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Original Article

Phenotypic description of cardiac findings in a population of Dogue de Bordeaux with an emphasis on atrial fibrillation

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ABSTRACT

The aim of this study was to describe the clinical phenotype of Dogue de Bordeaux (DdB) referred for cardiac investigation, with particular reference to the prevalence of atrial fibrillation and associated features. Review of canine medical records of two United Kingdom veterinary referral hospitals identified 64 DdB with available echocardiographic and electrocardiographic (ECG)/Holter data. Atrial fibrillation was documented in 25 (39%) dogs and supraventricular tachycardia was recorded in five (7.8%) dogs. In a subset of 34 dogs, excluding congenital heart disease ($n = 17$), presence of a cardiac mass ($n = 7$) and non-cardiac neoplasia ($n = 6$), 19 (56%) dogs had atrial fibrillation, with a median heart rate of 200 beats per min (bpm) on presentation. Atrial fibrillation was inconsistently associated with cardiac chamber remodelling, but was frequently associated with systolic dysfunction (13/19, 68.4%) and right sided atrial or ventricular dilatation (14/19, 73.7%) in dogs with atrial fibrillation in this subset. No dogs in this subset had right sided atrial or ventricular dilatation in the absence of supraventricular arrhythmia or systolic dysfunction. The absence of structural heart disease in some dogs with supraventricular arrhythmias suggests that an underlying primary arrhythmic process might be responsible for initiating remodelling, although a primary cardiomyopathy cannot be ruled out.

Introduction

The Dogue de Bordeaux (DdB) is a large brachycephalic breed of dog, originating in France. The population and cardiac pathology of DdB in the United Kingdom (UK) has not been well described; however, anecdotal reports suggest that atrial fibrillation (AF) is prevalent in this breed and a recent study suggested that the breed may have a high incidence of sudden and unexpected death (McAulay et al., 2018). The DdB is affected by a range of cardiac conditions, including subaortic stenosis (SAS), tricuspid dysplasia and dilated cardiomyopathy (DCM) (Borgarelli et al., 2006; Höllmer et al., 2008; Martin et al., 2009; Oliveira et al., 2011; Ohad et al., 2013). A breed predisposition to supraventricular tachyarrhythmia has been suggested (Locatelli et al., 2011). In a study by Ohad et al. (2013), all DdB diagnosed with tricuspid dysplasia had AF.

Atrial fibrillation has a complex pathophysiology, whereby functional and structural mechanisms promote electrical re-entry (Brundel et al., 2005). Atrial fibrillation is frequently associated with heart disease; increased atrial dimensions, inflammation, fibrosis, alterations in autonomic tone and ion channel expression promote development of AF. Large breeds of dog might be predisposed to AF because their atrial dimensions provide the critical atrial mass required to support wavelet re-entry (Moore and Spear, 1987; Guglielmini et al., 2000). Atrial fibrillation in the absence of structural heart disease has been described as 'lone' AF (Menaut et al., 2005). Frequent arrhythmia, including AF, can promote cardiac chamber remodelling and a dilated cardiomyopathy (DCM) phenotype, designated tachycardia-induced cardiomyopathy (Shinbane et al., 1997).

Since AF can be a cause, or consequence, of structural or functional disease, clarifying the association of AF with phenotype may be helpful in defining the underlying disease process. This study sought to describe the phenotype of DdB within a cardiac

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referral population, specifically with reference to the prevalence and associated features of AF. We hypothesised that AF is the predominant arrhythmia in DdBs undergoing cardiac investigation and that AF reflects a primary arrhythmia, rather than consequence of structural heart disease. We hypothesised that AF would occur in some dogs in the absence of cardiac chamber remodelling.

Materials and methods

Study group

This study was approved by the Royal Veterinary College Ethics and Welfare Committee, (approval number 1296; date of approval 16th October 2014). The records of The Queen Mother Hospital for Animals, Royal Veterinary College, Hatfield, UK, and Small Animal Teaching Hospital, University of Liverpool, Neston, UK, were searched for DdB presenting to the cardiology services from March 2005 to July 2013. Dogs were excluded if echocardiographic or electrocardiographic (ECG) data were unavailable.

