

Atrial Fibrillation Cycle Length and Atrial Size in Horses with and without Recurrence of Atrial Fibrillation after Electrical Cardioversion

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Background: Atrial fibrillation (AF) cycle length (CL) and atrial size have been used in humans to characterize electrical and structural remodeling to predict outcome of cardioversion of AF and risk for AF recurrence (rAF).

Hypothesis: Atrial fibrillation cycle length can be determined in horses with AF, and AFCL and atrial size are related to risk for rAF.

Animals: Eighteen horses with naturally occurring AF that were successfully converted to sinus rhythm (SR) by transvenous electrical cardioversion (TVEC).

Methods: Prospective study. Horses with severe valvular regurgitation, left atrial enlargement, or that required sedation for catheter placement were excluded. In all horses intra-atrial electrograms were recorded and estimated AF duration and echocardiographic parameters were determined before TVEC. The follow-up time was 1 year after TVEC.

Results: Atrial fibrillation cycle length could be determined in all horses. The AFCL and the shortest 5th percentile (p5) AFCL in horses with rAF (n = 6 or 33%) were (mean ± SD) 157 ± 28 and 134 ± 24 milliseconds, respectively, and in those maintaining SR (n = 12 or 67%) 166 ± 13 and 141 ± 13 milliseconds, respectively. Significant parameters to predict rAF were (1) the ratios of the p5AFCL to the left atrium (LA) sizes corrected to the size of aorta (AO) and (2) LA sizes corrected to the size of AO.

Conclusions and Clinical Importance: Before TVEC, assessment of LA size and atrial electrophysiologic characteristics might help to identify horses at increased risk for AF recurrence.

Key words: Atrial effective refractory period; Atrial size; Electrophysiology; Recurrence of atrial fibrillation.

Atrial fibrillation (AF) is the most important supraventricular dysrhythmia in horses with an impact on athletic performance. AF can be treated pharmacologically using quinidine sulfate (QS) or by transvenous electrical cardioversion (TVEC).^{1–4} Currently, there are no studies that compare success rates between the 2 techniques. Recurrence rate after QS treatment is between 15 and 40% and AF duration is a major risk factor.^{1,5} Data for the recurrence rate after TVEC are currently lacking, but recurrence rate is probably independent of the treatment technique and therefore is likely to be similar to that reported for pharmacologic conversion of AF.⁶ Objective criteria that allow prediction of AF recurrence (rAF) after successful TVEC are currently unavailable in horses. In 2 studies on AF in horses, recurrences became more frequent when AF was present for a longer period of time before treatment.^{5,7} Atrial size, duration of AF, and atrial fibrillation cycle length (AFCL) are parameters used in human medicine to predict recurrence of AF after successful treatment.^{8,9} AFCL is an index of

Abbreviations:

A	area
AERP	atrial effective refractory period
AF	atrial fibrillation
AFCL	atrial fibrillation cycle length
AO	aorta
LA	left atrium
la	long-axis
L	left
mSR	maintenance of sinus rhythm
p5AFCL	shortest 5th percentile atrial fibrillation cycle length
rAF	recurrence of atrial fibrillation
R	right
sa	short-axis
SR	sinus rhythm
TVEC	transvenous electrical cardioversion

atrial effective refractory period (AERP), an electrophysiologic parameter strongly related to AF susceptibility. AF-induced electrical remodeling shortens AERP and leads to increased AF sustainability.^{10,11} After restoration of sinus rhythm (SR), reverse electrical remodeling to pre-AF levels takes time, during which the atria are vulnerable to early rAF.^{2,10,12}

The purpose of this study was to describe a method to record right intra-atrial electrograms in horses with AF and to identify possible factors that might be related to rAF after successful TVEC.

