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Incidence, recurrence, and outcome of postrace atrial fibrillation in Thoroughbred horses

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Abstract

Background: Atrial fibrillation (AF) impacts performance and horse and jockey safety. Understanding the outcomes of AF identified postrace will better inform regulatory policy.

Hypothesis/Objectives: To investigate the outcomes after episodes of AF identified postrace and determine whether affected horses are at increased risk of additional episodes compared to the general racing population.

Animals: Total of 4684 Thoroughbred racehorses.

Methods: Race records for Thoroughbred horses racing in Hong Kong from 2007 to 2017 were reviewed. Horses that performed below expectation were examined by cardiac auscultation and ECG. Incidence and recurrence of AF were compared between horses with and without a history of AF and between horses with paroxysmal and persistent episodes using Fisher's exact test.

Results: There were 96 135 race starts during the study. Atrial fibrillation was identified in 4.9% of horses, with an overall incidence of 2.7 episodes per 1000 starts. The incidence of AF in horses after any previous episode (12.8 per 1000 starts) was higher than for horses with no previous episode (2.4 per 1000 starts; odds ratio [OR], 5.3; 95% confidence interval [CI], 3.8-7.6). Recurrence was seen in 64% of horses previously treated for persistent AF, which was higher than recurrence in horses with paroxysmal AF (23%; OR, 5.9; 95% CI, 1.6-21.2). Median duration between episodes was 343 days (range, 34-1065).

Conclusions and Clinical Importance: Thoroughbreds are at increased risk of recurrent AF after both paroxysmal and persistent episodes, but the duration of time between episodes varies widely. These findings support a substantial burden of AF among individual Thoroughbred racehorses.

KEYWORDS

arrhythmia, atrial fibrillation, cardiology, electrocardiography, epidemiology, equine

Abbreviations: AF, atrial fibrillation; CI, confidence interval; HKJC, Hong Kong Jockey Club; OR, odds ratio.

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In athletic horses, atrial fibrillation (AF) is an important cause of poor and erratic performance. Occasionally, cardiac arrhythmias, including AF, result in collapse or sudden cardiac death (SCD), as a result of which riders often are injured.¹⁻⁵ Cardiac arrhythmias of supraventricular and ventricular origin frequently are identified by ECG during and immediately after exercise.⁶⁻⁹ Atrial fibrillation is the most commonly recognized arrhythmia in poorly performing horses, with an estimated prevalence among racehorses of 0.11% to 0.29%.¹⁰⁻¹³ In racehorses. AF usually is paroxysmal, converting to sinus rhythm within 72 hours without specific treatment.^{11,14} Detectable structural heart disease usually is absent, and the condition previously has been referred to as lone AF.^{4,15,16} However, underlying microstructural myocardial lesions and electrical remodeling that cannot be readily detected by clinical examination are suspected to contribute to the development of AF in horses with recurrent episodes.¹⁷ Recently, electro-anatomical mapping has identified pulmonary vein firing initiating AF in a horse.¹⁸ Atrial fibrillation is not entirely benign and such individuals might also be susceptible to arrhythmias originating in the ventricular myocardium.¹⁹ Although rarely documented in horses, ectopy arising from both the atrial and ventricular myocardium in the same individual can precede development of ventricular fibrillation and SCD.³ The role of exercise-induced myocardial remodeling in the promotion of AF is supported by experimental studies in rodents.²⁰⁻²² In human athletes, the risk for AF is related to cumulative volume of exercise training.^{23,24} Although not vet evaluated in horses, it is evident that cardiac remodeling in athletes is not entirely benign and could parallel pathological heart disease, increasing risk for arrhythmias and SCD.23,25

Persistent AF can be converted to sinus rhythm using either transvenous electrocardioversion or pharmacologic intervention, most commonly using quinidine sulfate, and generally carries an excellent prognosis for future athleticism.^{4,16} After conversion to sinus rhythm, AF recurrence in horses with AF of recent onset is approximately 15% to 40%.^{16,17,26-28} A longer duration of AF,²⁶ which induces structural, mechanical, and electrical cardiac remodeling.^{27,29-32} is associated with increased risk of AF recurrence. Other factors influencing recurrence of AF include the burden of atrial premature depolarizations,¹⁷ mitral regurgitation,²⁷ and left atrial size.²⁸

Because of concerns for the health and welfare of horses and jockeys, and the impact of erratic performance on betting markets, many jurisdictions impose sanctions on horses after episodes of AF. The Hong Kong Jockey Club (HKJC) provides a unique opportunity to investigate the epidemiology of AF because it manages a large population of horses with detailed veterinary records. The proportion of horses in the field examined postrace typically is 22% (Weir J., personal communication, 2020), which is a substantial cohort for the evaluation of postrace AF. Our objectives were to: (a) describe the incidence, recurrence, and outcome of postrace AF and (b) describe the ECG characteristics of AF in the postrace AF are at increased risk for future episodes compared to horses without a history of AF.

2 | MATERIALS AND METHODS

2.1 | Animals

A retrospective, longitudinal cohort study of Thoroughbreds racing in Hong Kong from 31 July 2007 until 31 July 2017 was performed. All horses registered to race within the study period were collated from the HKJC racing database, which comprised a study population of 4684 horses (Figure 1). A start was defined as a registration of an individual horse to start in a specific race. There were 96 135 race starts during this study period (Figure 1). The HKJC clinical records were searched for all starts at which an episode of AF was diagnosed on postrace veterinary inspection. Episodes were defined as presumed AF, characterized by an irregularly irregular rhythm on cardiac auscultation, occurring within 60 minutes after a race, and were used to determine the incidence of postrace AF.