Echocardiography

Echocardiographic examinations were performed as described by Thomas et al. (1993), using a Vivid 7 (GE Healthcare), with simultaneous ECG recording, and reviewed and measured using EchoPAC Clinical Workstation Software (GE Healthcare). Left ventricular measurements were obtained in M-mode using the leading edge to leading edge method (Sahn et al., 1978). The mean of three measurements for dogs in sinus rhythm and five measurements for dogs with arrhythmia were recorded for each variable. Left ventricular systolic and diastolic measurements were normalised to body weight (Cornell et al., 2004). Normalised left ventricular systolic diameter (LVDsn) measurements exceeding 95% confidence interval (CI) predicted values were defined as a marker of systolic dysfunction (LVDsn > 1.26). Normalised left ventricular diastolic diameter (LVDdn) measurements exceeding 95% CI predicted values were defined as a marker of ventricular dilatation (LVDdn >1.85).

The pre-ejection period to ejection time ratio (PEP:ET) was calculated from Doppler interrogation of aortic flow obtained from the left apical five chamber or subcostal view (de Madron, 2015). Left atrial diameter was indexed to aortic diameter (LA:Ao) (Hansson et al., 2002). Right sided dilatation was defined as right ventricular diastolic dimensions exceeding 50% of the diameter of the left ventricle or right atrial dimensions that were subjectively larger than the left atrium in any view (Bright et al., 2005; Menaut et al., 2005; Palermo et al., 2011). If dogs exhibited left ventricular dilatation, right ventricular dilatation was assessed subjectively on the basis of clinical experience.

Pulmonary hypertension (systolic) was diagnosed when Doppler-derived tricuspid regurgitation velocity exceeded 3.1 m/s (>38 mmHg) (Stepien, 2009) and was classified as mild (<50 mmHg), moderate (≥50 mmHg to <80 mmHg) or severe (≥80 mmHg). The aortic valve, outflow tract and Doppler profile were assessed; velocities > 2.5 m/s were considered to be consistent with SAS (Bussadori et al., 2000; Höllmer et al., 2008). Pulmonic valve morphology was assessed according to Bussadori et al. (2000); pulmonic stenosis was defined by pulmonic velocities > 2.25 m/s.

Electrocardiography

ECG data were collected from the original ECG, Holter, echocardiographic timing ECG and attending clinicians' records. Holter data were quantitatively analysed by Laboratory Corporations of America, Ambulatory Monitoring Services. For initial analysis, AF and supraventricular tachycardia (SVT) were described collectively as 'supraventricular arrhythmia' (Santilli et al., 2008). Atrial fibrillation was diagnosed when QRS complexes occurred without periodicity in the absence of P waves or flutter waves (Miller et al., 1999). Supraventricular tachycardia was defined as three or more QRS complexes < 0.07 s duration, occurring regularly at an instantaneous rate > 160 beats per min (bpm), paroxysmally or persistently, and deemed to be physiologically inappropriate by the attending clinician or on review of Holter data with reference to the Holter activity diary. Dogs in sinus rhythm with no evidence of paroxysmal supraventricular arrhythmia on review were classed as 'sinus rhythm'. Ventricular arrhythmia was described as 'isolated' if only individual ventricular premature complexes (VPCs) were identified, or 'complex' if couplets, triplets, bigeminy, trigeminy and/or ventricular tachycardia were documented. Dogs with only isolated VPCs on Holter were dichotomised with a cut off of 100 VPCs/24 h.

Statistical analysis

After initial assessment of the whole population, dogs with congenital heart disease, cardiac masses and non-cardiac neoplasia were excluded from further assessment, and the clinical, echocardiographic and ECG findings of the remaining subset (non-CHDN) were explored further.

