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Using rumination and activity data for early detection of anaplasmosis disease in dairy heifer calves

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ABSTRACT

Bovine anaplasmosis causes considerable economic losses in dairy cattle production systems worldwide, ranging from $300 million to $900 million annually. It is commonly detected through rectal temperature, blood smear microscopy, and packed cell volume (PCV). Such methodologies are laborious, costly, and difficult to systematically implement in large-scale operations. The objectives of this study were to evaluate (1) rumination and activity data collected by Hr-Tag sensors (SCR Engineers Ltd.) in heifer calves exposed to anaplasmosis; and (2) the predictive ability of recurrent neural networks in early identification of anaplasmosis. Additionally, we aimed to investigate the effect of time series length before disease diagnosis (5, 7, 10, or 12 consecutive days) on the predictive performance of recurrent neural networks, and how early anaplasmosis disease can be detected in dairy calves (5, 3, and 1 d in advance). Twenty-three heifer calves aged 119 ± 15 (mean ± SD) d and weighing 148 ± 20 kg of body weight were challenged with 2×10^7 erythrocytes infected with UFMG1 strain (GenBank no. EU676176) isolated from *Anaplasma marginale*. After inoculation, animals were monitored daily by assessing PCV. The lowest PCV value (14 ± 1.8%) and the finding of rickettsia on blood smears were used as a criterion to classify an animal as sick (d 0). Rumination and activity data were collected continuously and automatically at 2-h intervals, using SCR Heatime Hr-Tag collars. Two time series were built including last sequence of −5, −7, −10, or −12 d preceding d 0 or a sequence of 5, 7, 10, or 12 d randomly selected in a window from −50 to −15 d before d 0 to ensure a sequence of days in which PCV was considered normal (32 ± 2.4%). Long short-term memory was used as a predictive approach, and a leave-one-animal-out cross-validation (LOAOCV) was used to assess prediction quality. Anaplasmosis disease reduced 34 and 11% of rumination and activity, respectively. The accuracy, sensitivity, and specificity of long short-term memory in detecting anaplasmosis ranged from 87 to 98%, 83 to 100%, and 83 to 100%, respectively, using rumination data. For activity data, the accuracy, sensitivity, and specificity varied from 70 to 98%, 61 to 100%, and 74 to 100%, respectively. Predictive performance did not improve when combining rumination and activity. The use of longer time-series did not improve the performance of models to predict anaplasmosis. The accuracy and sensitivity in predicting anaplasmosis up to 3 d before clinical diagnosis (d 0) were greater than 80%, confirming the possibility for early identification of anaplasmosis disease. These findings indicate the great potential of wearable sensors in early identification of anaplasmosis diseases. This could positively affect the profitability of dairy farmers and animal welfare.

Key words: artificial intelligence, machine learning, sensors, *Anaplasma marginale*

INTRODUCTION

Bovine anaplasmosis caused by *Anaplasma marginale* is endemic in some countries, causing considerable economic losses due to mortality, especially in young animals, reducing animal performance, and increasing costs related to medicines and veterinary services (Kocan et al., 2003; Aubry and Geale, 2011; Ueti et al., 2012). Bovine anaplasmosis is listed as an impor-

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tant disease by World Organization for Animal Health report (OIE, 2019). The mortality caused by anaplasmosis can reduce the number of weaned calves by 3.6% and increase the mortality rate in adult cattle by up to 30% (Zabel and Agusto, 2018). Anaplasmosis is one of the most common postweaning diseases in tropical countries, and it is responsible for generating annual economic losses of $300 million in the United States and $900 million in Latin America, in the dairy and beef cattle industries (Kocan et al., 2003).

Current procedures used for diagnosis of anaplasmosis are based on laboratory analyses of blood smears using a binocular microscope (Vidotto and Marana, 2001; Aubry and Geale, 2011), and packed cell volume (**PCV**; Radostits et al., 2007). Another way to diagnose anaplasmosis is through clinical symptomatology, which includes: fever, mild to severe anemia, jaundice without hemoglobinemia and hemoglobinuria, loss of appetite and weight, dehydration, abortion, anorexia, and lethargy (de Souza et al., 2001; Kocan et al., 2003; 2010; Oliveira Júnior et al., 2018). The serological and molecular methods to measure *Anaplasma* spp. antibodies (Aubry and Geale, 2011) include ELISA (Araújo et al., 2005), the indirect immunofluorescence reaction (**RIFI**) (Visser et al., 1992), and PCR (Molad et al., 2006). Such methods present high specificity (**SPE**) and sensitivity (**SEN**); however, they are expensive and difficult to perform routinely on commercial farms. Additionally, systematic monitoring of individual animals for anaplasmosis detection requires time, training, and specialized labor, which become limiting factors in large-scale livestock operations (Kocan et al., 2003; Silvestre et al., 2016; Oliveira Júnior et al., 2018).

Although the on-farm diagnosis of anaplasmosis disease is based on clinical signs, the peak of anemia occurs only 2 d after the peak of parasitemia, and 1 d after the peak in rectal temperature (Coelho, 2007). Consequently, on-farm anaplasmosis diagnosis usually occurs when the disease has already caused damage to health and economic losses. Therefore, strategies for its early detection would improve disease prognosis and efficiency of the diagnosis, maximizing the sustainable use of antimicrobials.

Precision farming technologies appear as an option for early disease detection. Continuous sensor-based monitoring of rumination (**RUM**) and activity (**ACT**) has the potential to be used for herd health management decisions (Reiter et al., 2018) and to evaluate animal welfare (Jaeger et al., 2019) through early diagnosis of diseases such as ketosis (Sturm et al., 2020), hypocalcemia (Goff et al., 2020), lameness (Alsaaod et al., 2019), diarrhea (Belaid et al., 2020), and respiratory disease (Timsit et al., 2011; Swartz et al., 2017; Hixson et al., 2018). However, the use of such sensor devices to create predictive models for detection of diseases such as anaplasmosis has not been extensively explored in dairy heifer calves. Souza et al. (2021) recommended a protocol based on blood smears associated with rectal temperature for bovine tick fever monitoring. Such protocol avoided unnecessary treatments, drove the correct treatment, and decreased the unnecessary use of medicines. Continuous sensor-based monitoring can automate animal screening for application of the Souza et al. (2021) protocol.

