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Electrocardiographic abnormalities are frequently detected in healthy adult Borzoi with a normal echocardiogram

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OBJECTIVE
Borzoi reportedly experience sudden death. The objective of this study was to report ECG intervals, amplitudes, and frequency of ECG abnormalities in clinically healthy Borzoi.

METHODS
98 clinically healthy Borzoi were prospectively recruited and underwent echocardiogram, ECG, and cardiac troponin I testing between October 2020 and December 2022. Standard ECG measurements were obtained. Early repolarization notches and slurs were recorded.

RESULTS
Of 82 Borzoi with a structurally normal echocardiogram, ventricular arrhythmias were documented in 8 (10%) dogs, all of which had normal cardiac troponin I concentrations. Median P wave duration was 55 milliseconds (range, 45 to 70 milliseconds). Median PR interval was 125 milliseconds (range, 80 to 175 milliseconds). Thirty-one (38%) Borzoi had first-degree atrioventricular block (PR interval > 130 milliseconds). Median QRS duration was 65 milliseconds (range, 48 to 90 milliseconds). Median QT interval was 235 milliseconds (range, 185 to 275 milliseconds). Twenty-nine (35%) and 15 (18%) of 82 Borzoi had QT intervals > 240 or > 250 milliseconds, respectively. Sixty-seven of 82 (82%) Borzoi had early repolarization notches or slurs. Seventeen of 82 (21%) Borzoi had an abnormality of the ST segment, most commonly convexity/doming. Convexity of the ST segment was intermittent (n = 9) or persistent (4).

CONCLUSIONS
Ventricular arrhythmias, early repolarization, prolonged QT intervals, and ST segment abnormalities are not infrequent in clinically healthy Borzoi. P, PR, and QRS durations are commonly prolonged compared to general canine reference intervals.

CLINICAL RELEVANCE
Future study into heritable channelopathies in Borzoi is warranted given the frequency of ventricular arrhythmias, repolarization abnormalities, and sudden death in the breed. Breed-specific ECG reference intervals are needed.

Keywords: sighthound, Brugada, long QT syndrome, sudden death, ventricular arrhythmia

Borzoi are athletic sighthounds that are reportedly predisposed to dilated cardiomyopathy (DCM), ventricular arrhythmias, and sudden death.[1,2] In humans, approximately 85% of sudden deaths have an underlying cardiac origin.[3] Coronary artery disease, the leading cause of sudden cardiac death (SCD) in humans, is rarely identified in dogs and unlikely to play an important role in SCD in this species. Cardiomyopathies and cardiac channelopathies, on the other hand, are recognized causes of SCD in humans, some of which have established corollaries in veterinary medicine.[4]

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With regard to cardiomyopathies, both DCM and arrhythmogenic right ventricular cardiomyopathy are known causes of SCD in dogs, similar to humans. Cardiac channelopathies leading to SCD in humans include long QT syndrome (LQTS), short QT syndrome, Brugada syndrome, and catecholaminergic polymorphic ventricular tachycardia.[3] Cardiac channelopathies are rarely recognized in veterinary species; however, heritable ventricular arrhythmias have been identified in young dogs of several breeds, including German Shepherd Dogs,[5] Rhodesian Ridgebacks,[6] and Leonbergers,[7] and LQTS has been reported once in a single family of English Springer Spaniels.[8]

In the Borzoi breed, athleticism must also be considered when interpreting an increased tendency for ventricular arrhythmias and possible SCD. Borzoi may actively train and compete in high-level athletic competition, particularly in sprint-type events such as lure coursing. In human athletes, physiological remodeling in response to exercise can result in a proarrhythmic state.[9] This can be attributed to sporting events serving as an arrhythmia trigger when a preexisting cardiac condition already exists, physical activity promoting the development or progression of an arrhythmic substrate, or exercise in and of itself serving as an arrhythmia substrate inducer.[9] Both canine athletes and canine exercise physiology models have demonstrated the potential for increased susceptibility to ventricular arrhythmias.[10–12]

The recognition of an early repolarization pattern is also a common ECG finding in human athletes; however, the pattern of early repolarization is then subclassified as benign or malignant on the basis of the appearance of the ST segment following the early repolarization notch or slur, also termed a J wave.[13] The malignant early repolarization form exhibits a horizontal or down-sloping ST segment following the notch or slur and is associated with idiopathic ventricular fibrillation and increased mortality, whereas a rapidly ascending ST segment is considered benign.[13] Early repolarization patterns have not been widely investigated in dogs. Historically, J waves have been largely considered a normal variant in dogs, with 1 study[14] demonstrating that the frequency of J waves varies on the basis of breed. The morphology of the ST segment following J waves has not been described in dogs.

The objective of the present study, therefore, was to report ECG intervals, amplitudes, and the frequency of ECG abnormalities in a sample of clinically healthy adult Borzoi. We also aimed to investigate the frequency of early repolarization and ST segment abnormalities in Borzoi.

Methods

Clinically healthy, adult Borzoi were prospectively recruited as part of a larger prospective cohort study[2] between October 16, 2020, and December 1, 2022, and underwent a standard echocardiogram, a 3-minute ECG, and cardiac troponin I (cTnI) testing. Dogs were enrolled either on-site at Texas A&M University's Small Animal Veterinary Medical Teaching Hospital or off-site at the 2022 National Borzoi Specialty Show cardiac screening event. The study was approved by the Texas A&M University IACUC (protocol 2020-0032 CA). All owners provided informed signed consent.

Demographic data, medical history, and exercise/training level over the preceding 6 months were provided by owners. The training level was assessed by use of an athletic training score as follows: 0, sedentary, minimal activity (ie, only goes outside to urinate/defecate, no walks, no training); 1, mild, sporadic activity (ie, walks < 2 miles 1 to 3 times/wk, no training); 2, moderate, regular activity (ie, walks 2 to 4 miles, 3 or more times/wk); 3, rigorous, regular activity (ie, spends majority of day running on land, moderate level of training/competing, walks/runs > 4 miles, 3 or more times/wk); and 4, high-level athlete, regular high-intensity training (ie, 5 to 7 d/wk of rigorous training, the most active of dogs).

