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Heart rate variability derangements in dogs with Chagas disease: a potential indicator of autonomic and cardiac disruption

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Objective
To assess heart rate variability (HRV) as a marker of autonomic nervous system disruption and its role in disease progression in dogs with Chagas disease (CD), and to evaluate arrhythmias and conduction abnormalities in symptomatic and asymptomatic groups.

Methods
A prospective observational study was conducted on dogs treated at a small animal hospital in central Texas from August to December 2023. Ambulatory 24-hour Holter monitoring was conducted to assess HRV metrics (proportion of pairs of successive NN intervals differing by > 50 milliseconds and root mean square of the successive differences), arrhythmias, and conduction abnormalities. Heart rate variability parameters were categorized as high, normal, or low. Dogs were classified as symptomatic or asymptomatic on the basis of clinical presentation, and comparisons of HRV and ECG findings between groups were performed.

Results
112 client-owned dogs with confirmed *Trypanosoma cruzi* infection were included. Of the 112 dogs, 46 (41.1%) were symptomatic and 66 (58.9%) were asymptomatic. Heart rate variability disruptions were observed in 63% of dogs, underscoring early and widespread autonomic dysregulation in *T cruzi* infection. Symptomatic dogs had more arrhythmias (1.54 vs 1.02) and a higher prevalence of second-degree atrioventricular blocks (0.19 vs 0.03), but HRV abnormalities were similar between groups.

Conclusions
Heart rate variability abnormalities were prominent across all dogs with CD, regardless of symptoms, suggesting their utility as early markers of autonomic and cardiac dysfunction. These findings highlight HRV's potential for monitoring disease progression, particularly in asymptomatic dogs, supporting its inclusion in routine assessments for *T cruzi* infections.

Clinical Relevance
Heart rate variability analysis may enhance early detection and management of CD, an emerging One Health issue, by addressing underdiagnosed autonomic and cardiac dysfunction in dogs.

Keywords: cardiac arrhythmia, cardiac conduction defect, Chagas disease, dogs, heart rate variability

Chagas disease (CD) is an important veterinary zoonotic disease in the US, affecting domestic animals like dogs, cats, and horses. Chagas disease is caused by the protozoan *Trypanosoma cruzi*. The triatomine bug (*Triatoma* spp), also known as the *kissing bug*, serves as the host for the parasite. Transmission occurs in both dogs and humans through several routes: ingestion of the bug or its excreta, contamination of a bite wound with the bug's feces, vertical transmission from mother to fetus, consumption of infected carrion from reservoirs, blood transfusion, or inhalation of the parasite.[1] The kissing bug inhabits 29 southern states in the US, with canine CD cases reported across all 50 states of the US and estimates indicating a prevalence ranging from 3% to 31%,[2–6] surpassing other vector-borne diseases like *Dirofilaria immitis* infection. The dog's ability to serve as a competent reservoir host[7]

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for *T cruzi* as well as deforestation and human migration into rural areas where vectors are abundant also contribute to high infection rates.

The pathophysiology of CD revolves around direct parasite tissue destruction, host immune response, and microvascular compromise,[8] particularly in the heart, resulting in fibrosis leading to arrhythmias, conduction abnormalities, structural changes, and systolic dysfunction. Dysautonomia has been extensively studied in humans with chronic Chagas cardiomyopathy (CCC), in which its presence is associated with poor outcomes, including high mortality rates and an increased risk of sudden cardiac arrest, even in patients with preserved cardiac structure and systolic function.[4,9–15] The prognostic value of dysautonomia in CCC underscores the importance of understanding its impact on affected animals.

Despite the recognized importance of cardiac autonomic dysfunction in humans,[4,12–15] research investigating the role of heart rate variability (HRV)—a biomarker of autonomic nervous system (ANS) function[16]—in canine CD is lacking. In humans, studies have demonstrated that HRV abnormalities correlate with markers of disease severity and progression, including morphofunctional cardiac parameters and mortality risk scores, such as the Rassi score. Silva et al[16] showed that HRV indices are strongly associated with echocardiographic findings and predict overall mortality in patients with CCC. These findings suggest that HRV could provide critical insights into disease status and progression.