We hypothesized that anaplasmosis causes changes in RUM time and ACT index in dairy heifer calves and that bovine anaplasmosis can be predicted based on either or both RUM and ACT data obtained from wearable sensors. The objectives of this study were to evaluate (1) RUM and ACT data collected from dairy heifers exposed to anaplasmosis, and (2) long short-term memory (**LSTM**) for detection of anaplasmosis using RUM, ACT, or both combined. Additionally, we aimed to investigate the effect of time series length on predictive performance of LSTM and to study how early anaplasmosis diseases can be accurately detected in dairy heifers using sensor data.

MATERIALS AND METHODS

This study was approved by the Embrapa Dairy Cattle Animal Care and Use Committee, Juiz de Fora, Minas Gerais, Brazil (number: 4498240316). The experiment was conducted from February to December 2019 at the Embrapa Dairy Cattle Experimental Farm located in Coronel Pacheco, Minas Gerais, Brazil. Data analysis was conducted at the University of Wisconsin-Madison.

Preweaning Period

Calves, Housing, and Management. Fifty-five Holstein calves with birth weight of 34.42 ± 6.25 kg (mean ± SD) were randomly selected from the Embrapa Dairy Cattle experimental farm. Calves were individually placed in pens (1.25 × 1.75 m) located in a shed protected by nylon screen and a double-screened door to prevent contact with flies and ticks, and exposure to anaplasmosis and other tick fever agents. Once a week, the shed was sprayed with imidacloprid (Rotam do Brazil Agrochemicals and Agricultural Products Ltda.) to keep away flies and mosquitoes. In addition to replacing thiamethoxan and Z-9-tricosene mosquito baits (Agita 10 Wg, Elanco) every 3 wk, a spray containing cypermethrin 15% + chlorpyrifos 25% + piperonyl butoxide 15% (Ciperclor Plus, Ceva Saúde Animal Ltda.) was administered to the animals weekly to prevent tick infestation. This drug was selected for

use based on a sensitivity test performed using ticks found on the experimental farm, as described by Drummond et al. (1973). In addition, the calves received a diazinon mosquito ring (Top Tag 180, Zoetis).

To ensure proper adaptation, one day after birth, each calf received an SCR Hr-Tag Heatime collar (SCR Engineers Ltd.) according to Rodrigues et al. (2019). The collars were adjusted routinely as the calves grew. Colostrum (≥25% Brix) was administered at a minimum of 10% of BW up to 6 h after birth (Lombard et al., 2020). To verify the quality of the transfer of passive immunity, plasma blood protein was measured 48 h after birth (Serum protein REF-301, Biocotek), and all animals presented adequate values (>5.5 g/dL) as recommended by McGuirk (2003). Calves received transition milk until 3 d of age, and from 4 to 75 d of age, they were fed whole milk (4.4 ± 1.0% fat and 3.1 ± 0.1% CP) using nipple buckets (Milk Bar). The volume of milk supplied was 8, 6, and 3 L/d from 0 to 30, 31 to 60, and 61 to 75 d of age, respectively. From 0 to 60 d of age, calves were fed twice daily (at 0800 and 1500 h) and from 61 to 75 d of age calves were fed a single meal (at 0800 h). A mixture of 95% starter (22% CP and 80% NDF) and 5% Tifton hay (8.5% CP and 69.9% NDF) was fed ad libitum from 0 to 60 d of age. After age 61 d, corn silage (6.8% CP and 42% NDF) was fed ad libitum in an individual bucket. Between 75 to 90 d of age, the calves were maintained in the same facilities, receiving only solid diet and water.

A clinical examination was performed daily at 0800 h to assess rectal temperature, nasal discharge, cough, eye discharge, ear positioning, and fecal score according to Larson et al. (1977) and McGuirk (2008). Animals presenting injuries or illness were treated in accordance with routine farm management practices. At 15 and 120 d of age, all animals received coccidiostat (Isocox) at a dose of 3 mL/10 kg, equivalent to 15 mg/kg of Toltrazuril. Two days after birth, individual blood samples were collected, via puncture of the jugular vein, and placed in vacuum tubes (EDTA, Vacutainer; Becton Dickinson and Co.) to determine the absence of *A. marginale*, *Babesia bovis*, and *Babesia bigemina* using PCR (da Silveira et al., 2014) and RIFI (Santos et al., 2017). Twenty-two calves tested positive and were excluded from the experiment to avoid interference from the antibodies that resulted from the responses to vertical transmission in the induced anaplasmosis challenge process.

Postweaning Period

Heifer Calves, Housing, and Management After the preweaning period, the remaining 23 dairy heifer calves averaging 119 ± 15 d of age and 148.4 ± 20.3 kg of BW were randomly grouped (8, 8, and 7 per group) and moved to 3 paddocks with a concrete floor (280 m^2) mechanically cleaned daily. The first 15 d of the experimental trial were used for socialization and adaptation of the animals.

In the postweaning period, calves were fed TMR (18% CP and 80% NDF) composed of whole corn silage, ground corn, soybean meal, monensin, and mineral-vitamin (Bovigold Prima). The TMR was provided twice a day (at 0800 and 1500 h) in 4 electronic feed bins per paddock (AF-1000 Junior; Intergado Ltda.). The refused feed was removed from the feed bins daily before the morning meals at 0900 h. The amount of feed offered was adjusted daily to reach approximately 10% refusal. Water was offered ad libitum by an electronic water bin available in each paddock (WD-1000 Junior, Intergado Ltda.).

The same clinical examination procedure adopted during the preweaning period was performed daily at 0800 to assess rectal temperature, nasal discharge, cough, eye discharge, ear positioning, and fecal score.

Anaplasmosis Inoculation Procedure Fifteen days before *A. marginale* inoculation, blood samples were collected to determine the absence of *A. marginale, B. bovis,* and *B. bigemina* using nested (n)PCR and RIFI techniques. Based on nPCR and RIFI results, all 23 animals averaging 119 ± 15 d of age and 148.4 ± 20.3 kg of BW tested negative and were challenged with a low virulence inoculum dosage (2×10^7 erythrocytes infected) of *A. marginale* UFMG1-EU676176, isolated from a naturally infected splenectomized calf and cryopreserved in liquid nitrogen using dimethyl sulfoxide (Bastos et al., 2010).