Materials and Methods

Study Population

Horses referred to the Department of Large Animal Internal Medicine for treatment of AF were included in this study. Mean

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age, body weight, and height at the withers were recorded (Table 1). All horses were treated by TVEC. If SR could not be restored by TVEC alone, horses received 5 mg/kg amiodarone IV over 30 minutes and TVEC was repeated. Horses that presented ≥ 30 atrial premature depolarizations in the first 15 minutes post-cardioversion received 5 mg/kg amiodarone IV over 30 minutes before they were allowed to recover from general anesthesia. Inclusion criteria were the availability of a clinical examination, a base-apex ECG recording, a full echocardiographic examination^a before TVEC, and successful restoration of SR. Horses with severe valvular regurgitation or enlargement of the left atrium (LA) (left parasternal long-axis view and during peak ventricular systole, >14.5 cm) were excluded from the study. Horses that required sedation for catheter placement, where excluded from the study. AF duration was estimated based upon history and previous examinations (Table 1). Only horses in which AF was determined for the first time were used in this study.

Left Atrial and Aortic Size and Area

The two-dimensional ultrasonographic measurements from the left (L) and right (R) parasternal long-axis (_{la}) and short-axis (_{sa}) view were performed. For the LA, the maximal internal diameter (LA) and area (LAA) were determined at ventricular end-systole. LA diameters, on the long-axis views, were measured from the interatrial septum to the atrial free wall, parallel to the mitral annulus (LLA and RLA_{la}).

From a right parasternal short-axis (_{sa}) view, maximal internal diameter and area (A) of LA (LA_{sa}, LAA_{sa}) and aorta (AO_{sa}, AOA_{sa}) during ventricular systole were obtained.¹² For the internal short-axis diameter of the LA, calipers were placed in a line extending from and parallel to the commissure between the noncoronary and left coronary aortic valve cusps to the distant margin of the LA.¹² For the internal short-axis diameter of the AO at valvular level, calipers were placed along the commissure between the non-coronary and right coronary aortic valve cusps. From a right parasternal long-axis view the aortic annulus diameter (AO_{la}) was determined by measuring the inner distance between the opened aortic valve leaflets during peak systole.¹³ From this diameter, aortic area (AOA_{la}) was calculated as $\pi \cdot (AO_{la}/2)^2$.

Left atrium diameters and areas measured from the right long- or short-axis view were indexed to size of the AO in the same view, to obtain a correction for horse size.

AFCL Recording

In the standing unsedated horse, a 14F introducer sheath^b was inserted in the lower half of the right jugular vein. Through this sheath 2 cardioversion catheters^c and 1 bipolar sensing/pacing electrode^d were inserted under echocardiographic guidance. The sensing/pacing catheter was positioned in the right atrium (RA) to record a bipolar intra-atrial electrogram during 15 minutes whereas cardioversion catheters were positioned in the left pulmonary artery and the RA. Digital electrogram recording was performed with a modified (K. Engel^e) ECG recording device (Televet 100 version 5.0.0^f) that allowed simultaneous recording of 2 independent bipolar traces, the intra-atrial and surface ECG trace. During off-line analysis, the time interval between consecutive intra-atrial depolarizations, which is the AFCL, was manually measured over 500 depolarizations using dedicated software^e (Fig 1). Paper speed and amplitude were 50 mm/s and 10 mm/mV, respectively. From these data a mean AFCL, a 5th percentile (p5) AFCL, and a ratio of p5AFCL to echocardiographic measurements were calculated.

After TVEC and recovery, surface electrocardiograms were recorded on days 1, 2, 7, and 49 after cardioversion in order to confirm the presence of SR or rAF. The follow-up period was 1 year after successful cardioversion. The local veterinarian checked the horse, at regular time intervals, for maintenance of SR or rAF by auscultation. If a dysrhythmia was present, an ECG was performed. In all patients, except 1 (recurrence of AF 2 days after TVEC), the recurrence of AF was determined by the local veterinarian (auscultation and ECG) (Table 1).

Statistical Analysis

All variables are reported as mean \pm SD. Independent samples *t*-tests were performed on all parameters shown in Table 2 between horses maintaining SR (mSR) and those who suffered from rAF. The level of significance was $\alpha = 0.05$.

Table 1. Detailed information about the patients with atrial fibrillation.

