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Exercise-associated rhythm disturbances in poorly performing Thoroughbreds: risk factors and association with racing performance.

Celia M Marr[1], Samantha Franklin[2,3], Georgie Garrod[1], Claire Wylie[1], Lewis Smith[1], Jo Dukes-McEwan[4], Jan Bright[5], Kate Allen[2]

1. Rossdales Diagnostic Centre, Cotton End Road, Exning, Newmarket, Suffolk, UK, CB8 7NN
2. Equine Sports Medicine Centre, Bristol Vet School, University of Bristol BS40 5DU UK
3. Equine Health and Performance Centre, University of Adelaide, Roseworthy Campus, South Australia. SA5371
4. Department of Small Animal Clinical Science (Cardiology Service), Institute of Veterinary Science, Leahurst Campus, University of Liverpool, Chester High Road, Neston, Cheshire CH64 7TE.
5. Colorado State University Veterinary Teaching Hospital, Fort Collins, Colorado, 80523, United States

Corresponding Author Celia M Marr, celia.marr@rossdales.com

Summary

Background Exercise-associated cardiac rhythm disturbances are common but there is a lack of evidence-based criteria on which to distinguish clinically relevant rhythm disturbances from those that are not.

Objectives To describe and characterise rhythm disturbances during clinical exercise testing; to explore potential risk factors for these rhythm disturbances and to determine whether they influenced future racing.

Study design Retrospective cohort using a convenience sample.

Methods Medical records were reviewed from two clinical services to identify horses with poor performance and/or respiratory noise with both exercise endoscopy and electrocardiography results. Respiratory and ECG findings recorded by the attending clinicians were described, and for polymorphic ventricular rhythms (n = 12), a consensus team agreed the final rhythm characterisation. Several statistical models analysing risk factors were built and racing records were reviewed to compare horses with and without rhythm disturbance.

Results Of 245 racehorses, 87 (35.5%) had no ectopic/re-entrant rhythms, 110 (44.9%) had isolated premature depolarisations during sinus rhythm and 48 (19.6%) horses had complex tachydysrrythmias. Rhythm disturbances were detected during warm-up in 20 horses (8.2%); during gallop in 61 horses (24.9%) and during recovery in 124 horses (50.6%). Most complex rhythm events occurred during recovery but there was one horse with a single couplet during gallop and another with a triplet during gallop. In 15 horses (1 with frequent isolated premature depolarisations and 14 complex rhythms) were considered by clinicians to be potentially contributing to poor performance. Treadmill exercise tests, the presence of exercise-associated upper airway obstructions and National Hunt racehorses all increased risk of rhythm disturbances. The proportion of horses racing again after diagnosis (82%) was similar in all groups and univariable analysis revealed no significant associations between subsequent racing and the presence of any ectopic/re-entrant rhythm, or the various subgroups based on phase of exercise in which this was detected.

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Main Limitations Reliance on retrospective data collection from medical records with no control group. Exercise ECGs were collected using only 1 or 2 leads. Variables examined as risk factors could be considered to be inter-related and our sub-groups were small.

Conclusions

This study confirms a high prevalence of cardiac rhythm disturbances, including complex ectopic/re-entrant rhythms, in poorly performing racehorses. Detection of rhythm disturbances may vary with exercise test conditions and exercise-associated upper airway obstructions increases the risk of rhythm disturbances.

Keywords: Arrhythmia, Cardiac, Exercise, Horse, Performance

Introduction

Exercise-associated cardiac rhythm disturbances have been reported in racehorses and horses involved in other athletic disciplines. However, their clinical relevance remains uncertain [1]. Whilst cardiac arrhythmias have been reported in poorly performing horses [2; 3], apparently healthy horses also experience premature depolarisations during and immediately after exercise [4-8].

The prevalence of exercise-associated rhythm disturbances varies between studies [8]. This variation may be related to several factors including breed, age, level of fitness, differences in exercise test protocols, exercise intensity, differences in the threshold set for identification of deviations in the RR intervals and difficulties in the interpretation of exercise electrocardiograms (ECGs) which are prone to artefact [9]. In strenuously exercising racehorses, cardiac arrhythmias (other than atrioventricular block and sinus arrhythmia) have

been reported to occur in up to 50% of examinations [4-6]. The immediate post-exercise period is a particularly vulnerable time for arrhythmia development, likely relating to rapid changes in autonomic tone (Physick Sheard and McGurrin, 2010).

There is a lack of evidence-based criteria on which to identify clinically relevant rhythm disturbances. Ventricular arrhythmias, particularly complex ventricular rhythms, are considered to be a potential trigger for sudden cardiac death during exercise and are often interpreted with caution. A better understanding of the safety risks for horse and rider is important. Increasing age has been identified as a risk factor for atrial fibrillation and other exercise-associated arrhythmias [7; 10]. However, other potential risk factors have not been well studied. Similarly, the effect on performance has received little attention.

The aims of this study were to describe exercise-associated rhythm disturbances in a group of Thoroughbred racehorses presented for poor performance and/or exercise-associated respiratory noise; to explore potential risk factors for these rhythm disturbances and to determine whether rhythm disturbances influenced future racing.