Laboratory and Hematological Evaluation The PCV count was performed using the microhematocrit method (Weiss, J.D., Wardrop, 2010) using heparinized blood in a capillary tube, which was then centrifuged (Spin 1000, Micro Spin) at 800 × *g* for 5 min without exceeding a temperature of 45°C (Schalm et al., 1975). Subsequently, the PCV value was obtained using a Hematocrit Reader Card (Spin). Blood smears were stained by the Romanowsky method (Panótico Rápido Laborclin Produtos para Laboratórios Ltda.). Rickettsemia was determined by observing 40 homogeneous fields in a binocular microscope (Nikon Instruments Inc.), at a 100-fold increase, to determine the percentage of hematocrit cells infected with *A. marginale* (IICA, 1987).

The PCV and rickettsemia values were used to monitor anaplasmosis progression. The average of PCV values performed once a week before inoculation were used to calculate the reference value for a healthy animal. After *A. marginale* inoculation, PCV procedures continued to be performed once a week, but after the

first identification of parasitized erythrocyte by *A. marginale* in a blood smear, PCV, and blood smears were performed every 48 h. Sequentially, as PCV decreased further, both procedures were performed every 24 h to establish the exact time to begin treatment. When PCV reached 50% of the healthy value, the animal was intramuscularly administered a single dose of 7.5 mg/kg of BW enrofloxacin (Kinetomax, Bayer) according to Facury-Filho et al. (2012).

Data Processing and Analysis

The animals were considered sick when PCV value dropped and achieved 50% or less of average (n = 23) healthy value (32 ± 1.49%), and the presence of anaplasma was confirmed in the blood smears. The animals were classified as healthy when they had no parasitized red blood cells and the PCR-RIFI test was negative for anaplasmosis. To standardize the days relative to sickness, d 0 was considered the day that the minimum PCV value was reached. The time from inoculation to clinical disease (d 0) averaged 35 ± 3 d.

Rumination (min/2 h) and ACT (index ranging from 0 to 255 bits/2 h) data were generated through 3-axis accelerometers and collected directly from the SCR software (Rodrigues et al., 2019), using the Hr-Tag recording standards of 2-h periods for ACT and RUM data. Activity measurement was based on the signal analysis of the head movements (proportional to the number, intensity, and direction of the neck movements) expressed by an index ranging from 0 to 255 bits for a 2-h interval (Van Hertem et al., 2014).

Data from 2 time series of 5, 7, 10, or 12 d were collected from each animal. The first consisted of data from 5, 7, 10, or 12 d before sickness (d 0), which was considered the sick pattern. The other comprised a sequence of consecutive 5, 7, 10, or 12 d randomly selected in a time window from −50 to −15 d before d 0, which was considered the healthy pattern. All calves included in the data set had both time series (healthy and sick) and each animal served as her own control.

A recurrent neural network called LSTM was used as a predictive approach to detect sick events (50% of healthy PCV value) at d 0, and 1, 3, and 5 d in advance. Long short-term memory was adopted due to its capacity of extracting patterns and learning temporal dependences of longitudinal data in sequence prediction problems (Hochreiter and Schmidhuber, 1997) Data analysis was implemented in Python 3.6 using the computational resources provided by UW-Madison Center for High Throughput Computing.

A random search was performed to find the best combination of hyperparameters. The random grid search was based on a single LSTM layer with 20, 40, 80, 100, or 200 neurons, then as activation function, dropout ranging from 0.001 to 0.01, and recurrent dropout varying from 0 to 0.05. All models tested used a batch size of 6, 50 epochs, a binary cross-entropy loss function, and *rmsprop* optimizer.

Model validation was performed using leave-one-animal-out cross-validation (**LOAOCV**). In each iteration, a pair of samples from each calf was deleted (healthy and sick) and used for test, and the remaining data set was used to train and tune the model. This approach was repeated n times (n = number of calves) until all calves were excluded once from the training set. For each LOAOCV iteration, hyperparameter tuning was performed using the remaining data set (n − 2), and the grid search was performed to define the best combination of hyperparameters through a second LOAOCV (nested in each iteration), and these combinations were ranked based on accuracy (Supplemental Tables S1 to S6; https://doi.org/10.17632/9yy4dvctnd.1). The best combination of hyperparameters was defined as the combination with the greatest frequency after all iterations. This combination was then adopted as the final architecture and used to reanalyze specific iterations. Such tuning approach was used to avoid overfitting, which frequently occurs when machine learning algorithms are applied to small data sets, and particularly when hyperparameters are chosen using the same data set as that used for model assessment.

To evaluate performance of the models, ACC, SEN, SPE, positive predicted value (**PPV**), and negative predicted value (**NPV**) were calculated using the following equations: Accuracy = (TP + TN)/(TP + TN + FP + FN), SEN = TP/(TP + FN), SPE = TN/(TN + FP), PPV = TP, where TP is true positive, FP is false positive, FN is false negative, and TN is true negative. A description of the strategy used for hyperparameter search and model training and testing is presented in Figure 1.

RESULTS

Alterations in PCV, rickettsemia, and rectal temperature due to exposure to *A. marginale* can be observed in Figure 2. The PCV value on d 0 was 14 ± 1.8%, which means 40% of the normal PCV value between −40 and −16 d (32 ± 1.49%). The mean rickettsemia value on d 0 was 6.12 ± 3.07%. Regarding rectal temperature, values in the normal physiological range (below 39.5°C) were observed 3 d before d 0 (−3 d). Rectal temperature was greater than 39.5°C from −3 to 0 d and reached an average value of 40.9 ± 0.5°C on d 0.