Patient	Estimated AF Duration (months)	MR	TR	AR	PR	Time of rAF (days)
1	9	—	Moderate	—	—	2
2	8	—	Trivial	—	Trivial	202
3	6	Mild	Moderate	Mild	—	72
4	6	Mild	Trivial	—	—	354
5	1.5	Trivial	Trivial	Trivial	Trivial	25
6	9	Mild	—	—	—	355
7	6	Mild	Trivial	Mild	Moderate	—
8	18	Mild	Mild	—	—	—
9	5	Mild	Mild	Moderate	Trivial	—
10	5	Trivial	Trivial	—	Moderate	—
11	5	Trivial	—	—	—	—
12	4	—	Moderate	Trivial	Trivial	—
13	6	—	Trivial	Trivial	Trivial	—
14	0.3	—	—	—	—	—
15	4	—	—	Mild	—	—
16	1.5	—	—	—	—	—
17	6	—	—	Trivial	—	—
18	1	Trivial	Trivial	Mild	Trivial	—

MR, mitral valve regurgitation; TR, tricuspid valve regurgitation; AR, aortic valve regurgitation; PR, pulmonic valve regurgitation; rAF, recurrence of atrial fibrillation.

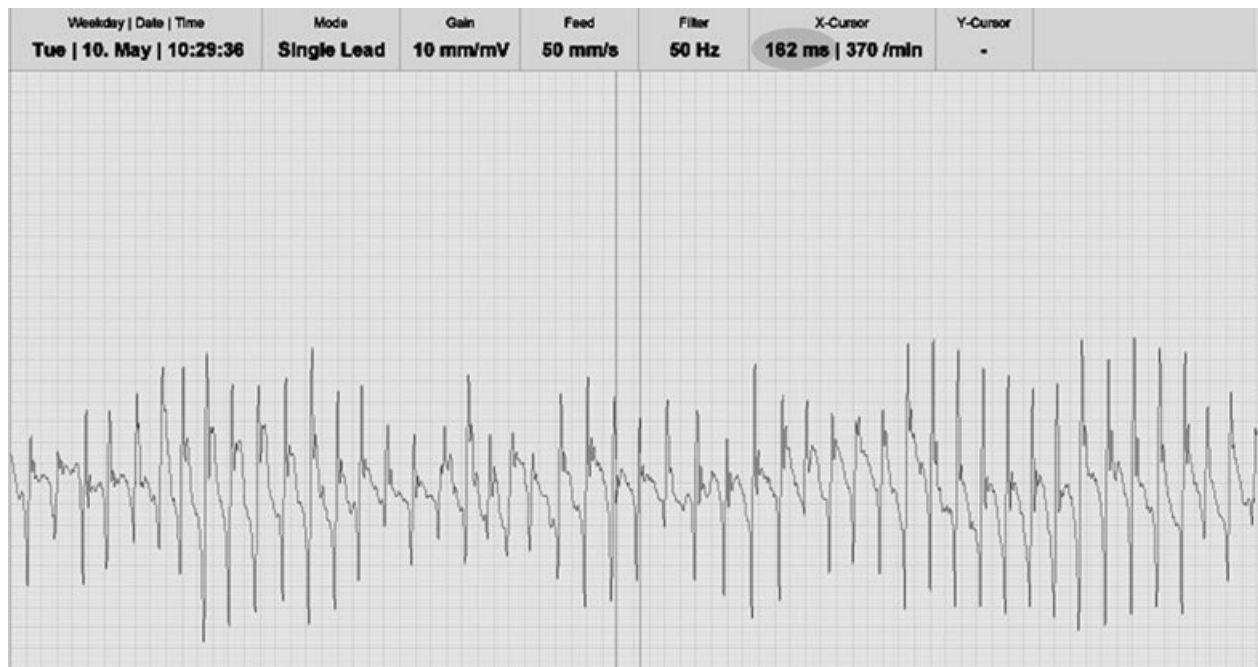


Fig 1. Intra-atrial electrogram from a horse with atrial fibrillation. The atrial fibrillation cycle length is the time (milliseconds) between 2 successive atrial depolarizations. The current measurement indicates an atrial fibrillation cycle length of 162 milliseconds (gray circle) which corresponds to a fibrillation rate of 370/min.

