Ventricular pre-excitation in cats: 17 cases

Sidler, M ; Santarelli, G ; Kovacevic, A ; Novo Matos, J ; Schreiber, Nora ; Baron Toaldo, Marco

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M. Sidler, Med. Vet[a], G. Santarelli, DVM, PhD[b], A. Kovacevic, Dr. Med. Vet[c], J. Novo Matos, DVM, PhD[d], N. Schreiber, Dr. Med. Vet[a], M. Baron Toaldo, DVM, PhD[a,*]

[a] *Division of Cardiology, Clinic for Small Animal Medicine, Vetsuisse Faculty, University of Zurich, Switzerland*
[b] *Department of Clinical Sciences, Faculty of Veterinary Medicine, University of Utrecht, the Netherlands*
[c] *Division of Small Animal Cardiology, Department of Veterinary Clinical Medicine, Vetsuisse Faculty, University of Bern, Switzerland*
[d] *Queen's Veterinary School Hospital, Department of Veterinary Medicine, University of Cambridge, UK*

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Abstract *Objectives:* Atrioventricular accessory pathways are abnormal electrical connections between the atria and ventricles that predispose to ventricular pre-excitation (VPE) and tachycardias.
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Results: Most cats with VPE were male (16/17 cats), non-pedigree cats (11/17 cats). Median age and mean body weight were 5.4 years (0.3—11.9 years) and 4.6 $\pm$ 0.8 kg, respectively. Clinical signs at presentation included lethargy (10/17 cats), tachypnea (6/17 cats), and/or syncope (3/17 cats). In two cats, VPE was an incidental finding. Congestive heart failure was uncommon (3/17 cats). Nine (9/17) cats had tachyarrhythmias: 7/9 cats had narrow QRS complex tachycardia and 2/9 cats had wide QRS complex tachycardia. Four cats had ventricular arrhythmias. Cats with VPE had larger left ($P < 0.001$) and right ($P < 0.001$)

* Corresponding author.
E-mail address: marco.barontoaldo@uzh.ch (M. Baron Toaldo).

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atria and thicker interventricular septum (P = 0.019) and left ventricular free wall (P = 0.028) than controls. Three cats had hypertrophic cardiomyopathy. Treatment included different combinations of sotalol (5/17 cats), diltiazem (5/17 cats), atenolol (4/17 cats), furosemide (4/17 cats), and platelet inhibitors (4/17 cats). Five cats died, all from cardiac death (median survival time 1882 days [2—1882 days]).
Conclusions: Cats with VPE had a relatively long survival, albeit showing larger atria and thicker left ventricular walls than healthy cats.

Abbreviation Table

AP	accessory pathway
CHF	congestive heart failure
HCM	hypertrophic cardiomyopathy
VPE	ventricular pre-excitation
ECG	electrocardiography

Introduction

Accessory pathways (APs) are abnormal sleeves of myocardium allowing an electrical connection between the atria and ventricles bypassing entirely or partially the normal atrioventricular conduction system [1,2]. Accessory pathways can have various locations and they can connect different portions of the atrial and ventricular myocardium or segment of the atrioventricular and ventricular conduction systems, such as the atrioventricular node, the His bundle, and the Purkinje fibers [3]. Moreover, AP can conduct the electrical impulse antegrade (from the atria to the ventricles), retrograde (from the ventricles to the atria), or bidirectionally. If the AP is located between the atrial and ventricular myocardium, and the electrical impulse is conducted antegrade, a ventricular pre-excitation (VPE) may occur. In case of VPE, a supraventricular impulse traveling across an AP bypasses the physiologic atrioventricular nodal delay and spreads gradually to the contralateral ventricular mass, activating the ventricles [3]. On surface electrocardiography (ECG), this aberrant ventricular excitation can result in a shortened PR interval and widened QRS complex containing a slurred upstroke, the delta wave, which represents the portion of the ventricle that is depolarized earlier than expected [3]. In some instances, a premature beat could trigger a macro re-entrant tachycardia, where the AP and the atrioventric-ular conduction system act as the limbs of the circuit. This arrhythmia is called atrioventricular reciprocating tachycardia, and it can be orthodromic (if the AP conducts retrogradely) or antidromic (if the AP conducts antegradely). In the former case, the surface ECG would show a narrow QRS complex tachycardia (in the presence of normal intraventricular conduction), while in the latter case, the tachycardia would have a wide QRS complex appearance [4]. In people, AP-mediated arrhythmias are associated with clinical signs, such as palpitations, fatigue, light-headedness, chest discomfort, dyspnea, presyncope, or syncope, arrhythmia-induced cardiomyopathy, or premature death [4]. Therefore, their detection and correct management are of critical importance.

Accessory pathways have been described in both animals and humans [1—6]. Two large independent studies have described clinical aspects and management in almost 200 dogs [5,6]. In dogs, APs are more often concealed, as they mainly conduct retrogradely, and therefore, VPE is not frequently observed in this species [5—11]. Ventricular pre-excitation has been rarely reported in cats, with sparse case reports present in the literature [12—16]. It has been described with structurally normal hearts, associated with cardiomyopathies, most commonly hypertrophic cardiomyopathy (HCM), congenital heart disease, or hyperthyroidism [8,12—17]. The reported clinical signs can be secondary to the underlying cardiac disease or to paroxysmal tachyarrhythmias mediated by the AP [12—17].

