The Veterinary Journal 261 (2020) 105476

Contents lists available at ScienceDirect

The Veterinary Journal

journal homepage: www.elsevier.com/locate/tvjl

Review

Ventricular arrhythmias in horses: Diagnosis, prognosis and treatment

Cristobal Navas de Solis

Department of Clinical Studies New Bolton Center, University of Pennsylvania, Kennett Square, PA 19348, USA

ARTICLE INFO

Keywords:
Arrhythmogenesis
Electrocardiogram
Equine
Sudden death
Tachycardia

ABSTRACT

Ventricular arrhythmias (VAs) are often incidental or coincidental with systemic disease. Ventricular arrhythmias are also the most likely cause of many sudden cardiac deaths in horses. This dichotomy creates challenges in the management of horses with VAs. This review presents current knowledge of diagnosis, prognosis and treatment of VAs in horses.

© 2020 Elsevier Ltd. All rights reserved.

Introduction

Ventricular arrhythmias (VAs) originate from the ventricular myocardium and include ventricular premature complexes (VPCs), ventricular tachycardia (VT), ventricular fibrillation, idioventricular (IVR) or accelerated idioventricular rhythms (AIVR) and ventricular escape rhythms.

There are three basic mechanisms for VAs: reentry, automaticity, and triggered activity but in most cases of equine VAs the mechanism remains unknown. In humans, reentry is commonly implicated as a mechanism causing VAs and scar due to previous infarction the most cited clinical scenario. Infarction is, however, uncommon in horses. Abnormal automaticity is seen in humans with ischemia, electrolyte disturbances and catecholamine stimulation. In horses, it is plausible that arrhythmias during exercise, excitement or arrhythmias secondary to systemic disease could be a consequence of enhanced automaticity. Arrhythmias associated with hypokalemia are a common example of enhanced automaticity of latent pacemakers in horses. Triggered activity is often the arrhythmogenic mechanism during reperfusion in acute infarction or with digitalis toxicity. Interestingly, high heart rates promote triggered activity and β-blockers may prevent them (Flinders and Roberts, 2000).

Definitions for VAs

Three or more consecutive VPCs in quick succession (instantaneous heart rate [HR] >120/min) are termed VT, although the precise rate for defining tachycardia has not been defined. The same rhythm at a slower rate is termed IVR or AIVR. The rhythm is characterized as paroxysmal if it terminates spontaneously or sustained when it persists (van Loon, 2019). When more than one ectopic QRS morphology is identified the rhythm is characterized as multiform (Fig. 3) and this raises concerns about the presence of more widespread myocardial pathology and a worse prognosis (Reef et al., 2014). R-on-T phenomenon is an electrocardiographic diagnosis in which an ectopic QRS merges with the preceding T (Fig. 4). Torsades de pointes (twisting of the points) is a type of wide complex polymorphic VT in which QRS complexes and T waves twist around the baseline of the ECG (Fig. 5). R-on-T phenomenon and torsades de pointes represent an unstable electrical activity that can deteriorate to ventricular fibrillation and cardiac arrest (Cohagan and Brandis, 2017).

Idioventricular rhythms are VAs in which the ventricular rate approximates or is slightly higher (accelerated idioventricular rhythm) than the prevailing sinus rate. A formal definition for which rate defines the line between AIVR and VT in horses does not exist. A rate of 60–80/min is commonly described as AIVR. This number is arbitrary, and rates can be lower in horses with AIVR (Fig. 2). Abnormal calcium-dependent automatism that affects the phase 4 slope of the action potential (ectopic automaticity) has been identified as the main electrophysiological mechanism for AIVR (Riera et al., 2010). Subsidiary pacemakers within the specialized conduction system of the ventricular Purkinje fibers become apparent in conditions such as endotoxemia, autonomic imbalance, acid-base disturbances, electrolyte abnormalities, use of anesthetic drugs, α2 adrenergic agonists, dobutamine or other catecholamine infusions and reperfusion (Karrasch et al., 2013). Idioventricular rhythms are considered benign in the absence of structural heart disease (Riera et al., 2010) in humans and the relevance of this arrhythmia in horses is uncertain.

Causes of VAs in horses

Electrophysiological studies of arrhythmias in horses are in their early stages (Van Steenkiste et al., 2020) and hence there is limited information about the specific mechanisms responsible for

E-mail address: navasdes@vet.upenn.edu (C. Navas de Solis).

http://dx.doi.org/10.1016/j.tvjl.2020.105476
1090-0233/© 2020 Elsevier Ltd. All rights reserved.

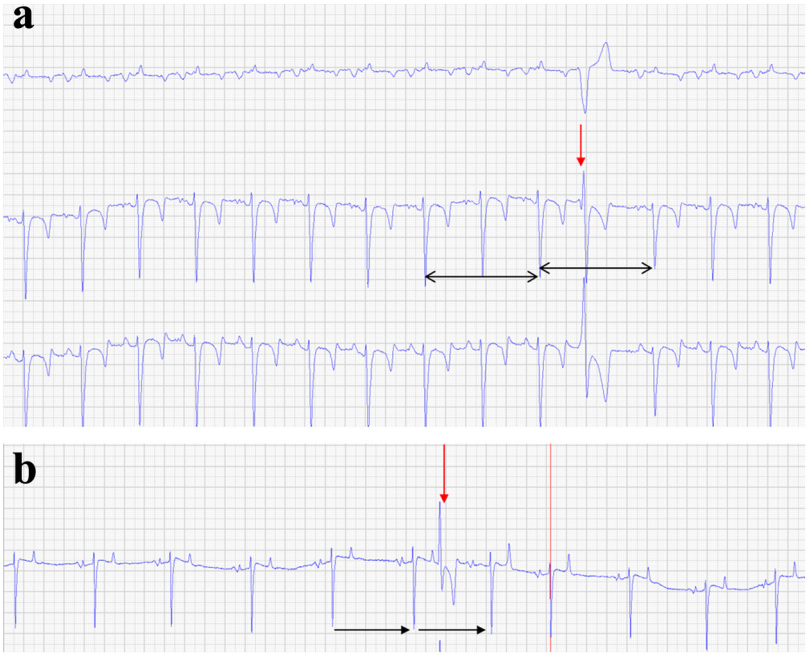

Fig. 1. (a) Single ventricular premature complex (VPC). The ectopic QRS is marked by a red arrow. A compensatory pause follows the VPC. Note the RR interval between the two normal QRS complexes separated by the VPC is twice the previous RR interval (black arrows). Paper speed is 25 mm/s and gain 20 mm/mV. Lead configuration is a modified lead I (the right arm electrode placed 20 cm lower than the withers in the right side of the horse and the left arm electrode placed 20 cm lower than the withers in the left side of the horse) for the top lead and a modified base-apex lead for the two leads at the bottom ('apex' electrode placed near the sternum and 'base' electrodes placed as described above for modified lead I). (b) Single VPC. The ectopic QRS is marked by a red arrow. A compensatory pause does not exist and the VPC is interpolated. Note the RR interval between the two normal QRS complexes separated by the VPC is the same than the previous RR interval (black arrows). Paper speed is 50 mm/s and gain 20 mm/mV. Lead configuration is a modified base-apex lead ('base' electrode was placed 20 cm lower than the withers in the right side of the horse and apex electrode placed near the sternum).

