later be unsatisfied with the result. In the following analyses, our interest always resided in predicting negative outcome, because that was the outcome one would want to avoid. For statistical considerations, a LAC of 0.79 mmol/L was attributed to the "LO" result from the clinical analyzer.

First, descriptive statistics were calculated and distributions inspected for LAC and HR. Box-Cox transformations (Box and Cox, 1964) were evaluated for their ability to improve normality of the L-lactate distribution. Box-Cox transformations provided, in general, only relatively modest improvements of the normality and L-lactate measures were, therefore, kept on the original scale to facilitate interpretation of the results.

Effect of the abomasal condition (RDA or AV) on the probability of a negative outcome was modeled using hierarchical logistic regression model taking into account clustering of observations by herd (GLIMMIX procedure of SAS using quadrature approximation with 7 points; version 9.2, SAS Institute Inc., Cary, NC). For median LAC and HR, differences between negative and positive outcomes for RDA or AV, and AV and RDA specifically were assessed through Wilcoxon rank sum tests.

Test Characteristics. In the current study, sensitivity (**Se**) was defined as the proportion of negative outcomes that were correctly predicted by the L-lactate measurement. Specificity (**Sp**) was defined as the proportion of positive outcomes that were correctly identified using L-lactate. Characteristics (**Se** and **Sp**) of the L-lactate test across a range of L-lactate values were explored. Sensitivity, **Sp**, positive predictive value (**PPV**), and negative predictive value (**NPV**) across L-lactate values were computed as indicated by Dohoo et al. (2009).

Prognostic Gain. An L-lactate receiver operating characteristic (**ROC**) curve was drawn, taking into account clustering of observations by herd (GLIMMIX procedure of SAS using quadrature approximation with 7 points), and visually compared with the HR ROC curve. Areas under the curve (**AUC**) of LAC and HR ROC curves, which indicate accuracy of tests to predict outcome across the range of potential thresholds, were then assessed (Dohoo et al., 2009). To assess which variable was the most accurate in predicting negative outcome, **AUC** of LAC and HR were compared by using the nonparametric approach of DeLong et al. (1988).

Potential Thresholds. To determine potential L-lactate thresholds above which a surgical correction may be too costly considering the probability of a positive outcome, plots of misclassification cost term against range of L-lactate values were drawn and visually inspected for a range of different plausible false negative-to-false positive cost ratios (ranging from 1:1 to 1:10). The misclassification cost term can be used to select cut-off values that consider that the cost (financial or other) of a false negative may be more undesirable than that of a false positive (or the other way around) and can be computed using the following formula (Greiner, 1996; Greiner et al., 2000):

$$\text{Misclassification cost term} = (1 - p) \times (1 - \text{Sp}) + rp(1 - \text{Se}),$$

where p is the disease prevalence, **Se** and **Sp** are the test sensitivity and specificity, and r is the false negative-to-false positive cost ratio. In the current study, the health cost of a false negative (i.e., test indicated that surgery would be valuable but a negative outcome occurred) was deemed to be less than or equal to that of a false positive (i.e., test indicated that the cow should be culled, but the outcome would have been positive if the surgery had been performed). In the first situation, the inappropriate decision would yield losses mainly from the unnecessary surgical correction and associated milk withdrawal time. In the case of a false positive, cost for replacement of the inappropriately culled cow would be

incurred, even though a simple surgical correction may have actually solved the problem.

Complementary Prognosis Value of L-lactate. Finally, to evaluate the usefulness of LAC measurement (when used with the proposed thresholds) to improve the prognosis that can already be established using the available HR, a log-likelihood ratio statistic comparing the full model (LAC and HR) to the reduced model (HR only) was used. For this purpose, logistic models taking into account clustering of observations by herd were used with a maximum likelihood approximation (GLIMMIX procedure of SAS using quadrature approximation with 7 points; SAS Institute Inc.). To assess which model (HR or HR and LAC) was the most accurate to predict negative outcome, **AUC** of both models were compared by using the nonparametric approach of DeLong et al. (1988). Results of all statistical analyses were considered significant when P -value < 0.05 .