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Materials and Methods

Study design

A retrospective cohort study was undertaken by clinical services offered at Rossdales Diagnostic Centre, Newmarket, England / Troytown Grey Abbey Equine Veterinary Services, Ireland (RDC/TT) and the University of Bristol (UOB), England. This study is presented considering the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [11].

Medical records were searched to identify all Thoroughbred racehorses examined between June 2003 and August 2013 for RDC/TT and 2007 to 2013 for UOB that were presented with a history of either poor performance or abnormal respiratory noise at exercise, in which both exercising endoscopy and exercising ECGs were performed. Horses were excluded if ECGs were of non-diagnostic quality or a peak heart rate of 200 or above had not been achieved.

Examination protocols

Treadmill – Horses underwent a minimum of 3 treadmill training sessions prior to testing. For the test, horses first undertook a warm-up consisting of 20 minutes on a mechanical walker or in hand plus exercise on the treadmill[a] for 2 minutes walk (1.8m/s), 4 minutes trot (3.5m/s) and 1 minute canter (6 or 7 m/s). The horse was removed from the treadmill to place the endoscope. For most horses a standardised incremental exercise test was performed, consisting of 1 min at each of 6, 8 and 10 m/s on a 10% incline, followed by further increments of 1 m/s at 1 min intervals. The exercise test was continued until a definitive diagnosis of upper airway obstruction was made. If this did not occur, horses continued to exercise to the point of fatigue, i.e. until the horse was no longer easily able to maintain its position on the treadmill despite encouragement. The mean test distance for tests concluding at 10m/s was 1805m, for 11m/s 2507m, for 12m/s 2970m and 13m/s 3831m. From 2012, a high-speed test was introduced for flat horses, where treadmill speed was accelerated up to 11m/s and maintained at this speed for 1 min at 11m/s followed by 1 min at 12m/s on a 10% incline, with a mean test distance of 1673m. Following strenuous exercise, horses were walked on the treadmill for 5 minutes recovery. The horse then walked for approximately 20 minutes. An ECG was placed for the duration of treadmill exercise, recording warm-up, exercise test and 5 minutes recovery.

Overground - The exact workload was not standardised and was determined by the trainers' usual regimen. Horses were typically warmed up at trot for around 15 minutes, then jockeys were instructed to gallop the horse at speeds emulating racing 1 - 3 times over grass or synthetic gallops of 4 - 8 F (~800-1600m) with variable incline. The recovery phase was conducted at the walk and typically lasted for 10 – 30 minutes. Speed was recorded using a GPS tracking device[b] worn by the jockey.

ECG Equipment

Three different ECG units were used at RDC/TT[c,d,e,] and one unit in Bristol[e]: one system[c] produced a paper trace, recorded at 25 mm/s and at 5 mm/mV. The other systems produced digital files, which could be displayed at a range of gains and paper speeds, depending on the operator's preference. The digital software included calipers to calculate heart rate based on individual R-R intervals and during real-time recordings, the heart rate was visible to the

treadmill operator but not to the veterinarian supervising ridden examinations.

ECG Recording Technique

Regardless of lead placement, ECGs were typically evaluated in Lead II (red-green) but other channels were used if they showed less artefact. In UOB, electrodes were placed in a modified base-apex conformation. The red (negative electrode) and black (earth) electrodes were placed on the left proximal scapular region and the green (positive electrode) and yellow (positive/negative electrode) electrodes on the left thorax at the level of the elbow, approximately 10 cm caudal to the girth. At RDC/TT, electrodes were positioned in a modified base-apex lead such that they could fit under the girth of a saddle without interfering with the rider. The red (negative) electrode was placed at the level of the left proximal scapula, the yellow (positive/negative) electrode was placed at the level of the point of the shoulder, the black (earth) electrode was placed at the level of the elbow and the green (positive) electrode was placed just to the right of the ventral midline.

ECG Interpretation

ECGs which were recorded on paper were assessed visually by one operator (CMM). Digital ECG recordings were initially inspected and classified by one of two operators (KA, CMM). Maximum heart rate during the exercise session was recorded in UOB whilst RDC/TT's records indicated that this exceeded 200 bpm but a specific peak heart rate was not consistently noted in the records.

Ectopic/re-entrant rhythms were classified as either as isolated premature depolarisations (one or more premature depolarisations that occurred singly, ventricular and/or supraventricular) or complex (two or more premature depolarisations that occurred in pairs, triplet or runs on at least one occasion). On this basis, three groups were identified, ie no rhythm disturbance (Group 0), isolated premature depolarizations or complex ectopic/reentrant rhythms.

The phase during which the rhythm disturbance(s) occurred was noted; warm-up (from start of recording to start of exercise test), gallop (peak exercise phase), and recovery (from heart rate decline after peak exercise to the end of the recording). For the purposes of the analysis

we further divided the three rhythm disturbance type groups into sub-groups, based on the timing of rhythm disturbances: warm-up phase only (subgroup A), gallop only (subgroup B1), gallop and recovery (subgroup B2), gallop, warm-up and recovery (subgroup B3), recovery phase only (C1) and recovery and warm-up phases (C2).

All ECGs (n = 12) in which tachycardias of likely polymorphic ventricular origin were identified were re-examined by two operators (JDM, JB) and consensus was reached on the specific classification.