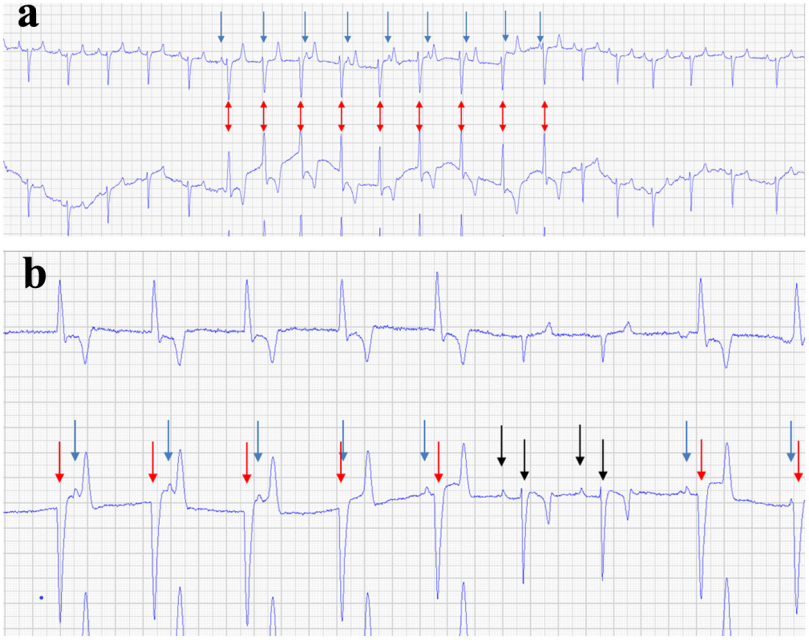

Fig. 2. (a) Paroxysmal accelerated ventricular rhythm (AIVR) at a rate of 75/min approximately). The recording illustrates the utility of multiple leads to detect abnormal QRS configuration. Blue arrows point to dissociated P waves (some buried in QRS complexes or T waves) and red arrows point to ectopic QRS complexes. Paper speed is 25 mm/s and gain 20 mm/mV. Both simultaneous leads are modified base-apex leads. ('Base' electrodes were placed 20 cm lower than the withers in the right and left sides of the horse and apex electrode placed near the sternum). (b) Idioventricular rhythm (IVR) at a rate of 44/min. Blue arrows point to dissociated P waves (some buried in QRS complexes or T waves) and black arrows point at associated P waves and QRS complexes. Red arrows point at ectopic (idioventricular QRS complexes). Paper speed is 25 mm/s and gain 30 mm/mV. The top lead is a modified lead I (right arm electrode placed 20 cm lower than the withers in the right side of the horse and left arm electrode placed 20 cm lower than the withers in the left side of the horse) and the bottom leads are modified base-apex leads (apex electrode placed near the sternum and base electrode placed 20 cm lower than the withers in the left right side of the horse).

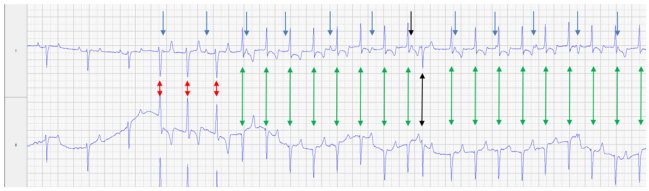

Fig. 3. Multiform ventricular ectopy. There are two ectopic QRS morphologies (small red arrows and larger green arrows) at rates of approximately 82/min and 100/min respectively. Blue arrows point to dissociated P waves (some buried in QRS complexes or T waves) and black arrows point at a P wave and capture beat. Paper speed is 25 mm/s and gain 20 mm/mV. Both simultaneous leads are modified base-apex leads ('base' electrodes were placed 20 cm lower than the withers in the right and left sides of the horse and apex electrode was placed near the sternum).

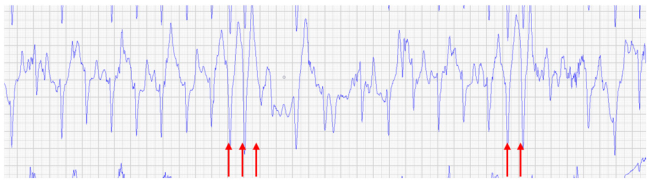

Fig. 4. Exercising ECG showing a triplet and couplet of ventricular premature complexes (VPCs; red arrows) and R on T phenomenon. Paper speed is 50 mm/s and gain 10 mm/mV. Both leads are modified base-apex leads. ('base' electrodes were placed 20 cm lower than the withers in the right and left sides of the horse and apex electrode placed near the sternum).

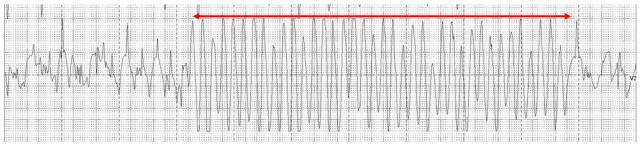

Fig. 5. Torsades de pointes. The recording shows atrial fibrillation during exercise followed by torsades de pointes (segment marked in red). Paper speed is 25 mm/s and gain 10 mm/mV. The lead is not a conventional lead (holter placed during exercise) and the horse is exercising over small fences in an arena.

arrhythmogenesis. As a result, most information is extrapolated from other species. Examination directed to assess whether there is extra-cardiac disease affecting myocardial function, or whether there is structural heart disease is relevant in horses with VAs. The presence of underlying cardiac disease or substrate ('a pre-existing condition that forms a prerequisite for the induction of an arrhythmia') (Coronel et al., 2001) and the clinical scenario can provide clues to the mechanism of the arrhythmia, treatment and prognosis (Roberts-Thomson et al., 2011). For example, ventricular remodeling, a sympathetic surge, increased myocardial oxygen demand, decreased diastolic time and decreased coronary perfusion are mechanisms that can contribute to arrhythmogenesis in the exercising horse with moderate or severe aortic regurgitation (AR). For this reason, horses with moderate or severe AR are monitored for ventricular arrhythmias and their presence considered when formulating a prognosis for the ability to safely perform athletic activities (Reef et al., 2014). Other examples of these considerations include, that β-blockers are indicated in arrhythmias associated with a sympathetic surge, that procainamide is likely to exacerbate hypotension and that Class 1C antiarrhythmics are contraindicated when structural heart disease is detected.

The use of performance enhancing, or illegal drugs is often a difficult discussion with horse owners or trainers but β- agonists and other anabolic steroids, thyroid hormones, cobalt chloride, caffeine, ephedrine and cocaine have arrhythmogenic properties and have been detected in horses as illegal substances (Thompson et al., 2011; Burns et al., 2018).

One of the most common clinical scenarios in the evaluation of horses and other animals with VAs is the detection of the arrhythmia incidentally or coincidentally with diseases not ascribed to the cardiovascular system. Extracardiac causes of VAs include systemic disease, hypoxia, acid–base or electrolyte disturbances, exhaustion, (Leroux et al., 1995) drugs (Karrasch et al., 2013), changes associated with the post-operative period (Morgan et al., 2011) or toxicity (Reimer et al., 1992; van Loon, 2019). Some common clinical scenarios of extracardiac causes for VAs are systemic disease causing an inflammatory response such as colitis, pneumonia or severe hemorrhage or hemolysis (Hondalus and Pipers, 1989; Wilkins and Bain, 1993; Navas de Solis et al., 2015). The cause of arrhythmias during Systemic Inflammatory Response Syndrome (SIRS) and other inflammatory states have not been completely elucidated. Autonomic imbalance, arrhythmogenic effect of inflammatory mediators, abnormal calcium handling, abnormal myocardial perfusion or edema, predisposition to atherosclerosis and coagulative states, myocardial dysfunction, and bacterial or viral effects have been proposed as contributing mechanisms (Schwartz et al., 2015; Yalta and Yalta, 2018; Shahreyar et al., 2018). Cardiac causes of VAs include myocardial disease such as myocarditis, ionophore intoxication or atypical myopathy, valvular or congenital heart disease causing enlargement and remodeling, pericarditis, endocarditis, aortocardiac fistula, cardiac trauma, fibrosis or rarely cardiac neoplasia or arteriosclerosis, (Machida et al., 1992; Coudry et al., 2007; Verheyen et al., 2012; Peters et al., 2013). Large adipose and fibrous tissue infiltration of the cardiac muscle has been described in three horses as a syndrome potentially comparable to arrhythmogenic right ventricular cardiomyopathy in boxers and humans and this relationship requires further investigation (Freel et al., 2010; Raftery et al., 2015).