Considering the scarce data available in VPE in cats, we aimed in this retrospective study to describe the signalment, clinical presentation, electrocardiographic and, when available, echocardiographic findings, treatment strategies and survival in cats with an ECG diagnosis of VPE.

Animals, materials, and methods

Study population

The medical databases of four veterinary teaching hospitals were retrospectively reviewed and searched for cats with a diagnosis of VPE.

Keywords used for the electronic search were 'ventricular pre-excitation', 'Wolff-Parkinson-White syndrome', 'WPW', and 'accessory pathway'. Only cats with ECG traces available showing VPE were included. All ECG traces were reviewed by a single board-certified cardiologist (MBT), who confirmed the diagnosis. In the present study, VPE was defined as follows: preserved atrioventricular synchrony, reduced PQ interval duration (<50 ms), increased QRS complex duration (>40 ms) with aberrant morphology, presence of a delta wave [8,17]. Analysis of ST segment and T wave was not performed for this study. These ECG findings are more likely to reflect an atrioventricular node bypass tract connecting the atrial and ventricular working myocardium (Kent bundle) [4,8]. The following data were collected and reviewed from the medical databases: signalment, presenting clinical signs, clinical examination findings, presence of congestive heart failure (CHF), circulating cardiac troponin I concentrations, ECG and Holter findings other than VPE, treatment, and outcome. Thoracic radiographs, when available, were reviewed by a board-certified radiologist at the time of presentation. Outcome, including death, follow-up time, and cause of death were recorded from the database or through a telephonic contact with the owners. Cardiac death was defined as sudden death or euthanasia from CHF or arterial thromboembolism.

A group of healthy age- and body weight-matched control cats was selected from the same electronic databases with the aim of comparing echocardiographic findings. Each center submitted a group of control cats matching their VPE cases. Control cats were breeding cats assessed for pre-breeding scans or cats referred for asymptomatic heart murmurs.

Echocardiography

Echocardiographic studies at presentation were performed by a board-certified cardiologist or a cardiology resident under supervision. All studies were then reviewed by a board-certified cardiologist in each center. The following echocardiographic measurements were recorded: left ventricular end-diastolic and end-systolic internal diameters, fractional shortening, end-diastolic interventricular septum, and left ventricular free wall thicknesses, obtained from a two-dimensional right parasternal short-axis view. Left and right atrial end-systolic maximal internal diameters, and right ventricular end-diastolic internal diameter at the level of the tricuspid valve annulus, were measured from a two-dimensional right parasternal long-axis view. Diagnosis of HCM was made in case of an end-diastolic maximal left ventricular wall thickness $\geq$6 mm [18].

Statistical analysis

Descriptive data are presented for each cat with VPE. Data were tested for normality graphically, and normally distributed data are reported as mean $\pm$ standard deviation and non-normally distributed data as median (range). Between group, comparisons (control cats versus cats with VPE) were analyzed with a two-sample Student's t-test or a Mann—Whitney U- test, as appropriate. Kaplan—Meier survival curve was created to analyze survival time in the entire population. Data were right censored if death was non-cardiac, or if they were lost from follow-up or still alive at the time of writing. The analysis was done with dedicated software[e] and level of significant was set at $P < 0.05$.

Results

Animals and clinical presentation

The database search performed using the previously mentioned keywords retrieved a total of 30 cats. Of these, 13 cats were excluded either because an ECG was not available to review or because of the absence of VPE based on previously established criteria. Therefore, 17 cats with VPE and 15 control cats were enrolled in the study. The most represented breed in the VPE group was European shorthair cats (11/17 cats), followed by Norwegian forest cat (2/17 cats), and one cat of each of the following breeds Oriental shorthair, Main coon, Persian, and Russian blue. In the control group, represented breeds were Bengal (4/15 cats), European shorthair (3/15 cats), Main coon (2/15 cats), Norwegian forest cat (2/17 cats), Sphynx (2/15 cats), British shorthair (1/15 cat), and Persian (1/15 cat). Most cats with VPE were male (14 castrated and two intact) and one was a female spayed. They were 5.4 years (0.3—11.9 years) old, with all but one cat being adults, and they weighted 4.6 $\pm$ 0.8 kg. The control group was well matched for age (6 years [0.6—14 years]) ($P = 0.88$) and body weight (4.6 $\pm$ 0.9 kg) ($P = 0.878$). Most cats presented with non-specific clinical signs, such as lethargy

[e] Prism8, GraphPad Software Inc., San Diego, CA.

Table 1 Signalment, clinical, radiographic, ECG and Holter findings in 17 cats diagnosed with ventricular pre-excitation.

