Risk Factors for Recurrence of Atrial Fibrillation in Horses After Cardioversion to Sinus Rhythm

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Background: Although atrial fibrillation (AF) can be successfully treated in horses, recurrence occurs frequently. In humans, atrial function after cardioversion can predict recurrence.

Objectives: To examine the prognostic value of atrial mechanical function at 24 hours after cardioversion and other potential predictor variables for AF recurrence in horses.

Animals: 117 horses treated for AF at 4 referral centers.

Methods: Retrospective study. Inclusion criteria were successful cardioversion, echocardiography at 24 hours after cardioversion and ≥4 months follow-up. To determine factors associated with AF recurrence, a multivariable survival model was built.

Results: 133 AF episodes in 117 horses were included. AF recurred in 36/100 horses with a first AF episode and in 57/133 AF episodes overall. Factors associated with recurrence in horses with a first episode were previous unsuccessful treatment attempt (hazard ratio HR 2.36, 95% confidence interval CI 1.11–4.99, P = .025) and mild or moderate mitral regurgitation (HR 2.70, 95% CI 1.23–5.91, P = .013). When the last AF episode of all horses was included, previous AF (HR 2.53, 1.33–4.82, P = .005) and active left atrial fractional area change ≤9.6% (HR 3.43, 1.22–9.67, P = .020) were significant predictors.

Conclusions and Clinical Importance: The only echocardiographic variable of left atrial function with significant prognostic value for recurrence was low active left atrial fractional area change. Further research is necessary to evaluate whether echocardiography at a later timepoint could provide more prognostic information.

Key words: Echocardiography; Quinidine sulfate; Tissue Doppler imaging; Transvenous Electrical cardioversion.

Atrial fibrillation (AF) is the most important arrhythmia causing poor performance in horses.[1] Heart rates 40–60 beats/minute higher than expected for the work performed are common in horses with AF, resulting in an important performance decrease at peak exercise. In horses performing rigorous work, cardioversion is desirable.[1] In horses used for less intense athletic work, cardioversion is advised if horses have disproportionate tachycardia, QRS broadening or R-on-T phenomenon during exercise, because of the potential risk of these arrhythmias for exercise-associated weakness, collapse, or even death.[2] Over the past decades, differ-

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Abbreviations:

a	maximal atrial contraction
Aduration	A_{peak} duration by tissue Doppler imaging
AF	atrial fibrillation
$Ao_{sx}A$	aortic internal area in short-axis view
$Ao_{sx}D$	aortic internal diameter in short-axis view
A_{peak}	peak atrial contraction velocity by tissue Doppler imaging
CI	95% confidence interval
diast	end ventricular diastole, one frame after mitral valve closure
$FAC_{LA}act$	active LA fractional area change
$FAC_{LA}pas$	passive LA fractional area change
$FS_{LA}act$	active LA fractional shortening
HR	hazard ratio
LA	left atrium
LAA	LA area in four-chamber view
LAD	maximal LA diameter in four-chamber view
$LA_{sx}A$	LA area in short-axis view
$LA_{sx}D$	LA internal diameter in short-axis view
p	at onset P
PW	pulsed wave
QG	quinidine gluconate
QS	quinidine sulfate
SD	standard deviation
Syst	end ventricular systole, one frame before mitral valve opening
tA_{onset}	time from onset electrocardiographic P wave to onset A_{peak} by tissue Doppler imaging
tA_{peak}	time from onset electrocardiographic P wave to A_{peak} by tissue Doppler imaging
TDI	tissue Doppler imaging
TVEC	transvenous electrical cardioversion

ent treatment options have been described. Medical treatment can be performed using quinidine sulfate (QS) administered via nasogastric intubation or quinidine gluconate (QG) administered IV. The use of amiodarone or flecainide has also been described although the success rate for conversion of naturally occurring AF using amiodarone (58%) and flecainide (10%) is rather low and treatment with flecainide can cause dangerous ventricular dysrhythmias. Therefore, these treatments are not routinely used.[3–8] Quinidine sulfate administered via nasogastric intubation has a success rate of 70–89%.[5,9–11] Cases can also be treated by transvenous electrical cardioversion (TVEC), with a reported success rate of 94–99%.[12–14] However, no direct comparison between cardioversion methods can be made from data in literature as the case populations differ between studies.