RESULTS

During the study period, 113 Holsteins cows presented with right-sided tympanic resonance; 103 of these cows had an RDA or AV and were recruited. Of the 10 excluded cows, 3 were diagnosed with duodenal sigmoid flexure volvulus, 3 were diagnosed with RDA and duodenal sigmoid flexure volvulus, which was considered different from a simple RDA (Vogel et al., 2012), 2 were diagnosed with an ileus, 1 had an omasal impaction, and 1 had an unknown diagnosis. Of the 103 cows recruited, 1 cow was excluded because she had been previously treated for ileus on numerous occasions before developing a RDA. The remaining 102 cows with RDA or AV were all included in the study (57 RDA and 45 AV).

The 102 cows originated from 64 commercial dairy herds milking between 25 and 230 cows (primarily Holstein cattle) and using mostly tiestall housing ($n = 53$). Most herds had only 1 case ($n = 45$) but some had up to 5 cases during the study period. Of the 102 cows, 87 had an omentopexy, 12 had a pyloro-omentopexy, 1 had a pyloropexy, and 2 died during surgery before any abomasal correction could be performed. Of the 10 different surgeons, 3 treated cows that later had positive outcomes only ($n = 11$), whereas 1 surgeon had treated only 1 cow that later had a negative outcome ($n = 1$). Of the 6 other surgeons, the probability of negative outcome ranged from 8 to 32%. Of the 102 cows, 80% received antimicrobial therapy, 56% received nonsteroidal antiinflammatory drugs, 51% received intravenous calcium fluids, 25% received intravenous dextrose fluids, and 28% received intravenous hypertonic fluids. All but 7 cows were in lactation. Among these dry cows,

5 had AV (1 positive and 4 negative outcomes) and 2 had RDA (2 positive outcomes). Descriptive data from study population are presented in Table 1. Negative outcome (%; 95% CI) was significantly more frequent for AV (40%; 26–54) compared with RDA (5.3%; 0–11; $P = 0.005$). Median LAC was significantly higher in cows with negative outcome (2.7 mmol/L) than positive outcome (0.8 mmol/L; $P < 0.001$). Median HR was also significantly higher in cows with negative outcome (100 beats/min) compared with positive outcome (80 beats/min; $P < 0.001$). In cows with AV, median LAC and HR were also significantly higher for negative outcome (3.0 mmol/L and 104 beats/min) than for positive outcome (1.2 mmol/L and 88 beats/min; $P < 0.001$, and $P = 0.005$, respectively). In cows with RDA, no significant differences in median LAC or HR could be seen between negative (1.0 mmol/L and 72 beats/min) and positive outcomes (0.8 mmol/L and 80 beats/min; $P = 0.66$ and $P = 0.25$, respectively).

Relationships between LAC, HR, and probability of a negative outcome are presented in Figure 1. The probability of a negative outcome was higher as LAC or HR increased. Furthermore, the association between LAC and the probability of a negative outcome appeared to be stable across HR categories because the slopes of the 3 curves on Figure 1 were very similar. Consequently, for an increment of 1 unit of LAC (e.g., 4 to 5 mmol/L), the probability of negative outcome increased almost equally for the 3 categories of HR (<90 beats/min: 0.21 to 0.33%; 90 to 110 beats/min: 0.46 to 0.62%; and >110 beats/min: 0.64 to 0.77%). If the association was not stable, the curves would diverge (crossing slopes). Therefore, for an increment of 1 unit of LAC, the probability of negative outcome would increase differently from one category of HR to another.

Test Characteristics

Receiver operating characteristic curves displaying the general characteristics of LAC as a prognostic in-

Figure 1. Relationship between L-lactate concentration and probability of a negative outcome (NO) across 3 categories of heart rate (HR) for 102 cows with diagnosis of right abomasal disorders; NO is defined as an unsatisfied owner 30 d postoperatively, or a cow that was culled or died.

indicator of negative outcome are presented in Figure 2. The AUC (95% CI) of the ROC curve for LAC alone was 0.92 (0.87–0.97), significantly higher ($P = 0.013$) than that of HR alone (0.77; 0.64–0.90), which indicates that LAC, in general, performed better than HR alone to predict negative outcome. Prognostic predictive performance of LAC and HR were, however, relatively equivalent when cut-off values with high Sp (>0.90) were chosen (Figure 2).