Case	Breed Sex	Age (Y) BW (kg)	Presentation complains	Relevant clinical findings	CHF	Thoracic radiography	cTnI (ng/ml)	ECG	Holter
1	Oriental shorthair MN	5.4 4.4	Dyspnea, syncope, lateral recumbency	HR 160 bpm, T 33.6 °C, tachypnea, pale/ cyanotic MM	Yes	Decompensated cardiomegaly	3.24	Pre-excited SR	Phases of pre-excited SR, phases of narrow QRS complex tachycardia (HR 250 bpm)
2	Main Coon MN	5.1 5.1	Anorexia, lethargy	HR > 300 bpm, galopp rhythm, T 35.7 °C, pale MM	No	/	/	Pre-excited SR (HR 140 bpm); sustained narrow QRS complex tachycardia with P′ inscribed in the ST segment (HR 340 bpm)	Almost constant pre-excited SR (HR 100—150 bpm), rare ventricular escape rhythm during sinus bradycardia
3	Norwegian forest cat MN	14.1 5.5	Anorexia, lethargy, weakness	HR 280 bpm, HM, gallop rhythm	No	Moderate compensated cardiomegaly	0.71	Pre-excited SR (HR 160 bpm); sustained narrow QRS complex tachycardia with P′ inscribed in the ST segment (HR 260 bpm)	Constant pre-excited SR (HR 120—140 bpm); phases of sustained narrow QRS complex tachycardia with P′ inscribed in the ST segment (HR 240—260 bpm)
4	ESH MN	1.9 5.1	Weakness, lethargy, syncope, coughing	HR 120—200 bpm, arrhythmic, HM.	No	/	0.05	Pre-excited SR; non-sustained wide QRS complex tachycardia, suspected pre-excited SVT (HR 333 bpm)	Pre-excited SR, long phases of sustained wide QRS complex tachycardia, suspected pre-excited SVT (HR 350 bpm), some atrial premature beats.

(*continued on next page*)

Table 1 (*continued*)

Case	Breed Sex	Age (Y) BW (kg)	Presentation complains	Relevant clinical findings	CHF	Thoracic radiography	cTnI (ng/ml)	ECG	Holter
5	ESH MN	11.9 4.6	Hit by car	HR 180 bpm, HM, pale MM	No	Compensated cardiomegaly	/	Pre-excited sinus arrhythmia (HR 160 bpm)	Almost constant pre-excited SR, rare supraventricular premature beats
6	ESH MN	12.3 6.7	Deceleration trauma	HR 240 bpm, tachypnea, T 31.5 °C, pale MM.	Yes	Decompensated cardiomegaly	/	Pre-excited SR (HR 180 bpm)	/
7	ESH M	11.9 6.2	Tachypnea, syncope	HR 370 bpm, tachypnea	No	Normal findings	/	Pre-excited SR with (HR 200 bpm); sustained narrow QRS complex tachycardia (HR 375 bpm)	Constant pre-excited SR, some atrial premature beats
8	ESH MN	10.9 4.2	Lethargy, tachypnea, disorientation, tachycardia	HR 200 bpm, tachypnea	No	/	/	Pre-excited SR (HR 180/min); narrow QRS complex tachycardia (HR 330/min)	Alternating SR with and without pre-excitation, phases of narrow QRS complex tachycardia
9	Norwegian forest cat MN	3.5 5.5	Cough	HR 180 bpm	No	PPDH	/	Pre-excited SR (HR 240 bpm)	/
10	ESH MN	5 4.2	Lethargy, anorexia, arrhythmia	HR 120 bpm, arrhythmic	No	Compensated cardiomegaly	0.13	Pre-excited SR (HR 160 bpm); complex ventricular arrhythmia (bigeminy, trigeminy, and VT, HR 220 bpm)	/
11	Persian FS	6.5 3.6	Lethargy, dyspnea	HR 210 bpm, arrhythmic, tachypnea, HM	Yes	/	/	Pre-excited SR (HR 200 bpm)	/

12	ESH MN	2.5 4.5	Lethargy, weakness, diarrhea, vomitig.	HR 300 bpm, tachypnea	No	/	/	Pre-excited SR (HR 140 bpm); sustained narrow QRS complex tachycardia (HR 420 bpm)	/
13	ESH MN	1 4	Lethargy	HR 240 bpm, T 35.1 °C, pale MM	No	/	>24.9	Pre-excited SR, ventricular premature beats, wide QRS complex tachycardia	/
14	ESH M	0.3 2.8	Dyspnea, weakness, lethargy	HR 300 bpm, jugular distension	No	/	/	Pre-excited SR, narrow QRS complex tachycardia	/
15	ESH MN	11.3 5.1	Weakness	HR 180 bpm, arrhythmic, HM	No	/	0.22	Pre-excited sinus tachycardia, ventricular premature beats	/
16	ESH MN	10 4.3	Bradycardia	HR 110 bpm, arrhythmic, HM	No	/	/	Pre-excited sinus bradycardia, ventricular premature beats	/
17	Russian blue MN	7 4.7	Hyporexia, lethargy, arrhythmia	HR 210 bpm, arrhythmic	No	/	/	Intermittent pre-excited SR	/

bpm: beats per minute; BW: body weight; CHF: congestive heart failure; cTnI: cardiac troponin I; ESH: European shorthair; FS: female spayed; HM: heart murmur; HR: heart rate; M: male; MM: mucous membranes; MN: male neutered; PPDH: peritoneal-pericardial-diaphragmatic hernia; SR: sinus rhythm; SVT: supraventricular tachycardia; T: temperature; VT: ventricular tachycardia; Y: years.