Atrial contractile dysfunction is evident after cardioversion of experimental and naturally occurring AF in horses, likely because of AF-induced atrial remodeling.[15–17] Atrial myocardial remodeling protects the cardiomyocytes against intracellular Ca^{2+} overload caused by the high fibrillatory rate during AF. Electrical, contractile, and structural remodeling and reverse remodeling after cardioversion occurs in goats and dogs with experimental disease.[18] After cardioversion in horses there is a gradual improvement of atrial contractile function measured by 2D echocardiography and tissue Doppler imaging (TDI).[19] In human medicine, TDI-based left atrial electromechanical conduction time after cardioversion of AF is a predictor of 6-month sinus rhythm maintenance.[20] In horses, AF recurrence occurs in 15–40% after successful treatment.[9–12,21,22] Recurrence rate is independent of treatment modality but influenced by AF duration, atrial size and electrophysiological properties.[9,22] However, a large multicenter study on AF recurrence in horses including different treatment methods and measurements of atrial contractile function is currently lacking.

The primary aim of this study was to determine whether echocardiography at 24 hours after cardioversion could be used to predict AF recurrence in horses successfully treated for AF. In addition, signalment, AF history, cardiac comorbidities such as valvular regurgitation, method of treatment, and administration of drugs at or after cardioversion were included as potential prognostic factors.

Materials and Methods

Study Set-up

A retrospective multicenter study was performed to determine the risk of recurrence after AF cardioversion and associated risk factors. At 4 university referral centers, namely Ghent University (Belgium), New Bolton Center (University of Pennsylvania, USA), University of Zurich (Switzerland) and The Ohio State University (USA), clinical records of horses admitted between January 2005 and May 2013 were retrospectively reviewed for AF cases. Inclusion criteria were successful cardioversion, availability of digitally stored echocardiographic recordings suitable for assessment of left atrial mechanical function performed 24 hours after cardioversion

and after at least 4 months follow-up. Based on the history, racing performance and previous examinations by the local veterinarian, AF duration was estimated and previous AF episodes and treatment attempts were recorded. Follow-up was performed by telephone contact with the horse owners, trainers, or local veterinarians or by follow-up visits to the clinic. Recurrence was defined as the presence of an irregular rhythm consistent with AF detected by cardiac auscultation or AF confirmed by ECG. The follow-up time was defined as the time to recurrence or in horses without recurrence as the time period until the date of interview with the owner or the last veterinary examination.

Echocardiography

In all horses, echocardiography had been performed 24 hours after cardioversion using a similar ultrasound system in the different centers. Offline analysis was performed by a single observer (A.D.) using dedicated software. Measurements included a classification of valvular regurgitation, 2D echocardiographic measurements of left atrial (LA) size and function and tissue Doppler (TDI) measurements of LA function.[15,19,23,24] A detailed description of the imaging and analysis protocol is available online as Data S1.

Statistics

Data are reported as mean ± standard deviation (SD) for normally distributed data or as median (range) for nonnormally distributed data. The underlying assumptions of normality were checked by visual inspection of the raw data plots and by using the Shapiro-Wilk test of linearity and Kolmogorov-Smirnov test of sample cumulative distribution.[a] To determine factors significantly associated with the hazard of AF recurrence, two survival models were built. In a first model, only horses with a first AF episode were included. Predictor variables of interest were: body weight, age, sex, breed (Warmblood, Standardbred or trotter, Thoroughbred, other), use (racing or other), referral center, previous unsuccessful treatment attempt (0/1), previous AF (0/1), AF duration, valvular regurgitation when in atrial fibrillation (none, trivial, mild, moderate), method of treatment (medical or electrical), total dose of quinidine administered, total J administered during TVEC, administration of amiodarone, digoxin, or other antiarrhythmic drugs at cardioversion, administration of ACE-inhibitors, digoxin, dexamethasone or KCl supplementation after cardioversion and the echocardiographic variables measured at 24 hours after cardioversion (Table 1). The group of horses with moderate mitral regurgitation was subsequently pooled with the group with mild mitral regurgitation after it was determined that mild mitral regurgitation was a significant predictor of recurrence. Interactions between predictor variables were examined using chi-square tests for categorical variables, independent t-tests for comparing continuous normally distributed variables in 2 groups or a one-way analysis of variance with post-hoc Bonferroni correction for comparing continuous normally distributed variables in 3 or more groups. Nonnormally distributed data were compared using the Mann-Whitney U-test. Initially, all predictors were tested univariably and hazard ratios (HR) and 95% confidence intervals (CI) were calculated (Cox proportional hazards model). Those predictors with $P < .20$ were withheld for multivariable analysis. Possible associations between these predictor variables were explored by the chi-square test for categorical variables and by Pearson r and Spearman's r_s correlations for continuous variables. For variables with over 60% correlation, only the variable which was most significantly associated with recurrence was included in the multivariable model. This multivariable Cox regression model was built by stepwise backward selection, gradually excluding nonsignificant