2.2 | Postrace veterinary inspection

A diagnosis of presumed AF was made at postrace inspection of horses that were examined by veterinarians after a race. Such inspections were performed mainly at the request of race day stewards when horses delivered a disappointing racing performance, an indication of an abnormality was noted during or after racing, or based on a jockey's postrace report.³³ Veterinary inspections were performed within 30 minutes of the race and consisted of cardiac and respiratory auscultation, lameness examination and palpation of musculoskeletal structures, and upper airway endoscopy. Electrocardiography also was performed within 60 minutes in many, but not all, cases using either the Televet 100 or Schiller MS-3 ECG V 2.05 ECG units. Echocardiography was not performed.

2.3 | Veterinary records

Electrocardiographs and electrocardiographic reports pertaining to the episode of AF were collated from the veterinary records and evaluated. Veterinary records also were used to determine whether the episode was paroxysmal (converting spontaneously to sinus rhythm within 72 hours) or persistent (lasting beyond 72 hours). After consultation with the trainer, conversion to sinus rhythm was attempted in horses with persistent AF by nasogastric administration of quinidine sulfate.²⁶ Sinus rhythm was documented by a veterinarian before a horse was allowed to continue in training or present for any race or trial. Veterinary records were used to determine whether an episode of AF occurred at any veterinary inspection before or after the episode of postrace AF to determine the rate of recurrence.

2.4 | Electrocardiographic classification

Electrocardiographs were visually inspected by a certified specialist in equine medicine (L.C. Nath) and a certified specialist in equine sports medicine (S. Franklin) to achieve consensus classification of the arrhythmia. The number of leads recorded was 1 to 3. Previously

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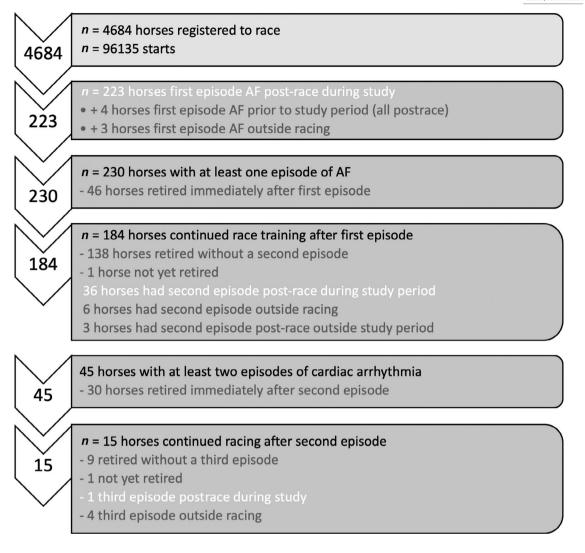


FIGURE 1 Detail of cohort included in study. Total population N = 4684 horses presenting to 96 135 starts. There were 280 episodes of atrial fibrillation (AF) in 230 horses. Incidence data were generated only from 260 postrace episodes occurring during the study period. All 280 episodes were included for analysis of recurrence. +, entry to study. -, exit from study. White, episodes used to calculate incidence

published criteria^{5,34} were used determine the rhythm abnormality and to develop a novel method of classification of AF that included a description of QRS morphology. The morphology of the QRS complexes was not further interpreted as being supraventricular with aberrant conduction or ventricular in origin. Arrhythmias were classified as sinus rhythm with ectopy or AF. Atrial fibrillation was further subclassified as AF uniform (all complexes showed similar QRS conformation), AF nonuniform (QRS complexes differed in conformation with a single monomorphic change), or AF multiform (AF with QRS complexes of \geq 3 different morphologies).

2.5 | Statistical analysis

2.5.1 | Defining variables

The incidence of AF was defined as the proportion of episodes per start in horses that had been exposed (diagnosed with) any previous,

1 previous or 2 previous episodes compared to horses that had never been exposed (diagnosed with) a previous episode. Incidence of AF per horse was defined as the proportion of horses in the registered population that had any diagnosis of postrace AF (single episode, 2 episodes or 3 episodes). The overall incidence of AF included all horses in the study period. Only episodes of AF diagnosed at postrace inspection within the study period were included in the estimation of incidence. Horses that were identified as having arrhythmia during the study period then were searched across their entire careers in Hong Kong for additional episodes of arrhythmia. For all horses, the earliest identified episode was regarded as the first episode and therefore the first episode occurred before the study period for some horses. For these horses, the second or third recurrent episode occurred during the study. Recurrence was defined as the proportion of horses that continued training after a previously diagnosed episode of AF and had a subsequent episode. Recurrence in horses that were exposed to 2 previous episodes was compared to horses with 1 previous episode. Recurrence in horses that were exposed to a previous American College of Veterinary Internal Medicine

persistent episode was compared to horses with a previous paroxysmal episode. Episodes of AF occurring outside the study period or at times other than postrace were included for estimation of recurrence. Therefore, for analysis of recurrence, horses with episodes of AF occurring at rest, or after training or racing, during, before, or after the study period were included. Horses that were retired immediately after the first episode were excluded from further analysis of recurrence and outcome (Figure 1). Career duration was defined as the number of days and starts between the first diagnosed episode of arrhythmia and either the last start in the racing index³⁵ or last date of diagnosis of AF. Horses that were not retired as of 22nd June 2020 were excluded from analysis of career duration. Only horses that presented for a race start or official trial after the first episode of AF were included in analysis of career duration. Career duration was compared between horses having a single episode or 2 or 3 episodes over their careers. The HKJC racing index³⁵ of horses with any episode of postrace AF was reviewed to determine the number of wins after the first episode of AF and to determine the rating of each horse at the time of the first episode of arrhythmia and any subsequent start. A change in career rating was calculated by averaging the rating of the horse at each start of their career after the first episode of AF and deducting that rating from the rating at the time of the first episode. Therefore, a negative value for rating change reflects a decline in performance and a positive rating change reflects an improvement in performance.