Exercise-associated upper airway diagnoses

An endoscopic[f,g,] examination of the upper airway was performed during the exercise test. The attending clinicians' diagnosis was obtained from case records and conditions were described using standard terminology [12]. Exercise-induced upper airway obstructions were classified as present/absent for subsequent analysis.

Additional Clinical Information

Cases in which the cardiac rhythm was considered by the attending clinician as potentially contributing to poor performance alone or in combination with other clinical conditions were identified and their medical records were reviewed to extract additional clinical information recorded during the poor performance investigation.

Outcome measures

Racing records were retrieved from an online racing results archive[h] in April 2014 for variable periods with a minimum of 8 months after the date of examination. Horses were recorded as having raced or not, and the number of races the horse started in post examination was noted. For horses with tachycardia (i.e. > 4 complexes in a run, n = 14) and one other which were considered by the attending clinician to warrant further cardiological investigation, racing records were scrutinised in more detail and for descriptive purposes these were classified as not raced, raced successfully (won or were placed at least once) or raced unsuccessfully (did not win or gain a place).

Data analysis

Normality of numerical variables was tested using the Shapiro-Wilk test. Mean ± standard deviation is reported for normally distributed data and median with interquartile range is reported for non-normally distributed data. For proportions, confidence intervals were calculated.

The following variables were examined as potential risk factors for the presence of ectopic/re-entrant rhythms: clinic (RDC/TT or UOB), sex (female or male), age (categories based on quartiles: ≤3, 4, 5&6 and >6 years), peak heart rate during exercise (categories based on quartiles: ≤214, 215-222, 223-227, >227 beats per minute (bpm)), upper airway abnormalities (absent or present), exercise technique (overground or treadmill), maximal speed (categories based on quartiles: ≤11, 11.1-12, 12.1-13.6, >13.6 metres per second, (m/s)), use at time of the examination (Flat, National Hunt or Point-to-point), season at the time of examination (winter (December, January, February), spring (March, April, May), summer (June, July, August), autumn (September, October, November).
Unconditional ordinary logistic regression was conducted [13] to obtain odds ratios (OR) with 95% confidence intervals (CI) and examine associations between all variables of interest and binary outcomes (rhythm disturbances present/absent). Missing data were left as missing.

The binary outcomes examined were:

(i) Model 1: Presence of rhythm disturbance: The goal of this analysis is to compare horses with and without abnormal rhythms and the sub-groups modelled are No ectopic/re-entrant rhythm (group 0) vs. ectopic/re-entrant rhythm at any exercise phase (i.e. subgroups A, B1, B2, & B3 and C1 & C2)

(ii) Model 2: Rhythm disturbance at gallop: The goal of this analysis is to compare horses with rhythm disturbances that were present at gallop with horses that had normal rhythm at gallop and and the sub-groups modelled are No ectopic/re-entrant rhythm (group 0) and ectopic/re-entrant rhythm at warm-up (subgroup A) or recovery (subgroups C1 & C2) vs. ectopic/re-entrant rhythm at gallop only (subgroup B1) and gallop and other phases (subgroups B2 & B3).

(iii) Model 3: Character of rhythm disturbance: The goal of this analysis is to compare horses with isolated premature depolarisations vs. complex ectopic/re-entrant

rhythms without differentiating the exercise phase at which the rhythm disturbance was identified.

Univariable analysis for these three models was performed in (a) the overall population, (b) the treadmill exercise population and (c) the overground exercise population.

Multivariable logistic regression models were built using data from the overall population using a manual stepwise forward selection method considering all variables associated at a level of P<0.20 [14]. A variable was retained if exclusion resulted in a likelihood ratio test statistic (LRS) of P<0.05. For highly correlated variables considered to measure similar exposures, one was selected based on biological plausibility [15] therefore clinic was excluded prior to development of the final multivariable models as it was highly correlated with examination overground or on the treadmill. Hosmer and Lemeshow goodness of fit test was used for each resulting model, and then models that passed the test were compared using likelihood ratio test and the area under the curve of the receiver operator characteristic [14].

Finally, associations between the three model outcomes and the binary outcome 'raced' (yes/no) were tested using Chi-squared ($\chi 2$) or Fisher's exact contingency table analysis, unconditional ordinary logistic regression and the similarities in proportions evaluated by examination of CI. A five percent level ($P<0.05$) was taken to indicate statistical significance throughout. *P*-values were not adjusted for multiple comparisons [16; 17]. All analyses were performed in STATA/IC Statistical Package[i].

Results

Descriptive analyses

There were 245 individual racehorses included in the analysis: ECGs from 89 horses (36.3%) were examined at RDC /TT and ECGs from 156 horses (63.7%) were examined at UOB. Thirty-seven (15.1%) were females and 208 (84.9%) were males. The median age was 4.8 years, IQR 3.4-6.4 years. At the time of examination, 134 (54.7%) were in National Hunt racing, 106 (43.3%) were in flat racing and 5 (2.0%) were point-to-pointers (racing over fences with amateur riders). During the examinations the median maximal speed was 12m/s (IQR 11-13.6,

not recorded in 14 cases (12 RDC/TT; 2 UOB) and the median peak heart rate (recorded in UOB only) was 212 beats-per-minute (IQR 201-222). An exercise-induced upper airway obstruction was diagnosed in 192 horses (78.4%) (Supplementary item 1). The months after examination where race performances were reviewed ranged from 8.1 to 131.2 months (median 38.8 months). Forty-four horses did not race after examination. In the 201 horses (82%) that raced after assessment, the median number of races after examination was 5 (IQR 1-11).