Table 1. Echocardiographic measurements of left atrial dimensions and atrial function in 133 AF episodes at 24 hours postcardioversion.

	Mean	SD	N	Reference range*
Heart rate (bpm)	42	7	133	37 ± 5
LADdiast (cm)	11.9	1.3	126	9.9 ± 0.8
LADsyst (cm)	12.7	1.2	126	11.3 ± 0.7
LADp (cm)	11.7	1.2	126	10.6 ± 0.7
LADa (cm)	11.1	1.2	126	9.3 ± 0.7
$FS_{LA}act$ (%)	5.2	2.5	126	12.3 ± 2.1
LAAdiast (cm^2)	90.0	18.2	126	65.0 ± 9.1
LAAsyst (cm^2)	108.9	20.3	126	87.5 ± 9.9
LAAp (cm^2)	85.8	16.9	126	69.9 ± 8.9
LAAa (cm^2)	79.6	16.2	126	57.8 ± 8.0
$FAC_{LA}act$ (%)	7.3	3.3	126	17.4 ± 2.9
$FAC_{LA}pas$ (%)	21.1	4.4	126	20.1 ± 3.1
$LA_{sx}D$ (cm)	10.2	0.92	111	9.5 ± 0.7
$LA_{sx}D/Ao_{sx}D$	1.4	0.13	111	1.4 ± 0.09
$LA_{sx}A$ (cm^2)	126.0	21.0	111	102.1 ± 13.2
$LA_{sx}A/Ao_{sx}A$ (cm^2)	2.5	0.40	111	2.4 ± 0.28
color TDI A_{peak} (cm/s)	2.1	1.2	80	4.3 ± 1.3
color TDI tA_{peak} (ms)	266	45	80	238 ± 28
color TDI tA_{onset} (ms)	200	40	80	164 ± 24
color TDI $A_{duration}$ (ms)	131	19	80	140 ± 16
PW TDI A_{peak} (cm/s)	3.1	1.6	72	5.4 ± 2.9
PW TDI tA_{peak} (ms)	255	46	72	190 ± 21
PW TDI tA_{onset} (ms)	186	40	72	147 ± 12
PW TDI $A_{duration}$ (ms)	149	20	72	126 ± 18

LAD, maximal left atrial diameter from four-chamber view; diast, end-diastole; syst, end-systole; p, at onset P wave on the ECG; a, at maximal atrial contraction; $FS_{LA}act$, active left atrial fractional shortening; LAA, left atrial area from four-chamber view; $FAC_{LA}act$, active left atrial fractional area change; $FAC_{LA}pas$, passive left atrial fractional area change; $LA_{sx}D$, left atrial internal diameter at end ventricular systole from short-axis view; $LA_{sx}D/Ao_{sx}D$, ratio of left atrial to aortic internal diameter at end ventricular systole; $LA_{sx}A$, left atrial area at end ventricular systole from short-axis view; $LA_{sx}A/Ao_{sx}A$, ratio of left atrial to aortic area; A_{peak}, peak velocity during atrial contraction; tA_{peak}, time from onset P to A_{peak}; tA_{onset}, time from onset P to onset A_{peak}; $A_{duration}$, A_{peak} duration.
*Based on previous publications[19,24] and unpublished data ($FAC_{LA}pas$-in 37 horses, age 8 ± 4 years, body weight 552 ± 58 kg).