This study aimed to address this gap by investigating the prevalence of cardiac abnormalities and dysautonomia in symptomatic and asymptomatic *T cruzi*–infected dogs with the use of 24-hour continuous ECG monitoring (Holter) to detect arrhythmias and conduction abnormalities. Heart rate variability parameters were also analyzed to evaluate their potential as markers of disease progression.

Methods

Patient selection

A cross-sectional survey was conducted on a cohort of 112 client-owned dogs positive for *T cruzi* at a small animal hospital in central Texas from August to December 2023. Prior diagnosis of CD was confirmed by at least 1 serologically reactive test within 60 days of presenting at the hospital, employing immunofluorescent antibody testing (IFA) or ELISA. The IFA was conducted at the Texas Veterinary Medical Diagnostic Laboratory in College Station, Texas, while the ELISA was performed at VRL Laboratories in San Antonio, Texas. Both tests have been validated internally for use in canines. Animals were cared for according to the principles outlined in the NIH *Guide for the Care and Use of Laboratory Animals*.[17] The study design was approved by the animal hospital's advisory board, and owners were appropriately informed of the procedures for their dogs. Eligibility requirements included dogs seropositive for *T cruzi* infection and whose owner opted for pretreatment Holter monitoring and subsequent treatment at the hospital. Patients whose owner refused a Holter monitor were excluded from the study. Recruited dogs were followed up until January 2024.

The dogs were categorized into 2 groups: asymptomatic and symptomatic. Asymptomatic patients were those that appeared clinically normal according to both the owner and attending veterinarian, with no clinically detectable abnormalities on physical examination or diagnostic testing and with CD testing conducted at the owner's request to assess serological status. Symptomatic patients were dogs with a history of symptoms supportive of CD and/or findings on veterinary examination suggestive of CD. Alongside physical examination, additional modalities such as radiology, electrocardiography, clinical pathology, and echocardiography were utilized to ascertain symptomatic criteria. Specific criteria are outlined in **Table 1**.

Patient characteristics

Arrhythmias were categorized as either present or absent, with detailed notation of the number and type of arrhythmia observed including ventricular premature contraction, premature atrial contractions, ventricular tachycardia, and atrial fibrillation. Similarly, conduction abnormalities were recorded, including the number and type (first-, second-, and third-degree atrioventricular [AV] block; sinus arrest; atrial standstill; bundle branch block; sinus arrhythmia; sinus bradycardia; and sinus tachycardia). Sinus arrest was defined as a pause in the sinus rhythm that lasted for > 2 normal R-R intervals.[18,19] Sinus arrhythmia was defined as any irregular R-R interval episodes that occurred in a 7.5-second period identified during the Holter monitor data analysis.

Sinus bradycardia was characterized by an average heart rate < 60 beats/min (bpm), minimum heart

Table 1—Characteristics of symptomatic patients based on physical examination, radiology/imaging, and clinical pathology. Patients with 1 or more of the following were classified as symptomatic.

	Characteristics of symptomatic patients
Physical examination	Arrhythmia, murmur, distended jugular veins, capillary refill time > 2 seconds, uveitis, blindness, hepatosplenomegaly, ascites, icterus, seizure or other neurological deficits
Radiology/imaging	Cardiomegaly, congestive heart failure, distended pulmonary A/V, hepatosplenomegaly, systolic dysfunction
Clinical pathology	Monocytosis, thrombocytopenia, anemia, neutrophilia, eosinophilia, leukocytosis, proteinuria, hyperglobulinemia
ECG	Arrhythmias and conduction abnormalities

A/V = Artery/vein.

rate < 30 bpm, time with heart rate < 50 bpm for > 350 minutes (> 24%). Sinus tachycardia was defined as > 200 bpm for > 350 minutes (> 24%).[20] Unless stated otherwise, normal values of ECG parameters were defined as proposed by Tilley et al.[19]

Heart rate variability

We used HRV analysis to indirectly evaluate the state of the ANS by comparing R-R interval oscillation patterns between dogs with CD and healthy dogs with the use of 2 key parameters: root mean square of the successive differences (RMSSD) and proportion of pairs of successive NN (R-R) intervals differing by > 50 milliseconds (pNN50). The RMSSD, which measures beat-to-beat SD and is commonly assessed in veterinary Holter monitor evaluations, strongly correlates with parasympathetic modulation.[21] Additionally, we chose pNN50 for its ability to gauge parasympathetic regulation of the heart.[21]

