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Heart rate variability in newborn foals and its association with illness: a pilot study

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ABSTRACT

This study aimed to investigate differences in heart rate variability (HRV) between healthy and sick neonatal foals with a variety of diagnosis and to verify whether some HRV parameters could be associated with sepsis and/or survival. Twenty-one foals were included in the study: nine were healthy and 12 were sick. Retrospectively, sick foals were divided into sub-groups (non-septic vs. septic and non-survivor vs. survivor) for statistical analysis. Heart rate was recorded daily for 20 min and a 5-min period was used for heart rate variability analysis. Data on HRV variables were analysed using a linear model. Least-square means with their standard errors were reported, and treatment effects were declared significant at $p < .05$. To isolate the group that differed from the others, Tukey's test was used as a multiple comparison procedure. Pearson's correlations between variables were calculated, to estimate their relationship. Standard Deviation of the RR intervals and Standard Deviation 2 by the Poincaré plot was significantly lower in sick foals compared with healthy subjects, but there were no differences between survivors and non-survivors. Healthy foals presented a significantly lower Sample Entropy and heart rate compared with sick foals. HRV analysis is a non-invasive, rapid, and economical measurement tool that can be added to other parameters to improve the accuracy of predicting in-hospital mortality in foals. Further studies should be conducted with a larger sample of foals to confirm these findings and to evaluate the clinical usefulness of HRV analysis during neonatal diseases.

HIGHLIGHTS

- This study investigated differences in heart rate variability (HRV) between sick and healthy neonatal foals
- Standard Deviation of the RR intervals was significantly lower in sick compared with healthy foals, but there were no differences between survivors and non-survivors.
- HRV analysis is a non-invasive, rapid, and economical tool that can be added to other parameters to improve the accuracy of predicting mortality in foals.

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Introduction

Sepsis in neonatal foals remains a leading cause of morbidity and mortality despite the improvement in survival that has been reported over the last 25 years (Hytychová and Bezděková 2015; Taylor 2015; Wong et al. 2018). Identifying the right biomarkers is key to an earlier and accurate diagnosis of sepsis in the horse (Pusterla et al. 2006; Bonelli et al. 2015a, 2015b; Taylor 2015; Bonelli et al. 2017). The survival of septic foals varies within a range of 45–81% (Corley and Furr 2003; Slack et al. 2005; Castagnetti and Veronesi 2008). Since intensive care for newborn foals is very

expensive, the early prognosis for survival on admission or during the first few hours of hospitalisation should be considered to identify neonates with a higher chance of survival (Castagnetti and Veronesi 2008; Wong and Wilkins 2015).

By assigning numerical values to several clinicopathological variables, Brewer and Koterba (1988) developed a sepsis scoring system that originally had an 86% specificity and 93% sensitivity. More recently, the accuracy of this system has been questioned (Corley and Furr 2003; Wong et al. 2018) and other prognostic indicators have been sought (Pusterla et al. 2006;

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Gold et al. 2007a, 2007b; Armengou et al. 2008; Hollis et al. 2008; Hurcombe et al. 2008; Paltrinieri et al. 2008; Hurcombe et al. 2009; Barsnick et al. 2011).

Heart rate variability (HRV) is a non-invasive measurement that can be used to investigate the balance of sympathetic and vagal activity (Task Force of the European Society of Cardiology, North American Society of Pacing and Electrophysiology 1996). HRV is measured by determining the continuously changing time interval between successive heartbeats (R–R intervals). It is based on the antagonistic oscillatory influences of the sympathetic and parasympathetic nervous systems on the *nodus sinuatrialis* (Stucke et al. 2015). HRV is increasingly used in animal research to analyse changes in the sympathovagal balance related to disease, psychological and environmental stressors, or individual characteristics, such as temperament and coping strategies (Von Borell et al. 2007; Stucke et al. 2015).

In human medicine, HRV has also been used to predict prognosis in septic patients (Bonjorno Junior et al. 2019; Prabhakar et al. 2019), and several studies have reported that a decrease in HRV indices is associated with higher mortality in critically ill patients (de Castilho et al. 2018). HRV analysis has been used especially in neonatal medicine to predict mortality in infants (Beuchée et al. 2009; Lake et al. 2014).