variables. Wald's test was used to assess parameter estimate significance. Final model variable pair-wise interactions were evaluated and compliance with the assumptions of proportional hazard models was checked by log cumulative hazard plots and Schoenfeld residuals. Kaplan-Meier survival curves were generated to visualize possible associations between the studied factors and recurrence. The follow-up time was used as time variable and AF recurrence was used as outcome variable. Horses with loss of follow-up were right censored at the time of last confirmed AF absence. Continuous variables were both analysed as a continuous variable and as a categorical factor. Categories were based on quartiles. If an ordinal increase or decrease in the hazard was present with each quartile, these parameters were taken forward as continuous. If 1 or more quartiles had significantly different survival curves, these variables were taken forward as categorical data using cut-offs based on the values of the differing quartile(s).

To determine whether horses which already experienced an AF recurrence have a higher risk for AF recurrence after cardiover-

sion, a second multivariable survival model was built using the last AF episode of all horses in the database. The HR and 95% CI were calculated (Cox proportional hazards model). In the multivariable models, significance was set at $P < .05$.

Results

The study included 133 AF episodes that were successfully converted in 117 horses. A detailed description of the study population including AF history and treatment methods is available online as Supplementary Information (Data S1).

The echocardiographic measurements are listed in Table 1. Color and PW TDI measurements were available in 80/133 cases and 72/133 cases respectively. Atrial contractile function based on 2DE (ie $FS_{LA}act$, $FAC_{LA}act$) and TDI variables was impaired compared to the normal reference range.[19,24]

In the group of horses with a first AF episode, horses treated by TVEC showed a significantly higher body-weight, age, and AF duration compared to horses treated medically (Table S1). The left atrial dimensions, time to A_{peak} by color TDI and time to onset A_{peak} by color TDI were also significantly higher (Table S1). Several other interactions between risk factors were present. AF duration was significantly shorter in racehorses (median 21 days, range 2–365) compared to other breeds (median 105 days, range 5–720, $P < .001$). Similarly, significant interactions between referral center, breed, AF duration, and drug treatment were present. Over all episodes, 69% of medical treatments and only 18% of TVEC treatments were performed in racehorses compared to Warmbloods and other breeds. 82% of TVEC treatments were performed at Ghent University and 75% of medical treatments at the New Bolton Center. Amiodarone was exclusively used in Warmbloods, while digoxin was mainly used in Standardbreds and trotters. Horses with mild or moderate mitral regurgitation were predominantly Warmbloods (69%) and showed significantly larger left atrial dimensions compared to horses without and with trivial mitral regurgitation (Table S2).

The recurrence rate, median time to recurrence and median follow-up time are listed in Table 2. Factors univariably associated with an increased hazard of AF recurrence were a previous unsuccessful treatment attempt, mitral regurgitation, higher total dose of quinidine administered, $FAC_{LA}act \leq 9.6\%$, higher $FAC_{LA}pas$, and lower $FS_{LA}act$ ($P < .20$, Table 3, Fig. 1–2). These factors did not show high correlation with each other and were therefore all included in the multivariable model. All other factors were not significantly associated with recurrence.

In the multivariable proportional hazards model based on 100 observations including only horses with a first AF episode, previous unsuccessful treatment attempt (HR 2.36, 95% CI 1.11–4.99, $P = .025$) and mild or moderate mitral regurgitation (HR 2.70, 95% CI 1.23–5.91, $P = .013$) were associated with recurrence. In the multivariable proportional hazards model including the last AF episode of 117 horses, previous AF (HR

Table 2. Recurrence rate and median, minimum and maximum time to recurrence and time of follow-up in all 133 AF episodes and in 100 first AF episodes.

	Recurrence	All cases (n = 133)	First AF episodes (n = 100)
At 4 months	Recurrence	30 (22.6%)	20 (20.0%)
	No recurrence	103	80
At 1 year	Recurrence	47 (42.7%)	32 (39.0%)
	No recurrence	63	50
	Unknown	23	18
Overall	Recurrence	57 (42.9%)	36 (36.0%)
	Time to recurrence (days)	113 (3–1427)	113 (3–1427)
	No recurrence	76	64
	Follow-up time (days)	510 (123–2403)	544 (123–2403)

Table 3. Univariable predictors of recurrence in 100 horses successfully treated for a first episode of atrial fibrillation.