Daily RUM and ACT patterns are described in Figure 3. There was a reduction of RUM from −4 d until d 0. Rumination time decreased 34% from 566 ± 78

min/d (between −20 to −15 d) to 372 ± 140 min/d (between −1 d to 0 d) from healthy and sickness time. Activity index was on average 453 ± 65 (−20 to −15 d) and 405 ± 59 (−1 to 0 d) and decreased about 11%, respectively. The architectures of LSTM algorithms with best performance for each time series length (5, 7, 10, and 12 d), and each day relative to anaplasmosis (0, −1, −3, and −5 d), are shown in Tables 1, 2, and 3, respectively. The performance of the remaining tested architectures (total of 345) is shown in supplementary tables. The ACC of LSTM algorithms for the detection of anaplasmosis ranged from 87 to 98% when using RUM data (Table 1). The ACC values were 95, 97, 88, and 90% for 0, −1, −3, and −5 d, decreasing 5% when the prediction time changed from 0 to −5 d. The SEN and SPE decreased 8 and 2% comparing 0 to −5 d in early predictions, respectively (Table 1). Changes in time series length did not substantially affect the ACC values of the predictive models (93, 93, 92, and 93% for of 5, 7, 10, and 12 d, respectively).

The ACC of predictive models for the detection of anaplasmosis ranged from 70 to 98% using ACT data (Table 2). The ACC values were 95, 92, 87, and 80% for 0, −1, −3, and −5 d time series length, respectively (Table 2). Regardless of time series length, ACC values were 92, 92, 87, and 85% for 5, 7, 10, and 12 d, respectively, decreasing 8% comparing the time series of 5 and 12 d.

The ACC of predictive models for the detection of anaplasmosis based both on RUM and ACT data ranged from 85 to 98%. The ACC (95, 97, 89, and 89% for 0, −1, −3, and −5 d before d 0) decreased 7% when the prediction was done −5 d in advance compared with 0 d (Table 3). The length of time series had little influence on ACC values, with 92, 92, 93, and 94% for the time series of 5, 7, 10, and 12 d, respectively.

DISCUSSION

The current study was designed to assess the feasibility of using a commercial system (SCR Heatime Hr) for early detection of anaplasmosis in dairy calves based on challenge model with a low virulence inoculum of *A. marginale* UFMG1-EU676176. Using clinical reference assessments and artificial intelligence, we found that RUM and ACT data collected every 2 h can be used for the early detection of anaplasmosis in calves up to 5 d in advance of clinical signs.

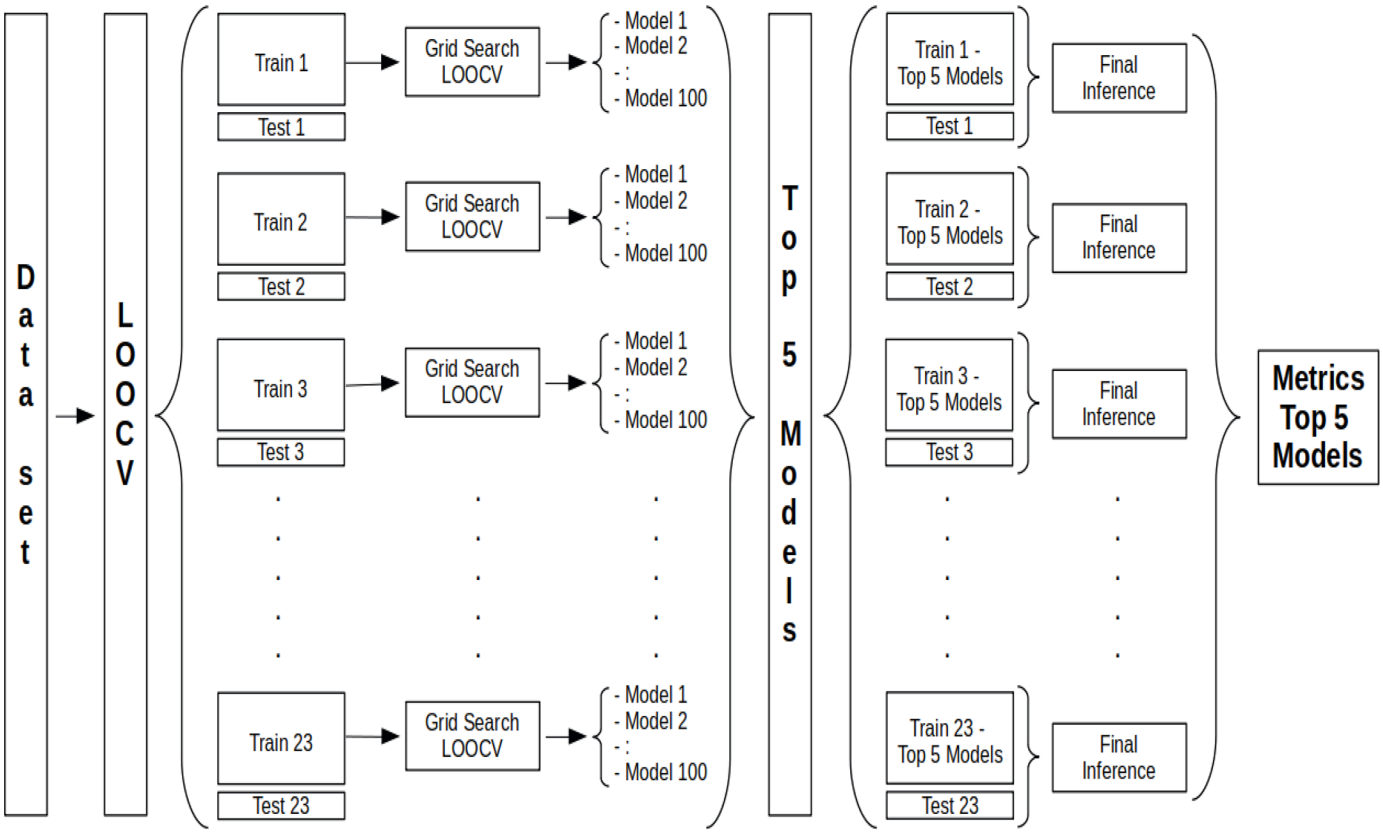

Figure 1. Strategy used for hyperparameter search and model training and testing.