The HRV analysis utilized 2 distinct time-domain metrics: pNN50 and RMSSD. The normal pNN50 range was 46% to 67% and RMSSD was 102 to 443 milliseconds.[21] Time-domain metrics assess HRV in a set time frame by estimating the variability in measurements of the interbeat interval.[22] These metrics were selected because of their specificity in assessing the parasympathetic nervous system (vagally mediated changes to heart rate)[21] and their ability to distinguish between the 2 branches of the ANS.

Heart rate variability was determined and categorized as high, normal, and low on the basis of pNN50 and RMSSD measurements. A higher value of either variable indicates an increase in parasympathetic expression, while lower values suggest increased sympathetic stimulation. Patients with pNN50 < 46% and RMSSD < 207 milliseconds were considered low, pNN50 > 66% and RMSSD > 443 milliseconds were considered high, and values falling within these ranges were considered normal. The HRV data were also compared between groups on the basis of body weight with a χ^2 test of independent association. Dogs were classified as small (< 15.9 kg [< 35 lb]), medium (15.9 to 29.5 kg [35 to 65 lb]), large (> 29.5 to 34.0 kg [> 66 to 75 lb]), or giant (> 34.0 kg [> 75 lb]) for comparison.

Data collection

An ambulatory ECG Holter monitor (model DR400; Northeast Monitoring Inc), was placed on the shaved and prepped ventral left thoracic space, with electrodes attached and secured with a bandage and vest as per the manufacturer's recommendations. All patient ECGs were recorded in the home environment for 24 hours at a rate of 25 mm/s, utilizing a lead configuration of V1, V2, and V5. After the monitoring period, patients returned for device removal. Data collection occurred upon dog's recruitment until January 2024.

Collected data were analyzed with ALBA Medical Systems software (ALBA Medical Systems Inc), and reports were reviewed by the veterinarian for various parameters, including the following: duration of analysis, heart rate (minimum, mean, and maximum), presence and number of supraventricular and ventricular contractions, occurrence of supraventricular tachycardia, number of pauses exceeding 3 seconds, longest pause exceeding 4 seconds, presence of second- and third-degree AV blocks, irregular RR interval, nonrespiratory sinus arrhythmia, sinus arrest, RMSSD, and pNN50. To reduce the risk of potential bias, Holter data were analyzed by staff blinded to the diagnosis and history/clinical evaluation of the patient.

Statistical analysis

All statistical analyses were conducted with R statistical software (version 4.1.2; R Core Team) to investigate potential differences between outcomes measured within the symptomatic and asymptomatic populations. To assess differences in the number of arrhythmias and conduction abnormalities between symptomatic and asymptomatic patients, a Wilcoxon test was employed via the wilcox.test() function in R. The Wilcoxon test was preferred over the traditional 2-sample *t* test because of the nonnormal distribution of the data and relatively small sample sizes.

To evaluate differences in the incidence of various cardiac events (eg, sinus bradycardia, premature atrial contraction [supraventricular arrhythmia], ventricular premature complexes, ventricular tachycardia, AV block, atrial fibrillation, sinus arrhythmia, tachycardia, and sinus arrest) between symptomatic and asymptomatic patients, a 2-sample proportion test was utilized with the prop.test() function in R.

Given the qualitative nature of HRV, a Pearson χ^2 test was conducted to examine whether HRV (ie, low, normal, high) differed between the symptomatic and asymptomatic patients. This test was conducted with the chisq.test(.) function in R. All statistical conclusions were drawn at the significance level of $\alpha = 0.05$.