Characteristics of L-lactate measurement as a diagnostic test to predict negative outcome are presented in Figure 3. The PPV (the probability that a cow had negative outcome when LAC would predict so) rapidly increased up to a value of 50% (corresponding to a LAC of 2 mmol/L). The PPV was relatively stable between LAC from 2 to 4 mmol/L and a second improvement

Table 1. Important characteristics of a cohort of 102 cows with surgical diagnosis of right displaced abomasum or abomasal volvulus¹

Variable	Right displaced abomasum		Abomasal volvulus	
	PO	NO	PO	NO
Number of cows	54	3	27	18
Lactation ²	3 (1–3)	4 (2–4)	2 (1–3)	2.5 (2–3)
DIM ²	14 (7–45)	5 (4–6)	19 (7–45)	26.5 (8–45)
L-Lactate ² (mmol/L)	0.8 (0.79–1.2)	1.0 (0.79–1.8)	1.2 (0.79–2.3)	3.0 (2.4–6.6)
Heart rate ² (beats/min)	80 (72–88)	72 (60–80)	88 (78–100)	104 (92–120)

¹PO (positive outcome) is defined as a satisfied owner 30 d postoperatively; NO (negative outcome) is defined as an unsatisfied owner 30 d postoperatively, or a cow that was culled or died.
²Median (25th and 75th percentiles).

Figure 2. Receiver operating characteristic curves displaying the general characteristics of L-lactate measurement, heart rate (HR), and L-lactate and HR together as diagnostic tests to predict negative outcome in 102 cows with diagnosis of right displaced abomasum or abomasal volvulus; areas under the curves (AUC) and their 95% CI are reported for each test or combination of tests; receiver operating characteristic curves take into account clustering of observation by herd.

was seen up to a value of approximately 7 mmol/L. No further improvement of PPV was observed with higher LAC cut-offs. The NPV, on the other hand, slowly decreased to approximately 80% at LAC of 3 mmol/L and remained stable thereafter.

Potential Thresholds

Misclassification cost term across the range of L-lactate values and false negative-to-false positive health cost ratios ranging from 1:1 to 1:10 are presented in Figure 3. The observed decrease in misclassification cost term from 80% at LAC of 0.8 mmol/L to 20% at LAC of 2 mmol/L indicated that a large proportion of the misclassification cost could be controlled when using a 2 mmol/L threshold. Similar misclassification cost term patterns were observed among the different false negative-to-false positive health cost ratios: first, an important misclassification cost term reduction up to LAC of approximately 2 mmol/L followed by an additional but relatively smaller misclassification cost term decrease up to LAC of approximately 6 mmol/L. No important gain in misclassification cost term could be observed for LAC above 6 mmol/L (Figure 3). Values of 2 mmol/L and 6 mmol/L were, therefore, selected

Figure 3. Characteristics of different L-lactate cut-points as a diagnostic test to predict negative outcome in 102 cows with diagnosis of right displaced abomasum or abomasal volvulus. Sensitivity (Se), specificity (Sp), positive predictive value (PPV), and negative predictive value (NPV) are reported for the range of L-lactate values observed. Misclassification cost term (MCT) is reported for a range of false negative (FN)-to-false positive (FP) health cost ratios (r ; from 1:1 to 1:10) and across the range of L-lactate values observed; thresholds of 2 and 6 mmol/L to predict negative outcome are represented by vertical dashed lines.

as potential cut-offs for subsequent analyses because they corresponded to the inflection points where the misclassification costs could be controlled. Sensitivity, Sp, PPV, and NPV of 76.2, 82.7, 53.3, and 93.1%, and of 28.6, 97.5, 75, and 84% were observed for the 2 and 6 mmol/L thresholds, respectively.

