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Diurnal modulation and sources of variation affecting ventricular repolarization in Warmblood horses

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Abstract *Objectives:* Irregularities in cardiac repolarization are known to predispose for arrhythmias and sudden cardiac death in humans. The QT interval is a quantitative measurement of repolarization, and clinically, the QT_c (QT interval corrected for heart rate) and T_{peak} to T_{end} intervals (T_pT_e) are used as repolarization markers. To support the use of these markers in horses, we sought to describe the possible influence of the environment, time of day, day-to-day effects, T wave conformation, age, body weight (BW), and horse-to-horse variation on repolarization measurements.
Animals: 12 Warmblood geldings, age 10.8 ± 4.8 years.
Methods: Holter ECGs were performed on days 0, 7 and 14. Measures of RR, QT, QT_p, QT_c and T_pT_e intervals and T wave conformation were obtained each hour during the recordings. An ANCOVA analysis was performed to estimate diurnal variation and the sources of variation affecting these intervals.
Results: Differences between individual horses were the largest source of repolarization variability although the environment had a significant effect on

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repolarization as well. Diurnal variation affected both the RR interval and the repolarization markers. The QT, QT_c and T_pT_e intervals were prolonged on day 0. Biphasic T waves shortened the T_pT_e interval approximately 10 ms. Age and BW did not appear to affect repolarization.
Conclusions: Equine repolarization markers exhibit significant variation. Factors affecting repolarization measurements include horse-to-horse variation, diurnal variation, the environment, and T wave conformation. These factors must be considered if markers of equine repolarization are used diagnostically.

Abbreviations

2 AV block	second-degree atrioventricular block
ANS	autonomic nervous system
BPM	beats per minute
BW	body weight
CI	confidence interval
CR	coefficient of repeatability
HR	heart rate
LQTS	long QT syndrome
M cell	midmyocardial cell
PNS	parasympathetic nervous system
QT	time interval from Q wave onset to T wave end (myocardial depolarization and repolarization)
QT_c	QT interval corrected for heart rate
QT_p	time interval from Q wave onset to T wave peak (conduction of the electrical impulse from the sinoatrial node to the ventricular muscle)
RR	R_{peak} to R_{peak} interval (cardiac cycle length)
SA block	sinoatrial block
T_pT_e	time interval from T wave peak to T wave end (repolarization of the ventricular wall)

Introduction

Disturbances in myocardial repolarization can be induced by pathological and structural changes in the heart, as well as drugs that block cardiac potassium channels.[1,2] In particular, long QT syndrome (LQTS), which includes both a congenital and an acquired form of delayed cardiac repolarization, has been shown to be of clinical importance in both human and canine patients.[3,4] Since even small irregularities have been shown to be a strong indicator of cardiovascular mortality, precise quantification of cardiac repolarization is important.[5] The QT interval measured on the surface ECG reflects the duration of the myocardial depolarization and repolarization. As depolarization is fairly short and constant, the QT interval is routinely used as an indirect measurement of repolarization duration.[6] However, using the QT interval as a diagnostic tool is challenging in any species as some physiological parameters can cause significant variations. Most importantly, the QT interval is known to vary as a function of heart rate (HR)/cardiac cycle length (RR interval). Thus, rate correction is performed in both humans and horses using different formulas in an attempt to compensate the influence of HR. This facilitates comparison of corrected QT durations (QT_c) at different HRs.[7,8] Additionally, studies in humans and horses have also shown that gender, age and body weight (BW) have influence on the QT interval.[8–13] A further factor for consideration when estimating the QT interval in both humans and horses is the repeatability of measurements. Hence, inter- and intra-observer variability has been studied in both manual and automated measurements in humans and in manual measurements of horses.[8,14,15]

Human studies have shown a significant influence of the autonomic nervous system (ANS) on the QT interval. Diurnal fluctuations in the activity of the human ANS are well known, and especially during sleep, the parasympathetic (cholinergic) effect on the heart is increased, prolonging the QT interval.[16–18] Diurnal fluctuations of the ANS have also been described in horses, but in contrast to humans and other animal species, the parasympathetic nervous system (PNS) dominates completely in the resting awake horse.[19–21] No studies of diurnal variations of the QT interval exist in horses.

In healthy humans, psychosocial factors have been shown to be responsible for inducing sympathetic imbalances which cause QT prolongation.[22] It is well known that horses are generally