Results

Patient characteristics

A total of 112 *T cruzi*–seropositive (ELISA or IFA) dogs were enrolled and monitored continually for 24 hours on a Holter. There was no loss to follow-up. Among them, 66 (58.92%) were asymptomatic, while 46 (41.08%) were symptomatic. Ages ranged from 6 months to 16 years, with a mean age of 5.21 years. The cohort encompassed 33 distinct dog breeds, including mixed breed, which was the most common (n = 37 [33.04%]), followed by Border Collie (9 [8.04%]), Labrador Retriever (7 [6.3%]), and Australian Shepherd (7 [6.3%]). Weights varied from 2.7 to 73.9 kg, with a mean of 21.07 kg. The sex distribution consisted of 54 males (48.22%) and 58 females (51.78%). Only 13 males (11.61%) and 13 females (11.61%) were not neutered or spayed. Most dogs were either neutered males (n = 41 [36.60%]) or spayed females (45 [40.18%]).

Characteristics of symptoms

Figure 1 summarizes the distribution of symptomatic patients by type of symptoms. Among

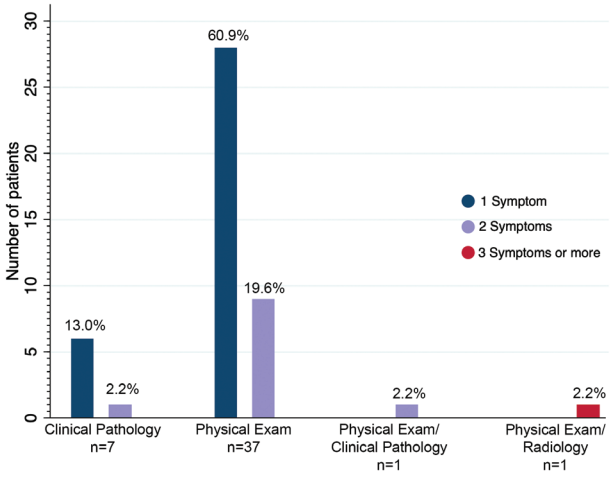

Figure 1—Frequency of patients' symptoms stratified by type and number of symptoms. Patients with multiple symptoms may have either more than 1 symptom from the same type or a combination of symptoms from different types.

the 46 symptomatic patients, 37 (80.5%) exhibited symptoms on physical examination, 60.9% of which had 1 symptom. Next, there were 7 patients (15.2%) with clinical pathology findings, the majority with a single finding (13.0%). Patients with > 1 symptom were more likely to have symptoms from the same type and were identified during the physical examination (19.6%). There was one patient (2.2%) with 2 symptoms identified on physical examination and clinical pathology and another patient (2.2%) with 3 symptoms or more, including a combination of physical examination findings and radiology findings.

A total of 109 dogs (97.3%) had at least 1 arrhythmia or conduction abnormality, and 71 dogs (63.3%) showed HRV abnormalities. Conduction abnormalities occurred more often, observed in 99 dogs (88%), compared to arrhythmias, which occurred in 75 dogs (67%). The mean number of types of arrhythmias was significantly higher in symptomatic patients compared to asymptomatic patients (1.54 vs 1.02; P = .02). However, there was no significant difference in the mean number of conduction abnormalities between symptomatic and asymptomatic patients (1.52 vs 1.35; P = .34; **Table 2**).

The distribution of arrhythmias and conduction abnormalities is summarized in **Table 3**. Sinus bradycardia emerged as the predominant conduction abnormality, affecting 64.6% (64 of 99) of cases across both groups, while ventricular premature contractions were the most frequently observed arrhythmia, accounting for 61.3% (46 of 75) of instances. There were no statistical differences between groups except that a higher proportion of symptomatic dogs had second-degree AV block (0.19 vs 0.03; P = .01).

On Holter findings, 37 dogs (33%) did not have arrhythmias, 13 (11.6%) did not have conduction abnormalities, and 3 (2.7%) had normal Holter readings. Concerning HRV, 58 dogs (51.79%) had high HRV, 41 dogs (36.61%) had normal HRV, and 13 dogs (11.61%) had low HRV. However, the differences in HRV between groups did not reach statistical significance (P = .90), with a higher proportion of dogs demonstrating high indices, followed by normal and low HRV **(Table 4)**.

Table 2—Sample mean and SD of the numbers of arrhythmias and conduction abnormalities stratified by symptomatic status.