(10/17 cats), weakness (5/17 cats), and anorexia (3/17 cats). Three cats had syncopal events. Six cats presented with tachypnea, of these three had CHF (two of them confirmed having lung edema on thorax radiographs, while one had mild pericardial and pleural effusion with dilated right atrium on echocardiography). The remaining three cats with tachypnea were not assessed to have CHF based on either thorax radiographs or echocardiography. Two cats presented for trauma, and VPE was an incidental finding. Cardiac auscultation revealed an arrhythmia in 6/17 cats, gallop sound in 2/17 cats, systolic heart murmur in 6/17 cats, and/or fast regular tachycardia ($\geq$300 beats per minute) in 4/17 cats. Five cats had pale mucous membranes and low rectal temperature. Thoracic radiographs were available in 7/17 cats, 5/7 had cardiomegaly, and 2/7 cats had lung edema. One cat had a peritoneal-pericardial-diaphragmatic hernia, and 1/7 cat had a normal thoracic radiograph. Cardiac troponin I was measured in 6/17 cats with VPE, and it was elevated ($\geq$0.2 ng/mL [19]) in 4/6 cats. Table 1 summarizes the clinical data in the 17 cats with VPE.

Electrocardiographic findings

All 17 cats had at least one lead surface ECG trace showing sinus rhythm, sinus bradycardia, or sinus arrhythmia associated with VPE. In 4/17 cats, pre-excited sinus rhythm was the only observed rhythm abnormality. Additional ECG and Holter findings included: narrow QRS complex tachycardia with a P′ in the ST segment, suggesting an orthodromic atrioventricular reciprocating tachycardia (2/17 cats); wide QRS complex tachycardia with preserved atrioventricular synchrony, evidence of P′ waves, short P′Q interval, and the presence of a delta wave, suggesting a pre-excited supraventricular tachycardia (1/17 cat); narrow QRS complex tachycardia without evidence of P′ waves (5/17 cats); wide QRS complex tachycardia without clear atrioventricular synchrony nor dissociation (1/17 cat); ventricular arrhythmias of variable severity, including single ventricular premature beats (3/17 cats), bigeminy, trigeminy, and ventricular tachycardia (1/17 cat); single atrial/supraventricular premature complexes (3/17 cats) (Table 1, and Figs. 1 and 2).

Echocardiographic findings

Echocardiographic studies were available in 15/17 cats with VPE, therefore only 15 matched-control cats were selected. Cats with VPE had larger left ($P < 0.001$) and right ($P < 0.001$) atrial diameters, and thicker interventricular septum ($P = 0.019$) and left ventricular free wall ($P = 0.028$) than controls. Two cats had a left atrial diameter >20 mm (21 and 23 mm). Three cats (case numbers 5, 15, and 16) had a maximal end-diastolic left ventricular wall thickness of 7.0 mm, 7.5 mm, and 7.6 mm, respectively, and were therefore diagnosed with HCM. Excluding the cats with HCM, cats with VPE still had larger left ($P = 0.002$) and right ($P < 0.001$) atrial diameters, and thicker left ventricular free wall ($P = 0.041$). Additionally, right ventricular end-diastolic internal diameter was larger in cats with VPE when three cats with HCM were excluded ($P = 0.047$). One cat had a left atrial thrombus. Table 2 summarizes the echocardiographic findings in the cats with VPE and control cats.

Treatment and outcome

Treatment strategies are summarized in Table 3 and described as three different treatment protocols, according to the clinician's decision of modifying the therapy based on the patients' response. Antiarrhythmics included sotalol (5/17 cats), diltiazem (5/17 cats), and atenolol (4/17 cats), alone or in combination. Additional medications included furosemide (4/17 cats), platelet inhibitors (aspirin or clopidogrel) (4/17 cats), heparin (1/17 cat), terbutaline (1/17 cat), pimobendan (1/17 cat), and benazepril (1/17 cat). One cat, presented for deceleration trauma, received a single dose of furosemide because of concern of mild pulmonary edema on thoracic radiographs. Four cats received no treatment, while one cat received only short-term intravenous fluid therapy. One cat with sinus bradycardia at the time of presentation was under treatment with atenolol, and this was discontinued.

At the time of writing, 5/17 cats with VPE had died, all of cardiac causes. Causes of death are summarized in Table 3. Median survival time for the entire population was 1882 days (2—1882 days) (Fig. 3). The cat that died two days after admission was presented with a left atrial thrombus and was euthanized due to an arterial thromboembolism despite emergency treatment.