Abnormal HRV measurements, such as decreased approximate entropy, decreased sample entropy, reduced variability, and transient decelerations have been significantly associated with sepsis or sepsis-like illness in premature neonates (Beuchée et al. 2009). Early in the course of neonatal sepsis, there are reduced heart rate variability and transient decelerations similar to the foetal distress that appears before the clinical diagnosis of sepsis or systemic inflammatory response syndrome (Griffin et al. 2005; Bohanon et al. 2015). In animal models, HRV assessment may provide insights into the acute effect of sympathetic and cholinergic anti-inflammatory pathways (Zila et al. 2015). According to some clinical studies, HRV analysis might play an important role in the continuous monitoring of severe infection (Fairchild et al. 2009; Jarkovska et al. 2015). HRV has been evaluated in newborn foals (Nagel et al. 2012; Nagel et al. 2015) however, to the best of the authors' knowledge, no studies have been conducted to analyse HRV in sick or septic foals.

The aim of this study was thus to investigate differences in HRV between healthy and sick neonatal foals with a variety of diagnosis. We wanted to verify whether some HRV parameters could be associated

with sepsis or could represent early markers of survival in neonatal foals referred to the hospital.

Materials and methods

A total of 21 foals were included in the study. Ethical approval (n° 2825/2014) by the Ethics Committee on Animal Experimentation of the University of Pisa and an owner's written consent were obtained. Nine of the foals were healthy Standardbreds, that had been born on the same stud farm, had undergone similar management conditions, and were used as a control group. The following inclusion criteria were set for the 'control group': (1) normal gestation length (>320 days) (Lester 2011); (2) unassisted delivery; (3) mares treated for gastrointestinal parasites and vaccinated for equine influenza, tetanus, and equine herpes virus-1; (4) Apgar Score ≥ 7 within 5 min of birth (Stoneham 2006); (5) good passive transfer of immunity at 24 h of age (Immunoglobulin G ≥ 800 mg/dL)¹; (6) righting reflex immediately after birth and sucking reflex within 20 min, sternal recumbence within 2 min, standing position within 120 min, first suckling within 180 min (Stoneham 2006); and (7) normal at physical examination throughout the study period.

In addition, 12 sick client-owned foals were included. All the foals were referred with different complaints to two different veterinary teaching hospitals providing secondary health care during one year. The foals were managed under similar circumstances in both the VTHs. Using data from clinical history, physical examination, and clinicopathological analysis collected on admission, a sepsis score was calculated for each foal (Wong et al. 2018). Based on the sepsis score and results of blood culture, each foal was assigned to 1 of 2 patient groups: a sick non-septic group (sepsis score < 7 and negative results of bacteriological culture of blood; $n = 6$ foals) or a septic group (sepsis score ≥ 7 with or without positive results of bacteriological culture of blood or sepsis score < 7 with positive results of bacteriological culture of blood; $n = 6$ foals). Retrospectively, the foals enrolled in the study were grouped according to the outcome into survivors ($n = 7$) and non-survivors ($n = 5$). The foals were considered survivors if they had been discharged from the hospital, while they were considered non-survivors if they died or had been humanely euthanised due to their severe medical prognosis and not for economic reasons. For details regarding all foals included in this study, see Table 1.

Heart rate was recorded in all foals using a heart rate monitor² (connected by a chest belt, as previously

Table 1. Foals included in this study were divided into three groups (healthy, sick survivor, and sick non-survivor).

