



Breed predisposition and heritability of atrial fibrillation in the Standardbred horse: A retrospective case–control study

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KEYWORDS

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Abstract Objectives: To assess evidence for genetic contributions to atrial fibrillation (AF) in the Standardbred horse.

Animals: Equine referrals to the Ontario Veterinary College Health Sciences Centre (OVCHSC) for 1985–2009, and age and gait matched breed registry controls.

Methods: Breeds presenting ≥ 5 times annually were tabulated (admission year and diagnosis; total 40,039; AF 396; no AF 39,643), and breed and year effects examined. Heritability and inbreeding coefficients were determined for Standardbred AF cases and racing contemporaries, and odds ratios for AF were calculated for frequently occurring sires.

Results: Year and breed effects on diagnosis were highly significant (Chi-Square 212.85, $p < 0.0001$, and 304.25, $p < 0.0001$, respectively). Year effect on diagnosis by breed was significant from 1997, and due to Standardbred admissions each year. Quarterhorses were significantly less likely to present with AF (OR 0.0578–0.6048), Standardbreds were more likely (OR 4.3874–10.9006). Heritability of AF on the underlying scale (h^2_u) was estimated at $29.6 \pm 3.9\%$ and on the observed binomial scale

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(h_o^2), at 9.6%. For horses born in 1994 or later, h_u^2 was $31.1 \pm 4.3\%$ and h_o^2 , 10.1%. Of 22 first generation sires appearing ≥ 10 times in the case/control file, seven pacing and one trotting sire produced affected horses more frequently than expected (OR 2.66–66.32). Inbreeding was not a factor.

Conclusions: There is genetic liability to AF in Standardbred horses, likely due to more than single genes with simple Mendelian inheritance. Genomic studies are required.

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Abbreviations

σ_a^2	additive genetic variance
σ_p^2	additive phenotypic variance
AF	atrial fibrillation
CMLE	conditional maximum likelihood estimate
F	coefficient of inbreeding
h_u^2	heritability on the underlying continuous scale
h_o^2	heritability on the observed binomial scale
MUE	median unbiased estimate
OR	odds ratio
OVCHSC	Ontario Veterinary College Health Sciences Centre
REML	restricted maximum likelihood estimate

Introduction

Over the last 20 years, there has been a progressive rise in the number of active Standardbred racehorses presented at the Ontario Veterinary College Health Sciences Centre (OVCHSC) with a diagnosis of atrial fibrillation (AF). Frequency of presentation appeared to exceed the number expected based on the general referral population, while particular pedigrees occurred often. Very few horses were phenotypically predisposed to arrhythmias since evidence of clinically significant organic heart disease was generally absent, and a diagnosis of lone AF (AF without clinical evidence of predisposing organic heart disease) was made in all cases.

Atrial fibrillation is of growing importance in humans, with increase in cases being attributed in part to an ageing population and genetic contributions.^{1–3} Ageing does not apply in the Standardbred racehorse, however, where average age is

low.^{4,5} Genetic contributions to AF of both familial and non-familial forms have been described in humans,^{6,7} but no arrhythmia with a genetic basis has been described to date in the horse. The objectives of the present investigation were to assess evidence supporting a genetic liability for AF in the Standardbred horse, and to gain insight into the mode of inheritance if such liability were found. These objectives were approached through a retrospective case–control study of the OVCHSC referral population for the period of 1985–2009 inclusive.

Animals, materials and methods

The investigation was divided into three components, as follows:

Study 1 – analysis of hospital referral population

Reference population for this study was horses of any breed living in the catchment area of the OVCHSC, which included the Province of Ontario and adjacent areas of the United States. Study population was horses referred to the hospital for any reason. The medical records database of the hospital was searched from 1985 to 2009 inclusive to determine by breed, annual equine admissions and annual number of these admissions in which a diagnosis of stable (persistent) AF was made. The diagnosis of AF was confirmed on ECG. Cases in which AF arose spontaneously during systemic illness, and then resolved, were not included. For study 1, these populations constituted the case group (all horses with stable AF) and control group (all other equine admissions). Throughout the study period, all presenting problems and clinical findings were routinely recorded in the medical record. Arrhythmias (whether historical, evident during examination or noted during hospitalization) were routinely evaluated by ECG and diagnoses of AF were recorded. Hospital controls

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