Ventricular arrhythmias are common in equine athletes. Complex VAs were identified post-race in 15.9% race events in Standardbreds (Physick-Sheard and McGurrin, 2010) but VAs during peak exercise are not common if single occasional VPCs are excluded (Navas de Solis, 2016). It is paramount in clinical decision making to define the use of the horse, circumstances of the rider, clinical scenario, presence of cardiac and extracardiac disease and the presence of other arrhythmias. It is also important to define if the arrhythmia happens at rest, during submaximal, maximal exercise or in the recovery period in the equine athlete. For example, VPCs in an event horse ridden by an underage rider with a history of collapse and with areas of abnormal echogenicity in the ventricle compared with VPCs that only occur in the post exercise period in a dressage horse without identifiable cardiac or extracardiac disease will lead the clinician to very different conclusions.

Diagnosis

Clinical presentation

Presenting complaints of horses with VT include colic, anxiety, signs of depression or exercise intolerance (Mitchell, 2017) and VAs are often suspected in cases of sudden death without relevant postmortem findings (Lyle et al., 2011). Horses with VAs can have an abnormal auscultation. Ventricular premature complexes are characterized by earlier than anticipated S1 and S2 usually followed by a compensatory pause. Auscultation of horses with VT often reveals a regular rhythm with booming heart sounds. Prominent jugular pulses, variable blood pressure, variable peripheral pulses or pulse deficits (Reef et al., 2014) are other common findings in the physical examination of horses with VAs. Signs of congestive heart failure such as ventral edema, distended veins or increased respiratory rate or effort are possible in horses

with sustained VT (Mitchell, 2017) due to long term effects of reduced cardiac filling as a result of the persistent tachycardia.

Electrocardiograms

Electrocardiograms (ECGs) are necessary to confirm VAs. Atrioventricular (AV) dissociation is the most useful electrocardiographic feature to differentiate supraventricular and ventricular arrhythmias (Roberts-Thomson et al., 2011). Ventricular impulses are not commonly conducted retrograde from the ventricles to the atria and therefore they do not affect the activity of the sinoatrial (SA) node. This independent activity of the SA node and the refractory period of the AV node and ventricles after a depolarization causes the presence of compensatory pauses when single VPCs occur. That is, the interval between the R wave of the complex preceding the VPC and the R wave of the complex after the VPC (and so encompassing the VPC) should be twice the normal RR interval. (Fig. 1a). The long RR interval between the ectopic QRS and the following (normal) QRS (the pause) 'compensates' for the short RR interval between the ectopic QRS and the preceding (normal) QRS. If the ventricles are not refractory when the SA node generated impulse reaches them after the ectopic QRS, the VPC will become interpolated (Fig. 1b) and a pause will not exist (Roberts-Thomson et al., 2011). If during a dissociated rhythm an impulse generated in the SA node is transmitted to the ventricles a QRS with normal morphology and duration occurs and this is referred to as a capture beat (Fig. 3). If impulses generated from two different locations (most often the SA node and an area in the ventricles) act upon the same area simultaneously a fusion beat is generated. Fusion and capture beats imply AV dissociation and are typically present in ventricular rhythms (Roberts-Thomson et al., 2011).

P waves might be difficult to identify during VT or AIVR as they can be buried in QRS complexes or T waves. The presence of P waves and recognition of AV dissociation is, however, key to the electrocardiographic diagnosis of VA. Examining different leads and using calipers may help increase the confidence in the identification of buried P waves (Fig. 2).

Ventricular rhythms often (but not always) have an underlying regularity and QRS complexes of abnormal morphology and longer duration (wider). This is due to electrical impulses being conducted via slow cell-to-cell conduction. In some VAs QRS complexes can have near normal morphology if they are partially conducted over the bundle of His or originate from areas near the normal conduction system. In these cases, differentiation of ventricular, supraventricular and nodal arrhythmias can be difficult and multiple leads helpful (Fig. 2; van Loon, 2019). Ventricular pre-excitation due to accessory pathways can cause aberrant QRS morphology in horses (Viu et al., 2018). In humans, premature supraventricular complexes might cause bundle branch block and alter QRS morphology and duration. These aberrant QRS complexes might be hard to distinguish from a VPC especially if the P wave cannot be identified. It has been described in horses that the QRS morphology following an atrial premature complex might be different (especially amplitude) than the QRS generated during sinus rhythm (Broux et al., 2016). Although bundle branch block is likely to be present in horses, it has not been fully characterized.

Echocardiography

Echocardiography is the main tool used in horses to detect underlying cardiac disease that can become the arrhythmogenic substrate for VAs. The sensitivity of echocardiograms in this scenario is uncertain but there are reports of the echocardiographic diagnosis of several conditions causing or predisposing to VAs (Traub-Dargatz et al., 1994; Sleeper et al., 2001; Schefer et al., 2011; Verheyen et al., 2012). In the absence of advanced imaging modalities capable of imaging the equine heart, echocardiography remains the most useful tool. The presence of underlying structural cardiac disease worsens the prognosis for resolution and recurrence of VAs and drastically changes the recommendation for athletic use in many instances (Reef et al., 2014; van Loon, 2019), although reports of horses returning to moderate athletic activity after severe VAs with persistent echocardiographic changes exist (Traub-Dargatz et al., 1994).

Exercising ECGs

Exercising ECGs are used in different scenarios in horses with VAs. Exercise tests are used in horses with occasional VPCs, AIVR, after therapy for VT or after myocardial damage and a period of rest. An exercise test should be performed at the same intensity or an intensity slightly above that required of the horse (Reef et al., 2014) The level of fitness should also be considered. The variability of the results of exercise tests (Navas de Solis et al., 2016) and the variability of their interpretation (Trachsel et al., 2010) are complicating factors. Clinicians may perform more than one exercise test, but the appropriate number of ECGs to accurately identify equine arrhythmias has not been determined. Occasional, non-complex VAs that are suppressed during exercise or occur only in the recovery period (Physick-Sheard and McGurrin, 2010; Reef et al., 2014) and in the absence of structural heart disease are considered to carry a good prognosis. Ventricular arrhythmias that increase during exercise, VT or other complex VAs (couplets, triplets, bigeminy or trigeminy patters or R on T) are cause for concern and are likely to negatively affect clinicians' recommendation for athletic activity (Reef et al., 2014). An exercise test is contraindicated in horses with severe arrhythmias such as VT or horses with demonstrated current myocardial injury (van Loon, 2019).