2.5.2 | Statistical analysis

Incidence within each group was estimated with a 95% confidence interval (CI) using a 1 sample binomial test (Clopper-Pearson) and reported as rate per 1000 starts and per 100 horses registered to race in the study period. The proportion of horses in each group that had recurrence of AF was estimated with a 95% CI using a binomial test (Clopper-Pearson). Estimates of incidence and recurrence in each group were entered into a contingency table and compared using Fisher's exact test from which odds ratios (ORs) were derived.³⁶ Career duration after the first episode of AF was assessed using the Kaplan-Meier method. Comparison of career duration was performed

by applying a log-rank (Mantel-Cox) test. For horses that continued training after the first episode, the difference in rating change between horses that had 1 episode compared to horses that had 2 or 3 episodes was nonnormally distributed and was compared using the Kolmogorov-Smirnov test. The difference in heart rate for each ECG classification of AF was compared by 1-way analysis of variance (ANOVA) with Tukey's post hoc multiple comparisons. Commercially available software (IBM SPSS Statistics version 25 and GraphPad Prism 8) was used for the analyses. For all analyses, significance was set at $P \leq .05$.

3 | RESULTS

3.1 | Animals

The search of the HKJC clinical records according to the inclusion criteria yielded 280 episodes of postrace AF in 230 horses (Figure 1). Of these 230 horses, 224 were geldings and 6 were intact males, reflecting the racing population of Hong Kong, which includes very few female horses. Mean age was 5.1 ± 1.4 years.

3.2 | Incidence

The overall incidence of postrace AF was 2.7 per 1000 starts (95% CI, 2.0-3.0; Table 1). The incidence of AF in horses after any previous episode (12.8 per 1000 starts) was higher than for horses with no previous episode (2.4 per 1000 starts; OR, 5.3; 95% CI, 3.8-7.6; P < .001; Table 1). The overall incidence of AF in horses registered to race during the study period was 4.9 (95% CI, 4.3-5.6) per 100 horses (Table 1).

3.3 | Recurrence

Overall, AF recurred after 50/199 (25%) episodes in 184 horses that continued racing after any episode (Table 2). In the 15 horses that

Type of previous episode (n AF/n starts)	Incidence per 1000 starts (95% CI)	Odds ratio (95% CI)	P value
Entire cohort (260/96135)	2.7		
No previous (223/93242)	2.4 (2-3)	1.0 (Ref)	
Any previous (37/2893)	12.8 (9-18)	5.3 (3.8-7.6)	<.001
One previous (36/2744)	13.1 (9-18)	5.5 (3.8-7.9)	<.001
Two previous (1/149)	6.7 (0-37)	2.8 (0.4-20.2)	.3
(n AF horses/n racing population)	Incidence per 100 horses (95% CI)		
Entire cohort (230/4684)	4.9 (4.3-5.6)		
Single episode (185/4684)	3.9 (3.4-4.6)		
Two episodes (40/4684)	0.85 (0.6-1.1)		
Three episodes (5/4684)	0.1 (0.0-0.2)		

TABLE 1Incidence per start for 260episodes of postrace atrial fibrillation (AF)in 230 horses during the 10 year studyperiod

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TABLE 2 Recurrence of atrial fibrillation in 184 horses that continued in race training after the first episode. Recurrence after previous paroxysmal AF which occurred in the first or second episode is compared to previous persistent episodes. Horses with 1 previous episode are compared to horses with 2 previous episodes. PE, previous episode. The duration of 4 episodes was unknown	Type of previous episode	n horses recurrence/ n horses with PE	Recurrence per horse (95% CI)	Odds ratio (95% Cl)	P value
	Following any episode	50/199	25.1 (19.2-31.8)		
	One previous	45/184	24.5 (18.4-31.3)	1.0 (Ref)	
	Two previous	5/15	33.3 (11.8-61.6)	1.5 (0.5-4.7)	.53
	Paroxysmal	42/184	22.8 (17.0-29.6)	1.0 (Ref)	
	Persistent	7 /11	63.6 (30.8-89.1)	5.9 (1.6-21.2)	.006

continued racing after 2 previous episodes, recurrence occurred in 5 (33.3%), which was not significantly different from horses with 1 previous episode (45 of 184 horses, 24.5%; P = .53). Eleven horses returned to training after an episode of persistent AF. The proportion of horses with recurrence after a previous episode of persistent AF (7 of 11, 64%) was higher than for horses with a previous paroxysmal episode (42 of 184, 23%; OR, 5.9; 95% CI, 1.6-21.2; P = .006; Table 2). The duration of 4 AF episodes was unknown. For the 45 horses that had 2 episodes, the median number of days and starts respectively between the first and second episode was 347 (range, 34-1065) days and 8.5 (range, 0-62) starts. For the 5 horses that had 3 episodes, there was a median of 229 (range, 93-388) days, and 0 (range, 0-4) starts between the second and third episode.

3.4 | Outcomes

After 2 episodes of postrace AF. 15 horses were embargoed and not allowed to start in any race for 6 months. Five horses were compulsorily retired after 3 episodes. Median career duration after the first episode is presented in Figure 2 and Table 3. Career duration was not significantly different between groups when measured by either days (P = .72) or number of starts after first episode (P = .12). One horse died suddenly 735 days after a paroxysmal episode of AF, giving an incidence of sudden death in horses with a previous episode of AF of 0.35 per 1000 starts. The median rating of all horses at the time of the first episode of AF was 62 (range, 20-128). For horses that were not immediately retired after the first episode, the median change in rating was -1.5 (range, -62 to +37). The decline in performance as measured by the rating change was not significantly different between horses that did not have a recurrent episode (median, -2; range, -26 to +30) compared to horses that had ≥ 2 episodes (median, -1; range, -119 to +37; P = .70). Of 182 horses that presented for a race start after an episode of postrace AF, 117 (64%) won at least 1 race. The median number of races won was 2 (range, 1-10) races.

3.5 | Electrocardiography

An ECG documenting an arrhythmia was present in the record for 125/280 (44.6%) events in 108/230 (47.0%) horses.