Complementary Prognosis Value of L-Lactate

The log-likelihood ratio statistic comparing the full model and the reduced model indicated that the

ability to predict negative outcome was significantly improved when LAC was taken into account in addition to HR ($P < 0.001$). The AUC (95% CI) of the ROC curve of the model with LAC and HR was 0.93 (0.87–0.99) and was higher ($P < 0.001$) than that of the model with HR alone (0.77; 0.64–0.90; Figure 2). Moreover, compared with the model with only HR, considering LAC in addition to HR improved the Se of the test at cut-off values yielding higher Sp, which greatly improved accuracy when predicting negative outcomes, especially at intermediate LAC (between 2 and 6 mmol/L) and HR (between 90 and 115 beats/min) values (Figure 2; Table 2). Therefore, combining LAC with HR allowed a better classification of the prognosis for intermediate HR values (90 to 115 beats/min; Table 2). Thus, the proportion of cows that fell in the “gray zone” decreased from 31% (32/102; HR: 90–115 beats/min) to 13% (13/102; HR: 90–115 beats/min, and L-lactate: 2–6 mmol/L) by adding the measure of LAC.

DISCUSSION

This study is the first to evaluate the use of LAC measurement as an ancillary test that could be used in combination with HR to establish a presurgical prognosis for cows with RDA or AV in farm settings. In the current study, practitioners were blinded to LAC, and the LAC value could not influence the therapeutic plan proposed or prognosis given to the owner.

Our results indicated that increased LAC was associated with increased probability of negative outcome in cows with RDA or AV. Previous studies on the prognostic importance of lactatemia have given conflicting results (Hjortkjaer and Svendsen, 1979; Constable et al., 1998; Figueiredo et al., 2006). The prognostic importance of lactatemia was found in one recent study (Figueiredo et al., 2006) but not in a previous one (Constable et al., 1998). This difference could be explained by the fact that a longer follow-up (12 mo) period was used in the Constable et al. (1998) study for outcome

classification, which could lead to an increased number of reasons to cull unrelated to the negative outcome.

In the current study, 2 LAC thresholds stood out when predicting outcome for RDA or AV. Based on our results, cows with LAC ≥ 6 mmol/L could confidently be culled rather than surgically treated. This threshold appropriately controlled almost all of the health costs associated with diagnostic errors by optimizing PPV and NPV. Using such a threshold in a population similar to ours, a practitioner would have a 75% probability of making the right decision when deciding to cull a cow rather than to perform the surgery (PPV = 75%). The 6 mmol/L threshold would, therefore, be particularly useful to support a culling decision. To support a surgical correction decision, on the other hand, a different threshold may perform better. In this case, a threshold of LAC ≤ 2 mmol/L could be used to decide to treat a cow with RDA or AV. As can be seen from the misclassification cost term plot (Figure 3), with a 2 mmol/L threshold, a large part of the health costs associated with diagnostic errors would already be controlled. With this threshold and in a population similar to ours, a practitioner would have a 93% probability of making the correct decision when recommending surgical correction of the abomasal disorder (NPV = 93%). Thus, the 2 mmol/L threshold would strongly support a decision to perform surgical correction of RDA or AV. In the current study, only 23% of the cows recruited fell into the “gray zone” (LAC between 2 and 6 mmol/L). At these intermediate LAC values, the NPV was relatively stable at approximately 85%, but the PPV rapidly increased from 50 to 75% between LAC values of 4 to 6 mmol/L. Although a 50% probability of correctly recommending culling of a cow (at LAC from 2 to 4 mmol/L) rather than surgical correction may be a “leap of faith” for many practitioners, PPV values between 50 and 75% may be sufficient in some instances and could also be considered.

The fact that the misclassification cost term curves varied little with the different false negative-to-false positive ratios investigated is reassuring. This observation

Table 2. Negative outcome probability across categories of presurgical L-lactate concentration and heart rate in a cohort of 102 cows with surgical diagnosis of right displaced abomasum or abomasal volvulus¹

L-Lactate (mmol/L)	Heart rate (beats/min)			Overall
	<90	90–115	>115	
<2	7.5 (53)	0 (16)	33.3 (3)	6.9 (72)
2–6	14.3 (7)	53.8 (13)	66.7 (3)	43.5 (23)
>6	— ²	66.7 (3)	100 (4)	85.7 (7)
Overall	8.3 (60)	28.1 (32)	70.0 (10)	

¹Results presented as probability of negative outcome (no.); negative outcome is defined as an unsatisfied owner 30 d postoperatively, or a cow that was culled or died.