Statistical analysis was performed using Prism 6 (GraphPad Software). Data were assessed for normality visually and using the D'Agostino and Pearson omnibus normality test. Normally distributed data were expressed as mean ± standard deviation (SD). Non-normally distributed data were expressed as median and interquartile range (IQR). Normally distributed, continuous data were assessed by one-way analysis of variance (ANOVA). Non-parametric data were compared using the Kruskal–Wallis test and Dunns multiple comparisons test. Fisher's exact test was used to compare differences in proportions of categorical data. Statistical significance was set at $P = 0.05$.

Results

The study included 64 DdB (Fig. 1). Presenting clinical signs are summarised in Table 1. Six of 64 (9.4%) DdB had a prior diagnosis of non-cardiac neoplasia and were examined to evaluate myocardial function prior to chemotherapy. Seven of 64 (10.9%) DdB had a cardiac mass identified echocardiographically. No dogs with a cardiac mass had a prior diagnosis of non-cardiac neoplasia. Cardiac masses were in variable locations and all were suspected to be neoplastic, but only one case (with haemangiosarcoma) was confirmed using histopathology. Seventeen of 64 DdB were diagnosed with congenital defects. Twelve of 64 (18.8%) had SAS (median velocity 3.47 m/s, IQR 2.6–5.4). Five dogs had other congenital defects, including two with patent ductus arteriosus, and one each with pulmonic stenosis, ventricular septal defect and atrial septal defect.

Supraventricular arrhythmia was identified in 30/64 (46.9%) DdB, persistent AF in 25/64 (39.1%) and SVT in 5/64 (7.8%). Dogs with supraventricular arrhythmia had higher heart rates at presentation, more severe left ventricular dilatation and systolic dysfunction, reduced FS% and increased PEP:ET compared to dogs in sinus rhythm (Table 2). Dogs with supraventricular arrhythmia were more likely to have left and/or right sided atrial dilatation, or left ventricular dilatation, than those in sinus rhythm ($P = 0.001$). Dogs with right sided atrial or ventricular dilatation had higher heart rates than those without atrial dilatation (190 ± 77 bpm versus 125 ± 52 bpm; $P = 0.001$). There was no significant difference in the frequency of supraventricular arrhythmia between dogs with or without SAS ($P = 0.117$), other congenital disease ($P > 0.999$), a cardiac mass ($P = 0.433$) or non-cardiac neoplasia ($P = 0.1094$). No dogs with a prior diagnosis of non-cardiac neoplasia had supraventricular arrhythmia.

Systolic dysfunction was observed in 21/64 (32.8%) DdB and left ventricular dilatation in 13/64 (20%) DdB, occurring concurrently in 11/64 (17.2%) cases. Systolic dysfunction was evident in 5/34 (14.7%) DdB classified as having sinus rhythm (no evidence of

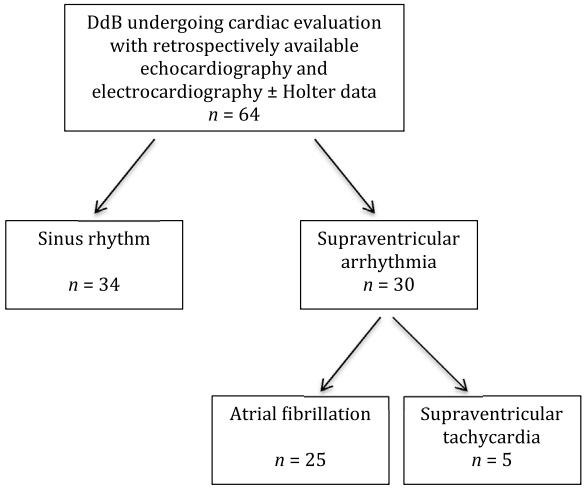

Fig. 1. Summary of 64 Dogue de Bordeaux (DdB) presented for cardiac evaluation. RVC, Royal Veterinary College; UoL, University of Liverpool.