Electrophysiological findings

A flow chart summarising the exercise phase during which rhythm disturbances were detected is presented in figure 1. Of the 245 horses, 87 (35.5%) had no ectopic/re-entrant rhythms. Rhythm disturbances were detected during warm-up in 20 horses (8.2%); during gallop in 61 horses (24.9%) and during recovery in 124 horses (50.6%).

Isolated premature depolarisations (ventricular and/or supraventricular) were detected in 110 (43.4%) horses (figure 1); which were identified during warm-up (15, hoses 13.6%), gallop (40 horses, 36.4%) and recovery (78, 70.9%). One horse with isolated premature depolarisations was diagnosed as having a performance-limiting cardiac problem. That individual had multiple isolated monomorphic ventricular premature depolarisations before and after peak exercise. Ambulatory ECG demonstrated that these were also numerous at rest. Initially echocardiography was unremarkable however over the subsequent months, ventricular dilation was documented (Supplementary Item 2).

Complex ectopic/re-entrant rhythms were detected in 48 (19.6%) horses (figure 1); in 26 horses (54.2%) rhythm disturbance was detected in only one exercise phase while 21 horses (45.8%) had a complex ectopic/re-entrant rhythm in one phase with additional rhythm disturbances at other phases. Complex rhythm events were most commonly detected in recovery (45 horses, 93.8%) of which 20 of these individuals also had additional rhythm disturbance during gallop, generally isolated premature depolarisations, and 2 horses had additional rhythm disturbances during warm-up, one of which had complex ectopic/re-entrant rhythms in both warm-up and recovery (Supplementary Item 2).

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Thirty-four horses with complex ectopic/re-entrant rhythms (70.8%. 95%CI 59-83.7%) had couplets or triplets, including one horse with a single couplet and several isolated premature depolarisations during intense exercise and no other rhythm disturbance and one other horse with a single triplet during intense exercise as well as an isolated premature depolarisation in warm-up and two isolated premature depolarisations in recovery.

Clinical and outcome information on the remaining 14 horses together with details of the rhythm disturbances are provided in Supplementary Item 2. Runs (i.e. four or more premature depolarisations) were not seen during gallop. Four horses had polymorphic ventricular tachycardia (figure 2), all following peak exercise, one of which also had monomorphic ventricular tachycardia during warm-up. A further three horses had a combination of complex supraventricular and ventricular rhythm disturbances. These ECGs were difficult to interpret and two had initially been considered to show concurrent atrial fibrillation, however, on discussion with the consensus team (JB and JDM), it was agreed that the rhythm was best characterised as polymorphic ventricular tachycardia with supraventricular ectopy and underlying sinus pauses relating to overdrive suppression of the sinus node (figures 3 and 4, supplementary item 2).

Four horses had paroxysms of accelerated idioventricular rhythm, one of which also had polymorphic ventricular tachycardia with supraventricular ectopy (figures 5, 6 and 7), another of which had isolated ventricular complexes with a different configuration, and one had numerous ventricular premature depolarisations detected on a subsequent resting ambulatory ECG. Three further horses had monomorphic ventricular tachycardia accompanied by additional ventricular premature depolarisations after exercise. In one of these that was the only rhythm disturbance, while one had isolated ventricular premature depolarisations before and during exercise and in the third the additional premature depolarisation included one of supraventricular origin. One horse developed atrial fibrillation immediately after peak exercise which lasted for approximately 2 hours (figures 8 and 9). Overall in these 14 horses, the outcomes were fairly successful, 8 raced and were placed or won, 3 more raced but were not placed while 3 did not race, including the one which was euthanased.

Risk factors for ectopic/re-entrant rhythms

Model 1: Presence of rhythm disturbance: No ectopic/re-entrant rhythm (group 0) vs. ectopic/re-entrant rhythm at any exercise phase (sub-groups A, B and C).

Findings on univariable analysis for the overall, treadmill and overground exercise populations are presented in supplementary item 3. Five variables were taken forward for multivariable model building (supplementary item 3). Exercise technique and the presence of upper airway obstructions were associated with ectopic/re-entrant rhythms (table 1). The model had a goodness-of-fit of 0.68 and an area under the curve of 0.66. Univariable analysis undertaken on the treadmill exercise population found horses with exercise-associated upper airway obstruction were more likely to have ectopic/re-entrant rhythm at any exercise phase (OR 2.62, CI 1.00, 6.86, P=0.05) and horses examined at RDC/TT were at decreased risk of ectopic/re-entrant rhythms on the treadmill compared to those at UOB (OR 0.05, CI 0.01,0.44, p <0.001), however because exercise technique and service were highly correlated this association is of uncertain significance. Univariable analysis undertaken on the overground exercise population found no significant associations.