²No animal in category.

)indicates that knowing the exact health costs involved would have little effect on the proposed cut-points, as long as the cost of a false negative is deemed to be equal to or lower than that of a false positive. In fact, misclassification cost term curves are influenced by combined variation of PPV and NPV across L-lactate values. If the cost associated with a false positive is greater than that associated with a false negative, then the misclassification cost term curve is more strongly influenced by variation of the PPV. Nevertheless, in an economic context where animal price and costs for replacement are high (false negative-to-false positive ratio = 1:10), a decision to perform the surgery would be economically justified at $\text{LAC} \leq 2$ mmol/L, and a decision to cull would be justified at $\text{LAC} \geq 6$ mmol/L. For LAC of 2 to 6 mmol/L, however, the practitioner could inform owners of their cow's probability of negative outcome and help them decide whether or not to treat the animal. In an economic context where costs for replacement are low (false negative-to-false positive ratio = 1:1), the decision to perform surgery on animals with $\text{LAC} \leq 2$ mmol/L would still be economically justified, but culling animals with $\text{LAC} > 2$ mmol/L would now be relevant. Although this last cut-point seems radical, it has been observed that 93.8% (95% CI: 82.8–98.7) of healthy early lactating Holstein cows had a $\text{LAC} < 0.8$ mmol/L, as measured by a portable clinical analyzer, which suggests that normal lactatemia for healthy cows seems to be less than the 2 mmol/L threshold proposed (G. Boulay, unpublished data). Results from the current study indicate, however, that regardless of the false negative-to-false positive ratio and, thus, the economic context, there is no economic advantage to performing surgery on commercial animals that have $\text{LAC} \geq 6$ mmol/L, and a poor prognosis should be reported to the owner.

Based on the ROC curves and their respective AUC, L-lactate seemed to be a better individual prognostic indicator than HR when considering the whole range of possible values. The observation that using LAC alone is better than using HR alone to predict surgical outcome of cows with RDA or AV was observed in another hospital-based study (Figueiredo et al., 2006). Many physiologic or pathologic pathways can increase HR without threatening animal survival, which indicates that this variable is certainly not specific to negative outcome of RDA and AV (Radostits et al., 2007). Heart rate, however, is an objective, inexpensive, and easily collected value, and this measure will always be available for dairy practitioners to establish a presurgical prognosis. For this latter reason, we believe that measuring L-lactate as an ancillary test should be assessed by comparing LAC and HR measurements together against HR measurement alone, as was done

in the current study. When such a comparison was made, predicting the surgical outcome was significantly improved by the complementary LAC measurement, and this gain was mediated, in part, by the gain in Se around threshold values yielding the highest Sp (Figure 2). Therefore, combining LAC with HR allowed better classification of the prognosis for intermediate HR values (90 to 115 beats/min; Table 2) and decreased the proportion of cows falling in the “gray zone.” Consequently, depending on which categories of HR and LAC the animal suffering from RDA or AV falls into, the practitioner would be able to provide an accurate probability of negative outcome (Table 2). Thus, RDA or AV would have a high probability of negative outcome if $\text{LAC} > 6$ mmol/L and $\text{HR} > 90$ beats/min or if LAC is between 2 and 6 mmol/L and $\text{HR} > 115$ beats/min. Right abomasal disorders would have a low probability of negative outcome when $\text{LAC} < 2$ mmol/L or between 2 and 6 mmol/L and $\text{HR} < 90$ beats/min. The probability of negative outcome would, however, be mitigated whenever LAC was between 2 and 6 mmol/L and HR between 90 and 115 beats/min.

It could be advantageous to use a multivariable model compared with a single value to predict outcome of cows with RDA or AV because multivariable analyses provide a more reliable prognosis prediction (Gröhn et al., 1990; Constable et al., 1991a). For instance, Figueiredo et al. (2006), in a hospital-based study, observed that the combination of LAC, chloride, and HR had a greater predictive power than a model with HR only. Currently, prognosis is mainly established based on clinical judgment, which is potentially a better prognostic indicator than HR or LAC or their combination. Clinical judgment is based on the interpretation, analysis, and synthesis of many clinical data, which are sometimes subjective and rely in part on the practitioner's clinical experience. Thus, further studies could evaluate if the proposed predictive models are superior to a practitioner's clinical judgment to predict negative outcome.