Factor	Level	n	HR	95% CI	P value
Previous unsuccessful treatment attempt	None	81	Reference		
	≥1	19	2.06	0.99–4.27	0.054
Mitral regurgitation	None	40	Reference		
	Trivial	30	1.08	0.44–2.66	0.88
	Mild or moderate	30	2.67	1.22–5.84	0.015
Total quinidine (g) (per unit increase in 1 g)			1.02	1.00–1.04	0.10
$FAC_{LA}act$	>9.6%	22	Reference		
	≤9.6%	73	2.72	0.96–7.70	0.061
$FAC_{LA}pas$ (%) (per unit increase in 1%)			1.09	1.01–1.18	0.030
$FS_{LA}act$ (%) (per unit increase in 1%)			0.91	0.80–1.05	0.19

HR, hazard ratio; $FS_{LA}act$, active left atrial fractional shortening; LAA, left atrial area from four-chamber view; $FAC_{LA}act$, active left atrial fractional area change; $FAC_{LA}pas$, passive left atrial fractional area change.

2.53, 1.33–4.82, P = .005, Fig. 3) and $FAC_{LA}act$ ≤9.6% (HR 3.43, 1.22–9.67, P = .020, Fig. 4) were significant predictors of recurrence. In horses with a second AF episode, the recurrence rate was 36.4% at 4 months and 52.6% at 1 year.

Discussion

This multicenter study describes the outcome of 133 successful AF cardioversions. A multivariable proportional hazards model identified previous unsuccessful treatment attempt and mitral regurgitation as factors associated with recurrence in horses treated for a first AF episode. Considering the risk factors present at the last AF episode, previous AF and atrial contractile dysfunction at 24 hours after cardioversion, assessed by 2D echocardiography, were identified as predictors of recurrence.

The cases described reflect the caseload of the centers involved in the study, as the study was in all centers part of prospective studies investigating atrial contractile dysfunction after cardioversion.[16,19] Therefore, all consecutive cases admitted for cardioversion were included in the study if they met the inclusion criteria. However, these criteria might have introduced a selection bias. Horses with AF recurrence within 24 hours after cardioversion were excluded from the analysis as no 24 hour echocardiography in sinus rhythm was available. AF horses which were not treated because of expected high risk of recurrence were also not included, such as horses with moderate to severe mitral regurgitation and associated LA dilatation.

The recurrence rate of 39% at 1 year after cardioversion in horses with a first AF episode is higher compared to reported recurrence rates in earlier studies, although a recurrence rate of 45% has previously been reported in horses with an AF duration longer than 1 month.[5,9–12,21,22] The majority of horses in our study were Warmbloods with long AF duration, which might explain the higher recurrence rate, although breed, use and AF duration were not significantly associated with recurrence.

