# Arrhythmogenic Right Ventricular Cardiomyopathy in the Boxer Dog: An Update

Kathryn M. Meurs, DVM, PhD*

**KEYWORDS**

• Boxer • ARVC • Cardiomyopathy • Arrhythmia

**KEY POINTS**

- Boxer arrhythmogenic right ventricular cardiomyopathy (ARVC) is an inherited myocardial disease resulting in ventricular arrhythmias, syncope, and sometimes sudden death; a small number of cases develop left ventricular myocardial dysfunction.
- Familial boxer ARVC has been associated with a deletion in the striatin gene in many families of boxers. Boxers that are homozygous (two copies) for the deletion seem to have more severe disease.
- Treatment is directed to management of the arrhythmia and sotalol and/or mexiletine are the most commonly prescribed antiarrhythmics.
- Although some affected boxers die of sudden death or develop congestive heart failure, many of them develop ventricular arrhythmias and still live a normal lifespan.

Harpster[1,2] first described a myocardial disease in the boxer dog in the early 1980s. It was characterized as a degenerative myocardial disease with unique right ventricular histologic findings that include myocyte atrophy and fatty infiltration. Affected dogs could be asymptomatic or syncopal with ventricular arrhythmias and they sometimes developed congestive heart failure. The disease seemed to have a greater prevalence in certain families of dogs.

More recently, careful evaluation of the disease demonstrated that this myocardial disease in the boxer dog had many similarities to a human myocardial disease called arrhythmogenic right ventricular cardiomyopathy (ARVC).[3] Similarities in clinical presentation, pathologic findings, and etiologic basis supported the reclassification of the disease as boxer ARVC.

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Department of Clinical Sciences, North Carolina State University College of Veterinary Medicine, 1060 William Moore Road, Raleigh, NC 27601, USA
* 1320 Ridge Road, Raleigh, NC 27607.
*E-mail address:* Kate_meurs@ncsu.edu

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## ETIOLOGY

ARVC in the boxer dog is a familial disease apparently inherited as an autosomal-dominant trait.[4] Although mutations that lead to the development of ARVC in humans have been identified in 20 different genes, only one mutation has been identified so far in the dog.[5,6] A genetic deletion mutation in the striatin gene was found to be associated with development of ARVC in many boxers.[6] Striatin is located in the intercalated disk region of the cardiac myocyte where it colocalizes to three desmosomal proteins (plakophilin-2, plakoglobin, and desmoplakin), all known to be involved in the pathogenesis of ARVC in humans. Desmosomes help maintain the structural integrity of the heart by assisting with myocyte adherence and helping to withstand shear forces.[7] Although the specific mechanisms that lead to the development of the fatty fibrous infiltration and arrhythmias in ARVC are not well understood, it has been theorized that abnormalities in desmosomal adherence may lead to cardiomyocyte death, inflammation, and replacement fibrosis.[7]

Although boxer ARVC is known to be an inherited disease associated with a deletion in the striatin gene in many cases, it is also a familial disease inherited with incomplete penetrance and variable expression. Therefore, not all dogs with the striatin deletion actually develop the disease and not all dogs that develop the disease demonstrate the same severity of disease. These phenomena are also observed in humans with this inherited disease. The factors that lead to incomplete penetrance and variable expression are poorly understood but are likely associated with other environmental or genetic factors that impact each individual dog. One factor associated with penetrance and expression is the individual dog's genotype. Dogs that are homozygous for the striatin deletion seem to exhibit a more severe form of ARVC demonstrated by a higher number of ventricular arrhythmias, sudden death events, and in some cases the development of the dilated form of the disease.[6,8]

## CLINICAL PRESENTATION

Boxer ARVC is an adult-onset myocardial disease. Most commonly, dogs are diagnosed between 5 and 7 years of age, although in some cases dogs may be diagnosed at 1 to 3 years of age. There is some indication that very young dogs are more likely to be positive homozygous for the striatin deletion. As originally proposed by Harpster, there seem to be three presentations of ARVC.[1] The first form is characterized by an asymptomatic dog with occasional ventricular premature complexes (VPCs) (**Fig. 1**). The second form is characterized by a dog with tachyarrhythmias and syncope or exercise intolerance. The third form, diagnosed least frequently, is characterized by a dog with myocardial systolic dysfunction and ventricular dilation, sometimes with evidence of congestive heart failure. Although it is likely that these three forms represent a continuum of the disease this has not been well documented. The form with myocardial dysfunction may be more frequently associated with a homozygous genotype for the striatin deletion.

## DIAGNOSIS

There is not a specific single diagnostic test for ARVC but rather, the diagnosis is best based on the presence of a combination of findings that may include the signalment of an adult to middle aged boxer and the presence of a ventricular tachyarrhythmia without other documentable causes for the arrhythmia. A family history of ARVC and a positive genetic test result for the striatin deletion are strong supportive findings, as is a history of syncope or exercise intolerance. However, many affected dogs are