Three-minute, 6- or 12-lead[15] ECGs were recorded in unsedated dogs lying in right lateral recumbency with a digital ECG system (Beecardia digital ECG; Witalize Ltd) and stored on the cloud-based system of the manufacturer. Standard ECG measurements were obtained by a board-certified cardiologist (BJ) offline in lead II at a paper speed of 50 mm/s with the automated "smooth" high-pass (50-Hz) ECG filter removed. Measurements included P wave duration (milliseconds) and amplitude (mV), PR interval (milliseconds), QRS duration (milliseconds), R wave amplitude (mV), and QT interval (milliseconds), as previously described.[16] Specifically, the QT interval was measured from the onset of the QRS depolarization to the end of the T wave. QT interval was corrected (QTc) by use of the Van de Water formula.[17] The ST segment was characterized by consensus of 2 board-certified cardiologists (BJ and SW) as previously described,[18] including the presence or absence of ST segment deviation, type of deviation (depression or elevation), morphological pattern of depression (horizontal, down-sloping, or up-sloping) or elevation (horizontal, concave, or convex), and maximal amplitude of the ST segment deviation (mV). If subtle variability existed in the ST segment morphology across the 3-minute ECG tracing, the predominant morphology was selected for characterization. The presence or absence of an early repolarization notch (defined as a low frequency deflection at the end of the QRS complex) or slur (an abrupt change in the slope of the last deflection at the end of the QRS complex) as defined by the American Heart Association was also recorded.[19] The T wave polarity was characterized in each dog as positive, negative, or biphasic on the basis of its appearance in lead II.

Standard echocardiograms including 2-D, M-mode, and Doppler imaging were performed in all dogs, with echocardiographic findings in this sample previously described.[2] Borzoi with structural cardiac abnormalities were excluded from analysis of the structurally normal group, but ECG abnormalities appreciated in this sample of Borzoi are provided in descriptive fashion.

Venous blood samples were obtained and immediately processed and aliquoted. Samples obtained off-site were immediately frozen at 0 °C for the duration of the clinic, then transferred frozen on dry ice and stored at –80 °C. Samples obtained on-site were immediately frozen at –80 °C after processing. High-sensitivity cTnI (HS-cTnI) was measured on stored samples as a batch analysis with a commercially available assay that has been validated in dogs at the Texas A&M Gastrointestinal Laboratory.[20]

Statistical analysis

Electrocardiogram data and HS-cTnI levels in Borzoi with structurally normal echocardiograms is presented as median (range) or proportion, where applicable. Simple linear regression was performed to examine the influence of exercise training on the basis of the athletic training score (the independent variable) on the QT and QTc intervals (the dependent variables). The assumption of linearity was confirmed by examining a graphical analysis of residuals. Regression equations and their associated unstandardized coefficients (with 95% CIs), SE, and T statistic were calculated. An ANOVA table was derived (based on 1 degree of freedom) to calculate F statistics and P values for both simple linear regression equations and to determine how well the regression models fit the data. The coefficient of determination or R^2 and SE of the estimate were also calculated for each simple linear regression equation. All analyses were performed with standard programs (Excel, version 16.82, Microsoft Corp; Online Statistics Calculator, DATAtab).

Table 1—Median and range values of standard ECG measurements in 82 clinically healthy adult Borzoi with a structurally normal echocardiogram recruited between October 16, 2020, and December 1, 2022.

ECG measurement	Median	Range
P wave duration (ms)	55	45–70
P wave amplitude (mV)	0.28	0.14–0.45
PR interval (ms)	125	80–175
QRS duration (ms)	65	48–90
R wave amplitude (mV)	1.96	0.45–3.7
QT interval (ms)	235	185–275
QTc interval (ms)	270	223–304
Average heart rate (bpm)	100	60–160

bpm = Beats per minute. QTc = Corrected QT.

Results

Electrocardiograms and echocardiograms were obtained for 98 Borzoi. The ECG was a 6-lead trace in 88 dogs and a 12-lead trace in 10 dogs. Eighty-two Borzoi had a structurally normal echocardiogram, while 16 had echocardiographic abnormalities, including occult DCM (n = 8), equivocal DCM (1), stage B1 myxomatous mitral valve disease (5), mild tricuspid valve dysplasia (1), and equivocal subaortic/aortic stenosis (1).

Descriptive data representing the median and range of standard ECG intervals and amplitudes in structurally normal Borzoi were derived **(Table 1)**. The median age of the structurally normal sample was 2.8 years (range, 1.0 to 11.4 years), and the median weight was 32.9 kg (range, 21.3 to 49.8 kg). There were 49 females (3 spayed) and 33 males (2 neutered). The exercise/training level was rated as 0 (n = 1), 1 (10), 2 (32), 2.5 (3), 3 (29), 3.5 (1), and 4 (6).