Discussion

Ventricular pre-excitation has been rarely reported in cats [8,12—17]. In this case series, we reported the clinical presentation, treatment, and outcome of 17 cats with VPE. Non-pedigree cats

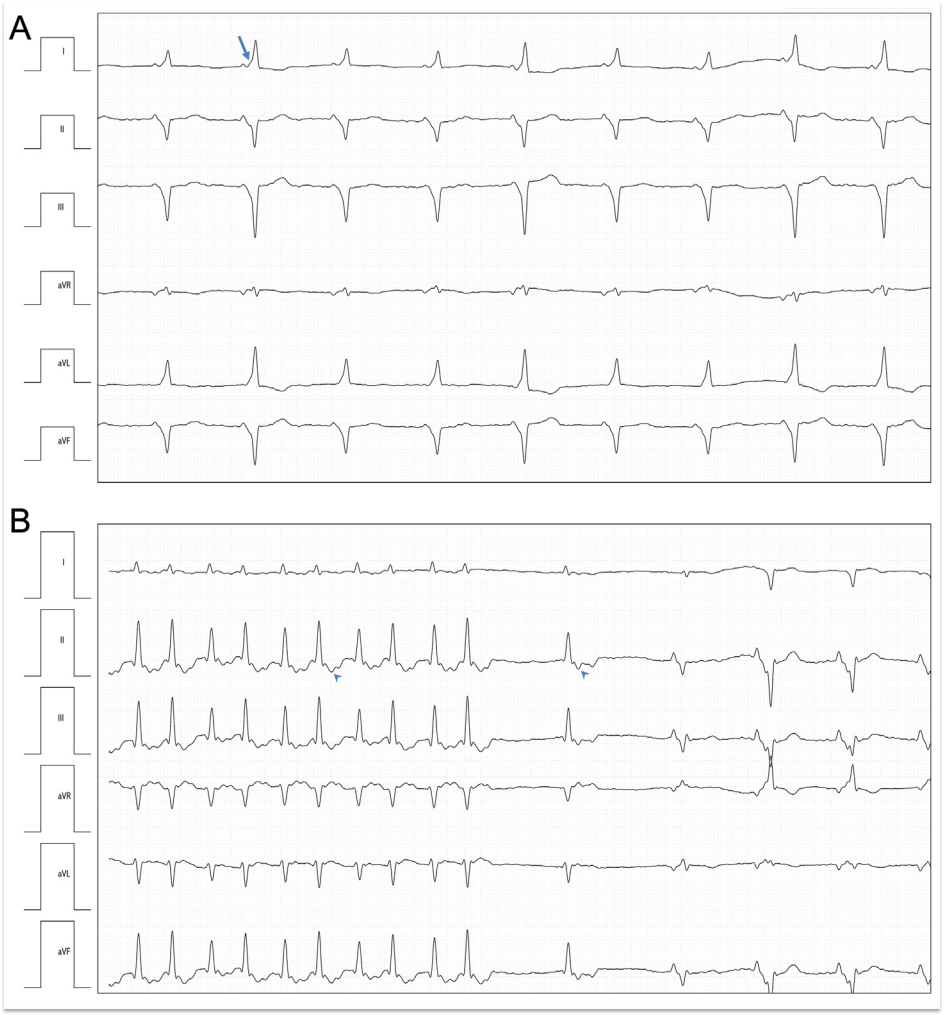

Fig. 1 Surface ECGs of a cat enrolled in the study. Pre-excited sinus rhythm, showing a short PQ interval, wide and bizarre QRS complex morphology, with a slurred upstroke, indicating a delta wave (arrow). Variation in R wave amplitude might indicate different degrees of pre-excitation according to small changes in sinus node cycle length (A). Amplitude 10 mm/mV; paper speed 50 mm/s. Same cat as (A), showing a mildly irregular narrow QRS complex tachycardia with evidence of negative P′ waves (arrowheads) inscribed in the ST segment (orthodromic atrioventricular reciprocating tachycardia). The tachycardia is followed by a pause interrupted by a possible junctional beat. Finally, a pre-excited sinus rhythm with different degrees of fusion occurs (last three beats) (B). Amplitude 20 mm/mV; paper speed 50 mm/s.

were the most represented breed, as previously described [8,12—17]. Male cats were over-represented in our study, but a previous case series [8] and a single case report [16] described female cats with VPE. Therefore, a clear sex predisposition cannot be confirmed. Clinical signs and reasons for presentation were variable in cats with VPE. In our study, and similarly to previous reports [8,12—17], signs can be related to the underlying cardiac disease, and CHF, or they can be more subtle, including lethargy and weakness. Syncope was present in three cats, and it could be attributed to phases of tachycardia, leading to reduced peripheral perfusion, dizziness, and discomfort, as described in cats with atrial fibrillation and supraventricular tachycardia [20]. Severe tachycardia in some cases could also explain tachypnea (if not associated with CHF) and vomiting. In some cases, VPE could not explain the clinical signs, or it was an incidental finding. Indeed, if not associated with tachycardias, the presence of an AP could be missed, as it might be completely asymptomatic.

We described different types of arrhythmias associated with VPE in cats. In most cases, sinus rhythm was constantly pre-excited. Intermittent VPE might occur with changes of heart rate, although other factors may play a role [10]. Since the AP usually has long refractory periods, an increase in heart rate would determine a typical conduction across the atrioventricular node [10].