However, the multivariable model could have been influenced by interdependence of the various risk factors. For example, AF duration was significantly longer in Warmbloods compared to racehorses. In addition, AF duration was estimated based on the time of diagnosis by the local veterinarian or the onset of signs noted by rider or driver. These signs are often subtle in Warmbloods and thus AF duration might have been underestimated.[2] In the multivariable proportional hazards model including the last AF episode of 117 horses, the effect of AF duration could be masked as owners will recognize the disease earlier in a horse with recurrent AF. However, AF duration was also not associated with recurrence in the model including only horses with a first AF episode.
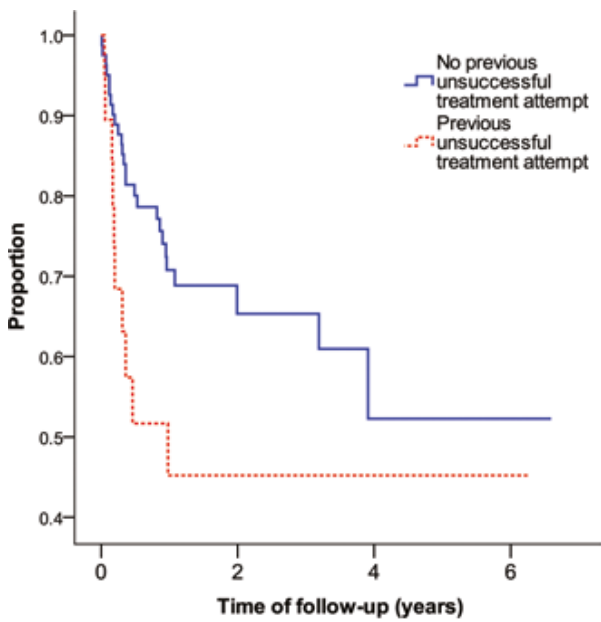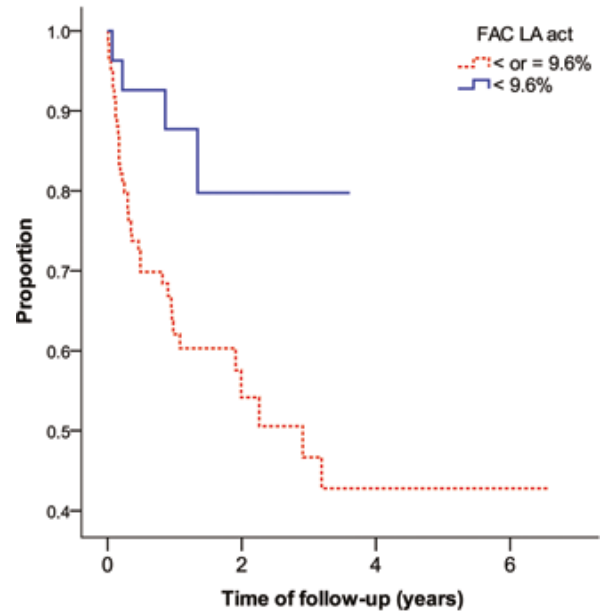
Fig 1. Kaplan–Meier survival curve for horses with a first episode of AF, with no, trivial and mild or moderate mitral regurgitation (n = 100). Proportion of horses without AF recurrence.
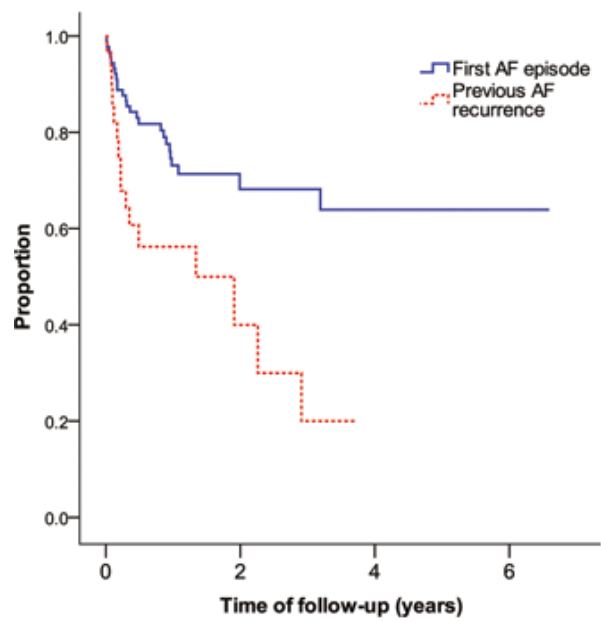
Fig 3. Kaplan–Meier survival curve for horses with a first AF episode or with previous AF, including the last AF episode of all horses (n = 117). Proportion of horses without AF recurrence.
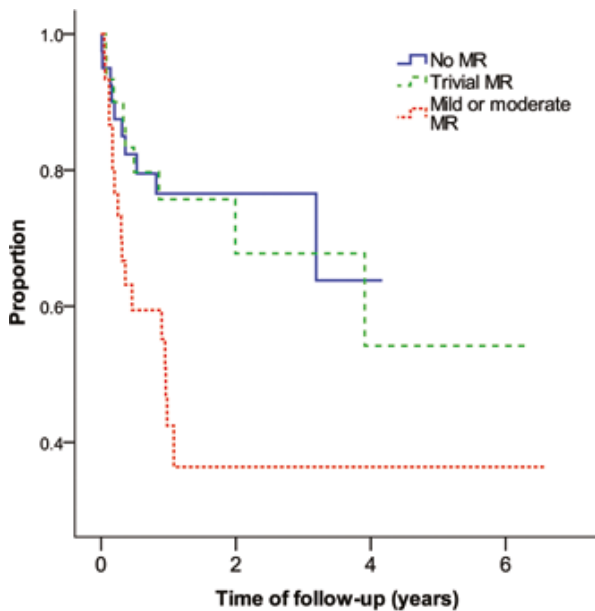
Fig 2. Kaplan–Meier survival curve for horses with a first episode of AF, with and without a previous unsuccessful treatment attempt for cardioversion of AF (n = 100). Proportion of horses without AF recurrence.