	Symptomatic dogs (n = 46)	Asymptomatic dogs (n = 66)	95% CI	*P* value
No. of types of arrhythmias (mean ± SD)	1.54 ± 1.24	1.02 ± 1.12	−1.0 to −1.2 X 10^{-5}	.02
No. of types of conduction abnormalities (mean ± SD)	1.52 ± 0.98	1.35 ± 0.83	−4.27 X 10^{-5} to 3.78 X 10^{-5}	.34

*Reported P values were obtained from Wilcoxon tests.

Table 3—Sample proportion of patients presenting with conduction abnormalities/arrhythmias stratified by symptomatic status.

Conduction abnormality/ arrhythmia	Proportion of symptomatic dogs (n = 46)	Proportion of asymptomatic dogs (n = 66)	95% CI	*P* value*
Sinus bradycardia (n = 64)	0.57	0.58	−0.18 to 0.21	≈ 1
Premature atrial contraction (n = 41)	0.46	0.30	0.30 to 0.46	.14
VPC (n = 46)	0.48	0.36	−0.32 to 0.09	.31
Ventricular tachycardia (n = 7)	0.07	0.06	−0.10 to 0.09	≈ 1
Second-degree AV block (n = 10)	0.19	0.03	−0.31 to 0.20	**.01**
Atrial fibrillation (n = 1)	0.00	0.02	−0.03 to 0.06	≈ 1
Sinus arrhythmia (n = 63)	0.63	0.52	−0.32 to 0.09	.31
Tachycardia (n = 10)	0.09	0.09	−0.11 to 0.11	≈ 1
Sinus arrest (n = 52)	0.57	0.39	−0.38 to 0.03	.11

**P* values were obtained from the 2-sample proportion tests. The bolded P value represents a significant value of $P < 0.05$.
AV = Atrioventricular. VPC = Ventricular premature contraction.

Table 4—Proportion of patients presenting with each heart rate variability (HRV) stratified by symptomatic status.

HRV	Symptomatic (n = 46)	Asymptomatic (n = 66)	*P value
Proportion low (n = 13)	0.10	0.12	.90
Proportion normal (n = 41)	0.39	0.35	
Proportion high (n = 58)	0.50	0.53	
Total	1.0	1.0	

*Reported *P* values were obtained from the Pearson χ^2 test.

Most dogs were in either the small or medium weight group (n = 85 [75.9%]). Additionally, the majority exhibited normal or high HRV. The distribution of HRV levels was similar across weight groups, with no statistically significant association (*P* = .916). Therefore, there was no association between HRV and weight.

Discussion

This study primarily investigated HRV as a marker for ANS dysfunction in dogs infected with *T cruzi*. Additionally, it examined arrhythmias and conduction abnormalities as secondary markers of cardiac electrical dysfunction. While arrhythmias were more prevalent in symptomatic dogs, the differences may lack clinical significance. The key finding is that HRV abnormalities were present in 63% of the dogs, with 98% exhibiting ECG abnormalities, regardless of clinical symptoms. This suggests widespread subclinical cardiac involvement and underscores HRV's potential as an early indicator of disease progression. This finding is not surprising, as CD unfolds as a multifaceted illness encompassing various clinical stages and a wide array of infiltrated organ systems and is distinguished by specific pathogenic characteristics. Its natural progression involves both acute and chronic phases, with the latter further divided into an indeterminate phase and a cardiomyopathic phase.[9,23] The indeterminate phase, also referred to as the transitional phase, is characterized by positive serological testing but generally lacks observable physical or clinical symptoms of the disease. Conversely, Chagas cardiomyopathy, known as the arrhythmic-congestive phase, presents a range of clinical features including arrhythmias, electrical conduction abnormalities, myocardial dysfunction, and thromboembolic events. Research indicates that individuals in the indeterminate phase may exhibit subclinical myocarditis, as evidenced by multiple studies revealing ongoing pathological changes in endocardial biopsies, even in the absence of clinically apparent disease.[11,24] Accurately predicting which patients will transition to Chagas cardiomyopathy or progress into fatal arrhythmias remains challenging until the mechanisms are fully elucidated. Several hypotheses have been proposed regarding the potential mechanisms underlying disease progression including tissue parasitism and direct tissue damage caused by the parasite immune-mediated myocardial injury, microvascular alterations, and the cardioneuromyopathic hypothesis.[9,10,25] In this study, 98% of the dogs, regardless of clinical symptoms, showed ECG abnormalities and 63% had HRV disruption. These changes are largely reflective of the ongoing complex physiopathological processes in canine CD, including damage to myocardial and neural tissue, the direct effects of the parasite, and the immune response, all of which contribute to the clinical disease. However, the extent of these interactions in canines is yet to be explored.