Foal	Group	Sex	Breed	Days of recording	Disease	Age at 1st recording (days)	Survivor/ not-survivor	Hospital
1	Healthy	M	Standardbred	12	–	1	–	–
2	Healthy	F	Standardbred	12	–	1	–	–
3	Healthy	M	Thoroughbred	12	–	1	–	–
4	Healthy	F	Thoroughbred	12	–	1	–	–
5	Healthy	M	Thoroughbred	12	–	1	–	–
6	Healthy	M	Thoroughbred	12	–	1	–	–
7	Healthy	M	Standardbred	12	–	1	–	–
8	Healthy	F	Standardbred	12	–	1	–	–
9	Healthy	M	Standardbred	12	–	1	–	–
10	Non-septic	F	Standardbred	12	Enteritis	1	Survivor	Pisa
11	Non-septic	M	Standardbred	12	Meconium impaction	1	Survivor	Pisa
12	Septic	F	Thoroughbred	8	Failure of passive transfer immunity and septic arthritis	11	Survivor	Pisa
13	Non-septic	F	Quarter horse	4	Hypoglycemia due to an aggressive mare	8	Survivor	Pisa
14	Septic	M	Arabian	12	Septic arthritis and enteritis; Blood culture: positive	11	Survivor	Barcelona
15	Non-septic	F	Thoroughbred	10	Failure of passive transfer immunity	1	Survivor	Pisa
16	Non-septic	M	Standardbred	12	Omphalophlebitis, umbilical hernia and enteritis	3	Survivor	Pisa
17	Septic	M	Thoroughbred	11	Septic arthritis and patent urachus	5	Non-survivor	Pisa
18	Non-septic	F	Standardbred	4	Hypoxic ischaemic encephalopathy	4	Non-survivor	Pisa
19	Septic	F	Standardbred	6	Omphaloflebitis and pneumonia	2	Non-survivor	Pisa
20	Septic	M	Andalusian	12	Enteritis and omphaloflebitis; Blood culture positive	10	Non-survivor	Barcelona
21	Septic	F	Arabian	1	Septicaemia and pneumonia	3	Non-survivor	Barcelona

M: male; F: female.

described (Nagel et al. 2012; Nagel et al. 2015). In healthy foals, heart rate was recorded daily for 20 min starting at 24 h of life for 12 consecutive days. The heart rate monitor belt was placed on the foals while they were in their usual stall with their dam. A 15-min period of familiarisation preceded the start of the heart rate recording so that the foal could regain calm. Using a closed-circuit television and a chronometer, the same (VV) operator recorded from outside whether the foal was awake or asleep, standing or lying down, or if it was running around the stall. This was used to select 5 min recordings for HRV analysis during which the foals were calm, but not sleeping. Data were always collected between 5:00 and 8:00 pm.

In sick foals, the heart rate was recorded daily for 20 min starting within 24 h from admission until discharge or death/euthanasia. As with the healthy subjects, the Polar belt was strapped to the foals in the hospital box in the presence of the dam. The recordings were performed after a 15-min period of acclimation, between 5:00 and 8:00 pm, without interfering with clinical procedures and avoiding medication or feeding times. Usually, the foals were lying down, however, if they were standing, an operator recorded its activity in the stall as with the healthy foals.

The data were entered into a computer and underwent automatic correction of artefacts using the available software³. A 5-min period from each 20 min recording was selected, in which the foals were at rest, also taking into account signal quality. Heart rate variability during this 5 min was subsequently analysed with a free software program designed for HRV

analysis⁴. The variables of HRV taken into account were: Heart Rate (HR; bpm); Standard Deviation of the RR intervals (SDRR; ms); Square root of the mean of the sum of the squares of differences between consecutive RR intervals (RMSSD; ms); Geometric Standard Deviations by Poincaré plot (SD1 and SD2; ms) and Sample Entropy (SampEn).

Data on HRV variables were assessed for distribution using the Shapiro-Wilk *W* test. Data relating to HRV variables were assessed by comparing first healthy, surviving, and non-surviving foals. Subsequently, healthy, septic, and non-septic foals were compared. Data on HRV were analysed by an ANOVA, to evaluate if there are significant differences between foals, classifying them as healthy, survivors, and non-survivors. Subsequently, the same statistical analysis was performed comparing healthy, septic, and non-septic foals.

In both cases, data on HRV were analysed using the following factorial mixed model⁵:

$$y_{ijz} = \mu + G_i + T_j + G_i \times T_j + H_z[G_i] + \varepsilon_{ijz}$$

where:

y_{ijz} = HRV variables: HR, SDRR, RMSSD, SD1, SD2, SampEn;

G_i = fixed effect of the *i*th group based on the following classifications of horse status, which were considered independently: (1) healthy vs. survivors vs. no survivors; (2) healthy vs. septic vs. no septic.