Fig 4. Kaplan–Meier survival curve for horses with an active left atrial fractional area change in ≤9.6% or >9.6%, including the last AF episode of all horses (n = 117). Proportion of horses without AF recurrence.

The treatment method (electrical versus medical) was not associated with recurrence. However, the study setup did not fully permit comparison as the treatment method was not randomized but instead reflected the clinicians' preference and typical case population. Quinidine was more often used for horses with short duration AF and racehorses, whereas TVEC was more often used in Warmbloods, horses with long duration AF or horses where previous QS treatment had failed. In 23/133 cases, a previous treatment attempt was reported. In 15 cases, this was unsuccessful medical treatment followed by successful TVEC. Higher success rates of TVEC have been reported in literature, although no direct comparison is available.[9–12,12–14] Antiarrhythmic

drugs were more frequently used in horses deemed more prone to recurrence by the clinician. This interdependence of various factors might have influenced the results of the multivariable model for predicting recurrence, especially concerning the effect of treatment.

We hypothesized that horses with more severe atrial contractile dysfunction at 24 hours after cardioversion would be more prone to recurrence. This time point was chosen as it was deemed to have most clinical applicability. Follow-up at a later time is often not feasible under clinical circumstances. However, the major limitation of echocardiography at 24 hours after cardioversion is the interference with antiarrhythmic drugs. QS shows a long and variable half-life in horses so low plasma concentrations can be expected at 24 hours.[25] QS plasma levels at the time of echocardiography were available in only 6 horses, in which low concentrations were found. The negative inotropic properties of QS have been documented in vivo in several species and are dose-dependent.[26,27] The potential influence of occurrence and severity of adverse quinidine effects was not considered within the scope of this study. The measurements at 24 hours could also be influenced by other antiarrhythmic drugs, such as amiodarone. Amiodarone shows few negative inotropic effects and even showed a positive inotropic effect at high concentrations on isolated atrial cardiomyocytes.[28] Amiodarone is highly lipophilic with a high volume of distribution and long elimination half-life. After a single intravenous dosage, the myocardial concentration decreases quickly when amiodarone is redistributed to fat but a secondary peak in plasma concentrations several hours after administration might be present because of entero-hepatic cycling.[29,30] The influence of TVEC treatment without drug administration on myocardial function is unknown, but no increase in cardiac troponin I levels could be detected at 24 hours after cardioversion in 72 AF episodes.[12] Echocardiography at 24 hours after cardioversion demonstrated atrial contractile dysfunction based on 2D echocardiography (ie $FS_{LA}act$, $FAC_{LA}act$) and TDI variables, similar to that previously reported.[15,16,19]

The factors univariably associated with recurrence in horses with a first AF episode were related to atrial function ($FAC_{LA}pas$, $FAC_{LA}act$, and $FS_{LA}act$), ease of treatment (previous unsuccessful treatment attempt and total quinidine administered) and presence of mitral regurgitation. $FAC_{LA}pas$ is related to left ventricular early diastolic filling. In man, this parameter decreases with age and mitral valve stenosis, whereas early diastolic filling is increased in case of mitral regurgitation.[31,32] The lower $FAC_{LA}act$ and $FS_{LA}act$ associated with recurrence reflect atrial contractile dysfunction. In human medicine, patients with AF recurrence showed deteriorated atrial mechanical function compared to patients in sinus rhythm after 1 month.[33] Left atrial electromechanical conduction time was included in our study as the time to onset and peak A measured by TDI. In our study, the time to onset A and peak A was prolonged at 24 hours after cardioversion compared to reference values.[19] This might be explained by larger atrial size or slower conduction caused by electrical remodelling. However, this variable did not show prognostic value. In man, this variable is a prognostic factor for AF recurrence as well as a predictor for new onset AF.[20,34,35] This might either be explained by the different pathophysiology of AF in human compared to horses or by the fact that echocardiography at 24 hours after cardioversion might be too early to detect differences in reverse remodeling.