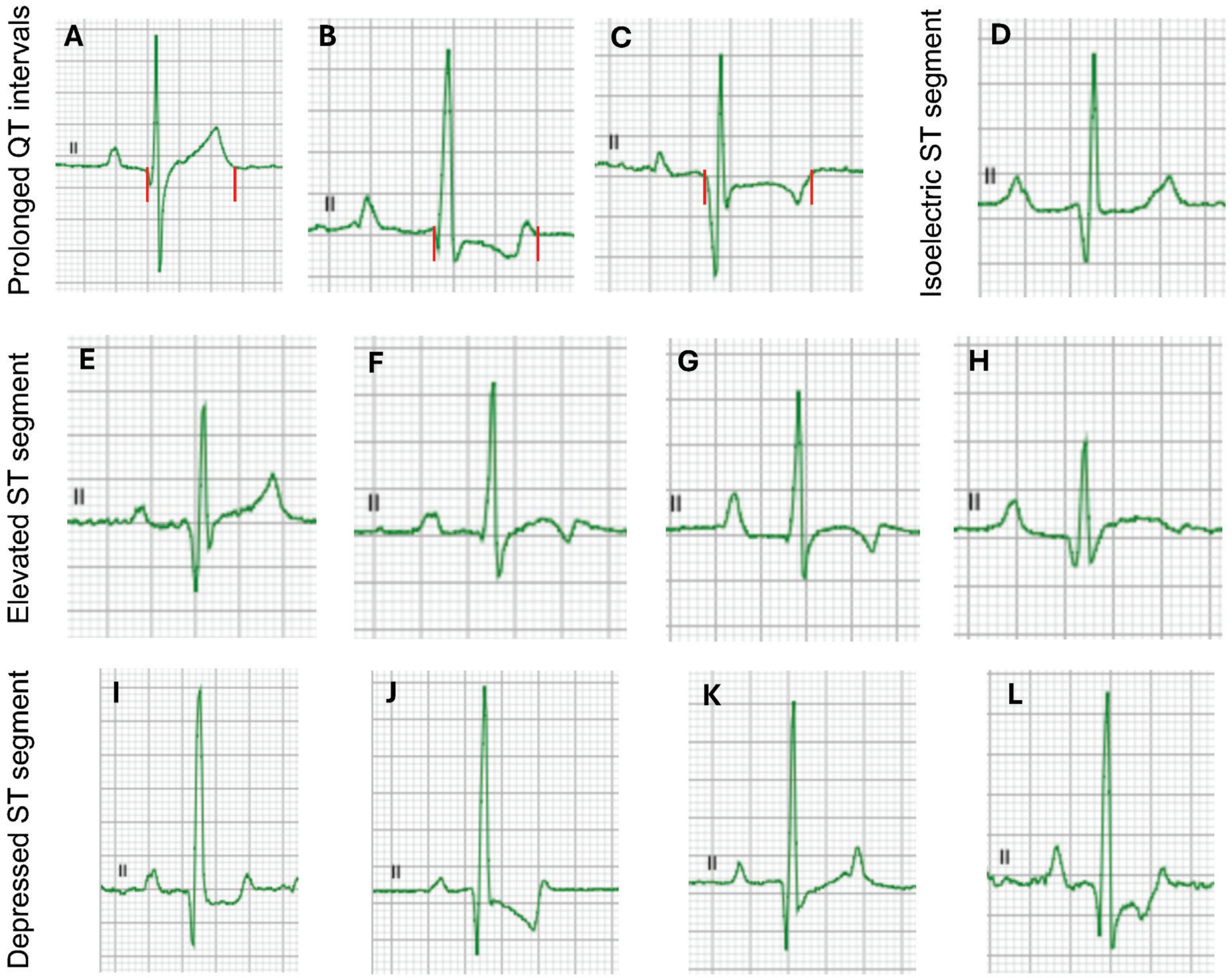

Figure 1—Selected example ECG traces (paper speed, 50 mm/s; amplitude, 10 mm/mV) in Borzoi exhibiting prolonged QT intervals (annotated with red lines at the beginning of the Q wave and the end of the T wave; A, B, and C) or various ST segment morphological patterns (D through L) from a sample of 82 healthy adult Borzoi with structurally normal echocardiograms recruited between October 16, 2020, and December 1, 2022. The QT durations shown are 275 milliseconds (A), 250 milliseconds (B), and 265 milliseconds (C). A horizontal, isoelectric ST segment is shown (D). E through H—Examples of ST segment elevation including up-sloping (E) and convex/domed morphological patterns (F, G, and H). I through L—Examples of ST segment depression including horizontal (I), down-sloping (J), up-sloping (K), and convex (L) morphological patterns.

All normal Borzoi exceeded the general P wave duration cutoff for normal dogs of < 40 milliseconds, and 73 of 82 (89%) exceeded the giant-breed cutoff of < 50 milliseconds.[16] Thirty-one of 82 (38%) Borzoi had first-degree atrioventricular block, defined as a PR interval exceeding 130 milliseconds.[16] Second-degree atrioventricular block (Mobitz type I) was appreciated in 2 (2%) Borzoi. The QRS duration exceeded the upper normal cutoff of < 70 milliseconds[16] in 33 of 82 (40%) Borzoi. Two Borzoi had a right axis shift, with a mean electrical axis of −120 and 180. The QT interval exceeded the upper normal cutoff of 240 milliseconds[16] in 29 of 82 (35%) Borzoi, with 15 (18%) of these dogs exceeding 250 milliseconds[21] and

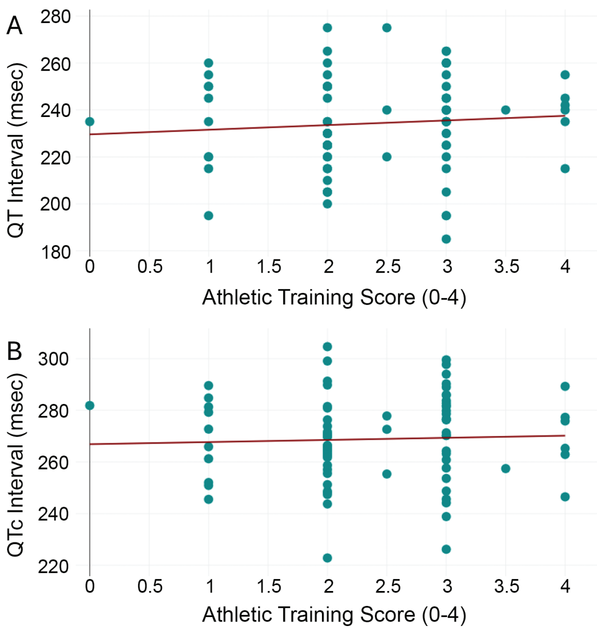

Figure 2—Scatterplots depicting the QT interval (panel A) and corrected QT interval (panel B) plotted against the athletic training score reported by the owner, with 0 being the least trained dogs and 4 being the most highly trained dogs in the sample described in Figure 1. A linear regression line is displayed for each, with an R^2 value of 0.01 and 0.0 for the QT interval and corrected QT interval, respectively.