T_j = fixed effect of the *j*th day of the survey (12 days)

$H_z[G_i]$ = random effect of the z th horse nested in the group.

ε_{ijz} = random residual

Least-square means with their standard errors were reported, and treatment effects were declared significant at $p < .05$. To isolate the group that differed from the others, HSD Tukey's test was used as a multiple comparison procedure. Finally, Pearson's correlations between variables were calculated, to estimate their relationship.

Results

Foals included in the study are described in Table 1. In the control group, HR was recorded for 11 consecutive days starting from 24 h of life. In the study group, 4 out of 5 non-survivor foals were euthanised, while one died naturally. In the survivors, the HR was recorded until discharge for 11 days in three foals, for 8 days in two foals, and 4 days in the other two subjects. In non-survivors, the heart rate was recorded until death in each foal for 11, 6, 4, and 1 day, respectively.

HRV parameters for healthy and sick foals, divided into survivor/non-survivors and septic/non-septic are reported in Tables 2 and 3.

When comparing the average values of the three groups, the healthy foals showed a significantly lower HR (96.23 vs. 114.79 bpm) and SampEn (0.82 vs. 1.22 ms), and higher SDRR (47.27 vs. 20.93 ms) and SD2 (65.72 vs. 27.89 ms) compared with non-survivor foals. Survivor foals showed intermediate values for all the variables considered. No significant differences were observed for RMSSD and SD1 in any of the groups.

An analysis of the differences over time revealed that non-survivor foals had a higher HR on all the days except on admission, while the survivor subjects had similar values to healthy foals except on days 7 and 8 when their HR was higher. SDRR and SD2 were significantly lower in sick foals compared with healthy subjects, but there were no differences between survivors and non-survivors. However, after 7 days, in survivor foals, these parameters were similar to those of the healthy groups.

Healthy foals presented a significantly lower SampEn (0.82 vs. 1.19 ms) and higher SDRR (47.27 vs. 25.51 ms) and SD2 (65.72 vs. 34.24 ms) compared with septic foals. Non-septic subjects showed intermediate values for all the variables considered. No significant differences were observed for HR, RMSSD, and SD1 in any of the groups.

An analysis of the differences over the time period in healthy foals revealed that the HR was lower from

Table 2. HRV parameters presented as mean \pm SEM for healthy, survivors and non-survivors and results of the statistical comparison.