Continuous ECGs

Continuous recordings over 24 h can be used to quantify the presence of VAs. Approximately one ectopic beat/h is commonly seen in normal horses and they are considered clinically irrelevant if they disappear with exercise (Reef, 1989). A recent study showed up to 1.8VPCs/h in normally performing event horses without detectable cardiac disease (Lorello et al., 2019). In human athletes, underlying heart disease is less likely when there are less than 2000 VPCs/24 h period, no sustained VT and no structural abnormalities (Stoebner et al., 2012). The number of VPCs that should be considered 'safe' in a horse is unknown. In boxers with arrhythmogenic right ventricular cardiomyopathy the presence of VT in 24 h recordings is associated with non-survival (Mõtsküla et al., 2013). It is uncertain if analogous criteria could be applied to horses, but the combination of exercising and continuous-resting ECGs seem complementary when interpreting clinical relevance of VAs in horses (Uhlendorf et al., 2013). The use of insertable cardiac monitors (loop recorders) has been described in horses for the evaluation of episodic collapse and can be a tool for clinicians suspecting sporadic VAs (Lyle et al., 2010).

Other diagnostic tests available to physicians such as cardiac MRI, genetic testing for channelopathies or angiography are not used in equine practice due to lack of availability of the imaging equipment and the different underlying diseases that cause VAs in horses compared to humans.

Cardiac troponins

Cardiac troponins (cTn) I and T are currently the most used and sensitive markers of myocardial damage. Cardiac troponins can be increased during primary cardiac disease (Cornelisse et al., 2000;

Verheyen et al., 2012; Nath et al., 2012). In the event of VAs, cTns can help assess the presence of myocardial injury and modify the therapeutic plan. It is important to recognize that increases in cTns can occur during systemic disease such as endotoxemia (Nostell et al., 2012), hemorrhage (Navas de Solis et al., 2015) or colic (Díaz et al., 2014), without the presence of primary myocardial injury. The increases in cTns may have short-term prognostic relevance in these cases but the long-term relevance has not been defined (Diaz et al., 2014). The kinetics of cTns have been described in horses after experimental injection of recombinant cTns and after exercise (Kraus et al., 2013; Rossi et al., 2019). The half-lives in these two studies were 6.4 h and 0.47 h respectively with the difference likely due to the different scenarios and the measurement of exogenous recombinant vs. endogenous cTns. The release of cTns has been proposed to occur in two phases corresponding to the early release of cytoplasmic cTns and later release of cTns bound to the contractile apparatus. Peak concentration of cTns has been described at 3–6 h after exercise with a return to baseline values within 24 h (Shields et al., 2018). After experimental administration of monensin, peak plasma concentration was detected 24–72 h after administration (Kraus et al., 2010). It is plausible that in common clinical scenarios kinetics will approximate these situations and the short half-life of cTns can be useful for monitoring purposes. In many occasions, ongoing damage and elimination are likely to overlap and the effective half-life may be longer than that described experimentally. High sensitivity assays have been validated for use in horses (van der Vekens et al., 2015; Shields et al., 2016) and the increased sensitivity coupled with lower limits of detection may be useful in some scenarios. It is currently uncertain if this better analytical performance translates into a clinical benefit in equine practice. It is relevant to recognize that cTnI assays are heterogenous and validated assays and reference ranges specific for the assay should be used. Only one cTnT assay currently exists and this has been validated in horses (van der Vekens et al., 2015).

Myocardial biopsies

Ventricular and atrial myocardial biopsies can be safely obtained using a transvenous approach with endomyocardial forceps in horses without evident cardiac disease (Decloedt et al., 2016). There are no data about the safety of this procedure in horses with underlying cardiac disease or its sensitivity to diagnose myocardial injury. If proven safe and sensitive in horses this could become a useful tool for selected cases of VAs (Strain et al., 1983; Vasichkina et al., 2017).

Treatment

Ventricular arrhythmias, especially when associated with structural heart disease, can predispose to VT or ventricular fibrillation and carry a risk for horses' health and riders' safety (van Loon, 2019). Treatment of VAs is initially directed at solving the underlying cardiac or systemic disease. Rest is often included in the treatment and the duration of the resting period varies from short periods if the arrhythmia is associated with underlying non-cardiac disease that resolves to longer periods for treatment of ongoing or more severe cardiac or extra cardiac diseases. An example of a suggested resting protocol after treatment for VT would be at least 4 weeks of rest after restoration of normal sinus rhythm followed by a 24-h continuous ECG and an exercising ECG. If these tests are considered normal, the horse can start mild and progressive exercise and another exercising ECG is performed when the horse is back into normal training (van Loon, 2019) and ready to perform an exercise test. The use of detraining periods of approximately 3 months have been suggested (Biffi et al., 2004; Pelliccia et al., 2005) and challenged (Delise et al., 2011) in human athletes with no underlying cardiac disease in which the arrhythmias are thought to be associated with training. The duration or presence of training associated arrhythmias in horses is uncertain but perhaps detraining could be a logical approach in some equine athletes with arrhythmias of unknown cause.

There are five classic scenarios in which pharmacological antiarrhythmic therapy is recommended (Mitchell, 2017). These are 1-symptomatic ventricular arrhythmias; 2-heart rate higher than 100–120/min, 3-multiform ectopy, 4-R on T and 5-torsades de pointes. Management of other VAs largely depends on whether structural heart disease is present or not, but antiarrhythmic therapy is often not recommended. It is important to obtain more information about outcomes after antiarrhythmic therapy in horses. Suppression of VAs is a pathophysiologically sound goal. The Cardiac Arrhythmia Suppression Trial (Cardiac Arrhythmia Suppression Trial (CAST) Investigators, 1989), performed in humans, highlights that prospective studies are necessary to support sound goals. Prior to CAST, physicians assumed that pharmacologic suppression of VPCs in patients at risk for VT was desirable, but CAST showed that antiarrhythmic drugs increased mortality. The underlying diseases causing or predisposing to VAs, the potential consequences of the arrhythmia and the availability of therapeutic and monitoring tools is different in horses and humans making the extrapolations challenging. Thus, pharmacologic treatment of arrhythmias should take place in a monitored setting with continuous ECG in initial stages.

Lidocaine is often the first-line antiarrhythmic followed or alongside magnesium sulfate. Procainamide, phenytoin, sotalol, quinidine, amiodarone, and β-blockers (atenolol, propranolol, esmolol) are other drugs that can be used in horses with VAs (Mitchell, 2017). Several reviews have recently compiled information regarding the use of antiarrhythmics in horses and Table 1 displays a summary of these reviews (Mitchell, 2017; van Loon, 2019; Redpath and Bowen, 2019).

Prognosis

The prognosis for resolution of VAs with treatment of the underlying disease or antiarrhythmic drugs is good. The largest case series of miscellaneous equine VAs reported restoration of normal sinus rhythm in 17/21 cases (81%) (Reimer et al., 1992). It is important to recognize that the methods for detection of underlying cardiac disease in horses are far from perfect. Horses treated for complex VAs should be reassessed frequently and people handling or riding these horses should be informed adults if these horses are to exercise at all (van Loon, 2019). The long-term prognosis for the horse to resume athletic activity is a complex topic and defining safety risks for horse and rider is key. The main concern is that VPCs represent a potential risk for deterioration into ventricular tachyarrhythmias such as VT, torsades de pointes, or ventricular fibrillation, which may cause poor tissue perfusion. These rhythms, when associated with demands of exercise, can cause weakness, collapse or sudden cardiac death. Risk stratification considers the likelihood of malignant arrhythmia development and the potential consequence of an adverse event. In many cases of VAs observation with no specific therapy is acceptable, although follow-up is advisable or mandatory.