Results

During the study period, 41 horses were presented for AF. Thirteen horses were not treated because the owner denied ($n = 6$) or because of underlying heart disease ($n = 7$). Three horses were treated with QS, administered via a nasogastric tube. In 1 horse QS treatment was terminated because of allergic reactions. In 25 horses TVEC was performed and 23 horses successfully converted of which 3 required preoperative amiodarone administration to achieve cardioversion. In all horses, high-quality intra-atrial electrograms could be recorded and allowed accurate determination of AFCL. Five horses were sedated for catheter placement and measurements were, therefore, excluded from the study. Eighteen horses (8 geldings, 5 mares, 5 stallions; 15 warmbloods, 1 Friesian, 1 Anglo-Arabian, 1 trotter horse) met the inclusion criteria. Three horses had ≥ 30 atrial premature depolarizations within 15 minutes after restoration of SR and received amiodarone IV. None of the horses that received amiodarone for cardioversion showed atrial premature depolarizations immediately postcardioversion. Six horses had rAF which occurred between day 2 and 355 (Table 1). Table 2 shows an overview of all measured parameters.

Values are shown for horses remaining in mSR ($n = 12$; 67%) versus horses suffering from rAF ($n = 6$; 33%). There was no significant difference for mean age, body weight, height at the withers, estimated duration of AF, LLA, RLA, RLAA, LA_{sa}/AO_{sa}, LAA_{sa}/AOA_{sa}, mean AFCL, p5AFCL, p5AFCL/LLA, p5AFCL/LLAA, p5AFCL/RLA,

p5AFCL/(RLA/AO), and p5AFCL/RLAA between horses who remained in SR and those suffering from rAF. The LLAA, RLA_{la}/AO_{la}, and RLA_{la}A/AOA_{la} were significantly higher in horses suffering from rAF. P5AFCL/(RLAA/AOA_{la}), p5AFCL/(LA_{sa}/AO_{sa}), and p5AFCL/(LAA_{sa}/AOA_{sa}) were significantly lower in horses suffering from rAF.

Individual results of mean AFCL as a function of estimated duration of AF are shown in Fig 2. There was a significant negative correlation between mean AFCL and estimated duration of AF (Spearman's rank correlation coefficient -0.628 ; $P = .005$).

Discussion

This study shows that AFCL can be recorded in standing horses. This study describes risk factors for rAF in horses after electrical cardioversion. The ratios of the p5AFCL to the corrected LA sizes and the corrected LA sizes were associated with rAF after restoration of SR.

Recurrence rate after TVEC of horses (56/63 were racehorses) with a median AF duration of 4 weeks is 15% (11/72).⁴ Overall recurrence rate after pharmacologic treatment of racehorses is 30% but appeared 15% for AF of <1 month duration, 14% for AF of <4 months duration, and 62% for horses with AF of more than 4 months.⁵ The recurrence rate in our study (33%), with most horses showing long-lasting AF, was comparable with pharmacologic treatment of AF. The high prevalence of chronic AF in our horse population was probably related to our horse population (16/18 were warmbloods) and the associated sport discipline (most horses used for jumping or dressage). Indeed,

Table 2. Baseline characteristics (mean ± SD) of the horses remaining in SR and those suffering from AF recurrence after transvenous electrical cardioversion.