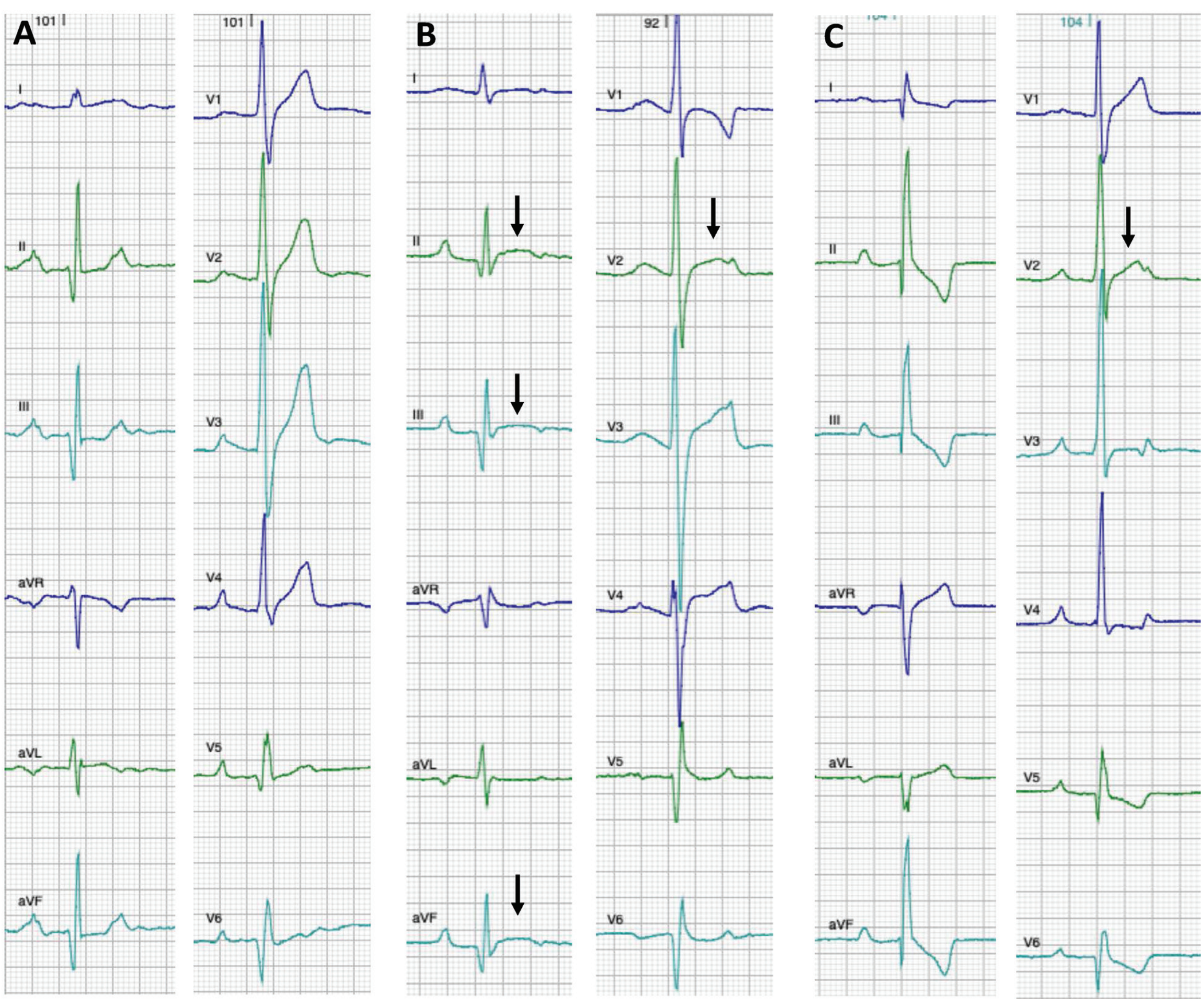

Figure 3—Limb and precordial ECG tracings in 3 Borzoi from the sample described in Figure 1. The dog in panel A exhibits a normal ST segment. The dog in panel B has a structurally normal echocardiogram but exhibits ST segment elevation with a convex or domed ST segment morphology in inferior limb leads as well as precordial lead V2. The dog in panel C has occult dilated cardiomyopathy. ST segment elevation with a convex or domed morphology is only clearly present in lead V2. Paper speed, 50 mm/s; amplitude, 10 mm/mV.

11 (13%) ranging between 260 and 275 milliseconds **(Figure 1)**. None of the dogs with a prolonged QT interval showed normalization of the QT interval when corrected for heart rate. The relationship between the QT and QTc intervals and owner-reported level of exercise training is plotted in scatterplot form **(Figure 2)**. For QT interval, the calculated regression equation was as follows: QT = 229.55 + 1.98 X athletic training score. Coefficients for the model and associated statistical values and 95% CIs are presented in tabular form **(Supplementary Table S1)**. The effect of athletic training on QT interval was not significantly different from zero (F = 0.59, P = .443, R^2 = 0.01, SE of the estimate = 19.54). For QTc interval, the calculated regression equation was as follows: QTc = 266.84 + 0.84 X athletic training score. Coefficients for the model and associated statistical values and 95% CIs are presented in tabular form. The effect of athletic training on QTc interval was not significantly different from zero (F = 0.15, P = .702, R^2 = 0.0, SE of the estimate = 16.62).

Of the 31 Borzoi with a prolonged PR interval, 11 of 31 (35%) also had a prolonged QRS duration and 17 of 31 (55%) or 8 of 31 (26%) had a QT interval > 240 or > 250 milliseconds, respectively. Of the 33 Borzoi with a QRS duration of 70 milliseconds or more, 15 of 33 (45%) and 8 of 33 (24%) had a QT interval > 240 or > 250 milliseconds, respectively. Eight of 82 (10%) or 3 of 82 (4%) structurally normal Borzoi had a PR interval > 130 milliseconds, a QRS duration > 70 milliseconds, and a QT interval > 240 or > 250 milliseconds, respectively.