HRV parameter	Days											p-Value			
	1	2	3	4	5	6	7	8	9	10	11	SEM	G	T	GxT
HR															
Healthy	101.84 cd	97.60 cd	95.18 cd	101.84 cd	97.60 cd	100.30 cd	96.86 cd	93.72 ad	91.36 ad	92.35 ad	89.85 ad	5.66	*	ns	*
Survivors	101.34 cd	101.02cd	93.49 ad	95.57 cd	102.91 cd	96.86 cd	108.05 bc	110.11 bc	97.11 cd	108.75 bc	98.96 cd				
Not survivors	111.39 ab	116.53 ab	114.30 ab	104.89 ac	102.56 cd	116.58 ab	123.99 ab	121.54 ab	108.69 bc	126.54 aa	116.07 ab				
SDRR															
Healthy	44.08 ab	52.80 aa	51.37 aa	49.77 ab	49.12 ab	46.60 ab	47.15 ab	46.37 ab	46.75 ab	41.16 ab	44.82 ab	6.52	**	ns	*
Survivors	21.15 ac	27.28 bc	44.42 ab	41.83 ab	35.34 ab	29.64 bc	41.58 ab	41.46 ab	45.89 ab	41.41 ab	37.91 ab				
Not survivors	24.14 ac	25.77 bc	19.22 ac	20.17 ac	22.25 ac	28.72 bc	24.30 ac	28.15 bc	8.65 ac	16.95 ac	15.25 ac				
RMSSD															
Healthy	16.49aa	17.69aa	18.61aa	13.68aa	17.16aa	13.56aa	16.51aa	16.31aa	19.04aa	15.04aa	15.40aa	3.57	ns	ns	ns
Survivors	10.11aa	17.64aa	21.60aa	15.29aa	12.54aa	16.74aa	14.60aa	12.75aa	17.15aa	12.87aa	17.49aa				
Not survivors	12.68aa	10.99aa	11.01aa	10.91aa	13.66aa	9.43aa	14.54aa	15.84aa	6.19aa	11.04aa	14.04aa				
SD1															
Healthy	11.68aa	12.50aa	13.18aa	9.69aa	12.12aa	10.36aa	11.67aa	11.50aa	13.46aa	10.66aa	11.89aa	2.23	ns	ns	ns
Survivors	7.16aa	12.49aa	15.30aa	10.82aa	8.87aa	11.87aa	10.34aa	9.01aa	11.12aa	9.15aa	12.39aa				
Not survivors	8.98aa	7.77av	7.77aa	7.75aa	9.69aa	6.69aa	10.25aa	8.30aa	9.40aa	7.85aa	9.90aa				
SD2															
Healthy	61.08 ab	73.57 aa	71.30 aa	69.66 aa	68.24 ab	65.04 ab	65.53 ab	64.50 ab	64.61 ab	57.15 ab	62.20 ab	8.53	**	ns	*
Survivors	28.85 ac	36.31 ac	60.61 ab	58.03 ab	48.96 ab	39.86 ab	57.55 ab	57.81 ab	64.96 ab	57.36 ab	51.84 ab				
Not survivors	32.74 ac	35.42 ac	25.12 ac	27.40 ac	29.59 ac	40.09 ab	32.56 ac	35.31 ac	11.31 ad	22.66 ad	19.31 ad				
SampEn															
Healthy	0.81 ac	0.72 ac	0.79 ac	0.70 ac	0.77 ac	0.81 ac	0.81 ac	0.90 ac	0.91 ac	0.93 ac	0.85 ac	0.13	*	ns	**
Survivors	1.21 ab	1.35 ab	1.06 bc	0.93 ac	0.98 ac	1.20 ab	0.90 ac	0.76 ac	0.96 ac	0.97 ac	1.09 bc				
Not survivors	1.05 bc	1.12 bc	1.16 bc	1.36 ab	1.17 bc	1.18 ab	1.22 ab	1.66 aa	1.11 bc	1.15 bc	1.29 ab				

HR: heart rate (beats/min); SDRR: standard deviation of RR (ms); RMSSD: square root of the mean of the sum of the squares of differences between consecutive RR (ms); SD1 and SD2: geometric standard deviation by Poincaré plot; SampEn: sample entropy; SEM: standard error mean; G: effect of group; T: effect of time; ns: not significant.

* $p < .05$, ** $p < .01$.

a, b, c means within an HRV parameter with different letters differ.

Table 3. HRV parameters presented as mean ± SEM for healthy, non-septic, and septic foals and results of the statistical comparison.