Career duration after first episode of arrhythmia

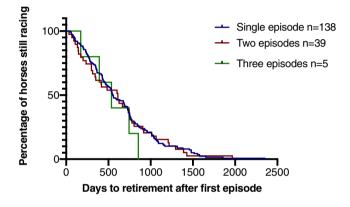


FIGURE 2 Kaplan-Meier survival curve depicting career duration in days after first episode of atrial fibrillation for n = 182 retired horses

The median duration of the recorded ECG was 67 seconds (range, 8-1120 seconds). Sinus rhythm with ectopy of narrow QRS conformation was observed in 5 events (4%; Figure 3A). Atrial fibrillation with QRS conformation of uniform morphology was observed in 40 events (32%; Figure 3B). Atrial fibrillation with nonuniform QRS conformation was observed in 32 events (26%; Figure 3C). Atrial fibrillation with multiform QRS conformation was observed in 48 events (38%) including 3 events with suspected R-on-T phenomenon (Figure 3D). An ECG was recorded in 18 recurrent episodes for which an ECG documenting the previous episode also was present. In 10/18 recurrent episodes, the ECG classification was the same as the previous episode, and in the remaining 8 episodes the ECG classification was different between episodes. The mean ± SD heart rate observed on post-race ECG was 144 ± 26 beats per minute (bpm). The mean ± SD heart rate for horses with AF and multiform QRS morphology was 156 ± 23 bpm which was significantly higher than in horses with AF of uniform morphology 131 ± 23 bpm (P < .001) and horses with sinus rhythm with ectopy 113 ± 19 bpm (P = .001; Figure 4). The mean \pm SD heart rate of horses with AF of nonuniform morphology was 146 ± 24 bpm which was significantly higher than in horses with AF of uniform morphology (P = .03) and horses that had sinus rhythm with ectopy (P = .02).

4 | DISCUSSION

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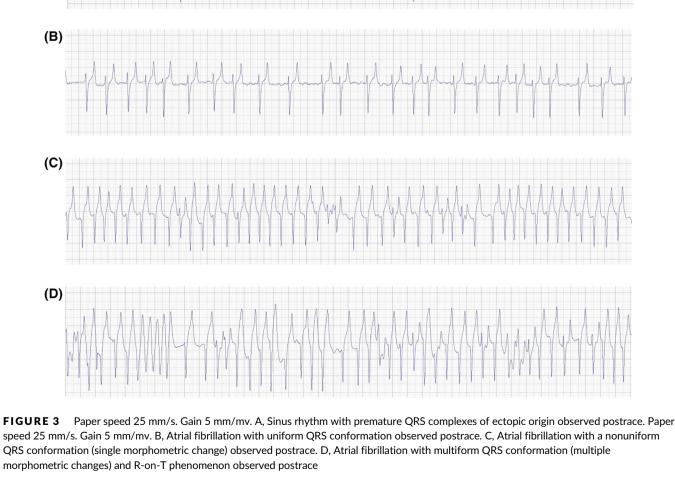
We identified several important findings on the recurrence of postrace AF in racehorses after both paroxysmal and persistent episodes. First, we determined that recurrence of AF is more

TABLE 3 Career duration for n = 182 retired horses presenting to an official start or trial after the first episode of atrial fibrillation. A log rank (Mantel Cox) test for survival confirmed there was no difference between groups in either median number of days (P = .72) or number of starts (P = .12) after the first episode

	Career duration after first episode		
Number of career episodes	Days median (range)	Starts median (range)	
One (n = 138)	550 (46-2352)	14 (1-87)	
Two (n = 39)	612 (34-1967)	13 (0-62)	
Three (n = 5)	536 (172-854)	7 (4-19)	

common after an episode of persistent AF than after paroxysmal AF. Second, although the rate of recurrence was high, the number of recurrent episodes did not impact career longevity or overall career performance. Finally, variation in QRS conformation was observed in most AF episodes and was associated with high heart rates, which could be suggestive of potential deterioration to an unstable rhythm.

In our study, a diagnosis of presumed AF was made based on cardiac auscultation of an irregularly irregular rhythm in the immediate postrace period. Approximately half of all events subsequently were documented using ECG. Heart rhythm irregularities are reliably identified by auscultation, but ECG is required to definitively determine the nature of the arrhyhmia.³⁷ In our study, the potential for misidentification of AF based on auscultation alone existed, because conditions considered to be normal findings after strenuous exercise in horses, such as sinus arrhythmia or second-degree atrioventricular block, may be confused with AF or ectopy.⁴ In a small proportion (4%) of events with a documented ECG, the ECG findings of sinus rhythm with



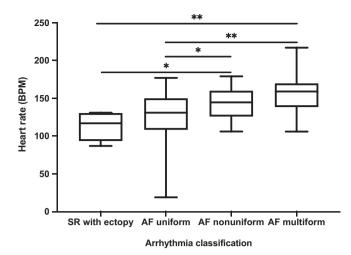


FIGURE 4 Heart rate of horses with each type of arrhythmia classification based on postrace ECG. Sinus rhythm with ectopy, sinus rhythm with either atrial or ventricular premature complexes; AF uniform, atrial fibrillation with uniform QRS morphology; AF nonuniform, atrial fibrillation with nonuniform (single morphometric change); AF multiform, atrial fibrillation with at least 3 different QRS morphologies. Single open circle represents outlier. *P < .05, **P < .001

ectopy differed from the auscultatory diagnosis of presumed AF. Sinus rhythm with ectopy was observed in a previous study of arrhythmias occurring after racing.¹¹ In our study, a delay occurred between auscultation and ECG recording, which might account for the different diagnoses based on these 2 methods. A previous study in horses identified an association between atrial premature beats postconversion and AF recurrence,¹⁷ and ectopy is important in triggering AF.³⁸ Episodes of sinus rhythm with ectopy were retained in our study because they could reflect an intermediate step in resolution of paroxysmal AF.