The American College of Veterinary Internal Medicine/ European College of Equine Internal Medicine joint document on recommendations for Management of Equine Athletes with Cardiovascular Abnormalities (Reef et al., 2014) is a useful reference for clinicians. The authors of this document admitted risk stratification for VAs is imperfect and in the absence of clear evidence recommendations are biased toward safety, as opposed to maintaining athletic activity. Future studies and information

Table 1
Summary of published information on antiarrhythmic drugs in horses.

Drug	Class	Dosage	Adverse effects	Comments
Lidocaine	Ib Na^+ channel blocker	0.5 mg/kg IV slowly every 5 min up to 1.5 mg/kg followed by a CRI of 0.05 mg/kg/min (van Loon, 2019)	Altered vision, eye blinking, close inspection of objects, anxiety, tremors, seizure and collapse (Meyer et al., 2001)	Adverse effect treated with diazepam and stopping infusion (van Loon, 2019). Lipid infusions have been described if large doses are given (Vieitez et al., 2017) Class Ib antiarrhythmics preferably bind damaged myocardial cells to prevent reentry (Redpath and Bowen, 2019) Hepatic metabolism highly dependent of hepatic blood flow and therefore caution should be exercised in horses with low cardiac output or liver failure (Meyer et al., 2001) Highly protein bound drugs may displace lidocaine increasing unbound concentrations and the risk of lidocaine toxicity (Milligan et al., 2006)
Magnesium sulfate	Physiologic Ca^{2+} channel blocker. Activator of membrane Na^+/K^+ ATPase	50–100 mg/kg IV diluted in 0.9% NaCl as a 15–25 min infusion (van Loon, 2019)	Rare. Overdose cause central nervous system depression, muscle weakness, trembling, bradycardia, hypotension, neuromuscular blockade, respiratory depression and cardiac arrest (Mitchell, 2017)	Drug of choice for torsades de pointes (van Loon, 2019) and contraindicated in bradycardia, SA and AV block
Procainamide	Ia Na^+ channel blocker	1 mg/kg/min IV up to 20 mg/kg total dose (Ellis et al., 1994)	Adverse effects are hypotension, QRS and QT prolongation, negative inotropism, arrhythmia, gastrointestinal and neurologic disorders (Mitchell, 2017; Ellis et al., 1994)	Contraindications: untreated heart failure, prolonged QRS or QT interval, complete AV block, digitalis intoxication. Interactions with hypokalemia, hypomagnesemia, acid-base disorders and quinidine or amiodarone described (Mitchell, 2017; Tartini et al., 1982)
Phenytoin	Ib Na^+ channel blocker	20 mg/kg PO twice daily for 2 days followed by 10–15 mg/kg twice daily 7.5 mg/kg IV (Wijnberg and Ververs, 2004)	Adverse effects are sedation, lip and facial twitching, gait deficits, excitation, seizures, arrhythmias and hepatotoxicity with chronic use (Redpath and Bowen, 2019) Contraindications are SA or AV block and sinus bradycardia (Mitchell, 2017)	Recommended for digoxin toxicity (van Loon, 2019) Monitor plasma drug concentrations (target 5–10 μg/mL) is recommended (Wijnberg and Ververs, 2004)
Quinidine	Ia Na^+ channel blocker	Sulfate: 22 mg/kg via nasogastric tube every 2 h for 4–6 doses followed by every 6 h (Reef et al., 1995) Quinidine gluconate (not available at the time of writing this manuscript): 1–2.2 mg/kg IV every 10 min up to 12 mg/kg total dose	Adverse effects: depression, flatulence, hypotension, diarrhea, colic, ataxia, nasal mucosal swelling, paraphimosis, urticaria, laminitis, acceleration of AV conduction and tachycardia, QRS and QT prolongation, VT, torsades de pointes, hypotension, negative inotropism, exacerbation of heart failure, cardiovascular collapse, sudden death. Therapeutic drug monitoring is recommended but availability of assays is limited. Target therapeutic concentration 2–5 μg/mL (Reef et al., 1995)	Contraindications: torsades de pointes, untreated heart failure, pre-existing QRS or QT interval prolongation, complete AV block, digitalis intoxication. Use with caution in patients with hypokalemia, hypomagnesemia, hypoxia, acid-base disorders or liver disease (Mitchell, 2017)
Propafenone	Ic Na^+ channel blocker	2 mg/kg IV or PO every 8 h (Puigdemont et al., 1990).	Adverse effects are gastrointestinal and neurologic disorders, bronchospasm, negative inotropism, exacerbation of heart failure, AV block, QRS and QT prolongation, arrhythmias (Mitchell, 2017)	Intravenous formulation not commonly available in many countries. Bioavailability is uncertain. Contraindications are structural heart disease, heart failure, SA or AV node dysfunction (Mitchell, 2017)
Flecainide	Ic Na^+ channel blocker	2 mg/kg as a 0.2 mg/kg/min infusion (Redpath and Bowen, 2019)	Sudden death. Colic, depression.	Not recommended for routine use due to very narrow safety profile (van Loon et al., 2004; Dembek et al., 2014). Contraindicated when structural heart disease is present (as for other Ic drugs).
Amiodorone	III K^+ channel blocker Also class I, II and IV effects.	5 mg/kg/h IV for 1 h, followed by 0.83 mg/kg IV for 23 h (De Clercq et al., 2007a, b)	Adverse reactions: hindlimb weakness, weight shifting, torsades de pointes, SA and AV nodal inhibition, bradycardia, hypotension. Prolonged treatment may affect lungs, liver, heart, thyroid gland, gastrointestinal tract, eyes, skin and nerves. (Mitchell, 2017)	Contraindications: sinus node dysfunction, bradycardia, AV block, cardiogenic shock, prolonged QT interval Oral absorption is low and variable and experience with oral use is anecdotal (de Clercq et al., 2007)

Table 1 (*Continued*)

Drug	Class	Dosage	Adverse effects	Comments
Sotalol	II/III β-blocker/K^+ channel blocker	1–2 mg/kg PO every 12 h for 1 day followed by 2–3 mg/kg PO every 12 h (Broux et al., 2018).	Adverse effects are QT prolongation, ventricular arrhythmias (Broux et al., 2018).	Good oral bioavailability. Well tolerated for long-term administration. Dosage should be gradually reduced before stopping. Contraindications: pre-existing QT prolongation. Use with caution in patients with uncorrected hypokalemia or hypomagnesaemia. (Mitchell, 2017)
Propranolol	II β_1/β_2-blocker	0.38–0.78 mg/kg PO every 8 h	Depression, lethargy, weakness, bradycardia, AV block, hypotension, negative inotrope, bronchoconstriction and aggravation of asthma (not at low doses) (Mitchell, 2017)	Indicated for tachyarrhythmias associated with exercise or other causes of increased sympathetic tone (Mitchell, 2017). Use preceded by α blockade in pheochromocytoma (Fouché et al., 2016). Variable or low bioavailability. Contraindications are bradycardia, high degree AV block, untreated heart failure, bronchopulmonary disease (Mitchell, 2017)
Esmolol	II β_1-blocker	200–500 ug/kg IV over 2–5 min, followed 25–100 ug/kg/min to effect.	Weakness, lethargy	Extrapolated dosage.
Atenolol	II/III β_1-blocker	0.5 mg/kg PO every 12 h	Weakness lethargy	Extrapolated dosage.
Dexamethasone	Anti-inflammatory	0.05–0.2 mg/kg IV or IM followed by a 3-week tapering course	Laminitis	Used when myocarditis is suspected in the absence of infection (van Loon, 2019)

gathered from large populations of horses are likely to help refine current guidelines. Specific '*Summary key recommendations for horses with VA*' are described in the above-mentioned consensus statement (Reef et al., 2014).