Deviation of the ST segment was appreciated in 49 of 82 (60%) Borzoi, with 41 of 50 being depressed and 8 of 50 being elevated. Only 4 (5%) dogs had ST segment deviation that exceeded 0.2 mV in limb leads. In dogs with ST segment depression, the morphological pattern was horizontal in 15 dogs, convex in 3 dogs, up-sloping in 6 dogs, and down-sloping in 17 dogs (Figure 1). The maximum amplitude of the ST segment depression ranged between 0.05 and 0.275 mV, with a median value of 0.125 mV. In dogs with ST segment elevation, the morphological pattern of elevation was up-sloping in 4 dogs and convex in 4 dogs **(Figure 3)**. The maximum amplitude of the ST segment elevation ranged between 0.075 and 0.2 mV, with a median value of 0.125 mV. Intermittent convexity of the ST segment was also identified in 6 dogs that were otherwise horizontal with no ST segment deviation. In total, convexity of the ST segment was identified in 13 (16%) dogs but was an intermittent finding in 9 and a persistent finding in 4. In one of the dogs with intermittent ST convexity, this ST segment change was only appreciated after ventricular premature complexes (VPCs; **Figure 4**).

Only 15 of 82 (18%) Borzoi did not have evidence of any early repolarization pattern. An early repolarization notch was present in 16 of 82 (20%) Borzoi, an early repolarization slur was present in 43 of 82 (52%) Borzoi, and a combination of notch and slur, depending on the ECG lead, was present in 8 of 82 (10%) Borzoi **(Figure 5)**. The ST segment in lead II following the early repolarization notch and/or slur was horizontal (n = 26), convex (4), horizontal to intermittently convex (8), rapidly up-sloping (15), rapidly up-sloping to intermittently convex (1), and rapidly down-sloping (13). All 33 Borzoi with a QRS duration of 70 milliseconds or higher had evidence of early repolarization.

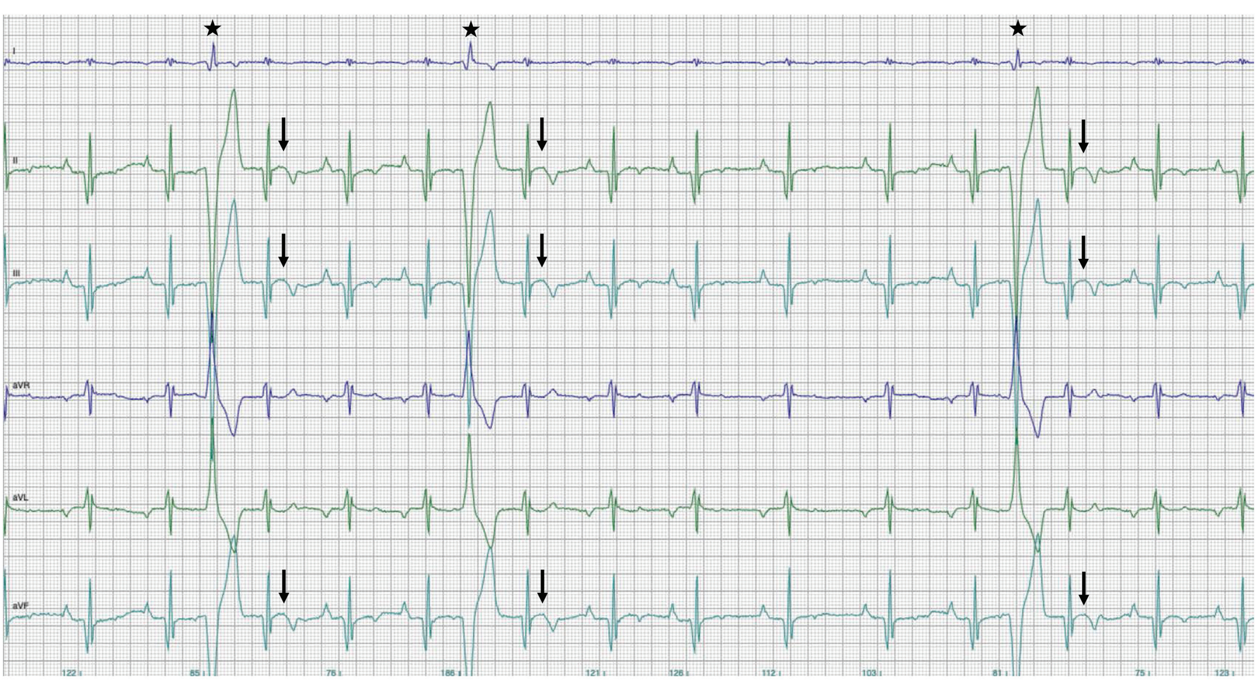

Figure 4—A 6-lead ECG tracing in a 2.6-year-old female Borzoi with a structurally normal echocardiogram from the sample described in Figure 1. The background rhythm is sinus, with 3 single ventricular premature complexes (black stars) present. The ST segment is isoelectric and horizontal prior to the ventricular premature beats, but after each of the ectopic ventricular beats the ST segment displays elevation with convexity in the inferior leads (black arrows). The convexity decreases over a 2- to 3-beat period, and the ST segment becomes horizontal again. Paper speed, 50 mm/s; amplitude, 10 mm/mV.