The overall frequency of postrace AF in Hong Kong (2.7 per 1000 starts) was higher than observed in previous studies conducted in the United Kingdom and Japan (0.2-0.3 per 1000 starts),^{12,13} but similar to a study of Standardbreds in the United States (1.4 per 1000 starts).¹⁰ The reported incidence of AF in our study should be considered a conservative estimate, because only horses performing below expectation were examined. Approximately 22% of horses in the field typically are examined after each race, and this method yielded a high incidence of AF. The true incidence of postrace AF might be higher than reported considering that a large proportion of horses that had performed to expectation were not examined, and some episodes of AF could have developed in the postrace period, thus not influencing race performance.^{10,11} A previous study of Standardbred racehorses found an incidence of any arrhythmia in the immediate postrace period of 27.8%.9 Because exercise-associated arrhythmias typically are short-lived,³⁵ the incidence of arrhythmia will be closely related to the timing between cessation of exercise and examination. In our study, some episodes of arrhythmia, that could have impacted the performance of the horse, might not have been detected because they resolved before veterinary examination. Given that arrhythmias American College of

also are observed after good race performances,^{10,11} the clinical relevance of arrhythmias that occur in the postrace period and their relationship to poor performance require further investigation.

Although only a small number of horses in this study continued to race after treatment for persistent AF, their recurrence rate was higher than that of horses with a paroxysmal episode. A recent study of a mixed population of horses, including both racing and performance horses, observed recurrence in 39% of horses 1 year after conversion to sinus rhythm.²⁷ Our study included only Thoroughbred racehorses, and suggests that recurrence of AF is likely to be higher in this group than previous estimates.^{2,16,26} Factors that influence risk for recurrence after persistent AF include mitral regurgitation,²⁷ increased left atrial size,²⁸ impaired left atrial function,²⁷ shorter AF cycle length,²⁸ and prevalence of atrial premature depolarizations¹⁷ after conversion. Echocardiography and follow-up ECG were not consistently performed in horses in our study. Therefore, the relationship between previously identified risk factors and recurrence of AF in this population could not be assessed. Additionally, the possibility of structural heart disease in some of the horses in our study cannot be excluded.

Recurrence of AF after paroxysmal episodes supports the concept that cardiac remodeling that promotes AF may be associated even with episodes of relatively short duration. Recurrence after paroxysmal episodes observed in our study is not dissimilar to findings in other studies largely comprised of racehorses with persistent AF.^{2,16,26} Atrial fibrillation rapidly induces atrial electrical and contractile remodeling, resulting in decreased atrial effective refractory period and impaired atrial contractility.³¹ The timeframe for return to normal function is proportional to the duration of AF, with a restoration of normal electrical and contractile function of <24 and 72 hours respectively after short duration AF.^{31,39} and 10 days and 1 to 2 months after AF of 6 months' duration.⁴⁰ Progression of paroxysmal AF to persistent AF is commonly recognized in humans.⁴¹ The impact of naturally occurring paroxysmal AF episodes on atrial remodeling in horses is yet to be investigated. Undetected, silent episodes of paroxysmal AF may occur frequently in training and racing, and the cumulative effect of such episodes may promote a higher burden of AF and AF of longer duration, which is more likely to limit performance and be detected clinically.

All horses in our study were regularly starting in Thoroughbred races. Previous studies in horses have shown that training induces cardiac remodeling, resulting in increased cardiac chamber size and a modest increase in myocardial wall thickness.⁴² Atrioventricular regurgitation occurs concurrently.⁴³ It is proposed that human athletes undertaking higher volumes and intensity of exercise are predisposed to development of AF.^{23,24,44} In rodents, myocardial inflammation and fibrosis after exercise training is considered to be a substrate for arrhythmia. ²⁰⁻²² Several studies have reported inflammatory and fibrotic changes in the myocardium of racehorses involving the atria, conduction system and ventricles^{3,45-49} Age is a risk factor for AF in racehorses,^{10,12} supporting the effect of volume of training and cardiac remodeling in the promotion of AF in this species. Although exercise likely promotes the onset of AF in horses, individual factors, such as atrial size and microstructural changes affecting electromechanical function, also are important in sustaining AF.^{27,28} In humans, the pulmonary veins are important AF triggers, and American College of Veterinary Internal Medicine

recent evidence supports that such also is the case in horses.¹⁸ Also in humans, lean body mass has been shown as the strongest anthropometric predictor of AF.⁵⁰ This observation is consistent with studies in horses, in which increased body mass is associated with risk of AF.^{51,52} Research in Standardbred racehorses has supported a genetic basis for AF based on epidemiology and pedigree analysis.^{51,53,54} Additional studies are needed to determine the role of genetics in AF in Thoroughbreds.

In our study of racehorses, arrhythmia recurrence did not impact career duration or performance, other than for horses that had 3 episodes and were compulsorily retired. An episode of AF was an important determinant in the decision to retire a horse, and many were retired immediately after the diagnosis. Horses with intermittent episodes of AF can perform successfully between episodes.¹⁴ Overall, a slight decline in rating, a proxy measure for performance, occurred from the time of the first episode of AF until retirement. However, most horses won at least 1 race after an episode of AF, and many horses experienced improvement in overall rating. Similar to other studies.^{27,55} it was observed that the time between episodes of AF was highly variable, and sometimes the recurrent episode was several years after the first episode. This finding suggests that individual horses remain vulnerable to repeated episodes of AF for a prolonged period, possibly because of clinically undetectable changes in myocardial substrate. In our study, 1 horse died 735 days after an episode of paroxysmal AF with multiform QRS morphology. The incidence of sudden death in Thoroughbred horses is 1 to 3 deaths per 10 000 starts, with approximately 50% of these estimated to be caused by fatal cardiac arrhythmia.⁴⁷ This finding is similar to the rate of sudden death observed in our study. Additional investigation is needed to determine the association between postrace AF and SCD.