Model 2: Rhythm disturbance at gallop: No ectopic/re-entrant rhythm at gallop (Group 0, Sub-group A & C1 and 2) vs. ectopic/re-entrant rhythm at gallop alone or gallop plus other phases (Sub-group B).

Findings on univariable analysis for the overall, treadmill and overground exercise populations are presented in supplementary item 4. Five variables were taken forward for multivariable model building (supplementary item 4), however only the variable for exercise technique was retained. Horses exercised on the treadmill were more likely to have ectopic/re-entrant rhythm at gallop (OR 3.47, CI 1.66, 7.26, P<0.001). Univariable analysis undertaken on the treadmill exercise population, found those with peak heart rate between >222 and ≤227 (OR 3.01, CI 1.04-8.75, p = 0.04), and those >227 bpm (OR 3.84, CI 1.37-10.75, P = 0.01) were more likely to have ectopic/re-entrant rhythm during gallop than those ≤214 bpm. Univariable analysis undertaken on the overground exercise population found that horses examined in the spring or summer were less likely to have ectopic/re-entrant rhythm during gallop than those examined in the winter (Spring vs Winter: OR 0.16,CI 0.03, 0.85,P=0.03; Summer vs Winter OR 0.11, CI 0.02, 0.68, P=0.02).

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Model 3: Character of rhythm disturbance: Isolated premature depolarisations vs. complex ectopic/re-entrant rhythm at any exercise phase.

Findings on univariable analysis for the overall, treadmill and overground exercise populations are presented in supplementary item 5. Six variables were taken forward for multivariable model building and two variables were retained (supplementary item 5): National Hunt horses were more likely to have complex rhythms compared to horses engaged in flat racing and inclusion of the exercise modality variable improved model fit (table 2). The model had a goodness of fit of 0.37 and area under the curve of 0.68. Univariable analysis undertaken on the treadmill population identified the same association; National Hunt horses were more likely to have complex ectopic/recurrent rhythm than flat racehorses (OR 3.26, CI 1.29, 8.27, P=0.01). Univariable analysis undertaken within horses examined overground found no significant associations.

Return to racing

There were no associations between clinic, sex, age, peak heart rate or presence of an upper airway obstruction with racing after examination. There was a significant association between racing after examination and season, with higher proportion examined in spring not racing (winter 11.1%, spring 29.7%, summer 8.6% and autumn 13.7%, P=0.004).

Univariable analysis revealed no significant associations between subsequent racing and the presence of any ectopic/re-entrant rhythm, or the various subgroups based on the phase of exercise in which this was detected (supplementary item 6). The CI around the proportions that did or did not race in horses with and without ectopic/recurrent rhythms overlapped suggesting that the diagnosis of these rhythm disturbances was not associated with failure to race again.

Discussion

This study has documented the prevalence of exercise-associated cardiac rhythm disturbances in a population of Thoroughbred racehorses presented for poor performance and/or exercise-associated respiratory noise. Some form of cardiac rhythm disturbance was

reported in 64% of horses and complex ectopic/re-entrant rhythms were found in 20% of horses.

An ectopic/re-entrant rhythm was identified in the gallop phase in 25% of horses and in the recovery phase in 51% of horses. The higher frequency of ectopic/re-entrant rhythms in the recovery period has previously been observed in both human and equine athletes and the immediate post-exercise period appears to be the most vulnerable time for the genesis of cardiac arrhythmias. Abnormal regulation of electrolytes and autonomic function may increase the incidence of arrhythmias during this time period [5; 18; 19].

The key findings from the multivariable analyses were the associations between ectopic/re-entrant rhythms and exercise type, upper airway obstructions and use. Exercise type was significant in all multivariable models, with risk of ectopic/re-entrant rhythms being higher during treadmill exercise test than during an overground test. There are several possible explanations for this. Firstly, the treadmill tests were designed to replicate the demands and fatigue that occur during racing. These exercise tests were typically undertaken over longer distances than the exercise tests undertaken overground and as a result high HRs are sustained for a much longer period. In some cases, overground exercise tests are undertaken in intervals and this may not replicate racing conditions well, as the intervals permit partial recovery [20]. In addition, for safety reasons, treadmill exercise tests are often concluded promptly, with the horse quickly being brought back down to walk at the point of fatigue. Whereas on the gallops the jockey slows the horse more gradually, resulting in a steady heart rate decline. Autonomic instability and increases in vagal tone during a rapid heart rate decline are thought to contribute to the increase in post-exercise rhythm disturbances observed during treadmill testing [5]. Furthermore, it has been proposed that arrhythmia risk may be associated with unusual exercise demands and that psychological stress may influence development of ventricular arrhythmias [5]. Treadmill testing will often be an unfamiliar exercising modality for the horse, and it is unclear whether this could influence arrhythmia presence. However, in contrast to gallop exercise tests it is unusual to see an anticipatory heart rate increase with treadmill testing, suggesting horses are more ‘excited’ with the gallop exercise tests as these are more familiar. It is known that treadmill training sessions are required to obtain reproducible cardiorespiratory parameters, however,

repeated treadmill exposure has been reported to have an adverse effect on acclimation, due to increased apprehension and excitement in anticipation of exercise [21; 22] Regardless of whether the testing is undertaken overground or on a treadmill it appears that it is the familiarity with the technique that leads to excitement and anticipatory heart rate increases. In contrast to the findings of this study, others have shown that exercise on the racetrack was associated with a higher prevalence of arrhythmias when compared to treadmill exercise in the same horses [8]. In that study, the horses were part of a research herd which regularly exercised on a treadmill whereas for our population, treadmill exercise was a relatively novel experience possibly having different psychological impact. Our overground and treadmill populations were not identical. Overall, the horses undergoing treadmill testing were older, more likely to be from National Hunt racing, more likely to have an upper airway obstruction, more likely to have a strenuous test over a longer duration and more likely to return to walk quickly.