The significant association between a previous unsuccessful treatment attempt and recurrence might suggest differences in atrial electrophysiology or the presence of underlying atrial myocardial disease in these horses. It has been demonstrated experimentally that atrial electrophysiological remodeling occurs during AF in horses.[15,36,37] These factors might provide a substrate for AF induction and maintenance. In addition to an AF substrate, triggers such as atrial premature depolarizations are needed for AF induction.[1] No ECG data were included in this study, although the presence of atrial premature depolarizations in the postcardioversion period might also be an important prognostic factor.

Mild or moderate mitral regurgitation was withheld as a prognostic factor in the multivariable model. If only mild mitral regurgitation was considered, a significantly higher recurrence rate was also found compared to none or trivial regurgitation. Mitral regurgitation induces atrial myocardial stretch and has previously been associated with AF in horses.[38] Chronic atrial stretch because of pressure and volume overload leads to changes in the cellular signaling pathways and the composition of interstitial matrix, thereby promoting atrial dilatation and AF in humans, dogs, rats, and presumably horses.[18]

A study limitation was that no echocardiographic measurements during AF were included. These might differ from measurements after cardioversion and would be useful in providing prognostic information before cardioversion is attempted. However, measurements during AF are difficult because of the large RR interval variations which influence cardiac diameters. In addition, the goal was to determine whether atrial contractile dysfunction had prognostic value. While echocardiography at 24 hours after cardioversion might be too early for reliably predicting AF recurrence, echocardiography in the first days to weeks after cardioversion might still be valuable as a prognostic indicator by identifying those horses with slow atrial functional recovery or to determine the period of rest before returning to exercise.[19] However, this was outside the scope of this study. The reliability of echocardiographic measurements might have been increased by using a higher number of nonconsecutive cardiac cycles in all horses.[39] In most horses, three consecutive cardiac cycles were measured as this has been shown in a previous study to yield repeatable results.[19] Finally, no information was included on physical activity during the follow-up period as this was highly variable and could not be reliably recorded to include in the model. Therefore, we have no information on the influence of

exercise on recurrence. Despite these limitations, the study population and study design reflected a realistic clinical scenario, in which not all factors can be controlled and interactions between different factors are inevitable.

Conclusions

After successful treatment of a first AF episode in horses, recurrence occurs in 39% at one year after cardioversion. In horses with a first AF episode, previous unsuccessful treatment attempt and mitral regurgitation were identified as risk factors for recurrence in a multivariable model. When horses with recurrent AF were included, previous AF and low active left atrial fractional area change observed at 24 hours after cardioversion were risk factors for recurrence in a multivariable model. Other echocardiographic measurements also demonstrated atrial contractile dysfunction but were not significant risk factors in the proportional hazards model. However, because of the limitations of this retrospective study, further research is necessary to evaluate whether echocardiography at a later time point could provide more prognostic information.

Footnote

Acknowledgments

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Supporting Information

Additional Supporting Information may be found online in Supporting Information:

Table S1. Comparison of signalment, AF duration, heart rate and echocardiographic variables measured 24 hours after successful cardioversion in horses with a first atrial fibrillation (AF) episode treated by transvenous electrical cardioversion (n = 56) or by medical (quinidine) cardioversion (n = 44).

Table S2. Comparison of signalment, AF duration, heart rate, and echocardiographic variables measured 24 hours after successful cardioversion in horses with no MR (n = 48), horses with trivial MR (n = 34) and horses with mild or moderate mitral regurgitation (MR) (n = 35).

Data S1. Supplementary information regarding methodology (imaging and analysis protocol) and results (detailed description of the study population including AF history and treatment methods).