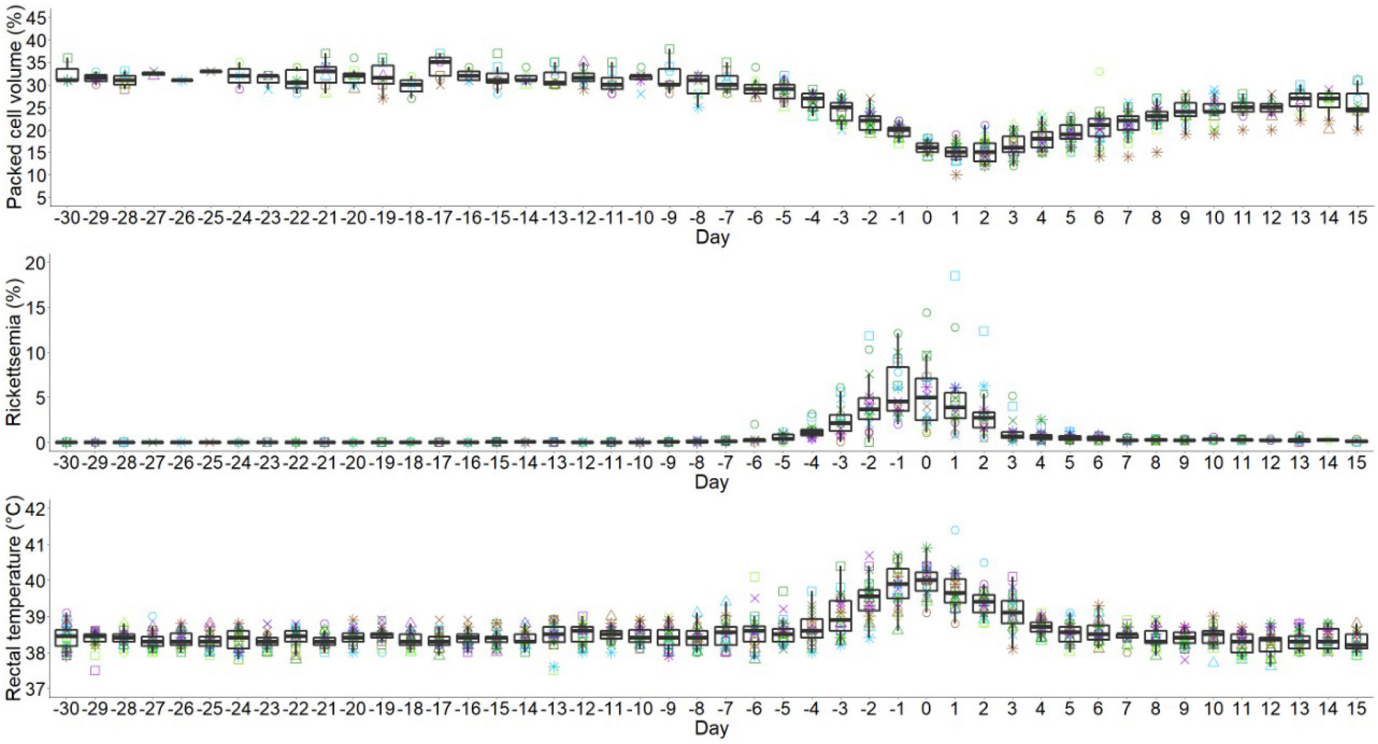

Figure 2. Boxplot representation of packed cell volume, rickettsemia, and rectal temperature in dairy heifer calves inoculated with *Anaplasma marginale* according to days relative to sickness. Each box indicates quartiles of distribution (Q1, median, and Q3); whiskers indicate minimum (Q1 − 1.5 × interquartile range) and maximum (Q3 + 1.5 × interquartile range) of data distribution. Datapoints are marked with different symbols and colors combinations by animal.

Healthy Status, RUM, and ACT During the Study

The peak of anemia occurs 2 d after the peak in rickettsemia, 1 d after rectal temperature peak, and is concurrent with clinical symptoms. The interrelationship between PCV, rectal temperature, and rickettsemia found in the current study agrees with Coelho (2007) and Oliveira Júnior et al. (2018). The decrease in PCV values is related to the virulence of the *A. marginale*-UFMG1 sample used, which is considered low (Coelho, 2007; Bastos et al., 2010; Silvestre et al., 2016), yet capable of triggering the disease in young calves. These authors, also working with *A. marginale,* found a lower (13.0 and 13.4%, respectively) average PCV value compared with our study (14%). The standard values of PCV normally vary 24 to 46% in cattle (Radostits et al., 2007). In our study, the peak of rickettsemia preceded the peak of lower PCV, which is corroborated by Coelho (2007) and Bastos et al. (2009).

The pyrexia released systemic inflammatory mediators, which can induce behavioral changes (Pecchi et al., 2009; Oliveira Júnior et al., 2018). In the current study, rectal temperature and rickettsemia increased gradually together, as described by Kocan et al. (2003) and Coelho (2007), which reported a positive correlation between rectal temperature and rickettsemia. Thus, the pathogeny and calves' physiological responses seem to be representative of ordinary anaplasmosis cases.

To the best of our knowledge, our study is the first that measures RUM and ACT through wearable sensors in Holstein calves challenged with anaplasmosis. The lower RUM and ACT associated with higher rectal temperature, rickettsemia, and decreased PCV on d −1 and 0 relative to sickness can be explained by the effects of anaplasmosis on immune response. Red blood cells parasitized by *A. marginale* induce a humoral immune response that causes antibodies to adhere to infected and uninfected cells. Consequently, these cells are quickly removed by the monocytic phagocytic system, resulting in anemia (Oliveira Júnior et al., 2018). In addition, changes such as weakness and lethargy can accompany severe anemia, which can mimic respiratory problems, because the animal must breathe faster and more deeply to compensate for the failure in blood oxygenation (Bastos et al., 2009; Silvestre et al., 2016). The increase in infected red blood cells also enhances the immune response, releasing inflammatory mediators that cause fever and lethargy (Coelho 2007).