National Hunt racehorses were more likely to have complex ectopic/re-entrant at any exercise phase than flat horses (Model 3: Character of rhythm disturbance). Compared to flat horses, National Hunt horses are older, often taller, and train and race over longer distances and thus high HRs are sustained for longer periods. Both age and training result in cardiac enlargement [23-26] and cardiac size is larger in National Hunt horses than flat horses [27]. Cardiac enlargement may play a role in the increased risk of complex ectopic/re-entrant rhythms. However, a previous study in 26 Standardbred horses did not show an association between heart size and prevalence of ventricular premature depolarisations [4]. A larger prospective study will be required to further elucidate whether such an association exists. In humans and laboratory animals, it is suggested that long-standing strenuous exercise is associated with adverse electrical remodelling as well as the better studied structural remodelling [28-31].

Several cases underwent detailed cardiological investigations, many had mild to moderate valvular regurgitation but none of these horses had cardiac enlargement. There was only one case (with frequent ventricular premature depolarisations at rest and during warmup and recovery) with echocardiographic evidence of ventricular enlargement, suggesting myocardial disease. A further case with complex supraventricular and ventricular rhythms

underwent post-mortem examination but no abnormalities were found, however this does not exclude the possibility of abnormalities at the cellular or sub-cellular level.

The presence of exercise-associated upper airway obstruction was identified as a risk factor for rhythm disturbances in Model 1: Presence of rhythm disturbance and horses with an upper airway obstruction were more likely to have rhythm disturbance at any exercise phase than those without. Exercise-associated upper airway obstructions result in a complex range of effects which may include reduced tidal volumes, more severe hypoxemia and hypercapnia, higher blood lactates, increased pleural pressures and increased work of breathing [32]. Which of these factors is the primary influence on rhythm disturbances during exercise is unclear. In horses with intermittent laryngospasm and dynamic pharyngeal wall collapse relating to hyperkalaemic periodic paralysis, ventricular arrhythmias were considered to be due to a combination of hypoxaemia and hyperkalaemia [33]. The psychological impact of upper airway obstructions is unknown but stressful conditions have been associated with ventricular rhythms in Standardbreds [5]. There has been little research investigating whether similar associations occur in human athletes with exercise-induced laryngeal obstructions. However, autonomic nervous system fluctuations, intermittent hypoxia, intrathoracic pressure swings leading to atrial stretch and hypercapnia are considered arrhythmogenic in people with obstructive sleep apnoea [34; 35].

The clinical relevance of equine arrhythmias is usually considered in terms of performance and safety to ride [1]. Although a high prevalence of rhythm disturbances were identified in this cohort of poorly performing horses, the extent to which these were definitely contributory to the poor performance is less clear. In very few horses was poor performance primarily attributed to the ectopic/re-entrant rhythm by the attending clinician. At the time of clinical investigation, some of the complex ectopic/re-entrant rhythms were considered potentially clinically relevant in terms of safety. A reduction in cardiac output is the primary mechanism through which a cardiac arrhythmia might affect athletic performance. Atrial fibrillation is the most important arrhythmia affecting performance in athletic horses [1]. In the case described here, atrial fibrillation did not develop until after intense exercise. The recurrence rate for paroxysmal atrial fibrillation is around 6% [10] and therefore it remains unclear whether the episode of atrial fibrillation found in this horse was relevant to its history

of poor performance and post-race distress and it subsequently returned to racing successfully.

With atrial fibrillation, poor performance arises because of the reduced cardiac output that occurs due to reduced ventricular filling. In contrast, the effect of supraventricular and ventricular premature depolarisations on performance is less clear. It is unlikely that occasional isolated premature depolarisations would have a detrimental effect on cardiac output and hence performance. There was one case with a single couplet and one with a single triplet at gallop and, while runs of abnormal complexes may reduce cardiac output, no ventricular tachycardia was seen during intense exercise and with one exception, all the episodes of ventricular tachycardia observed in the current population occurred in the recovery phase. One horse had a run of monomorphic tachycardia during warm-up. The significance to performance of rhythm disturbances that are only present in the post-exercise period is doubtful. However, it is possible that these are associated with an underlying abnormality e.g. hypoxaemia secondary to upper airway obstruction, which was present during the exercise period and was the cause of the poor performance.