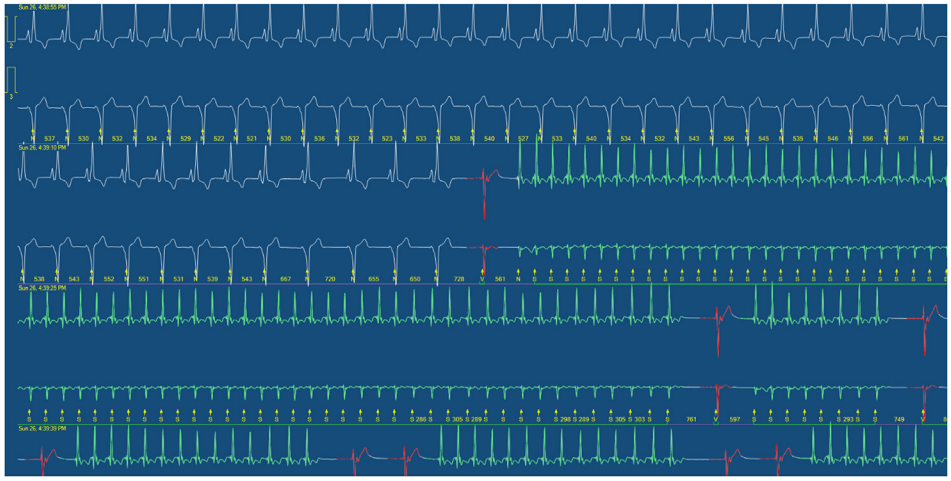

Fig. 2 Holter monitoring of a cat enrolled in the study. Pre-excited sinus rhythm (white complexes, marked with N), alternating with ventricular ectopic beats (red complexes, marked with V), and paroxysmal narrow QRS complex tachycardia (green complexes, marked with S) with negative P′ waves inscribed in the ST segment (orthodromic atrioventricular reciprocating tachycardia). Channels 2 and 3; amplitude 10 mm/mV; paper speed 25 mm/s.

Table 2 Clinical and echocardiographic variables in 15 cats diagnosed with ventricular pre-excitation and 15 healthy controls.

Variable	VPE group	Control group	P value
Age (years)	5.4 (0.3–11.9)	6 (0.6–14)	0.878
Body weight (kg)	4.6 ± 0.8	4.6 ± 0.9	0.871
LA_{max} (mm)	17.5 ± 2.7	14.3 ± 1	<0.001
RA_{max} (mm) (n, 11)	14.1 ± 1.8	11.3 ± 1	<0.001
RVIDd (mm) (n, 12)	8.7 ± 1.6	7.6 ± 1.3	0.068
LVIDd (mm)	17.1 ± 2.8	16.6 ± 1.6	0.610
LVIDs (mm)	10.7 ± 2.5	9 ± 2	0.053
LV FS (%)	39.6 ± 11.9	46 ± 9.8	0.121
IVSd (mm)	4.9 ± 1.2	4 ± 0.6	0.019
LVPWd (mm)	4.5 ± 1.1	3.7 ± 0.5	0.028

IVSd: end-diastolic interventricular septum thickness; LA_{max}: left atrial end-systolic maximal internal diameter; LV FS: left ventricular fractional shortening; LVIDd/s: left ventricular end-diastolic/end-systolic internal diameter; LVPWd: end-diastolic left ventricular free wall thickness; n: number; RA_{max}: right atrial end-systolic maximal internal diameter; RVIDd: right ventricular end-diastolic internal diameter; VPE: ventricular pre-excitation.

Besides pre-excited sinus rhythm, cats in our study frequently presented with tachycardias, that in some cases reached extremely high heart rates (>300/min). Accessory pathways can act as a limb of a re-entrant circuit leading to AP-mediated tachycardia (atrioventricular reciprocating tachycardia) [4]. When the supraventricular impulse reaches the ventricle through the physiological atrioventricular pathways, the QRS complex is narrow, while the subsequent atrial activation is initiated by the electrical impulse driving back through the AP producing a P′ inscribed in the ST segment (retrograde atrial activation), this is called an orthodromic atrioventricular reciprocating tachycardia [4,16]. In our study, this pattern of tachycardia could be observed in two cats, and it has been rarely reported in the literature [16]. Five other cats in our study had paroxysms of supraventricular tachycardia, that could not be further characterized, as no visible P or P′ waves were detected. It is possible that these cats also had paroxysmal non-sustained AP-mediated tachycardia, but other supraventricular tachyarrhythmias such as atrial tachycardia could not be excluded [20]. Moreover, in one cat, we suspected an antidromic atrioventricular reciprocating tachycardia. This arrhythmia occurs when the AP conducts the impulse antegrade from the atria to the ventricles, and the retrograde limb of the circuit is represented by the atrioventricular node