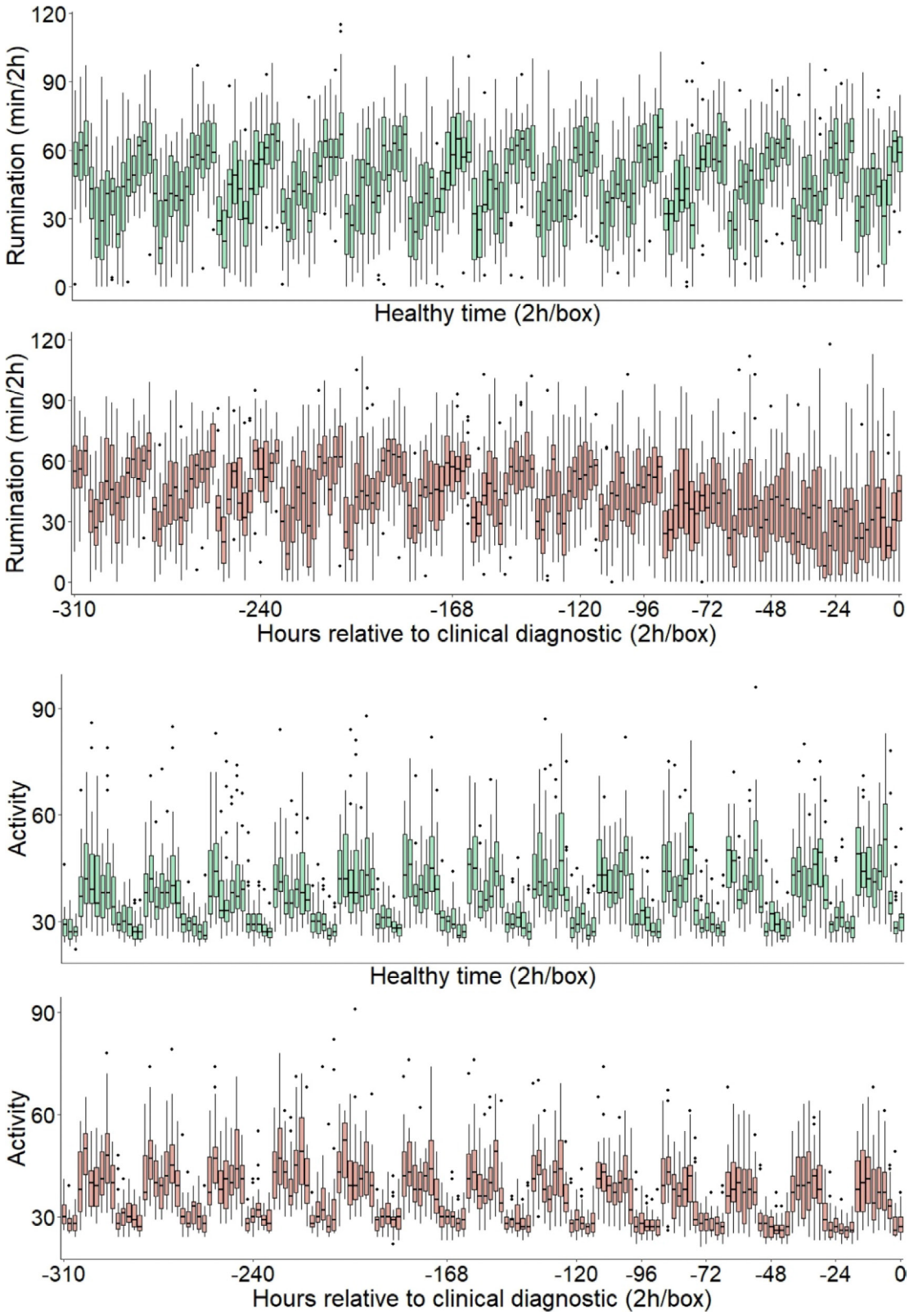

Figure 3. Boxplot representation of rumination time and activity index measured by SCR Heatime Hr collars (SCR Engineers Ltd.) in periods of 12 random days of healthy time (green) and 12 d before sickness (red) in dairy heifer calves. Each box indicates quartiles of distribution (Q1, median, and Q3); whiskers indicate minimum (Q1 − 1.5 × interquartile range) and maximum (Q3 + 1.5 × interquartile range) of data distribution.

Table 1. Performance of different recurrent neural network models based on rumination time data to detect anaplasmosis using different time series length at different days relative to sickness (DRS) in dairy heifer calves

	Model description				Performance[1]				
Time series	DRS	Neurons	Dropout	Recurrent dropout	ACC	SEN	SPE	PPV	NPV
5 d	0	20	0.005	0.000	96	96	96	96	96
	−1	20	0.001	0.005	96	96	96	96	96
	−3	20	0.000	0.005	87	91	83	84	90
7 d	0	20	0.000	0.01	96	96	96	96	96
	−1	20	0.001	0.01	98	96	100	100	96
	−3	20	0.000	0.01	89	91	87	88	91
	−5	200	0.005	0.001	91	91	91	91	91
10 d	0	20	0.005	0.001	93	96	91	92	95
	−1	20	0.001	0.000	96	91	100	100	92
	−3	20	0.005	0.001	89	91	87	88	91
	−5	20	0.01	0.005	89	83	96	95	85
12 d	0	20	0.001	0.005	96	96	96	96	96
	−1	20	0.000	0.01	98	100	96	96	100
	−3	20	0.005	0.01	89	91	87	88	91
	−5	20	0.001	0.005	91	91	91	91	91

[1]Accuracy (ACC), sensitivity (SEN), specificity (SPE), positive predicted value (PPV), and negative predicted value (NPV). All models used a long short-term memory layer, a batch size of 6, and 50 epochs. Data were collected using SCR Heatime Hr-Tag collars (SCR Engineers Ltd.).

Rumination, ACT, or Both as Predictors

The reduction of RUM may be associated with reduced intake, which is often an early sign of illness (Johnson, 2002). Previous studies evaluating inoculation of *A. marginale* observed reduction in feed intake and ruminal movements in calves (de Andrade et al., 2001; Meneses, 2013). Additionally, altered eating behavior may be a result of fever, which is known to be associated with reduced motivation to eat and drink (Hart, 1988; Feitosa, 2008). Thus, anorexia and fever are common clinical signs of acute anaplasmosis (Rodríguez et al., 2000). Calves affected with tick-borne disease have reduced feed intake, frequency, and time spent in feed bins of about 35, 27, and 24% before the clinical symptoms of fever, anemia, and parasitemia (Oliveira Júnior et al., 2018).