The final aim of this study was to determine whether rhythm disturbances influenced future racing outcomes. In this regard the outcome used in this study was simply whether the horse continued to be used for its intended purpose. Return to racing does not necessarily mean that race performance met expectation. Additional performance analysis in this retrospective population of horses is difficult as the high proportion of additional clinical abnormalities such as upper airway obstructions is also likely to be detrimental to race performance. Furthermore, failure to return to racing may not be a result of a cardiac abnormality. In this population of horses, there were no statistically significant differences in the number of horses that returned to racing in the normal rhythm, isolated premature depolarisation(s) or complex ectopic/re-entrant groups. This observation is in line with two previous studies which have also not documented an association between presence of arrhythmia and race performance [3; 5]. Nevertheless, clinical decision-making around suitability for continued use for ridden activities in individual horses with complex ventricular rhythms is challenging. This case series demonstrates that a number of individual Thoroughbreds with complex ventricular arrhythmia in the recovery phase returned to racing successfully. It is also

noteworthy, that there were no cases with complex rhythms during intense exercise, a finding which should be regarded as increasing risk of collapse or sudden cardiac death [1; 8].

Limitations

This study is limited by its retrospective design. All these horses presented with poor performance and/or exercise-associated respiratory noise. We did not include horses without a clinical reason for investigation and the relevance of the cardiac rhythm disturbances to the presenting problem is uncertain as other studies have documented similar rhythm disturbances in horses which are apparently healthy [4; 5]. ECG classification was obtained from the medical records rather than being re-assessed in the majority of cases. Exercise ECG have frequent artefact. We have not reported the suspected origin of isolated premature depolarisations because ECGs were recorded on up to three external leads, and while this allows confident identification of ventricular origin due to abnormal QRS-T morphology in some cases, in others, where the complexes were narrow, it is not possible to state the origin based on morphology alone. Supraventricular complexes may or may not be associated with a premature p wave: at faster heart rates, the p wave may be buried in the preceding T wave. Although compensatory pauses typically follow ventricular premature depolarisations, neither complete or incomplete pauses can reliably be used to identify origin, particularly given the relative low sampling frequency of ECG devices used (500 Hz). Logistic models are sensitive to multicollinearity, and due to the likelihood of a close relationship between clinical service and treadmill exercise, clinical service was excluded as a potential associated factor in the development of our multivariable models, several variables examined as risk factors could be considered to be inter-related i.e. National Hunt horses are older, with males predominating in that population while in flat racing, horses are younger and males and females are more equally represented. More National Hunt horses were examined during treadmill exercise at UOB thus there may be unidentified relationships between the factors we have associated with the presence and character of rhythm disturbances. We used a convenience sample without *a priori* sample size calculation and the rhythm disturbance groups and exercise-phase sub-groups were small, multivariable models had moderate fit and confidence intervals around the odd ratios were wide.

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Conclusions

In conclusion, this study confirmed a high prevalence of cardiac rhythm disturbances, including complex ectopic/re-entrant rhythms immediately after intense exercise, in poorly performing racehorses. Tachycardias (runs of 4 or more abnormal complexes) were not seen at the gallop. This study revealed that detection of rhythm disturbances can vary with exercise test conditions and that concurrent disorders, such as exercise-associated upper airway obstructions, may increase the risk of rhythm disturbances developing. Horses returned to racing after diagnosis and these data contribute to a better understanding of which rhythm disturbances are clinically relevant and which are not.

Manufacturers Addresses

a Sato, Upsala, Sweden

b Garmin Forerunner, Garmin (Europe) Ltd, Southampton, UK (in case needed: SO40 9LR; www.garmin.com/en-GB

c ECG Lifescreen 8, Nihon Kohden, Chessington, Surrey, UK (KT9 1BD; www.nihonkohden.com)

d Lifecard Ambulatory ECG, Spacelabs Health Care, Hertford, UK (SG13 7DT, www.spacelabshealthcare.com)

e Televet 100, Kruuse UK- I think this should be Engel Engineering Services GmbH, Heusenstamm, *Germany* (http://www.televet.de)

f EG-2940 Gastroscope, Pentax UK Ltd, Langley, Slough UK

g Videomed GmbH, Munchen, Germany

h http://www.racingpost.com/

i Stata version 13.1© 2013 StataCorpLP

Conflict of Interest Statement

None of the authors has any personal or financial relationships that could inappropriately influence or bias the content of the paper.

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Ethical Animal Research

Research ethics committee oversight not required by this journal: retrospective study of clinical records and publicly available racing records.

Owner Informed Consent
Explicit owner informed consent for inclusion of animals in this study was not stated.

Data Accessibility Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request

Authorship

CM, CW and KA conceived the study, CW performed data analysis, all authors contributed to data collection and interpretation, manuscript preparation and approved the final version of the manuscript

Supplementary Material

1. Upper airway diagnosis in a cross-sectional study of 245 Thoroughbred racehorses investigated for poor performance and/or respiratory noise.
2. Case details of 15 Thoroughbred racehorses in which ectopic/re-entrant rhythms (14 complex ectopic/re-entrant rhythms, 1 frequent isolated premature depolarisations) were considered by the attending clinician to be potentially contributing to poor performance, alone or in combination with other clinical conditions.
3. Univariable and sub-group analysis for Model 1 examining factors associated with the presence of rhythm disturbance at any exercise phase in a cross-sectional study of 245 Thoroughbred racehorses investigated for poor performance and/or exercise-associated respiratory noise in the overall, treadmill and overground exercise populations.
4. Univariable analysis for Model 2 examining factors associated with rhythm disturbance at gallop in a cross-sectional study of 245 Thoroughbred racehorses investigated for poor performance and/or exercise-associated respiratory noise in the overall, treadmill and overground exercise populations.
5. Univariable and sub-group analysis for Model 3 examining factors associated with complex ectopic/re-entrant rhythms in 158 horses with rhythm disturbances in a cross-sectional study of 245 Thoroughbred racehorses

investigated for poor performance and/or exercise-associated respiratory noise in the overall, treadmill and overground exercise populations.