Table 3

Case	Treatment first line	Treatment second line	Treatment third line	Outcome	Survival/Follow-up time (days)
1	Furosemide 1 mg/kg q12h	Sotalol 10 mg q12h	Sotalol 10 mg q12h, Diltiazem 15 mg q12h	Sudden death	493
2	Sotalol 10 mg q12h, Diltiazem 15 mg q8h	Sotalol 10 mg q8h, Diltiazem 15 mg q8h	Unchanged	Alive	1562
3	Furosemide 1 mg/kg q12h, Pimobendan 1.25 mg q12h, Atenolol 6.25 mg q12h	Furosemide 1 mg/kg q12h, Pimobendan 1.25 mg q12h, Atenolol 12.5 mg q12h	Furosemide 1 mg/kg q12h, Pimobendan 1.25 mg q12h, Sotalol 10 mg q12h, Diltiazem 15 mg q12h, Clopridogrel 18.75 mg q24h	Euthanasia for recurrent symptoms	1682
4	Sotalol 10 mg q12h	Sotalol 20 mg q12h, Aspirin 25 mg q48h	Sotalol 20 mg q12h, Aspirin 25 mg q48h, Diltiazem 15 mg q12h	Alive	400
5	No treatment	NA	NA	Alive	2390
6	Furosemide 2 mg/kg once. Management of the trauma	NA	NA	Sudden death	1882
7	Atenolol 6.25 mg q12h, Benazepril 2.5 mg q24h, Aspirin 25 mg, q72h.	NA	NA	Alive	68
8	Atenolol 6.25 mg q12h	Sotalol 10 mg q12h	Unchanged	Alive	1661
9	No treatment	NA	NA	Alive	231
10	Terbutalin 1.25 mg q8h	Drug discontinued	NA	Alive	184
11	Furosemide 2 mg/kg q8h, Pimobendan 1.25 mg q12h, Clopidogrel 18.75 mg q24h	Unchanged	Unchanged	Alive	20
12	Atenolol 6.25 mg q24h	Unchanged	Unchanged	Alive	2250
13	Heparin	NA	NA	Euthanasia due to ATE	2
14	Diltiazem 1 mg/kg q12h	Unchanged	Unchanged	Alive	534
15	No treatment	NA	NA	Alive	599
16	No treatment	NA	NA	Euthanasia due to CHF	1771
17	Fluid therapy	NA	NA	Alive	811

ATE: arterial thromboembolism; CHF: congestive heart failure; NA: not applicable.

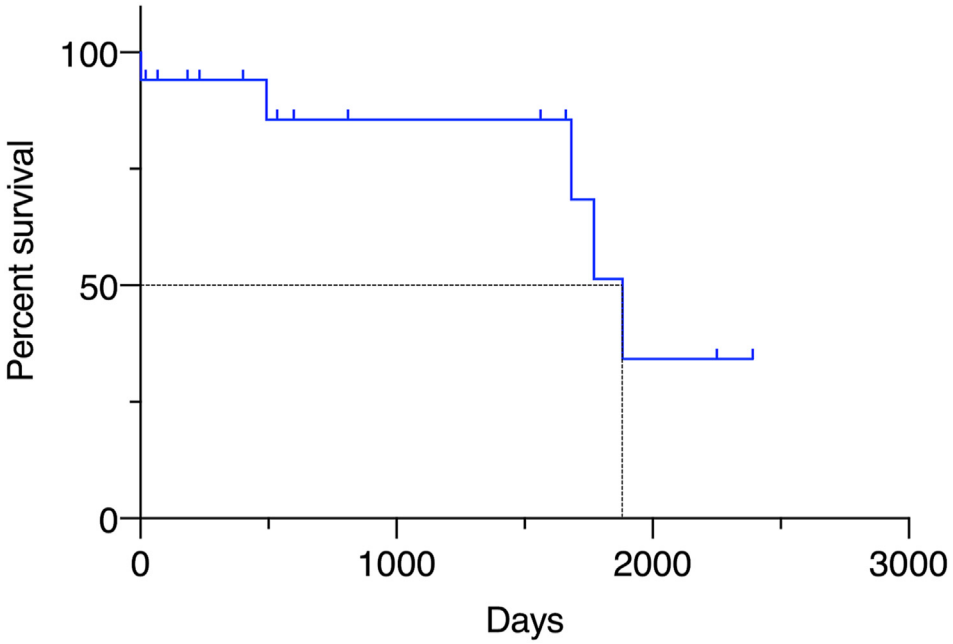

Fig. 3 Kaplan—Meier survival curve for the entire population of cats with ventricular pre-excitation. Cats still alive at the time of writing or cats lost from the follow-up were right censored. Median survival time was 1882 (2—1882) days.

[4]. One cat showed phases of wide QRS complex tachycardia, where no atrioventricular association could be seen. Differential diagnoses for this cat's rhythm are antidromic atrioventricular reciprocating tachycardia, supraventricular tachycardia with aberrancy or pre-excitation, or ventricular tachycardia secondary to myocardial damage [9]. In our study, tachycardias were often sustained with high heart rates, which might explain some of the clinical signs like syncope, weakness, and cardiogenic shock. Additionally, ventricular arrhythmias and atrial premature beats were observed, this might have been secondary to an underlying cardiac disease or associated with arrhythmic-induced myocardial damage. These might have represented a possible trigger for re-entrant tachycardias.