General rules included in the above-mentioned statement determine that circumstances considered to negatively affect safety are: 'structural heart disease, a history of collapse or cardiomegaly in a horse with VPCs, hypotension during VT, multiform ectopy, short coupling intervals and R on T, sustained VT, or couplets or triplets. On the other hand, rhythms generally considered benign, in the absence of other risks factors, are AIVR, occasional monomorphic VPCs overdriven with exercise or only detected in the immediate post-exercise period.

The relationship of arrhythmias that do not fit any of these categories with performance or safety is currently uncertain (Reef et al., 2014) and comparative information can give some perspective to equine medicine conundrums. Comparative aspects of exercising arrhythmias in horses and humans has been reviewed recently (Navas de Solis, 2016) and some markers of VA severity in humans mentioned in this review were: structural heart disease (Walker et al., 2010), presence of symptoms (palpitations, dizziness, dyspnea, chest pain, syncope, presyncope) (Giada et al., 2011); more than 2000 VPCs per 24-h period; non-sustained ventricular tachycardia (Stoebner et al., 2012); frequent VPCs during maximal or near maximal exercise; complex VAs at any time during an exercise test (Beckerman et al., 2005; Heidbüchel et al., 2003); VT or ventricular fibrillation at any time, multifocal VA; R-on-T phenomenon; VPCs with a short (<400 ms) RR interval (Giada et al., 2011); no arrhythmia reduction with deconditioning (Maron and Pelliccia, 2006). Direct extrapolation of information across species is not possible but the larger information available in humans vs. equine athletes make consideration of these guidelines interesting.

Conclusions

Ventricular arrhythmias can be incidental or life threatening. Determining the presence of underlying cardiac disease is key in the management of VAs. The evaluation, treatment and prognosis of horses with VAs require careful attention at factors that affect equine health and the safety of the human partner.

Conflict of interest statement

The author of this paper does not have a financial or personal relationship with other people or organisations that could inappropriately influence or bias the content of the paper.

References

Beckerman, J., Wu, T., Jones, S., Froelicher, V.F., 2005. Exercise test-induced arrhythmias. Progress in Cardiovascular Diseases 47, 285–305.

Biffi, A., Maron, B., Verdile, L., Fernando, F., Spataro, A., Marcello, G., Ciardo, R., Ammirati, F., Colivicchi, F., Pelliccia, A., 2004. Impact of physical deconditioning on ventricular tachyarrhythmias in trained athletes. Journal of the American College of Cardiology 2004, 1053–1058.

Broux, B., De Clercq, D., Decloedt, A., Van Der Vekens, N., Verheyen, T., Ven, S., Pardon, B., van Loon, G., 2016. Atrial premature depolarization-induced changes in QRS and T wave morphology on resting electrocardiograms in horses. Journal of Veterinary Internal Medicine 30, 1253–1259.

Broux, B., De Clercq, D., Decloedt, A., Vera, L., Devreese, M., Gehring, R., Croubels, S., van Loon, G., 2018. Pharmacokinetics and electrophysiological effects of sotalol hydrochloride in horses. Equine Veterinary Journal 50, 377–383.

Burns, T.A., Dembek, K.A., Kamr, A., Dooley, S.B., Dunbar, L.K., Aarnes, T.K., Bednarski, L.S., O'Brien, C., Lakritz, J., Byrum, B., Wade, A., Farmer, R., Tan, S., Toribio, R.E., 2018. Effect of intravenous administration of cobalt chloride to horses on clinical and hemodynamic variables. Journal of Veterinary Internal Medicine 32, 441–449.

Cardiac Arrhythmia Suppression Trial (CAST) Investigators, 1989. Preliminary report: effect of encainide and flecainide on mortality in a randomized trial of arrhythmia suppression after myocardial infarction. New England Journal of Medicine 10, 406–412.

Cohagan, B., Brandis, D., 2017. Torsade de pointes. StatPearls. StatPearls Publishing, Treasure Island (FL).

Cornelisse, C.J., Schott 2nd, H.C., Olivier, N.B., Mullaney, T.P., Koller, A., Wilson, D.V., Derksen, F.J., 2000. Concentration of cardiac troponin I in a horse with a ruptured aortic regurgitation jet lesion and ventricular tachycardia. Journal of the American Veterinary Medical Association 217, 231–235.

Coronel, R., Baartscheer, A., Rademaker, J.M.E., Vermeulen, J.T., de Bakker, J.M.T., 2001. The arrhythmogenic substrate in ischemic and non-ischemic cardiomyopathies. In: Liem, L.B., Downar, E. (Eds.), Progress in Catheter Ablation. Developments in Cardiovascular Medicine, vol. 241. Springer, Dordrecht.

Coudry, V., Jean, D., Desbois, C., Tnibar, A., Laugier, C., George, C., 2007. Myocardial fibrosis in a horse with polymorphic ventricular tachycardia observed during general anesthesia. Canadian Veterinary Journal 48, 623–626.