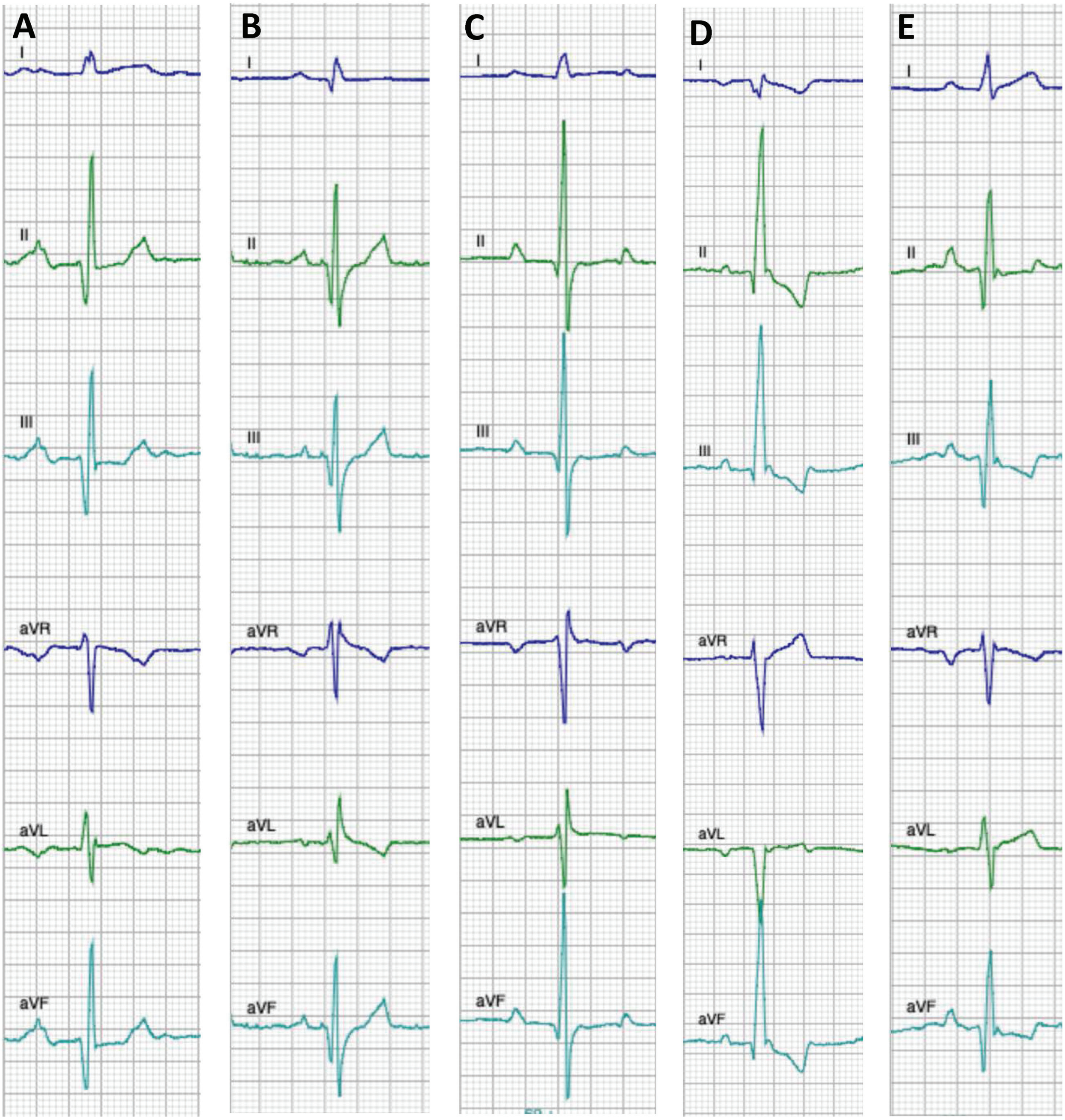

Figure 5—Electrocardiogram traces in 5 Borzoi with structurally normal echocardiograms from the sample described in Figure 1. Panel A demonstrates an isoelectric ST segment with no evidence of early repolarization. The dogs in panels B and C have early repolarization slurs with a rapidly ascending or up-sloping ST segment following the slur in panel B compared to a horizontal ST segment following the slur in panel C. The dogs in panels D and E have early repolarization notches followed by a down-sloping ST segment in panel D compared to a horizontal ST segment in panel E. Paper speed, 50 mm/s; amplitude, 10 mm/mV.

In the single dog of this cohort that experienced sudden death and for which an ECG was available, an early repolarization notch followed by a horizontal ST segment was appreciated. This male dog was 5.5 years of age, had an exercise/training score of 4 (high-level athlete), was observed to be normal a few minutes prior to death, and had a normal necropsy.

The T wave polarity was positive in 33 of 82 (40%) Borzoi, negative in 14 of 82 (17%) Borzoi, and biphasic in 35 of 82 (43%) Borzoi.

Of the 82 structurally normal Borzoi, ventricular arrhythmias were observed in 6 dogs during the 3-minute ECG, including 5 dogs with only single VPCs and 1 dog with single VPCs and 2 rapid ventricular couplets. Single supraventricular premature complexes were seen in 1 dog. Two additional structurally normal dogs had single VPCs appreciated during their echocardiogram but not during the 3-minute ECG, for a total of 8 of 82 structurally normal Borzoi (10%) with ventricular arrhythmias. The median age of these 8 dogs was 2.6 years (range, 1.1 to 5.1 years). The exercise/training level in dogs with ventricular arrhythmias was rated by the owner as 2 (n = 5) or 3 (3).

In dogs with structural cardiac abnormalities, 2 dogs with occult DCM and 1 dog with stage B1 myxomatous mitral valve disease had single VPCs. Four dogs had a QT interval > 240 milliseconds, with a QT interval of 245 milliseconds in 3 dogs and 260 milliseconds in 1 dog. Two of these Borzoi had occult DCM, and 2 had stage B1 myxomatous mitral valve disease. Four dogs with structural cardiac disease had abnormalities of the ST segment appreciated, including 3 with convex ST segments noted in precordial leads but not limb leads (Figure 3). Of these 3 dogs, 1 had occult DCM and 2 had stage B1 myxomatous mitral valve disease. One dog with occult DCM had ST segment depression. A variety of overlapping abnormalities were present in the same dog **(Supplementary Table S2)**.