Paroxysmal AF was the most commonly diagnosed arrhythmia in the postrace period in our study, a finding that concurs with those of previous studies.^{10-13,56} The potential for AF to deteriorate into an unstable ventricular rhythm, particularly in the setting of high sympathetic tone, is evidenced by reports of collapse and cardiac arrest.^{2,3} As has previously been reported in horses with AF,^{19,34,57,58} changes in conformation of QRS complexes frequently occur with strenuous exercise and increased sympathetic tone, and these complexes potentially may be dangerous. Atrial premature depolarizations also can be associated with changes in QRS morphology.⁵⁹ At high heart rates, the P wave typically is buried in the preceding QRS, making differentiation between supraventricular and ventricular complexes challenging.34,60,61 In exercising horses and at high heart rates, there is potential for errors in interpretation of the origin of abnormal QRS complexes based on morphology and timing alone.^{60,61} Recent studies have suggested that descriptive terminology be used to report ECG findings in studies of exercising horses with arrhythmias.^{60,61} Our study describes a method of AF classification to distinguish between cases of AF with uniform and nonuniform QRS morphology. In the setting of AF, both aberrant ventricular conduction of a supraventricular impulse or concurrent ventricular ectopy are possible underlying mechanisms for the abnormal QRS complexes. A clear association between the presence of QRS complexes of nonuniform and multiform morphology and increased heart rate in the postexercise recovery period was observed. However, ECG recordings generally were of short duration and made in 1 lead only. Therefore, it was not possible to determine whether the changes in conformation reflected ventricular ectopy or supraventricular conduction with aberrancy. In humans with AF, at high heart rates, impaired intraventricular conduction promotes aberrancy because of refractoriness of the right bundle branch.62 Although it is appreciated that increases in heart rate associated with enhanced sympathetic tone can promote aberrant conduction, increased sympathetic tone also promotes ventricular dysrhythmias.⁶³ In humans, ectopy occurring alongside AF can indicate underlying reentrant or aberrant pathways such as atrioventricular node reentry and ventricular preexcitation,⁶⁴ the latter of which also has been recognized in horses.^{65,66} A substantial proportion of horses in our study had AF and QRS conformation with \geq 3 different morphologies, which could reflect more widespread cardiac pathology and increased concern for deterioration into an unstable rhythm.4,34 More sophisticated ECG recording is needed to better identify and understand the origin of QRS complexes with abnormal morphology in horses.

In addition to not all horses having ECG confirmation of AF, a further limitation of our study was its retrospective nature. Many horses were retired immediately after the first episode of AF, dictating that potential for recurrence and impact of AF on performance could not be evaluated. Very few horses continued to race after 2 episodes of AF, which limited statistical power in detecting differences in recurrence among horses with multiple episodes of AF. The Hong Kong racing population differs from other jurisdictions because it has a predominantly male population and all horses are imported. Before import, horses are subject to veterinary examination to ensure soundness. Approximately half of all horses imported to Hong Kong have raced previously overseas and must have a rating of \geq 68 before import.⁶⁷ The unique features of this population may have impacted the high incidence and recurrence of AF observed in our study.

We identified a high rate of recurrence in Thoroughbred racehorses after both paroxysmal and persistent episodes of AF. This substantial AF burden could arise from underlying microstructural myocardial lesions and electrical remodeling. Although horses can have long and successful careers after AF, the arrhythmia should not be considered benign, and the suitability of horses to continue their racing careers should be assessed on an individual basis.

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CONFLICT OF INTEREST DECLARATION

Authors declare no conflict of interest.

OFF-LABEL ANTIMICROBIAL DECLARATION

Authors declare no off-label use of antimicrobials.

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INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION

Approved by the University of Adelaide Animal Ethics Committee (Science) Risk factors for exercise-induced arrhythmias in horses S-2017-088.

HUMAN ETHICS APPROVAL DECLARATION

Authors declare human ethics approval was not needed for this study.

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REFERENCES

- 1. Hitchens PL, Hill AE, Stover SM. The role of catastrophic injury or sudden death of the horse in race-day jockey falls and injuries in California, 2007-2012. *Equine Vet J.* 2014;48(1):50–56.
- Deem D, Fregin G. Atrial fibrillation in horses: a review of 106 clinical cases, with consideration of prevalence, clinical signs, and prognosis. *J Am Vet Med Assoc.* 1982;180:261-265.
- Kiryu K, Machida N, Kashida Y, Yoshihara T, Amada A, Yamamoto T. Pathologic and electrocardiographic findings in sudden cardiac death in racehorses. J Vet Med Sci. 1999;61:921-928.
- 4. Reef VB, Bonagura J, Buhl R, et al. Recommendations for management of equine athletes with cardiovascular abnormalities. *J Vet Intern Med.* 2014;28:749-761.
- Allen K, Young L, Franklin S. Evaluation of heart rate and rhythm during exercise. *Equine Vet Educ*. 2016;28:99-112.
- Martin BB Jr, Reef VB, Parente EJ, Sage AD. Causes of poor performance of horses during training, racing, or showing: 348 cases (1992-1996). J Am Vet Med Assoc. 2000;216:554-558.
- Jose-Cunilleras E, Young LE, Newton JR, Marlin DJ. Cardiac arrhythmias during and after treadmill exercise in poorly performing thoroughbred racehorses. *Equine Vet J Suppl.* 2006;38:163-170.
- 8. Ryan N, Marr CM, McGladdery AJ. Survey of cardiac arrhythmias during submaximal and maximal exercise in thoroughbred racehorses. *Equine Vet J.* 2005;37:265-268.
- 9. Physick-Sheard PW, McGurrin MK. Ventricular arrhythmias during race recovery in Standardbred Racehorses and associations with autonomic activity. *J Vet Intern Med.* 2010;24:1158-1166.
- Slack J, Boston RC, Soma LR, Reef VB. Occurrence of cardiac arrhythmias in Standardbred racehorses. *Equine Vet J.* 2015;47:398-404.
- 11. Holmes JR. Cardiac arrhythmias on the racecourse. *Equine Exerc Physiol.* 1987;2:781-785.
- 12. Ohmura H, Hiraga A, Takahashi T, Kai M, Jones JH. Risk factors for atrial fibrillation during racing in slow-finishing horses. J Am Vet Med Assoc. 2003;223:84-88.
- 13. Williams R, Harkins L, Hammond C, Wood J. Racehorse injuries, clinical problems and fatalities recorded on British racecourses from flat racing and National Hunt racing during 1996, 1997 and 1998. *Equine Vet J.* 2001;33:478-486.
- 14. Holmes JR, Henigan M, Williams RB, Witherington DH. Paroxysmal atrial fibrillation in racehorses. *Equine Vet J.* 1986;18:37-42.
- Nath L, Anderson G, Hinchcliff K, Savage C. Serum cardiac troponin I concentrations in horses with cardiac disease. *Aust Vet J.* 2012;90: 351-357.
- McGurrin M, Physick-Sheard P, Kenney D. Transvenous electrical cardioversion of equine atrial fibrillation: patient factors and clinical results in 72 treatment episodes. J Vet Intern Med. 2008;22:609-615.
- 17. Vernemmen I, De Clercq D, Decloedt A, Vera L, Van Steenkiste G, van Loon G. Atrial premature depolarisations five days post electrical cardioversion are related to atrial fibrillation recurrence risk in horses. *Equine Vet J.* 2020;52:374-378.