Negative outcome was more frequent for AV than for RDA. This observation has been reported previously (Fubini et al., 1991; Kümper, 1995). The proportion of negative outcomes for right-sided abomasal disorders was, however, lower in our study than in another study conducted on a referral population that reported 14.7% of negative outcome for RDA and 65% for AV (Figueiredo et al., 2006). Hospital-based studies may have a higher proportion of negative outcomes than farm-setting studies. Generally, cows referred to a veterinary hospital are more critically ill, partly because of the time required for transportation, which delays surgical correction, and are more likely to develop complications or to need additional supportive treatment

compared with cows treated on farm as a first-line medical intervention. For this reason, inferences from the current study should be drawn strictly for first-line RDA or AV presentation.

The current study has some limits. For example, animals that were excluded because of final diagnosis other than RDA or AV could have been included in this study. Inclusion of those cases might have helped our proposed model to more closely approach the practitioners' reality. As this situation only applied to 7 cases in our study, this approach could have slightly overestimated our model predictive performance. The fact that different surgeons participated in the current study could have affected the animals' progress because of differences in surgical experience and supportive medical treatments used. Four surgeons treated cows that later had only positive or only negative outcomes; therefore, it was impossible to determine the effect of different surgeons on the complete data set due to nonconvergence. Nonetheless, logistic regression on the 90 cows that were treated by the other 6 surgeons indicated that this variable did not influence prognosis ($P = 0.73$). Variability and type of supportive treatments might also have influenced results of the current study. The intensive medical treatment usually administered in a hospital setting, for instance, would likely yield different results, and the decision thresholds suggested in this study would not be suitable for such utilization. The strength of the current study was to adhere to field conditions that were representative of the practitioners' reality (i.e., different practitioners and various supportive treatments). Therefore, extrapolation of conclusions from this study to other populations should be made with caution. Furthermore, the measure of surgical outcome would have been more objective if death of the animal or level of milk production were used as the outcome of interest, as was done in other studies (Figueiredo et al., 2006; Roy et al., 2008). In the current study, the outcome definition was the satisfaction of the owner 30 d postoperatively and was chosen based on the assumption that the dairy producer would likely have decided not to have surgery performed if he had known that he would later be unsatisfied with the results. Asking about the satisfaction of the owner regarding the animal's progress implicitly includes a mixture of information on appetite, dairy production, complications, economics, and culling or survival status of the animal. Furthermore, such an aggregated measurement of these different components of "owner satisfaction" precludes any cost-benefit analysis associated with the use of this ancillary test. In our opinion, however, a positive surgical outcome cannot be defined solely by the cow's subsequent milk production or by its survival status. We strongly believe, however, that the

dairy producer's satisfaction would more completely encompass and summarize the different components that, together, can help define the outcome of the surgery.

Finally, thresholds proposed in this study cannot be validated using the same population, because using the same data to establish and validate LAC thresholds would likely introduce an upward bias. These thresholds will have to be validated in a future study in a distinct population. An economic study could then be performed to quantify the cost-benefit of using this ancillary test. Finally, although LAC plus HR allowed a better prediction of negative outcome compared with HR only for RDA or AV, it remains to be determined if this combination of variables is more effective and reliable than a practitioner's clinical judgment in providing an accurate preoperative prognosis.

CONCLUSIONS

This study indicated that LAC, in addition to HR, is a useful prognostic indicator for RDA or AV in dairy cows. The combination of LAC and HR significantly improved the predictive accuracy of a negative outcome compared with HR alone. A LAC ≤ 2 mmol/L seemed to be a good indicator of positive outcome and would be useful to support a surgical decision. Cows with LAC ≥ 6 mmol/L, on the other hand, had a very poor prognosis and should be culled in most instances (e.g., average commercial cows), without surgical treatment.

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