High-sensitivity cTnI concentrations were available in 85 Borzoi, 72 of which had a structurally normal echocardiogram and 13 of which had structural cardiac abnormalities. The median HS-cTnI concentration in the structurally normal Borzoi was 31 pg/mL (range, < 20 to 336 pg/mL). Seventy of 72 (97%) structurally normal Borzoi had an HS-cTnI within the reference interval proposed by the Texas A&M Gastrointestinal Laboratory of < 20 to 168 pg/mL, with 18 of 72 (25%) in the upper part of the reference interval between 50 and 168 pg/mL. The 2 dogs above this reference interval were 8.2 years of age (HS-cTnI, 184 pg/mL) and 9.8 years of age (HS-cTnI, 336 pg/mL), with these concentrations potentially related to the significant positive correlation between age and HS-cTnI for this assay that has been reported.[20] In all 8 structurally normal Borzoi with ventricular arrhythmias, HS-cTnI concentrations were normal, ranging between < 20 and 54 pg/mL. For the 13 Borzoi with structural cardiac abnormalities, all HS-cTnI concentrations were also within the canine reference interval, ranging between < 20 and 116 pg/mL.

Discussion

Ventricular arrhythmias, conduction system delays, and repolarization abnormalities were all appreciated in this sample of overtly healthy, largely young adult Borzoi. Ten percent of Borzoi with a structurally normal echocardiogram had ventricular arrhythmias. The underlying etiology of these ventricular arrhythmias in the absence of structural cardiac abnormalities remains unknown. Inflammation due to underlying myocarditis appears unlikely given the normal HS-cTnI concentrations. While these dogs were outwardly healthy, complete diagnostic evaluations were not performed, thus undiagnosed systemic disease as a trigger for ventricular arrhythmias cannot entirely be ruled out. Other Borzoi in this sample and in a previously described study[1] were diagnosed with DCM. Further longitudinal study is required to determine whether ventricular arrhythmias are a predictor of future development of DCM in the Borzoi breed, similar to the well-described natural history of the disease in Doberman Pinschers.[22]

Conduction system disturbances, such as prolonged PR, QRS, and QT intervals, were also common in structurally normal Borzoi. Prolonged PR intervals consistent with a diagnosis of first-degree atrioventricular block were appreciated in 38% of Borzoi. This could be a normal response to inherently increased vagal tone within the breed or be reflective of conduction system disease. It must also be considered that nearly all structurally normal Borzoi had wider P waves than what is reportedly normal for other breeds. This could suggest slower-than-typical intra-atrial conduction or conduction over a relatively larger atrial mass, either of which could play a role in prolonging the PR intervals. When first-degree atrioventricular block is present in combination with wide QRS complexes, however, a conduction delay involving the His bundle or proximal part of the left or right bundles is considered more likely than intra-atrial or intranodal conduction delay.[23] This was the case for 35% of the Borzoi with first-degree atrioventricular block in the present sample.

With regard to measurement of QRS duration, the phenomenon of early repolarization must also be considered. For this study, the authors used current recommendations published for dogs. Specifically, the QRS onset was defined as “coinciding with the first ECG deflection that interrupts the PQ segment” and the end of the QRS was defined as “the point where the last deflection of the ventriculogram intersects the isoelectric line, also called the J point or ST junction.”[16] This is consistent with past guidelines for humans in which terminal QRS slurs or notches were considered part of the QRS segment.[24] More recently, however, the American Heart Association proposed that the J point, where the QRS ends and the ST segment begins, should be measured to the peak of a notch or the onset of a slur when present.[19] These recommendations were made in an attempt to improve consensus over how early repolarization was both defined and measured. Eighty-two percent of Borzoi in the present sample had evidence of early repolarization, either in the form of a terminal QRS notch or slur. This included all 33 Borzoi with a prolonged QRS duration. Thus, it appears likely that an early repolarization phenomenon contributed to the prolonged QRS durations appreciated in 40% of the dogs and that these prolonged QRS durations may be within the realm of normal for the breed. Further, longitudinal study would help to confirm normalcy and rule out underlying conduction system disease. Improved standardization in veterinary medicine regarding measurement of terminal QRS notches and slurs in dogs may warrant further discussion.

In addition to its impact on QRS duration, the implication of simply identifying early repolarization on a canine or human ECG also warrants discussion. Although early repolarization has not been widely studied in dogs, it has historically been considered a benign variant, with a previous study[14] demonstrating that breed plays a role in the frequency with which it is identified. For example, 91% of Petit Basset Griffon Vendéens were found to have an early repolarization “J wave” notch or slur, compared to only 10% of Newfoundlands or 0% of Irish Wolfhounds.[14] On the basis of the present data, Borzoi also appear highly likely to have early repolarization identified on their ECGs.

In humans, early repolarization was originally considered a benign, normal ECG variant as well. However, knowledge advancement in recent decades has suggested that some forms of early repolarization are associated with malignant arrhythmias.[13,19,25–28] Specifically, the presence of an early repolarization notch or slur followed by a horizontal or down-sloping ST segment has been associated with increased arrhythmic risk, while the same finding followed by a rapidly ascending ST segment is considered benign.[25,28] Going a step further, Rollin et al[26] revealed the highest risk of all-cause and cardiovascular mortality was associated with the notched early repolarization pattern followed by a horizontal or nonascendent ST segment, with associated hazard ratios of 3.84 and 8.75, respectively. Whether these principles of benign versus malignant early repolarization patterns apply to canine ECGs requires further study, as attention has not previously been paid to the morphology of the ST segment after an early repolarization notch or slur. It is notable that the ECG of the highly athletically trained Borzoi in this cohort that experienced sudden death did have the highest-risk early repolarization pattern described in humans. In contrast, however, approximately 70% of Borzoi with early repolarization had horizontal, horizontal-to-convex, or down-sloping ST segments after their notch or slur, suggesting that the benign, up-sloping pattern in humans was less common in this cohort overall.