- Linz D, Hesselkilde E, Kutieleh R, Jespersen T, Buhl R, Sanders P. Pulmonary vein firing initiating atrial fibrillation in the horse: oversized dimensions but similar mechanisms. *J Cardiovasc Electrophysiol*. 2020; 31:1211-1212.
- Verheyen T, Decloedt A, van der Vekens N, Sys S, De Clercq D, van Loon G. Ventricular response during lungeing exercise in horses with lone atrial fibrillation. *Equine Vet J.* 2013;45:309-314.
- 20. Benito B, Gay-Jordi G, Serrano-Mollar A, et al. Cardiac arrhythmogenic remodeling in a rat model of long-term intensive exercise training. *Circulation*. 2011;123:13-22.
- Guasch E, Benito B, Qi X, et al. Atrial fibrillation promotion by endurance exercise: demonstration and mechanistic exploration in an animal model. J Am Coll Cardiol. 2013;62:68-77.
- Aschar-Sobbi R, Izaddoustdar F, Korogyi AS, et al. Increased atrial arrhythmia susceptibility induced by intense endurance exercise in mice requires TNFα. *Nat Commun.* 2015;6:6018.
- 23. La Gerche A, Heidbuchel H. Can intensive exercise harm the heart? You can get too much of a good thing. *Circulation*. 2014;130:992-1002.
- Elliott AD, Linz D, Verdicchio CV, Sanders P. Exercise and atrial fibrillation: prevention or causation? *Heart Lung Circ.* 2018;27:1078-1085.
- Maron BJ, Pelliccia A. The heart of trained athletes: cardiac remodeling and the risks of sports, including sudden death. *Circulation*. 2006;114:1633-1644.
- Reef VB, Levitan CW, Spencer PA. Factors affecting prognosis and conversion in equine atrial fibrillation. J Vet Intern Med. 1988;2:1-6.
- Decloedt A, Schwarzwald CC, De Clercq D, et al. Risk factors for recurrence of atrial fibrillation in horses after cardioversion to sinus rhythm. J Vet Intern Med. 2015;29:946-953.
- De Clercq D, Decloedt A, Sys SU, Verheyen T, Van Der Vekens N, van Loon G. Atrial fibrillation cycle length and atrial size in horses with and without recurrence of atrial fibrillation after electrical cardioversion. J Vet Intern Med. 2014;28:624-629.
- 29. Decloedt A, de Clercq D, van der Vekens N, Verheyen T, van Loon G. Noninvasive determination of atrial fibrillation cycle length by atrial colour tissue Doppler imaging in horses. *Equine Vet J.* 2014;46:174-179.
- Decloedt A, Verheyen T, Van Der Vekens N, Sys S, De Clercq D, van Loon G. Long-term follow-up of atrial function after cardioversion of atrial fibrillation in horses. *Vet J.* 2013;197:583-588.
- 31. De Clercq D, Van Loon G, Tavernier R, Duchateau L, Deprez P. Atrial and ventricular electrical and contractile remodeling and reverse remodeling owing to short-term pacing-induced atrial fibrillation in horses. *J Vet Intern Med.* 2008;22:1353-1359.
- Hesselkilde EZ, Carstensen H, Haugaard MM, et al. Effect of flecainide on atrial fibrillatory rate in a large animal model with induced atrial fibrillation. *BMC Cardiovasc Disord*. 2017;17:289.
- 33. Club HKJ. Department of veterinary regulation welfare and biosecurity policy. *Hong Kong Jockey Club*. 2019;54.
- 34. de Solis CN. Ventricular arrhythmias in horses: diagnosis, prognosis and treatment. *Vet J.* 2020;261:105476.
- Hong Kong Jockey Club racing index; 2020. https://racing.hkjc.com/ racing/english/index.aspx
- Kim H-Y. Statistical notes for clinical researchers: chi-squared test and Fisher's exact test. *Restor Dent Endod*. 2017;42:152-155.
- Naylor JM, Yademuk LM, Pharr JW, Ashbumer JS. An assessment of the ability of diplomates, practitioners, and students to describe and interpret recordings of heart murmurs and arrhythmia. J Vet Intern Med. 2001;15:507-515.
- Chen S-A, Hsieh M-H, Tai C-T, et al. Initiation of atrial fibrillation by ectopic beats originating from the pulmonary veins: electrophysiological characteristics, pharmacological responses, and effects of radiofrequency ablation. *Circulation*. 1999;100:1879-1886.
- Schwarzwald CC, Schober KE, Bonagura JD. Echocardiographic evidence of left atrial mechanical dysfunction after conversion of atrial fibrillation to sinus rhythm in 5 horses. J Vet Intern Med. 2007;21:820-827.