HRV parameter	Days											p-Value			
	1	2	3	4	5	6	7	8	9	10	11	SEM	G	T	GxT
HR															
Healthy	101.84 bc	97.60 ac	95.17 cd	101.84 bc	97.60 ac	100.30 bc	96.86 ac	93.72 cd	91.36 ad	92.35 cd	89.85 ad	5.94	ns	*	**
Non-septic	107.26 bc	106.61 bc	99.61 bc	99.66 bc	106.95 bc	99.37 bc	108.82 ab	112.10 ab	105.80 bc	112.93 ab	103.14 bc				
Septic	103.10 bc	108.78 b	105.64 bc	99.34 bc	100.25 bc	111.43 ab	122.95 aa	119.98 ab	95.91 cd	121.16 aa	110.69 ab				
SDRR															
Healthy	44.09 aa	52.80 aa	51.38 aa	49.78 aa	49.12 aa	46.60 aa	47.16 aa	46.38 aa	46.76 aa	41.17 aa	44.82 aa	6.52	*	ns	ns
Non-septic	19.53 aa	25.46 aa	41.51 aa	38.41 aa	31.97 aa	30.69 aa	39.89 aa	41.15 aa	42.53 aa	39.73 aa	36.23 aa				
Septic	26.42 aa	28.78 aa	24.13 aa	25.41 aa	28.26 aa	26.16 aa	30.04 aa	30.28 aa	23.84 aa	21.00 aa	19.30 aa				
RMSSD															
Healthy	16.49 aa	17.69 aa	18.61 aa	13.68 aa	17.16 aa	13.56 aa	16.51 aa	16.31 aa	19.04 aa	15.04 aa	15.40 aa	3.57	ns	ns	ns
Non-septic	8.33 aa	14.79 aa	20.19 aa	14.28 aa	11.47 aa	17.51 aa	11.05 aa	12.15 aa	15.40 aa	11.57 aa	16.19 aa				
Septic	15.18 aa	16.17 aa	13.67 aa	12.39 aa	14.54 aa	10.12 aa	19.39 aa	21.39 aa	11.66 aa	12.85 aa	15.85 aa				
SD1															
Healthy	11.68 aa	12.50 aa	13.18 aa	9.69 aa	12.12 aa	10.36 aa	11.67 aa	11.50 aa	13.46 aa	10.66 aa	11.89 aa	2.23	ns	ns	ns
Non-septic	5.90 aa	10.46 aa	14.30 aa	10.09 aa	8.10 aa	12.42 aa	7.82 aa	8.58 aa	9.68 aa	8.20 aa	11.44 aa				
Septic	10.74 aa	11.46 aa	9.66 aa	8.81 aa	10.33 aa	7.18 aa	13.70 aa	15.13 aa	8.27 aa	9.14 aa	11.19 aa				
SD2															
Healthy	61.09 aa	73.58 aa	71.30 aa	69.67 aa	68.24 aa	65.04 aa	65.53 aa	64.50 aa	64.61 aa	57.16 aa	62.20 aa	8.53	*	ns	ns
Non-septic	26.84 aa	34.21 aa	56.59 aa	53.29 aa	44.34 aa	41.20 aa	55.70 aa	57.46 aa	60.62 aa	55.18 aa	49.66 aa				
Septic	35.56 aa	38.82 aa	31.89 aa	34.69 aa	38.07 aa	36.22 aa	39.99 aa	39.42 aa	32.46 aa	28.19 aa	24.84 aa				
SampEn															
Healthy	0.81 aa	0.72 aa	0.80 aa	0.70 aa	0.77 aa	0.82 aa	0.81 aa	0.90 aa	0.92 aa	0.94 aa	0.86 aa	0.13	*	ns	ns
Non-septic	1.13 aa	1.30 aa	1.05 aa	1.02 aa	0.98 aa	1.19 aa	0.85 aa	0.77 aa	0.95 aa	0.96 aa	1.08 aa				
Septic	1.17 aa	1.21 aa	1.19 aa	1.23 aa	1.12 aa	1.21 aa	1.21 aa	1.36 aa	1.09 aa	1.13 aa	1.27 aa				

HR: heart rate (beats/min); SDRR: standard deviation of RR (ms); RMSSD: square root of the mean of the sum of the squares of differences between consecutive RR (m); SD1 and SD2: geometric standard deviation by Poincaré plot; SampEn: sample entropy; SEM: standard error mean; G: effect of group; T: effect of time; ns: not significant.

* $p < .05$, ** $p < 0.01$.

a, b, c means within an HRV parameter with different letters differ.

the 7th day onwards compared with sick foals, but no other differences were observed. Furthermore, no differences were detected between septic and non-septic patients.

Discussion

Our study describes an HRV analysis on neonatal healthy and sick foals with a variety of clinical diagnoses. We found a statistically significant effect of illness on SDRR, SD2, and SampEn. However, no differences were found between survivors and non-survivors, or between septic and non-septic groups on admission.

Our results on HRV parameters in healthy foals are similar to those already described by Nagel and colleagues (Nagel et al. 2015). Data were collected at the same time of the day to prevent circadian interference.

The decrease in SDRR and SD2 in sick foals indicates the decreased long-term variability of cardiac activity (Von Borell et al. 2007). Similarly, in human infants, short-term variability has not been found to change in the presence of sepsis, while long-term variability is significantly lower (Bohanon et al. 2015).

