

# Clinical, echocardiographic, and electrocardiographic abnormalities in Boxers with cardiomyopathy and left ventricular systolic dysfunction: 48 cases (1985–2003)

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**Objective**—To identify clinical, echocardiographic, and electrocardiographic abnormalities in Boxers with cardiomyopathy and echocardiographic evidence of left ventricular systolic dysfunction.

**Design**—Retrospective study.

**Animals**—48 mature Boxers.

**Procedure**—Medical records were reviewed for information on age; sex; physical examination findings; and results of electrocardiography, 24-hour ambulatory electrocardiography, thoracic radiography, and echocardiography.

**Results**—Mean age of the dogs was 6 years (range, 1 to 11 years). Twenty (42%) dogs had a systolic murmur, and 9 (19%) had ascites. Congestive heart failure was diagnosed in 24 (50%) dogs. Seventeen (35%) dogs had a history of syncope. Mean fractional shortening was 14.4% (range, 1% to 23%). Mean left ventricular systolic and diastolic diameters were 4.5 cm (range, 3 to 6.3 cm) and 5.3 cm (range, 3.9 to 7.4 cm), respectively. Twenty-eight (58%) dogs had a sinus rhythm with ventricular premature complexes (VPCs), and 20 had supraventricular arrhythmias (15 with atrial fibrillation and 5 with sinus rhythm and atrial premature complexes). Sixteen of the dogs with supraventricular arrhythmias also had occasional VPCs. Morphology of the VPCs seen on lead II ECGs was consistent with left bundle branch block in 25 dogs, right bundle branch block in 8, and both in 11.

**Conclusions and Clinical Relevance**—Results suggest that Boxers with cardiomyopathy and left ventricular dysfunction frequently have arrhythmias of supraventricular or ventricular origin. Whether ventricular dysfunction was preceded by electrical disturbances could not be determined from these data, and the natural history of myocardial disease in Boxers requires further study. (*J Am Vet Med Assoc* 2005;226:1102–1104)

Three clinical categories of cardiomyopathy in Boxers have been described.<sup>1,2</sup> The first 2 are char-

acterized by recurrent arrhythmias of ventricular origin in dogs without any abnormalities of left ventricular size or systolic function. These forms have historically been classified as categories I and II Boxer cardiomyopathy on the basis of whether affected dogs do (category II) or do not (category I) have associated clinical signs (ie, syncope or collapse).<sup>2</sup> Recent studies<sup>3,4</sup> have suggested that categories I and II Boxer cardiomyopathy may be more appropriately referred to as **arrhythmogenic right ventricular cardiomyopathy (ARVC)** on the basis of clinical and pathologic similarities to a disease in humans.

The third clinical category of cardiomyopathy in Boxers (category III) is characterized by congestive heart failure with frequent tachyarrhythmias.<sup>1</sup> Because the original classification scheme was developed before the common use of echocardiography, limited information is available on ventricular dimensions and systolic function in Boxers with category III cardiomyopathy.<sup>1,2</sup> However, 1 study<sup>2</sup> did find that 4 of 5 dogs with category III cardiomyopathy had left ventricular dilatation and decreased left ventricular systolic function. The purpose of the study reported here was to identify clinical, echocardiographic, and ECG abnormalities in Boxers with cardiomyopathy and echocardiographic evidence of left ventricular systolic dysfunction.

## Criteria for Selection of Cases

Medical records of Boxers examined at The Ohio State University College of Veterinary Medicine, North Carolina State University College of Veterinary Medicine, or Texas A&M University College of Veterinary Medicine between 1985 and 2003 were reviewed. Dogs in which a clinical diagnosis of cardiomyopathy had been made by a veterinary cardiologist that also had M-mode echocardiographic evidence of reduced left ventricular systolic function (specifically, left ventricular fractional shortening [FS] < 25%<sup>4</sup>) were eligible for inclusion in the study.

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## Procedures

Information obtained from the medical records included age; sex; physical examination findings (specifically, findings related to physical examination of the cardiovascular system); and results of electrocardiography (ie, rhythm diagnosis and morphology of any ventricular premature complexes [VPCs]), 24-hour ambulatory electrocardiography, thoracic radiography, and echocardiography (2-dimensional and M-mode), when available. Echocardiographic measurements of the left atrium were not included in the present study because of variations among participating institutions in regard to measurement methods.

