Arrhythmogenic right ventricular cardiomyopathy in Boxer dogs: A retrospective study of survival.

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ARVC in Boxer dogs is a familial disease apparently inherited as an autosomal dominant trait. It is an adult-onset myocardial disease. Affected dogs can have many different presentations ranging from being totally asymptomatic to sudden cardiac death. The aim of the present study was to retrospectively evaluate survival in a population of 62 Boxer dogs with arrhythmogenic right ventricular cardiomyopathy (ARVC), without left ventricular systolic failure, based on the following factors: age of diagnosis, presence of syncopal episodes, Holter arrhythmia classification and administered treatment.

According to this study, the best prognosis is for the younger Boxer without syncope. There were no differences in survival times in relation to the different treatment options used.

The diagnosis inclusion criteria included presence of more than 1000 ventricular premature complexes (VPCs) in 24 hrs Holter recording and normal left ventricular chamber on echocardiographic examination. Some dogs also presented syncope or exercise intolerance and/or VPCs with increased complexity (couplets, triplets) and/or ventricular tachycardia (VT). The Kaplan-Meier method and plot time to event curves were used to estimate survival function. Survival time differences were assessed by log Rank test. The crosstabs, Fisher's exact test and odds ratio were used to estimate risk of death within a year. A Cox regression multivariable analysis (stepwise method for variable selection) was done. A P value <0.05 was considered significant. The statistical analyses were performed using a commercially available software program: SPSS version 19.0.

There was a significant association between median survival time (MST) and VT (P< 0.001); between survival and the number of VPCs in Holter monitoring (P=0.01); between survival and Holter class (P=0.03); between survival and presence or absence of syncopal episodes (P=0.012) and, finally, there was a significant association between survival and age at initiation of treatment (P<0.001). **Figure 1 & 2** There were no differences with regards to survival, among the three treatment options used, with a MST of 365 days for sotalol treatment, a MST of 365 days for mexiletine plus atenolol treatment and a MST of 547 for procainamide treatment. The probability of death within a year (odds ratio), of dogs with VT class II is 20 times greater (95% CI= 4-99.5; P<0.001) than in the group of dogs with VT class I. The probability of death within a year, of dogs with VPCs class B is 5.43 times greater (95% CI= 1.79-16.46; P=0.004) than in the group of dogs with VPCs class A. The probability of death within a year, of dogs with syncope is 4.875 times greater (95% CI= 1.48-15.99; P=0.013) than in dogs without syncope. The hazard ratio, for the complete duration of the study, calculated by Cox proportional hazard multivariable analysis, for VT was 4.8 (95% CI= 2.63-8.99; P<0.001). The hazard ratio, for one year, calculated by Cox proportional hazard multivariable analysis, for VT was 6.05 (95% CI= 2.92-12.51; P<0.001). There were no other variables (VPC, presence/absence of syncope, Holter class) statistically significant for this Cox proportional stepwise method.

The fact that Boxers with ARVC and syncope live less time, has been proved in the present study; the probability of death within a year is 4.875 times greater for dogs with syncope. In this report, it has been found that VT means a high risk of death within one year. It is probable that VT

degenerate into VF leading to sudden death in the dogs used in this study. Even though this disease seems to be progressive in nature in this report a better survival in younger dogs is found. One reason besides lack of evidences of inflammatory response could be that early treatment (drug and restriction of vigorous exercise) was able to slow down the progression of the disease. The presence of frequent VT episodes was associated negatively with survival in this study, unlike the findings reported in other studies. On the other hand, this was a retrospective cohort study with a fixed sample size and was susceptible to bias. Because of the retrospective nature we cannot establish a progression from arrhythmia to other forms of left ventricular dysfunction. As regards treatment, this study only considered the effect of the different protocols on survival time. It did not consider other clinical factors (e.g., frequency of syncope) that could improve the overall condition of the animal prior to death.

This study shows a MST significantly longer in young Boxers with ARVC, in dogs without syncopal episodes, and in the VT class I group. As regards therapeutic options there were no statistically significant differences in MST between the three groups. As far as the probability of death within the first year after diagnosis is concerned, this risk is doubled for cohort of dogs with syncope and VPCs more than 10.000 per day and 6 times more for dogs with VT episodes over 200 per day. The results of the present study could be useful as prognosis guide for general veterinarians.