	mSR	rAF	P value
Number of horses	12	6	—
Age (years)	10.1 ± 3.0	8.7 ± 4.1	.423
Body weight (kg)	571 ± 57	582 ± 70	.727
Height (cm)	170 ± 6	167 ± 9	.443
Estimated duration AF (months)	5.2 ± 4.5	6.6 ± 2.8	.491
LLA (cm)	13.1 ± 0.7	13.6 ± 0.9	.380
LLAA (cm ²)	91.7 ± 13.2	105.9 ± 9.8	.034
RLA _{la} (cm)	12.7 ± 1.2	13.4 ± 0.7	.218
RLA _{la} /AO _{la}	1.68 ± 0.12	1.84 ± 0.16	.022
RLA _{la} A (cm ²)	95.5 ± 14.6	106.7 ± 10.4	.114
RLA _{la} A/AOA _{la}	2.13 ± 0.28	2.61 ± 0.47	.016
LA _{sa} /AO _{sa}	1.04 ± 0.12	1.16 ± 0.11	.056
LAA _{sa} /AOA _{sa}	1.65 ± 0.25	1.91 ± 0.31	.073
Mean AFCL (milliseconds)	166 ± 13	157 ± 28	.351
p5AFCL (milliseconds)	141 ± 13	134 ± 24	.446
p5AFCL/LLA (ms/cm)	11.3 ± 1.6	10.3 ± 1.8	.228
p5AFCL/LLAA (ms/cm ²)	1.58 ± 0.33	1.29 ± 0.31	.095
p5AFCL/RLA _{la} (ms/cm)	11.2 ± 1.5	10.1 ± 1.7	.173
p5AFCL/(RLA _{la} /AO _{la}) (milliseconds)	126.5 ± 16.5	114.4 ± 16.7	.164
p5AFCL/RLA _{la} A (ms/cm ²)	1.52 ± 0.31	1.28 ± 0.30	.141
p5AFCL/(RLA _{la} A/AOA _{la}) (milliseconds)	67.7 ± 13.2	53.2 ± 13.1	.043
p5AFCL/(LA _{sa} /AO _{sa}) (milliseconds)	138.0 ± 19.7	116.1 ± 15.5	.031
p5AFCL/(LAA _{sa} /AOA _{sa}) (milliseconds)	87.7 ± 16.9	71.0 ± 10.9	.044

mSR, maintenance of sinus rhythm; rAF, recurrence of atrial fibrillation; LLA, left atrial diameter or area (LLAA) measured from the left parasternal long-axis view; RLA_{la}, left atrial diameter or area (RLA_{la}A) measured from the right parasternal long-axis view; LA_{sa}, left atrial internal diameter or area (LAA_{sa}) measured from the right parasternal short-axis view; AO_{la}, aortic diameter or area (AOA_{la}) measured from the right parasternal long-axis view; AO_{sa}, aortic diameter or area (AOA_{sa}) measured from the right parasternal short-axis view; AFCL, atrial fibrillation cycle length; p5, shortest 5th percentile; AF, atrial fibrillation.

compared to warmbloods, racehorses with AF are generally younger and AF is often of shorter duration because clinical signs are usually more obvious in racehorses compared to jumping or dressage horses.

The inducibility and sustainability of AF depends on the ability of the atria to maintain a critical number of re-entry circuits.¹⁴ Identified factors in favor of AF are large atrial size, short AERP, and atrial structural disease.^{10,11} In horses, there is no gold standard for determination of the most accurate LA diameter. Therefore, LA sizes from left and right parasternal views were obtained. Atrial sizes were indexed to the aortic size to obtain body size

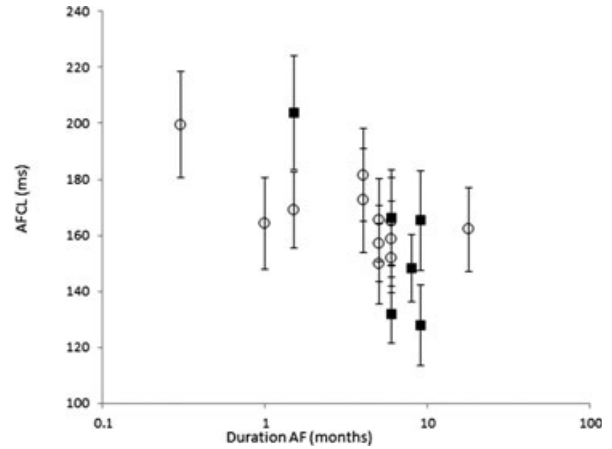


Fig 2. Scatterplot of atrial fibrillation cycle length (AFCL; milliseconds; mean ± SD) as a function of estimated atrial fibrillation duration on a logarithmic scale of horses with recurrence of atrial fibrillation (■) and those remaining in sinus rhythm (○) after successful transvenous electrical cardioversion. There is a significant negative correlation between mean AFCL and estimated duration of AF (Spearman's rank correlation coefficient -0.628 ; $P = .005$).

independent parameters.¹⁵ Similarly as previously reported, larger atria seemed to predispose to rAF,⁵ especially when atrial size was corrected for aortic size.