Left ventricular dilatation was diagnosed when left ventricular systolic and diastolic diameters, indexed to body surface area, exceeded 2.91 and 4.35 cm/m<sup>2</sup>, respectively.<sup>5</sup> The 24-hour ambulatory ECGs were analyzed to identify ventricular and supraventricular arrhythmias and total number of VPCs during the 24-hour measurement period. A ventricular arrhythmia grade ranging from 0 to 4 was assigned as follows: 0 = no VPCs; 1 = single, uniform VPCs; 2 = bigeminy, trigeminy, or both; 3 = ventricular couplets, triplets, or both; and 4 = ventricular tachycardia (ie,  $\geq 4$  consecutive VPCs).

Whether syncope or congestive heart failure had been diagnosed was also recorded. A diagnosis of congestive heart failure was made if left atrial and ventricular enlargement and pulmonary infiltrates consistent with pulmonary edema were seen with or without radiographic evidence of pleural effusion or ascites.

## Results

Forty-eight Boxers met the criteria for inclusion in the study. Of these, 7 (15%) were sexually intact females, 19 (40%) were spayed females, 13 (27%) were sexually intact males, and 9 (19%) were castrated males. Mean age was 6 years (range, 1 to 11 years).

Systolic murmurs were auscultated in 20 of the 48 (42%) dogs. Murmurs ranged from grade 1 to 4 on a scale from 1 to 6. Point of maximal intensity was identified as left basilar in 6 dogs and left apical in 8; point of maximal intensity was not specified for the remaining 6 dogs. A gallop sound was noted in 6 of the 48 (13%) dogs, and an abnormal cardiac rhythm was noted in 28 (58%). A fluid wave consistent with ascites was identified on physical examination in 9 (19%) dogs.

Results of thoracic radiography were available for 28 dogs. The most common findings were generalized cardiomegaly (19 dogs), left atrial enlargement (15), pulmonary edema (14), and pleural effusion (7).

Congestive heart failure was diagnosed in 24 of the 48 (50%) dogs on the basis of thoracic radiographic abnormalities, clinical signs, or both. A history of syncope was reported in 17 (35%) dogs.

Mean FS was 14.4% (range, 1% to 23%). Mean left ventricular systolic and diastolic diameters, measured by means of M-mode echocardiography, were 4.5 cm (range, 3 to 6.3 cm) and 5.3 cm (range, 3.9 to 7.4 cm), respectively. Mean left ventricular systolic and diastolic diameters indexed to body surface area were 4.7 cm/m<sup>2</sup> (range, 2.96 to 6.70 cm/m<sup>2</sup>) and 5.5 cm/m<sup>2</sup> (range, 3.85 to 7.48 cm/m<sup>2</sup>), respectively. Left ventricular systolic

diameter indexed to body surface area exceeded the reference value<sup>5</sup> (2.91 cm/m<sup>2</sup>) in all 48 dogs, and left ventricular diastolic diameter indexed to body surface area exceeded the reference value<sup>5</sup> (4.35 cm/m<sup>2</sup>) in 42 of the 48 (88%) dogs. Four of the dogs had been examined previously because of subclinical ventricular tachyarrhythmias and had had an FS  $\geq 25\%$  at that time but had evidence of left ventricular systolic dysfunction 6 to 30 months later.

For 28 of the 48 (58%) dogs, a sinus rhythm with VPCs was seen on an ECG obtained while the dog was hospitalized. The remaining 20 dogs had supraventricular rhythm disturbances, including 15 (31%) with atrial fibrillation and 5 (10%) with sinus rhythm and atrial premature complexes. Sixteen of these dogs also had occasional VPCs. Morphology of the VPCs seen on lead II ECGs was consistent with **left bundle branch block (LBBB)** in 25 dogs, with **right bundle branch block (RBBB)** in 8 dogs, and with both LBBB and RBBB in 11 dogs.

Twenty-four-hour ambulatory electrocardiography was performed in 27 dogs. Median number of VPCs during the 24-hour period was 1,007 (range, 0 to 15,560). Supraventricular tachyarrhythmias were observed in 2 dogs; one of these dogs did not have any evidence of ventricular arrhythmia (ventricular arrhythmia grade of 0), and the other had occasional single VPCs (ventricular arrhythmia grade of 1). Ventricular arrhythmias were observed in the remaining 25 dogs. Ventricular arrhythmias were classified as grade 1 in 5 of these dogs, grade 2 in 1, grade 3 in 7, and grade 4 in 12.

## Discussion

Arrhythmogenic right ventricular cardiomyopathy, previously termed Boxer cardiomyopathy, has been well documented in this breed,<sup>1,4,6,7</sup> but a less well-known form characterized by left ventricular systolic dysfunction and arrhythmias has also been described.<sup>2</sup> The present study included 48 mature Boxers with cardiomyopathy and left ventricular systolic dysfunction.