The depression of HRV in conditions of systemic inflammation has been repeatedly shown in humans



Figure 1.

(Griffin et al. 2005; Prabhakar et al. 2019), experimental animals (Jarkovska et al. 2015; Zila et al. 2015), and adult horses (McConachie et al. 2016a, 2016b; Vitale et al. 2020). As no changes were observed in RMSSD and SD1, we cannot associate the decrease in HRV in sick animals with a decreased parasympathetic tone but rather with a possible autonomic dysfunction (Vitale et al., 2020). Bonjorno Junior et al. (2019) already speculated that the reduced HRV in sepsis may indicate early autonomic dysfunction due to attenuation of the adrenergic response at the cardiomyocyte level.

When considering the HR in foals we must take into account that the physiology of the cardiovascular system is slightly different from those of adults. Foals cannot readily increase their stroke volume, thus, to

maintain an adequate cardiac output they have to increase their HR (Carr, 2014). This might influence the HRV which is difficult to quantify at this point due to the low number of cases included. Nevertheless, HR was not found different between septic, non-septic and healthy foals while other HRV parameters were.

Our study demonstrates that also in foals, HRV is different according to the state of health. The lack of significant differences between the different groups of sick foals during the initial 24 h suggests that HRV analysis performed on admission may not be useful when predicting survival or septicemia. It is also true that the number of sick foals enrolled in this study was low which might have been a bias for the statistical analysis.

A recent study reported that when the HRV responses to porcine moderate sepsis without organ failure and to a porcine progressive lethal septic shock were compared, no differences were found (Jarkovska et al. 2015). This probably indicates that the sensitivity of HRV to systemic inflammation is high but, on the other hand, HRV does not allow the illness to be scaled. A reliable staging of inflammatory processes likely requires an integrative approach with additional parameters, such as clinical, hematological, and biochemical variables (Peek et al. 2004; Bohanon et al. 2015; Jarkovska et al. 2015; Wong et al. 2018).

Although the accuracy of the sepsis score developed by Brewer and Koterba (1988), has been questioned (Corley and Furr 2003; Slack et al. 2005; Castagnetti and Veronesi 2008; Wong and Wilkins 2015; Wong et al. 2018), it remains the best predictor of survival, with the survival rate decreasing as the sepsis score increases (Peek et al. 2004; Wilkins 2018; Wong et al. 2018).

Nevertheless, a variety of 'new vital signs', such as tissue oxygenation and HRV, have been emerging in medicine. These can be associated with blood analysis and other vital parameters to obtain more detailed information on the health status of the patient, and thus produce a more reliable prognosis (Bohanon et al. 2015). In addition, in studies on humans, several data points are usually obtained to predict the risk of death in these patients (Bonjorno Junior et al. 2019). The values of SDRR and SD2 in the sick survivors became similar to those of the healthy foals starting from the seventh day of observation, while in the non-survivor group the values remained higher. These results support the hypothesis that HRV parameters return to normal values in foals that recover from illness.

When comparing foals according to their septic status, the changes observed were similar. This is probably because the majority of septic foals died (4/6) and the majority of non-survivors were septic (4/5).

Several limitations need to be considered in the interpretation of the current results. Firstly, the recruitment of patients was limited as it was related to the equipment and manpower available. Secondly, the ages of sick foals are quite different, and this could have influenced the results. Thirdly, although we selected our HRV parameters based on a literature review, there may have other suitable HRV variables for a comparison between groups.

Conclusions

In conclusion, HRV analysis is a non-invasive, rapid, and economical measurement tool, which requires a common heart rate monitor which is nearly always freely available in a referral equine hospital, as the software for HRV analysis. Adding HRV to other commonly used parameters may improve the accuracy of predicting in-hospital mortality in foals. Further studies should be conducted with a larger sample of foals to confirm these findings and to evaluate the clinical usefulness of HRV analysis during neonatal diseases.

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Disclosure statement

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Data availability statement

The authors confirm that the data supporting the findings of this study are available within the article.

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