De Clercq, D., van Loon, G., Baert, K., Tavernier, R., Croubels, S., De Backer, P., Deprez, P., 2007a. Effects of an adapted intravenous amiodarone treatment protocol in horses with atrial fibrillation. Equine Veterinary Journal 39, 344–349.
De Clercq, D., van Loon, G., Baert, K., De Backer, P., Deprez, P., 2007b. Treatment with amiodarone of refractory ventricular tachycardia in a horse. Journal of Veterinary Internal Medicine 21, 878–880.
Decloedt, A., de Clercq, D., Ven, S., van der Vekens, N., Chiers, K., van Loon, G., 2016. Right atrial and right ventricular ultrasound-guided biopsy technique in standing horses. Equine Veterinary Journal 48, 346–351.
Delise, P., Lanari, E., Sitta, N., Centa, M., Allocca, G., Biffi, A., 2011. Influence of training on the number and complexity of frequent VPBs in healthy athletes. Journal of Cardiovascular Medicine (Hagerstown) 12, 157–161.
Dembek, K.A., Hurcombe, S.D., Schober, K.E., Toribio, R.E., 2014. Sudden death of a horse with supraventricular tachycardia following oral administration of flecainide acetate. Journal of Veterinary Emergency and Critical Care 24, 759–763.
Díaz, O.M., Durando, M.M., Birks, E.K., Reef, V.B., 2014. Cardiac troponin I concentrations in horses with colic. Journal of the American Veterinary Medical Association 245, 118–125.
Ellis, E.J., Ravis, W.R., Malloy, M., Duran, S.H., Smyth, B.G., 1994. The pharmacokinetics and pharmacodynamics of procainamide in horses after intravenous administration. Journal of Veterinary Pharmacology and Therapeutics 17, 265–270.
Flinders, D.C., Roberts, S.D., 2000. Ventricular arrhythmias. Primary Care Care 27, 709–724.
Fouché, N., Gerber, V., Gorgas, D., Marolf, V., Grouzmann, E., van der Kolk, J.H., Navas de Solis, C., 2016. Catecholamine metabolism in a Shetland pony with suspected pheochromocytoma and pituitary pars intermedia dysfunction. Journal of Veterinary Internal Medicine 30, 1872–1878.
Freel, K.M., Morrison, L.R., Thompson, H., Else, R.W., 2010. Arrhythmogenic right ventricular cardiomyopathy as a cause of unexpected cardiac death in two horses. Veterinary Record 166, 718–721.
Giada, F., Conte, R., Pescatore, V., Brugin, E., 2011. Sports and arrhythmias. Minerva Medica 102, 239–247.
Heidbüchel, H., Hoogsteen, J., Fagard, R., Vanhees, L., Ector, H., Willems, R., Van Lierde, J., 2003. High prevalence of right ventricular involvement in endurance athletes with ventricular arrhythmias. Role of an electrophysiologic study in risk stratification. European Heart Journal 24, 1473–1480.
Hondalus, M.K., Pipers, F.S., 1989. ECG of the month. Paroxysmal ventricular tachycardia in a horse with diarrhea. Journal of the American Veterinary Medical Association 195, 1222–1223.
Karrasch, N.M., Scansen, B.A., Aarnes, T.K., Hubbell, J.A., Bonagura, J.D., 2013. ECG of the month. Accelerated idioventricular rhythm during anesthesia. Journal of the American Veterinary Medical Association 243, 1260–1262.
Kraus, M.S., Jesty, S.A., Gelzer, A.R., Ducharme, N.G., Mohammed, H.O., Mitchell, L.M., Soderholm, L.V., Divers, T.J., 2010. Measurement of plasma cardiac troponin I concentration by use of a point-of-care analyzer in clinically normal horses and horses with experimentally induced cardiac disease. American Journal of Veterinary Research 71, 55–59.
Kraus, M.S., Kaufer, B.B., Damiani, A., Osterrieder, N., Rishniw, M., Schwark, W., Gelzer, A.R., Divers, T.J., 2013. Elimination half-life of intravenously administered equine cardiac troponin I in healthy ponies. Equine Veterinary Journal 45, 56–59.
Leroux, A.J., Schott 2nd, H.C., Hines, M.T., 1995. Ventricular tachycardia associated with exhaustive exercise in a horse. Journal of the American Veterinary Medical Association 207, 335–337.
Lorello, O., Ramseyer, A., Burger, D., Gerber, V., Navas de Solis, C., 2019. Cardiovascular variables in eventing and endurance horses over a season. Journal of Veterinary Cardiology 21, 67–78.
Lyle, C., Turley, G., Blissitt, K., Pirie, R., Mayhew, I., McGorum, B., Keen, J., 2010. Retrospective evaluation of episodic collapse in the horse in a referred population: 25 cases (1995–2009). Journal of Veterinary Internal Medicine 24, 1498–1502.
Lyle, C.H., Uzal, F.A., McGorum, B.C., Aida, H., Blissit, K.J., Case, J.T., Charles, J.T., Gardner, I., Horadagoda, N., Kusano, K., Lam, K., Pack, J.D., Parkin, T.D., Slocombe, R.F., Stewart, B.D., Boden, L.A., 2011. Sudden death in racing Thoroughbred horses: an international multicentre study of post mortem findings. Equine Veterinary Journal 43, 324–331.
Machida, N., Nakamura, T., Kiryu, K., Haramaki, S., Too, K., 1992. Cardiopathological observation on a case of persistent ventricular tachycardia in a pony mare. Journal of Veterinary Medical Science 54, 1213–1216.
Maron, B.J., Pelliccia, A., 2006. The heart of trained athletes: cardiac remodeling and the risks of sports, including sudden death. Circulation 114, 1633–1644.
Meyer, G.A., Lin, H.C., Hanson, R.R., Hayes, T.L., 2001. Effects of intravenous lidocaine overdose on cardiac electrical activity and blood pressure in the horse. Equine Veterinary Journal 33, 434–437.
Milligan, M., Kukanich, B., Beard, W., Waxman, S., 2006. The disposition of lidocaine during a 12-hour intravenous infusion to postoperative horses. Journal of Veterinary Pharmacology and Therapeutics 29, 495–499.
Mitchell, K.J., 2017. Practical considerations for diagnosis and treatment of ventricular tachycardia in horses. Equine Veterinary Education 29, 670–676.
Morgan, R.A., Raftery, A.G., Cripps, P., Senior, J.M., McGowan, C.M., 2011. The prevalence and nature of cardiac arrhythmias in horses following general anaesthesia and surgery. Acta Veterinaria Scandinavica 53, 62.
Mõtsküla, P.F., Linney, C., Palermo, V., Connolly, D.J., French, A., Dukes McEwan, J., Fuentes, V.L., 2013. Prognostic value of 24-hour ambulatory ECG (Holter) monitoring in Boxer dogs. Journal of Veterinary Internal Medicine 27, 904–912.
Nath, L., Anderson, G., Hinchcliff, K., Savage, C., 2012. Serum cardiac troponin I concentrations in horses with cardiac disease. Australian Veterinary Journal 90, 351–357.
Navas de Solis, C., 2016. Exercising arrhythmias and sudden cardiac death in horses: review of the literature and comparative aspects. Equine Veterinary Journal 48, 406–413.
Navas de Solis, C., Dallap Schaer, B.L., Boston, R., Slack, J., 2015. Myocardial insult and arrhythmias after acute hemorrhage in horses. Journal of Veterinary Emergency and Critical Care 25, 248–255.
Navas de Solis, C., Green, C., Sides, R., Bayly, W., 2016. Arrhythmias in Thoroughbreds during and after treadmill and racetrack exercise. Journal of Equine Veterinary Science 42, 19–24.
Nostell, K., Bröjer, J., Höglund, K., Edner, A., Häggström, J., 2012. Cardiac troponin I and the occurrence of cardiac arrhythmias n horses with experimentally induced endotoxaemia. The Veterinary Journal 192, 171–175.
Pelliccia, R., Fagard, H.H., Bjørnstad, A., Anastassakis, E., Arbustini, D., Assanelli, A., Biffi, M., Borjesson, F., Carrè, D., Corrado, P., 2005. Recommendations for competitive sports participation in athletes with cardiovascular disease: a consensus document from the study group of sports cardiology of the working group of cardiac rehabilitation and exercise physiology and the working group of myocardial and pericardial diseases of the European society of cardiology. European Heart Journal 26, 1422–1445.
Peters, S.T., Hopkins, A., Stewart, S., Slack, J., de Solis, C.N., 2013. Myocardial contusion and rib fracture repair in an adult horse. Journal of Veterinary Emergency and Critical Care 23, 663–669.
Physick-Sheard, P., McGurrin, M., 2010. Ventricular arrhythmias during race recovery in Standardbred racehorses and associations with autonomic activity. Journal of Veterinary Internal Medicine 24, 1158–1166.
Puigdemont, A., Riu, J.L., Guitart, R., Arboix, M., 1990. Propafenone kinetics in the horse. Comparative analysis of compartmental and noncompartmental models. Journal of Pharmacology Methods 23, 79–85.
Raftery, A.G., Garcia, N.C., Thompson, H., Sutton, D.G., 2015. Arrhythmogenic right ventricular cardiomyopathy secondary to adipose infiltration as a cause of episodic collapse in a horse. Irish Veterinary Journal 68, 24.
Redpath, A., Bowen, M., 2019. Cardiac therapeutics in horses. Veterinary Clinics of North America Equine Practice 35, 217–241.
Reef, V.B., 1989. Frequency of cardiac arrhythmias and their significance in normal horses. Journal of Veterinary Internal Medicine 3, 506–508.
Reef, V.B., Reimer, J.M., Spencer, P.A., 1995. Treatment of atrial fibrillation in horses: new perspectives. Journal of Veterinary Internal Medicine 9, 57–67.
Reef, V.B., Bonagura, J., Buhl, R., McGurrin, M.K., Schwarzwald, C.C., van Loon, G., Young, L.E., 2014. Recommendations for management of equine athletes with cardiovascular abnormalities. Journal of Veterinary Internal Medicine 28, 749–761.
Reimer, J.M., Reef, V.B., Sweeney, R.W., 1992. Ventricular arrhythmias in horses: 21 cases (1984-1989). Journal of the American Veterinary Medical Association 201, 1237–1243.
Riera, A.R., Barros, R.B., de Sousa, F.D., Baranchuk, A., 2010. Accelerated idioventricular rhythm: history and chronology of the main discoveries. Indian Pacing Electrophysiology Journal 10, 40–48.
Roberts-Thomson, K., Lau, D., Sanders, P., 2011. The diagnosis and management of ventricular arrhythmias. Nature Reviews Cardiology 8, 311–321.
Rossi, T.M., Kavsak, P.A., Maxie, M.G., Pearl, D.L., Pyle, W.G., Physick-Sheard, P.W., 2019. Post-exercise cardiac troponin I release and clearance in normal Standardbred racehorses. Equine Veterinary Journal 51, 97–101.
Schefer, K., Hagen, R., Ringer, S., Schwarzwald, C., 2011. Laboratory, electrocardiographic, and echocardiographic detection of myocardial damage and dysfunction in an Arabian mare with nutritional masseter myodegeneration. Journal of Veterinary Internal Medicine 25, 1171–1180.
Schwartz, A., Brotfain, E., Koyfman, L., Klein, M., 2015. Cardiac arrhythmias in a septic ICU population: a review. Journal of Critical Care Medicine (Universitatea de Medicina si Farmacie din Targu-mures) 1, 140–146.
Shahreyar, M., Fahhoum, R., Akinseye, O., Bhandari, S., Dang, G., Khouzam, R.N., 2018. Severe sepsis and cardiac arrhythmias. Annals of Translational Medicine 6, 6.
Shields, E., Seiden-Long, I., Massie, S., Passante, S., Leguillette, R., 2016. Analytical validation and establishment of reference intervals for a 'high-sensitivity' cardiac troponin-T assay in horses. BMC Veterinary Research 12, 104.
Shields, E., Seiden-Long, I., Massie, S., Leguillette, R., 2018. 24-hour kinetics of cardiac troponin-t using a "high-sensitivity" assay in Thoroughbred chuckwagon racing geldings after race and associated clinical sampling guidelines. Journal of Veterinary Internal Medicine 32, 433–440.
Sleeper, M.M., Durando, M.M., Miller, M., Habecker, P.L., Reef, V.B., 2001. Aortic root disease in four horses. Journal of the American Veterinary Medical Association 219, 491–496.
Stoebner, R., Bellin, D.A., Haigney, M.C., 2012. Cardiac electrophysiology and the athlete: a primer for the sports clinician. Current Sports Medicine Reports 11, 70–77.
Strain, J.E., Grose, R.M., Factor, S.M., Fisher, J.D., 1983. Results of endomyocardial biopsy in patients with spontaneous ventricular tachycardia but without apparent structural heart disease. Circulation 68, 1171–1181.
Tartini, R., Kappenberger, L., Steinbrunn, W., Meyer, U.A., 1982. Dangerous interaction between amiodarone and quinidine. Lancet 12, 1327–1329.
Thompson, J.A., Mirza, M.H., Barker, S.A., Morgan, T.W., Bauer, R.W., McConnico, R.S., 2011. Clenbuterol toxicosis in three Quarter Horse racehorses after administration of a compounded product. Journal of the American Veterinary Medical Association 239, 842–849.