Dysautonomia in CD has been described and demonstrated in humans through various mechanisms, including anatomical descriptions of decreased cardiac autonomic innervation and functional tests.[16,26–29] Autonomic innervation destruction in cardiac tissue results from direct or indirect effects of *T cruzi* through cell toxicity and inflammation.[16] In dogs, potential mechanisms of cardiac damage include parasite-induced immune response due to toxic parasitic products toward cardiomyocytes and cardiac autonomic nervous cells and autoreactivity to infection, as seen in humans.[30] *Trypanosoma cruzi* has a direct cytopathic effect on myocardium by causing cell toxicity and inflammation.[28] Recent studies[9,31] of humans have increasingly emphasized the role of the ANS in the pathogenesis of Chagas cardiomyopathy. Autonomic abnormalities, particularly parasympathetic dysautonomia leading to reflex sympathetic activation, have been extensively documented.[9,32] However, the underlying causes of these neurogenic disturbances, whether resulting from the direct action of the parasite or abnormal neuroimmunomodulatory effects of autoantibodies, remain incompletely understood. Nevertheless, it is hypothesized that such autonomic dysautonomias may precipitate complex arrhythmogenic disturbances, ultimately leading to sudden death.[33,34] This scenario of autonomic arrhythmogenesis has been associated with a decrease in cardiac intramural neurons and ganglion cells, resulting in various chronotropic, dromotropic, and inotropic alterations.[9] These changes subsequently elicit electrophysiological responses, which can be evaluated by analyzing HRV as a surrogate marker of disease progression.[16]

Heart rate variability is increasingly recognized as a critical biomarker for autonomic function and overall cardiac health in various diseases, including CD. In this study, 63% of dogs demonstrated abnormal HRV, consistent with previous findings that suggest autonomic dysfunction as a feature of chronic CD. However, the analysis did not identify significant differences in HRV parameters between symptomatic and asymptomatic dogs.

This absence of statistical differences warrants careful interpretation, especially considering studies of humans demonstrating the prognostic significance

of HRV in CCC. Dysautonomia, a well-established component of CCC in humans, underpins HRV abnormalities. Research by Silva et al[35] has highlighted the association of HRV with echocardiographic parameters indicative of morphofunctional cardiac changes in CD patients. Furthermore, additional research by Silva et al[16] demonstrated that HRV indices correlate strongly with mortality risk, as assessed by the Rassi score, a predictive tool for CCC outcomes.[25]

Extrapolating from these human studies, it is plausible that HRV abnormalities in dogs with CD, even in the absence of marked clinical distinctions between symptomatic and asymptomatic groups, may still hold prognostic value. In asymptomatic dogs, HRV changes could reflect subclinical autonomic dysfunction, potentially serving as an early marker of disease progression before overt clinical signs emerge. Conversely, in symptomatic dogs, HRV abnormalities might indicate advanced autonomic involvement and greater disease severity.

These findings suggest that HRV, though not statistically differentiated between groups in the current analysis, may still be an essential tool for evaluating disease status in canine CD. Longitudinal studies are warranted to elucidate the role of HRV as a predictive marker for clinical progression and survival in dogs. The integration of HRV assessment into routine diagnostic protocols for canine CD could provide valuable insights into autonomic dysfunction and aid in risk stratification and therapeutic decision-making.