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- van Loon G. Atrial Pacing and Experimental Atrial Fibrillation in Equines Faculty of Veterinary Medicine. Merelbeke, Belgium: Ghent University; 2001.
- 41. De Vos CB, Pisters R, Nieuwlaat R, et al. Progression from paroxysmal to persistent atrial fibrillation: clinical correlates and prognosis. *J Am Coll Cardiol*. 2010;55:725-731.
- 42. Young LE. Cardiac responses to training in 2 year old thoroughbreds: an echocardiographic study. *Equine Vet J.* 1999;31:195-198.
- Young LE, Wood JL. Effect of age and training on murmurs of atrioventricular valvular regurgitation in young thoroughbreds. *Equine Vet* J. 2000;32:195-199.
- 44. Sanchis-Gomar F, Perez-Quilis C, Lippi G, et al. Atrial fibrillation in highly trained endurance athletes—description of a syndrome. *Int J Cardiol.* 2017;226:11-20.
- 45. Else RW, Holmes JR. Cardiac pathology in the horse. 2. Microscopic pathology. *Equine Vet J.* 1972;4:57-62.
- Boden LA, Charles JA, Slocombe RF, et al. Sudden death in racing Thoroughbreds in Victoria, Australia. *Equine Vet J.* 2005;37: 269-271.
- 47. Lyle CH, Uzal FA, McGorum BC, et al. Sudden death in racing Thoroughbred horses: an international multicentre study of post mortem findings. *Equine Vet J.* 2011;43:324-331.
- DeLay J. Postmortem findings in Ontario racehorses, 2003-2015. J Vet Diagn Investig. 2017;29:457-464.
- Molesan A, Wang M, Sun Q, et al. Cardiac pathology and genomics of sudden death in racehorses from New York and Maryland racetracks. *Vet Pathol.* 2019;56(4):575–585.
- Frost L, Overvad K, Tjønneland A, Fenger-Grøn M. Lean body mass is the predominant anthropometric risk factor for atrial fibrillation. J Am Coll Cardiol. 2016;69:2488-2497.
- Physick-Sheard P, Kraus M, Basrur P, McGurrin K, Kenney D, Schenkel F. Breed predisposition and heritability of atrial fibrillation in the Standardbred horse: a retrospective case-control study. J Vet Cardiol. 2014;16:173-184.
- Leroux A, Detilleux J, Sandersen C, et al. Prevalence and risk factors for cardiac diseases in a hospital-based population of 3,434 horses (1994–2011). J Vet Intern Med. 2013;27:1563-1570.
- Kraus M, Physick-Sheard P, Brito LF, Sargolzaei M, Schenkel FS. Marginal ancestral contributions to atrial fibrillation in the Standardbred racehorse: comparison of cases and controls. *PLoS One*. 2018;13:e0197137.
- Kraus M, Physick-Sheard P, Brito L, Schenkel F. Estimates of heritability of atrial fibrillation in the Standardbred racehorse. *Equine Vet J*. 2017;49:718-722.
- McGurrin MKJ, Physick-Sheard PW, Kenney DG. Transvenous electrical cardioversion of equine atrial fibrillation: patient factors and clinical results in 72 treatment. *Episodes*. 2008;22:609-615.

- Rosanowski S, Chang Y, Stirk A, Verheyen K. Descriptive epidemiology of veterinary events in flat racing thoroughbreds in Great Britain (2000 to 2013). *Equine Vet J.* 2017;49:275-281.
- 57. Heliczer N, Mitchell K, Lorello O, et al. Atrial fibrillation management in a breeding stallion. *J Vet Cardiol*. 2017;19:299-307.
- Buhl R, Carstensen H, Hesselkilde EZ, et al. Effect of induced chronic atrial fibrillation on exercise performance in Standardbred trotters. *J Vet Intern Med.* 2018;32:1410-1419.
- Broux B, De Clercq D, Decloedt A, et al. Atrial premature depolarizationinduced changes in QRS and T wave morphology on resting electrocardiograms in horses. J Vet Intern Med. 2016;30:1253-1259.
- 60. Reef V, Davidson E, Slack J, Stefanovski D. Hypercapnia and hyperlactatemia were positively associated with higher-grade arrhythmias during peak exercise in horses during poor performance evaluation on a high-speed treadmill. *Vet J*. 2020;266:105572.
- Slack J, Stefanovski D, Madsen T, Fjordbakk C, Strand E, Fintl C. Cardiac arrhythmias in poorly performing Standardbred and Norwegian– Swedish Coldblooded trotters undergoing high-speed treadmill testing. Vet J. 2020;267:105574.
- Suyama AC, Sunagawa K, Sugimachi M, Anan T, Egashira K, Takeshita A. Differentiation between aberrant ventricular conduction and ventricular ectopy in atrial fibrillation using RR interval scattergram. *Circulation*. 1993;88:2307-2314.
- 63. Zipes DP. Heart-brain interactions in cardiac arrhythmias: role of the autonomic nervous system. *Cleve Clin J Med.* 2008;75:S94.
- Chang S-L, Tai C-T, Lin Y-J, et al. Electrophysiological characteristics and catheter ablation in patients with paroxysmal supraventricular tachycardia and paroxysmal atrial fibrillation. J Cardiovasc Electrophysiol. 2008;19:367-373.
- Jesty SA, Kraus MS, Johnson AL, Gelzer AR, Bartol J. An accessory bypass tract masked by the presence of atrial fibrillation in a horse. *J Vet Cardiol.* 2011;13:79-83.
- Viu J, Armengou L, Decloedt A, Jose-Cunilleras E. Investigation of ventricular pre-excitation electrocardiographic pattern in two horses: clinical presentation and potential causes. J Vet Cardiol. 2018;20:213-221.
- PPS import criteria; 2020. https://racing.hkjc.com/racing/english/ racing-info/pps_import_critieria.asp

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