The underlying cause of the myocardial disease in the dogs described in the present report was not known. Approximately 20% of human patients with ARVC eventually develop left ventricular dilatation and systolic dysfunction, mimicking dilated cardiomyopathy.<sup>3,8</sup> Similarly, 4 of the dogs in the present report were initially examined because of ventricular tachyarrhythmias and later developed left ventricular dysfunction. However, because of the retrospective nature of the present study, most of the dogs had not previously undergone cardiac evaluations. Thus, our results do not allow us to establish a progression from arrhythmia to left ventricular dysfunction. It is possible, for instance, that some of these dogs had concurrent idiopathic dilated cardiomyopathy or left ventricular systolic dysfunction associated with primary valvular disease. In addition, the role of myocardial carnitine deficiency in Boxers with left ventricular dysfunction is not well understood<sup>9</sup> and was not addressed in the present study.

Ventricular tachyarrhythmias, particularly those with a morphology characteristic of LBBB, are characteristic of

ARVC in Boxers.<sup>1,2,10</sup> Supraventricular tachyarrhythmias also have been reported in Boxers with myocardial disease.<sup>2</sup> In the original description of Boxer cardiomyopathy, approximately 13% of the affected dogs had atrial fibrillation or supraventricular tachycardia.<sup>1,2</sup> Furthermore, atrial fibrillation as well as ventricular ectopy were observed in a family of Boxers with myocardial L-carnitine deficiency.<sup>9</sup>

The morphology of VPCs observed in Boxers with ARVC has previously been described as being consistent with LBBB, with the primary deflection of the QRS complex in leads II, III, and AVF being positive.<sup>1,2,10</sup> On the basis of results of pace-mapping studies, this morphology is believed to be associated with a right ventricular origin for the VPCs in affected dogs and is consistent with right ventricular myocardial disease.<sup>10</sup> However, some of the dogs included in the present study had VPCs with a morphology consistent with RBBB, while others had VPCs with morphology consistent with both RBBB and LBBB. It is possible that dogs with VPCs with RBBB morphology had a ventricular septal site of origin for the ventricular ectopy.<sup>10</sup> It has been suggested that portions of the ventricular septum may produce VPCs similar in morphology to those originating in the left ventricle.<sup>10</sup> It is also possible that dogs with VPCs with RBBB morphology had more substantial left ventricular involvement and that the VPCs in these dogs were of left ventricular origin. Particularly in the present study, for which left ventricular systolic dysfunction was the major selection criterion, ventricular ectopy from a left ventricular origin would be possible.

The frequency of murmurs among dogs in the present study was comparable to that reported previously in studies<sup>1,2</sup> of Boxers with cardiac disease; however, the most commonly auscultated murmur was a systolic, left apical murmur consistent with mitral regurgitation. This murmur was most likely associated with mitral valve regurgitation secondary to left ventricular dilatation. However, without postmortem examination, primary valve disease cannot be ruled out. Possible explanations for the relatively low prevalence of murmurs include the high heart rates at the time of initial examination, difficulties with auscultation of brachycephalic dogs resulting from respiratory noise, and a lack of a thorough physical examination because dogs were examined on an emergency basis. Aortic stenosis is well recognized in Boxers, but physiologic murmurs are also thought to be common in these dogs.<sup>11,12</sup> Doppler echocardiography was not performed on all dogs to detect flow disturbances.

The major criterion for inclusion of Boxers in the present study was echocardiographic evidence of left ventricular systolic dysfunction. Additional measure-

ments that evaluate more global aspects of systolic function, such as ejection fraction, might have further qualified the degree of left ventricular dysfunction. Additionally, no objective measures of right ventricular function were available. An additional limitation of this study was the lack of consistent testing of all animals. For instance, only 27 of the 48 dogs underwent 24-hour ambulatory electrocardiography. Therefore, the extent of arrhythmias in some of the dogs may have been underestimated. Finally, the study was limited by the absence of postmortem examinations. A complete necropsy would have greatly assisted with the classification of these dogs.

In conclusion, we believe that the dogs described in the present report may be representative of the category III Boxer cardiomyopathy as described by Harpster.<sup>1</sup> These dogs had a high prevalence of arrhythmias of supraventricular and ventricular origin as well as a high prevalence of congestive heart failure. Whether ventricular dysfunction is preceded by electrical disturbances cannot be determined from these data, and the natural history of myocardial disease in Boxers requires further study.

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