Since the length of a wavelet circulating in the atria is the product of conduction velocity and AERP, a decrease in either conduction velocity or AERP will lead to an increase in the maximum number of wavelets that can coexist in the atria.¹⁶ AERP can be determined in horses during SR by programmed electrical stimulation using temporary or implanted pacing devices.¹⁷⁻¹⁹ However, during AF this technique cannot be used. AFCL and minimum AFCL (5th percentile of AFCL, p5AFCL) have been shown to be an index of AERP.^{20,21} From reports investigating the effects of AF on atrial electrophysiology it has been concluded that AFCL and AERP shorten with maintenance of AF, and prolong progressively after medical treatment or ablation.^{10,22-24} An experimentally induced AF model in ponies and horses showed that the shortening of AFCL occurs mainly in the first weeks after AF induction.^{12,18,25} Our study in horses with naturally occurring AF confirmed that increasing AF duration was significantly correlated with shortening of AFCL (Fig 2) ($P = .005$).

In humans, AF duration, left atrial size, and AFCL are the most important parameters to predict mSR after cardioversion.^{8,9,26-28} In 2 large studies in horses with AF, AF duration was related to recurrence rate.^{5,7} Our study did not identify AF duration as a significant risk factor for rAF (Table 2). This might be explained by the low number of horses in our study, especially of horses with short AF duration before TVEC.

We obtained AFCL from the RA. In humans, left atrial electrophysiologic measurements are performed

by introducing a catheter in the LA through a transseptal puncture, a procedure that has not yet been done in horses. Besides electrical remodeling, atrial size, and AF duration other factors should be considered in determining the risk of rAF. Documented additional factors potentially triggering and promoting AF are ectopic atrial foci, rotors, and structural remodeling of the atria.^{29,30} Changes in the distribution of the protein connexin 40, myolysis characterized by disruption of the sarcoplasmic reticulum, accumulation of glycogen and the presence of apoptosis or fibrosis have been shown to influence the outcome of cardioversion and rAF in human patients.^{31–33} Also in horses, atrial fibrosis has been associated with AF.³⁴ Currently no additional information is available about the importance of these mechanisms in horses.

Our study included a number of limitations. A first limitation of our study is that baseline AERP (AERP during normal SR) was not measured. We measured AFCL which represents the AERP after electrical remodeling because of AF. AF duration but also individual degree of AF-induced remodeling may differ between horses. In addition, the relation between baseline AERP and AERP in the remodeled atrium may show individual differences. A second limitation of this study was that the presence of atrial structural lesion could not be established. In a number of horses, date of diagnosis of AF by the local veterinarian was used to estimate AF duration. However, as clinical signs of AF are less obvious in warmbloods compared to racehorses, real AF duration was probably even longer.

In conclusion, RA AFCL can be determined in standing horses. Despite the small number of horses, this study shows that recurrence of AF is associated with differences in left atrial size and electrophysiologic characteristics. Pretreatment measurement of these parameters might provide a risk assessment for rAF.

Footnotes

^a GE Vivid 7 Dimension, GE Healthcare, Horten, Norway and a 3S Phased Array Transducer, GE Healthcare

^b Triport; Mansfield EP, Watertown, MA

^c Custom catheter; Rhythm Technologies Inc, Irvine, CA

^d Bipolar intracardiac electrode, USCI; C. R. Bard, Inc, Lowell, MA

^e Engel Engineering Services GmbH, Offenbach an Main, Germany

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