Sinus arrhythmias can be normal in dogs, especially those associated with respiration or high vagal tone.[36] In resting dogs, the heart rate decreases and increases with the breathing cycle owing to waxing and waning vagal activity, known as respiratory sinus arrhythmia (RSA).[37] The usual pattern is acceleration with inspiration and deceleration with expiration, occasionally reversed.[36] Rapid beats in RSA often occur in sets of 2 (bigeminy), 3 (trigeminy), or 3 with a fourth beat during expiration in resting dogs.[36] Cyclic changes in R-R interval duration are often accompanied by cyclic alterations in ECG complexes' amplitude and, sometimes, T wave form (and occasionally polarity). Both software and manual detection of irregular RR intervals were utilized in this study to define sinus arrhythmia, allowing for the exclusion of dogs meeting RSA criteria. Heart rate variability analysis also enabled deeper observation into the ANS to determine whether the rate variation in dogs with sinus arrhythmias was normal variation or overexpression of the parasympathetic nervous system. We found that 63 of the 112 dogs had a sinus arrhythmia, indicative of profound parasympathetic influence over the heart rhythm. Since this was not associated with respiration, we concluded that this most likely reflected *T cruzi*–induced myocardial damage, affecting the ANS by disrupting the sympathetic arm, allowing the parasympathetic overexpression (high HRV and sinus arrhythmia). While there are other factors that can influence the parasympathetic system and thus cause this type of arrhythmia, it is unlikely that over half the dogs in this study would present with this symptom if the cause was another confounding variable. In addition, we attempted to reasonably rule out comorbidities with additional diagnostics.

While this study provided valuable insights, several limitations should be noted. The single-center design and sample size may limit generalizability. Additionally, the inability to correlate ECG findings with anatomical pathology constrains the conclusions regarding underlying mechanisms. Nonlinear HRV metrics, which offer a more comprehensive assessment, were not included due to their complexity and limited clinical applicability. Further research is warranted to explore these areas and elucidate the interplay between autonomic, electrical, and structural changes in canine CD.

Unlike the Rassi score used in humans, there is no equivalent scale for canines, which limits the ability to extrapolate the effects of HRV on disease progression, morbidity, and mortality in dogs with CD. The classification for heart failure in dogs, such as the modified New York Heart Association scale, primarily assesses the functional capacity and clinical severity of heart failure. While this functional scale does not predict patient outcomes, it is complemented by the human American Heart Association/American Stroke Association guidelines for heart failure.[38] Although these guidelines are not specific for CD, they can be extrapolated to the management of heart disease caused by *T cruzi* by standardizing severity assessment, guiding treatment decisions, and monitoring disease progression. However, because these scales do not predict mortality, their utility in canine CD management remains limited. Further studies are warranted to address these questions.

Chagas disease remains an important disease in both dogs and humans and is a good example of the One Health initiative: synergism in collaboration between veterinarians and health care providers. To this point, dogs are actually considered to be the most important reservoir for the transmission of *T cruzi* and sentinels for human infections, while perpetuating parasite transmission in endemic regions.[39] The data herein will hopefully prompt clinicians to pursue Chagas infection on the differential list for those patients with arrhythmias, conduction abnormalities, or HRV derangements.

Chagas disease is a neglected disease in humans, and unfortunately this may be the case for dogs too, with several factors contributing to underdiagnosis and mismanagement. Inadequate education in veterinary medicine regarding the disease, misinformation on its prevalence, and ignorance regarding the availability of diagnosis and treatment options leads to frequent misdiagnosis and mismanagement of affected pets. The knowledge gap is particularly alarming, with only 51% of veterinary cardiologists reporting comfort with their understanding of canine CD and 28% of those specialists having never even tested for it.[14]

Although these findings revealed no significant differences in HRV parameters between symptomatic and asymptomatic dogs, 63% of infected dogs

exhibited HRV abnormalities, suggesting subclinical autonomic dysfunction. By extrapolating from human studies, HRV may serve as an early marker of disease progression in asymptomatic dogs and a marker of disease severity in symptomatic cases. These findings highlight the importance of further research to validate HRV as a tool for monitoring and risk stratification in canine CD.

This study also underscored the role of HRV in identifying early autonomic and cardiac dysfunction in CD-infected dogs, supporting the hypothesis that dysautonomia would be an early and pervasive feature of CD. By integrating HRV assessment into diagnostic protocols and fostering veterinary-medical collaboration, clinicians can improve the detection and management of this neglected disease, ultimately enhancing outcomes for both canine and human populations.

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