In the present study, the RUM returned to normal values 2 d after d 0, probably due to early antimicrobial treatment provided when the PCV reached 50% of the healthy value. Rumination time remained low during the days after anaplasmosis treatment, probably due to the time needed to restore the PCV, acid-base balance, and hydration (Meneses, 2013). Contrastingly, in practical or on-farm conditions, diagnosis of anaplasmosis is usually performed when the disease has already

Table 2. Performance of different recurrent neural network models based on activity index data to detect anaplasmosis using different time series length at different days relative to sickness (DRS) in dairy heifer calves

	Model description				Performance[1]				
Time series	DRS	Neurons	Dropout	Recurrent dropout	ACC	SEN	SPE	PPV	NPV
5 d	0	100	0.001	0.05	98	100	96	96	100
	−1	100	0.001	0.05	93	96	91	92	95
	−3	100	0	0.05	85	91	78	81	90
7 d	0	100	0	0.05	93	87	100	100	88
	−1	100	0	0.05	93	100	87	88	100
	−3	200	0.001	0.005	93	96	91	92	95
	−5	200	0.005	0.001	91	91	91	91	91
10 d	0	40	0.001	0	91	87	96	95	88
	−1	40	0	0	91	100	83	85	100
	−3	200	0.005	0.001	87	91	83	84	90
	−5	200	0	0.005	80	87	74	77	85
12 d	0	100	0.01	0	96	100	91	92	100
	−1	100	0.01	0	93	100	87	88	100
	−3	100	0	0.01	83	87	78	80	86
	−5	200	0.01	0	70	61	78	74	67

[1]Accuracy (ACC), sensitivity (SEN), specificity (SPE), positive predicted value (PPV), and negative predicted value (NPV). All models used a long short-term memory layer, a batch size of 6, and 50 epochs. Data were collected using SCR Heatime Hr-Tag collars (SCR Engineers Ltd.).

Table 3. Performance of different recurrent neural network models based on rumination time and activity index data to detect anaplasmosis using different time series length at different days relative to sickness (DRS) in dairy heifer calves

	Model description				Performance[1]				
Time series	DRS	Neurons	Dropout	Recurrent dropout	ACC	SEN	SPE	PPV	NPV
5 d	0	20	0.005	0.005	93	91	96	95	92
	−1	20	0.005	0.005	93	91	96	95	92
	−3	20	0.005	0.005	91	96	87	88	95
7 d	0	20	0.001	0.001	96	96	96	96	96
	−1	20	0.01	0.005	98	96	100	100	96
	−3	20	0.005	0.05	89	91	87	88	91
	−5	20	0.01	0.005	85	91	78	81	90
10 d	0	20	0.001	0.000	96	96	96	96	96
	−1	20	0.000	0.05	98	96	100	100	96
	−3	20	0.001	0.005	89	91	87	88	91
	−5	20	0.000	0.05	89	96	83	85	95
12 d	0	20	0.000	0.05	96	96	96	96	96
	−1	20	0.01	0.01	98	96	100	100	96
	−3	20	0.01	0.01	89	87	91	91	88
	−5	20	0.005	0.000	93	91	96	95	92

[1]Accuracy (ACC), sensitivity (SEN), specificity (SPE), positive predicted value (PPV), and negative predicted value (NPV). All models used a long short-term memory layer, a batch size of 6, and 50 epochs. Data were collected using SCR Heatime Hr-Tag collars (SCR Engineers Ltd.).

reached an advanced stage, basically by inspecting the animals. Behavioral changes are visible to farm staff when anemia is already more severe and, often, with a PCV well below 50% of the normal value. Therefore, on many dairy farms, the adverse effects of anaplasmosis on RUM, ACT, PCV, and rickettsemia may be greater than the values reported in this study.

The RUM data obtained from Hr-Tag sensors were important predictors of anaplasmosis disease in the current study. Based on previous literature, predicted RUM time for heifers and calves may not be highly accurate when compared with human observation (Burfeind et al., 2011; Goldhawk et al., 2013; Lopreiato et al., 2018; Rodrigues et al., 2019). However, our results demonstrate that accuracy bias does not restrict its applicability for detection of diseases.

Visually, anaplasmosis had a subtler effect on ACT than did on RUM (Figures 3 and 4), but predictive models based on both RUM and ACT data had high predictive quality to detect anaplasmosis. When combining RUM and ACT as predictors, no improvements were observed on models' performance (Table 3). The ACC average for models based on combined RUM and ACT was similar to that of ACT or RUM separately. There-