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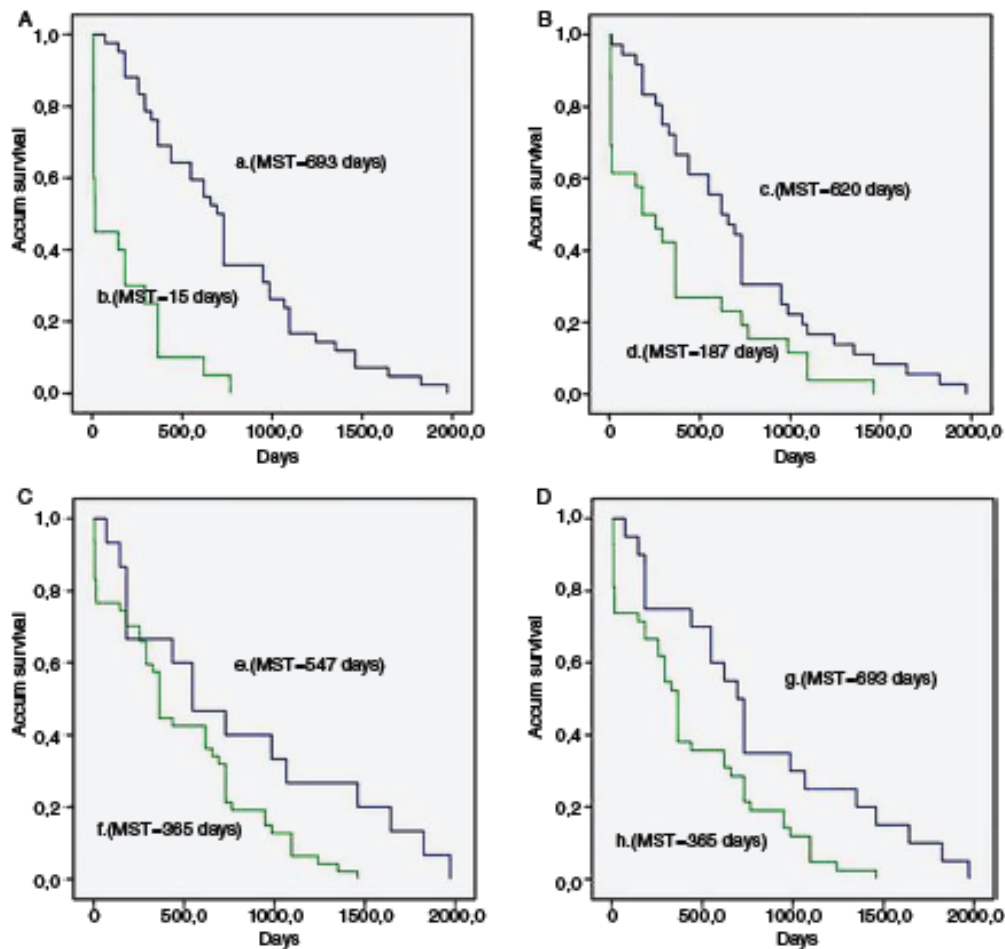
Figure 1: Kaplan-Meier survival curves in the Boxer dogs with ARVC according to:
(A) VT classification
   a.   Kaplan-Meier survival curve in ARVC dogs, VT class I
   b.   Kaplan-Meier survival curve in ARVC dogs, VT class II
(B) VPC classification
   c.   Kaplan-Meier survival curve in ARVC dogs, VPC class A
   d.   Kaplan-Meier survival curve in ARVC dogs, VPC class B
(C) Holter classification
   e.   Kaplan-Meier survival curve in ARVC dogs, Holter class 2
   f.   Kaplan-Meier survival curve in ARVC dogs, Holter class 4
(D) Presence or absence of syncope
   g.   Kaplan-Meier survival curve in ARVC dogs without syncope
   h.   Kaplan-Meier survival curve in ARVC dogs with syncopal episodes
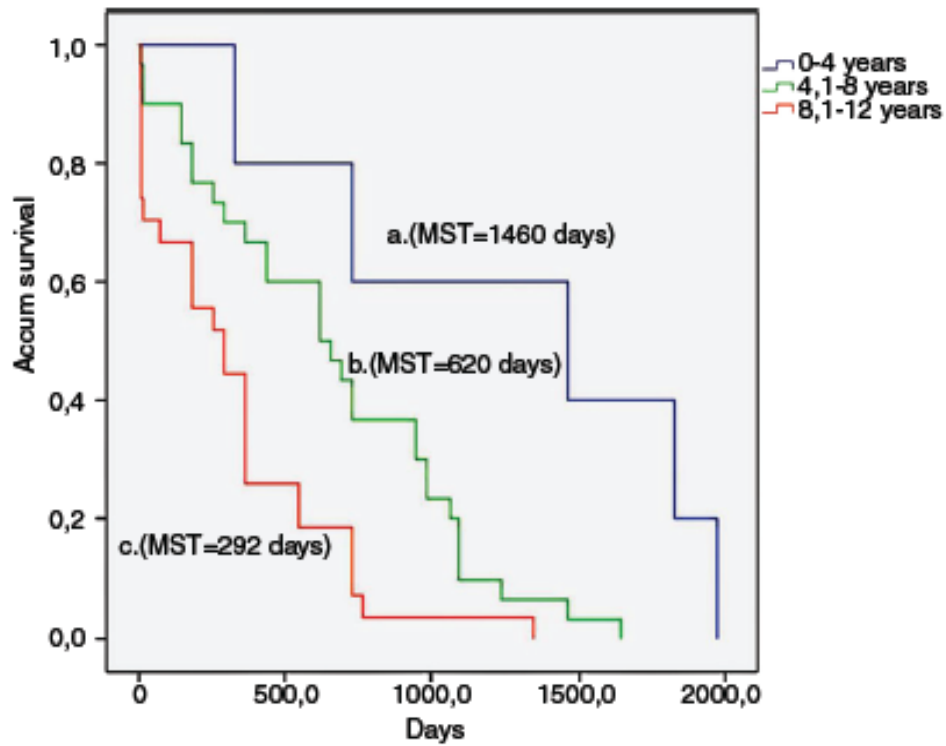
Figure 2: Kaplan-Meier survival curves in the different groups of Boxer with ARVC according to age of initial diagnosis.

  a. Kaplan-Meier survival curve in ARVC dogs younger than 4 years old
  b. Kaplan-Meier survival curve in ARVC dogs between 4 and 8 years old
  c. Kaplan-Meier survival curve in ARVC dogs older than 8 years