Cats with VPE had larger atria and thicker left ventricular walls than controls. After removing the three cats with HCM from the analysis, both atria and the right ventricle diameters were larger, and the left ventricular free wall was thicker in cats with VPE. These cats could be classified as a cardiomyopathy of non-specific phenotype according to recent guidelines [21]. Alternatively, these changes may be secondary to the observed tachyarrhythmias. Arrhythmia-induced cardiomyopathy occurs in case of sustained tachycardia or frequent arrhythmias leading to a reduced cardiac output and subsequent myocardial remodeling [22]. This condition could potentially resolve if the arrhythmia is adequately controlled. Cats with arrhythmia-induced cardiomyopathy have been rarely documented in the literature [23,24]. However, similar cardiac structural changes to our study were described in a case series of cats diagnosed with supraventricular arrhythmias [20]. Another potential mechanism that might lead to a dilated heart in the absence of tachyarrhythmias is sustained VPE, as seen in our cats. In people, VPE causes interventricular and intraventricular dyssynchrony due to eccentric ventricular activation, which can induce progressive myocardial dysfunction and dilatation, even in cases with normal heart rate [25,26]. These mechanisms might explain the dilatation of the cardiac chambers as observed in this case series, but not the thickened ventricular walls. As concentric wall hypertrophy is not a typical feature of arrhythmia-induced cardiomyopathy, other factors that could clarify this finding are a possible concomitant form of primary left ventricular hypertrophy/HCM as observed in people with VPE [27,28]. Since HCM has a relatively high prevalence in cats, and this increases with age [29], it could be that mild/equivocal forms of HCM were present in our population.

Three cats in our study had an HCM phenotype. Previous reports of cats with VPE showed conflicting data in regard to the presence of structural heart disease [8,12—17]. A previous case series showed that 6/9 cats with VPE had an underlying cardiomyopathy. These included five HCM and one

restrictive cardiomyopathy. However, on that study, the diagnosis of cardiomyopathy was based on post-mortem histological analysis [8]. Other reported cardiac diseases associated with VPE in cats included dilated cardiomyopathy, Ebstein's anomaly with tricuspid valve dysplasia, cardiomyopathy of non-specific phenotype, and not better specified congenital cardiac disease [17]. Uncommonly feline VPE has been described in the presence of a normally structured heart [12,17]. In people, VPE can be associated with an HCM phenotype [27]. Certain HCM phenocopies have been shown to have a high prevalence of VPE, such as metabolic and glycogen storage diseases, like PRKAG2 syndrome and Danon disease [28]. In our study, 3/17 cats had HCM, and this most likely reflects the high prevalence of HCM in cats [29,30]. However, a potential association between VPE and cardiomyopathy cannot be excluded, and larger studies are required to further assess this association.

In our study, treatments were variable and non-standardized, as expected in a retrospective study. Besides heart failure and antithrombotic treatments, eight cats received antiarrhythmics, as monotherapy or in combination. Several classes of antiarrhythmics are recommended to treat atrioventricular reciprocating tachycardias in humans [4]. We mainly selected beta-blockers and diltiazem, for their action in blocking the AP mediated re-entrant circuits. This combination, however, could induce bradycardia, asystole, sinus arrest, QT prolongation, and possibly *torsades de pointes*, and ventricular fibrillation [31], and therefore, in theory, monitoring of QT duration should be considered after initiating this therapy. A possible definitive treatment for AP is represented by endocardial arrhythmia mapping and ablation of the AP insertion on the atrial side. This treatment option has been performed in dogs [5,6], but at the time of writing, it was not available for cats in the authors' institutions and, therefore, never attempted.

Our study suggests that prognosis in cats with VPE was good. Excluding one cat that died two days after presentation with a thromboembolism, all other cats survived a relatively long time, with 12 cats living more than one year after diagnosis, and with a median survival time of the overall population of 1882 days. The other four cats that died during the study period experienced a cardiac death. Prognostic information in cats with VPE are rarely reported in the literature. Data available for four cats from previous reports showed a poor prognosis, with a survival of 2—7 months [17]. Our study offers the largest information about prognosis in cats presented with VPE and it could be clinically useful in the future to help veterinarians and veterinary cardiologists facing this uncommon condition.

The first limitation of our study is its retrospective nature that did not permit standardized treatment strategies and follow-ups. We are aware that ideally, a Holter control for each cat should have been performed after initiating an antiarrhythmic treatment, as it would have offered a more objective assessment. Unfortunately, few cats had Holter controls available for review, and no standardized criteria are established in feline cardiology to assess response to antiarrhythmic therapy. Second, the small number of cases enrolled was larger than other studies, but still relatively low. This affected the survival analysis since only five cats died during the study period. Moreover, since two cats had no echocardiography available, information about underlying cardiac phenotype for these animals was missing. Third, in most cases, cats were admitted for symptoms attributable to VPE. This raised an inclusion bias, as likely the population here described includes mainly animals with symptomatic VPE, while excluding all cats that might have a compensated, and clinically irrelevant VPE. Indeed, in two cats admitted for trauma and one for cough, VPE was an incidental finding. Finally, an invasive diagnosis using endocardial electrical mapping was never attempted in these cats; therefore, more accurate information about the electrophysiologic properties of the AP could not be done.

Conclusions

This study described the clinical presentation and outcome of 17 cats with VPE. Our study suggests that cats with VPE frequently presented with non-specific clinical signs, but syncopal events and CHF can be seen at presentation. The overall prognosis of cats with VPE was good.

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Conflicts of Interest Statement

The authors do not have any conflicts of interest to declare.

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