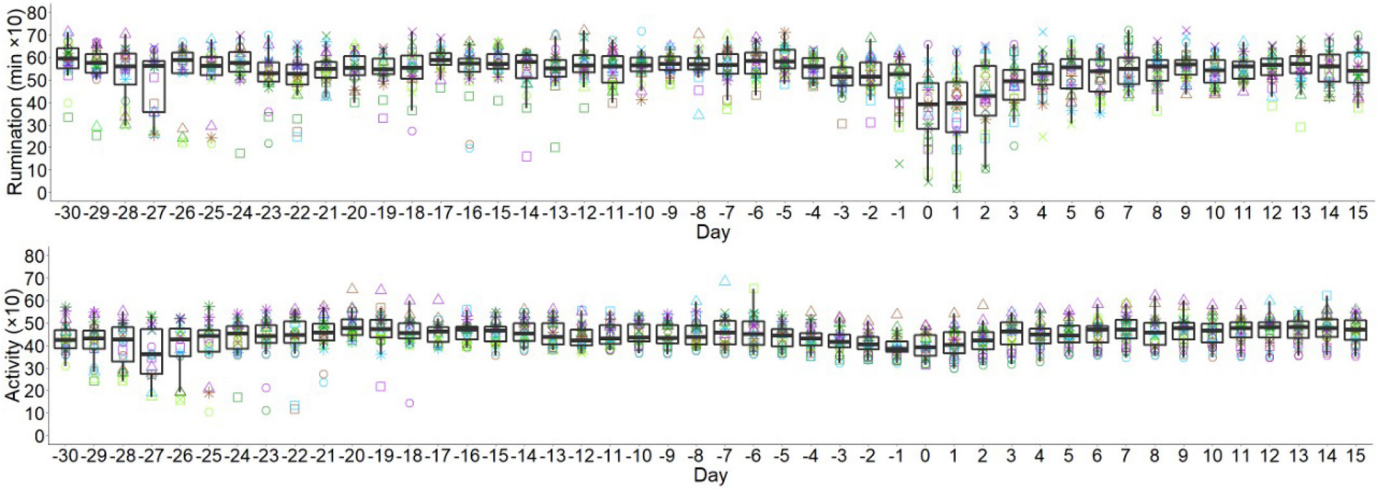

Figure 4. Boxplot representation of rumination time and activity index in dairy heifer calves inoculated with *Anaplasma marginale* according to days relative to sickness. Each box indicates quartiles of distribution (Q1, median, and Q3), whiskers indicate minimum (Q1 − 1.5 × interquartile range) and maximum (Q3 + 1.5 × interquartile range) of data distribution. Datapoints were marked with different symbols and colors combinations by animal. .

fore, it is possible to use models based only on RUM or ACT, which is interesting because a vast majority of commercial sensors do not have RUM functionality (Stygar et al., 2021). It is important to highlight that accelerometers are becoming less expensive and can be used to develop new commercial devices for early detection of specific diseases such as anaplasmosis.

Time Series Length Effects on Model's Predictive Quality

There was no benefit to using a longer time series for anaplasmosis detection. When comparing the 5- and 7-d time series, ACC, SEN, and SPE values were greater compared with time series at 10 and 12 d. Thus, time series between 5 and 7 d seem to be suitable for anaplasmosis detection. Similar results were observed for detecting estrus in dairy cows based on feeding behavior data, with equivalent performance for models using time series of −24 and −172 h relative to estrus (Cairo et al., 2020). The use of short time series can reduce the demand for computational resources in future development and deployments.

Perspectives of Early Detection of Anaplasmosis

The differences involving clinical signs, RUM behavior, and ACT index observed in this study are consistent with behavioral responses such as depression and lethargy that are part of animals' physiological response to *A. marginale* rickettsemia (Hart, 1988). Thus, the reduced behavioral ACT observed between −5 to 0 d compared with healthy periods, may be the result of fever, which is associated with the proliferation of parasitized cells and inflammation mediators (Bastos et al., 2009, 2010; Meneses, 2013).

The use of models that included 0 d in time series from sick animals was useful in detecting clinical disease and can be a safe threshold for prescribing treatment, as well as the fact that the health status of all animals in the current study was recovered after treatment with enrofloxacin. However, the great predictive performance of models to detect anaplasmosis 1 and 3 d in advance of clinical signs may allow the diagnosis of anaplasmosis disease at earlier stages of its development (when PCV values range between 50 and 70% of healthy time). This presents a great opportunity for early prescriptive treatments, including those that reduce disease morbidity and mortality. Additionally, after treatment with enrofloxacin, anemia is not eliminated quickly due the slow reduction in rickettsemia (Facury-Filho et al., 2012). Thus, early diagnosis and treatment may promote faster animal recovery. Treatment in the early stages can eliminate the need for supplementary treatment with support medications such as blood transfusions and fluid therapy, which are expensive and laborious. The ACC of models to predict anaplasmosis 5 d in advance was reduced; however, it remained greater than 70%, which may suggest the possibility of the usefulness of tracking of anaplasmosis disease based on ACT data. Early detection of the anaplasmosis event based on ACT data (−1, −3, and −5 d) reduced the model's accuracy by 2, 8, and 15%, respectively, compared with predictions including 0 d.

The satisfactory performance of −5 d prediction models can be explained by the ability of machine learning algorithms to grasp complex relationships between input and output information, capturing nonlinear relationships (Srivastava et al., 2014), and temporal dependencies with longitudinal data (Hochreiter and Schmidhuber, 1997). Contrastingly, Belaid et al. (2020) used a multivariate logistic regression model based on ACT-monitoring device data to predict sickness in veal calves, and reported ACC, SEN, and SPE of 62, 63, and 61%, respectively, with −3 d in advance.

The ACC values for 1 and 3 d in advance were similar compared with the 0 d predictions for all time series based on RUM data. Therefore, −1 and −3 d predictions based only on RUM can be used for early treatment prescription. The −5 d predictions based on RUM had SEN and SPE of 88 and 92%, respectively, which demonstrate the high potential of machine learning models to recognize the onset of disease, when the PCV represents 80% of normal healthy value. Therefore, the early prescription of treatment can be based both using RUM or ACT and may improve the efficiency of treatment and reduce calves' morbidity and mortality caused by anaplasmosis.

Implications

The impressive performance of machine learning models in predicting anaplasmosis using RUM and ACT data from Hr-Tag sensors observed in this study pointed out the possibility for use of such device as an auxiliary tool for precision tick fever therapy (Souza et al., 2021), avoiding the indiscriminate use of antimicrobials and development of antimicrobial resistance (Aslam et al., 2018; Haley et al., 2020; Lei et al., 2020). At the same time, this approach can improve prognosis due to early detection and can result in better animal welfare (Relić et al., 2020). In addition, the proposed approach can reduce the amount of labor spent on the diagnostic procedures and secondary support treatment (e.g., transfusion and fluid therapy).

Our results were obtained in a fully controlled experiment, where only anaplasmosis affected the evaluated variables. Under farm conditions, there are several dis-

tinct pathogens that can cause health problems. Therefore, future studies under farm conditions including a larger number of animals should be performed to check the viability of using commercial devices to identify specific diseases such as anaplasmosis as well as the performance of the developed algorithms.

CONCLUSIONS

The presence of anaplasmosis changed the daily pattern and reduced RUM time and ACT index. Our results suggest that monitoring both RUM time and ACT index may be useful for early detection of anaplasmosis in calves. The use of RUM and ACT combined did not improve the capacity of the models to detect anaplasmosis. There was no benefit to using time series longer than 7 d to detect anaplasmosis. The predictive performance of machine learning models including data from the day of disease is greater compared with early detection. However, the anaplasmosis diagnosis prediction up to 5 d before the disease provided satisfactory results and can be useful for early treatment prescription, improving the prognosis and the recovery of animals exposed to anaplasmosis.

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