Trachsel, D.S., Bitschnau, C., Waldern, N., Weishaupt, M.A., Schwarzwald, C.C., 2010. Observer agreement for detection of cardiac arrhythmias on telemetric ECG recordings obtained at rest, during and after exercise in 10 Warmblood horses. Equine Veterinary Journal Supplement 38, 208–215.
Traub-Dargatz, J.L., Schlipf Jr, J.W., Boon, J., Ogilvie, G.K., Bennett, D.G., Wingfield, W.E., Hutchison, J.M., 1994. Ventricular tachycardia and myocardial dysfunction in a horse. Journal of the American Veterinary Medical Association 205, 1569–1573.
Uhlendorf, F., Gehlen, H., Stadler, P., 2013. Comparative techniques for the diagnosis of rhythm abnormalities in horses. Tierärtzliche Praxis Grosstiere 41, 305–314.
van Der Vekens, N., van Dievoet, M.A., De Puydt, H., Decloedt, A., Ven, S., De Clercq, D., Deprez, P., van Loon, G., 2015. Analytical validation of a high-sensitivity cardiac troponin T assay in horses. Journal of Veterinary Diagnostic Investigation 27, 504–509.
van Loon, G., 2019. Cardiac arrhythmias in horses. Veterinary Clinics of North America Equine Practice 35, 85–102.
van Loon, G., Blissitt, K.J., Keen, J.A., Young, L.E., 2004. Use of intravenous flecainide in horses with naturally-occurring atrial fibrillation. Equine Veterinary Journal 36, 609–614.
Van Steenkiste, G., De Clercq, D., Boussy, T., Vera, L., Schauvliege, S., Decloedt, A., van Loon, G., 2020. Three dimensional ultra-high-density electro-anatomical cardiac mapping in horses: methodology. Equine Veterinary Journal 00, 1–8.
Vasichkina, E., Poghosyan, H., Mitrofanova, L., Tatarsky, R., Lebedev, D., 2017. Right ventricular endomyocardial biopsy in children and adolescents with drug-refractory arrhythmia. Cardiology in the Young 27, 435–442.
Verheyen, T., Decloedt, A., De Clercq, D., van Loon, G., 2012. Cardiac changes in horses with atypical myopathy. Journal of Veterinary Internal Medicine 26, 1019–1026.
Vieitez, V., Gómez de Segura, I.Á., Martin-Cuervo, M., Gracia, L.A., Ezquerra, L.J., 2017. Successful use of lipid emulsion to resuscitate a foal after intravenous lidocaine induced cardiovascular collapse. Equine Veterinary Journal 49, 767–769.
Viu, J., Armengou, L., Decloedt, A., Jose-Cunilleras, E., 2018. Investigation of ventricular pre-excitation electrocardiographic pattern in two horses: clinical presentation and potential causes. Journal of Veterinary Cardiology 20, 213–221.
Walker, J., Calkins, H., Nazarian, S., 2010. Evaluation of cardiac arrhythmia among athletes. American Journal of Medicine 123, 1075–1081.
Wijnberg, I.D., Ververs, F.F., 2004. Phenytoin sodium as a treatment for ventricular dysrhythmia in horses. Journal of Veterinary Internal Medicine 18, 350–353.
Wilkins, P.A., Bain, F.T., 1993. ECG of the month. Journal of the American Veterinary Medical Association 203, 972–973.
Yalta, T., Yalta, K., 2018. Systemic inflammation and arrhythmogenesis: a review of mechanistic and clinical perspectives. Angiology 69, 288–296.