In addition to identifying early repolarization, other repolarization abnormalities including prolonged QT intervals and abnormal ST segments were also appreciated in these Borzoi. The upper normal limit of the QT interval in dogs at normal heart rates is reported to be 240 milliseconds[16] or 250 milliseconds,[21] depending on the reference used. In this sample of Borzoi, 35% or 18% exceeded those upper normal QT interval cutoffs, respectively. When the QT interval was corrected for heart rate, none of the dogs with prolonged QT intervals normalized. Furthermore, the QT interval duration did not appear to be correlated with owner-reported level of exercise/training, suggesting athleticism was unlikely to be playing a role. It is unknown whether these findings represent a form of LQTS, a heritable channelopathy in humans known to trigger arrhythmias and result in SCD.[29] Long QT syndrome has only been reported in a single family of English Springer Spaniels to date, with a KCNQ1 mutation identified in this family.[8] In the LQTS-affected dogs of that report, QT intervals between 260 and 270 milliseconds were reported, with QTc for the same dogs ranging between 304 and 314 milliseconds.[8] In the present sample of Borzoi, 11 dogs had QT intervals between 260 and 275 milliseconds, with QTc intervals for these dogs ranging between 278 and 304 milliseconds. Genetic sequencing, QT to TQ restitution, and longitudinal follow-up of these dogs will be important as the next investigative steps to help determine the significance of these findings. Until more information is available, it will be prudent to carefully assess the QT interval in Borzoi dogs with ventricular arrhythmias prior to choosing antiarrhythmic medications. Medications that prolong the action potential duration such as sotalol or amiodarone may need to be avoided in Borzoi with QT intervals that are already prolonged.

Lastly, the shape of the ST segment in a subset of these structurally normal Borzoi also varied from what has previously been described in normal dogs. The canine ST segment has received little study, with minimal diagnostic criteria for normalcy other than depression or elevation of > 0.2 mV in limb leads or > 0.25 mV in precordial leads being considered abnormal.[16] Additionally, ST segment shape alterations including coving, arching, or doming are also listed as abnormal,[16] although to the authors' knowledge these shapes remain unreported as naturally occurring in the canine literature. A retrospective review[18] of 180 healthy dogs revealed that 76% of healthy dogs had isoelectric ST segments, with 20% having a small amount of ST segment depression in a horizontal, up-sloping or down-sloping shape and a 4% minority having ST segment elevation, all of which had a concave shape. No healthy dogs had convex ST segments reported.[18] In contrast, 16% of Borzoi had fixed or intermittent convexity or "doming" of their ST segment.

Brugada syndrome is a heritable condition in humans that predisposes to syncope and cardiac arrest and is characterized by pathognomonic ECG changes including coved ST segment elevation with T wave inversion in the right precordial leads.[30–32] The characteristic ECG changes in patients with Brugada syndrome are often intermittent, with sodium channel blockers or fever sometimes required to provoke the abnormalities.[31,32] From an anatomic perspective, histological and electrophysiological changes within the right ventricular outflow tract appear to be the underlying substrate triggering abnormal repolarization and arrhythmogenesis in this disease.[32,33] To that end, repositioning of precordial ECG leads to better overlie the right ventricular outflow tract improves the sensitivity of diagnosis in humans.[33]

The implication of the ST segment changes in the Borzoi of this study remains unknown. Whether these changes could represent an underlying disease process similar to Brugada syndrome will require further study. To date, Brugada syndrome has not been described in a natural large animal model. In the majority of Borzoi in this study, precordial ECG tracings were not available. In those that were, the method of precordial lead placement was that of Kraus et al.[15] To optimally study the ST segment in Borzoi, future study will be needed using precordial leads in all dogs. Furthermore, precordial leads specifically positioned more cranially to overlie the right ventricular outflow tract within the markedly deep-chested Borzoi thorax may also be necessary.

Given the spectrum of abnormalities noted in structurally normal Borzoi, special investigation into the SCN5A gene may be relevant. This gene encodes the α-subunit of the cardiac sodium channel $Na_v1.5$ that is responsible for initiating and propagating the action potential. Various loss of function and gain of function mutations of the SCN5A gene can produce LQTS, Brugada syndrome, DCM, conduction system defects, and more, with various overlap syndromes reported in which loss of function and gain of function mutations and the deleterious consequences of these mutations are present at the same time in the same patient. Genetic sequencing of affected Borzoi will help to determine whether SCN5A mutations may play a role in the variety of abnormalities identified in this breed.

Limitations of the present study included the lack of exhaustive testing for noncardiac disease, particularly with regard to the identification of ventricular arrhythmias in dogs without structural cardiac disease. Additionally, various electrolyte abnormalities can affect a variety of ECG parameters. While all participating dogs were outwardly healthy and unlikely to have clinically important electrolyte derangements, normal electrolyte levels were not confirmed. Furthermore, approximately half of the study sample was recruited from Borzoi breeders within the geographic vicinity of the authors' institution, while the other half was drawn from Borzoi breeders across the US. While an effect of locally overrepresented genetics on the study results is possible, it is unlikely to be consequential given the relatively small gene pool and homogeneity of the Borzoi breed in general. Finally, assessment and measurement of the ST segment is inherently challenging. Baseline artifacts or use of ECG filters may affect interpretation. Additionally, variability in subtle morphological differences is possible within the same ECG tracing. To help address these challenges, the ST segment morphology of the Borzoi in the present study was assessed by 2 board-certified cardiologists to reach a consensus on each dog about the predominant morphology. However, repeatability of the ST segment morphology assessments was not investigated as a component of this study, and the ability for other operators to reach the same conclusions about similar ECG traces using the same or other ECG machines remains unknown.

In conclusion, ventricular arrhythmias, early repolarization, prolonged QT intervals, and ST segment abnormalities are not infrequent in clinically healthy adult Borzoi with normal echocardiograms. Whether these ventricular repolarization abnormalities relate to the reported predisposition for sudden death warrants further investigation, including genetic sequencing of affected Borzoi. P, PR, and QRS durations are also commonly prolonged compared to reference intervals in other dogs.

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Disclosures

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Supplementary Materials

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