5.6. Univariable associations between ECG findings and ability to race after examination in a cross-sectional study of 245 Thoroughbred racehorses presented for poor performance or respiratory noise, 201 of which raced after examination.

List of Figures

Figure 1: Flow chart of 245 Thoroughbred racehorses summarising the rhythm disturbances and the exercise phase during which they occurred. Horses were grouped according to the presence and nature of rhythm disturbance (ie absent, isolated premature depolarisations or complex ectopic/re-entrant rhythms) and sub-groups defined by the exercise phases in which rhythm disturbances were found. Percentages and 95% confidence intervals in sub-groups A, B1-3, and C1-3 relate to the percentage of horses that display either isolated premature depolarisations or complex rhythms. UAO = upper airway obstruction.

Figure 2: ECG image from recovery phase showing single (*) and a couplet of ventricular premature depolarisations (* *) and paroxysm of polymorphic ventricular tachycardia with possible torsades de pointes (red line). After the couplet and the paroxysm, there is first degree atrioventricular block

Figure 3: ECG image from recovery phase. The image shows a supraventricular premature depolarisation (3rd complex) and a paroxysm of SVT, followed by a pause then regular sinus rhythm although P waves difficult to discern (red line). This horse was originally considered to have paroxysmal atrial fibrillation, but subsequent review and consensus resulted in the rhythm disturbance being reclassified. The negative deflections in the baseline are most likely to be artefactual as they do not interrupt the underlying rhythm nor are they consistently associated with the QRS complexes.

Figure 4: ECG image from the recovery phase. The image shows three ventricular premature depolarisations (red *) of two different morphologies followed by sinus pauses potentially due to overdrive suppression of the sino-atrial node. This horse was originally considered to have paroxysmal atrial fibrillation, but subsequent review and consensus resulted in the rhythm disturbance being reclassified. Note red and dashed vertical lines are placed by an automated analysis tool available within the ECG software.

Figures 5, 6 and 7: Three consecutive ECG images from the recovery phase. Image 5 shows both supraventricular (blue *) and ventricular (red *) premature depolarisations. Images 6 and 7 show accelerated idioventricular rhythm of different morphologies (red brackets). Note red and dashed vertical lines are placed by an automated analysis tool available within the ECG software.

Figures 8 and 9: ECG images from recovery. Figure 8 shows sinus pauses (blue line) followed by supraventricular tachycardia (red line) leading to the onset of atrial fibrillation (red star). Figure 9 shows the atrial fibrillation with irregular RR intervals and f waves. Note red and dashed vertical lines are placed by an automated analysis tool available within the ECG software.

Table 1: Multivariable model for variables associated with ectopic/re-entrant rhythms (n = 158) in a cross-sectional study of 245 Thoroughbred racehorses presented for poor performance or respiratory noise (Model 1 presence of rhythm disturbance).

Risk Factor	Rhythm disturbance present	No Rhythm disturbance present	β-coefficient	Standard error β	Logistic Odds Ratio	Odds Ratio 95% CI	Wald P-value
Exercise-associated Upper Airway Obstruction							<0.001
Not present	23 (9.4%)	20 (12.2%)	Ref	Ref	Ref	Ref	Ref
Present	135 (55.1 %)	57 (23.8%)	0.81	0.34	2.26	1.16-4.39	0.02
Exercise technique							
Overground	38 (15.1%)	44 (18.0%)	Ref	Ref	Ref	Ref	Ref
Treadmill	120 (49.0%)	43 (17.6%)	0.97	0.30	2.63	1.47-4.72	0.001

Goodness of fit = $\chi 2$ P-value 0.68, ROC area under the curve of 0.66.

Table 2: Multivariable model for variables associated with complex ectopic/re-entrant rhythm in 158 of 245 Thoroughbred racehorses presented for poor performance or respiratory noise in which isolated premature depolarisations (n = 110) and complex ectopic/re-entrant rhythms (n = 48) were identified (Model 3 character of rhythm disturbance).

Risk Factor	Complex ectopic/rentrant rhythm	Isolated premature depolarisations	β-coefficient	Standard error β	Logistic Odds Ratio	Odds Ratio 95% CI	Wald P-value
Exercise technique							
Overground	4 (2.5%)	34 (21.5%)	Ref	Ref	Ref	Ref	Ref
Treadmill	44 (27.9%)	76 (27.8%)	1.14	0.59	3.14	0.99-10.01	0.05

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Use at exam							
Flat			Ref	Ref	Ref	Ref	Ref
National Hunt			1.02	0.43	2.77	1.20-6.36	0.02
Point-to-point			NA	NA	NA	NA	NA

Goodness of Fit = $\chi 2$ P-value 0.37, ROC Area Under Curve 0.68

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