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The canine T wave: a retrospective analysis on qualitative and quantitative T wave variables obtained in 129 healthy dogs and proposed reference intervals

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Abbreviation table

BW	body weight
FBs	French Bulldogs
MEA	mean electrical axis
RIs	reference intervals
R/T concordance	concordance between the R wave and T wave
Tpte	interval from the peak to the end of the T wave
Tpte/QT ratio	ratio between the duration of the Tpte and that of the QT interval
T/R %	ratio between the amplitude of the T wave and that of the R wave

Introduction

The surface electrocardiogram represents a non-invasive, inexpensive, and useful diagnostic tool which is widely available and has been routinely employed in small animal practice for decades [1]. It is primarily used to diagnose disturbances of cardiac rhythm; however, the electrocardiogram may also be used to monitor the response to antiarrhythmic drugs, unveil occult cardiomyopathies as well as cardiac chamber enlargement, and detect cardiac effects of extracardiac factors such as electrolyte abnormalities and drug toxicity [1,2]. The electrocardiographic waveforms are the expression of transmembrane action potentials of atrial and ventricular myocytes [1–3]. The main electrocardiographic components include the P wave, which represents atrial depolarization, the PQ interval, which represents atrioventricular conduction time, the QRS complex, which represents ventricular depolarization, the ST segment and the T wave, which represent the ventricular repolarization, and the QT interval, which provides information on both ventricular depolarization and repolarization [1–3]. In human medicine, the study of repolarization represents a central research topic given its close association with ventricular diastolic function and arrhythmogenesis [4,5]. In contrast, historically, veterinary cardiologists have focused mainly on disturbances of depolarization rather than those of repolarization [6,7]. Moreover, many studies aimed at evaluating electrocardiographic variables in healthy dogs did not analyze important components of ventricular repolarization, such as the ST segment and T wave [8–12]. It should also be highlighted that the few available reports providing data on the T wave in healthy dogs are affected by relevant shortcomings, including small study populations [13–20], a restricted number of breeds enrolled [14,16–19], and/or limited T wave features investigated by each study [13–21]. Consequently, although the history of electrocardiography dates back to the 19th century, the T wave is still considered a poorly characterized and hardly interpretable electrocardiographic variable in dogs [2,3]. A robust background knowledge on the normal features of the canine T wave is essential for a proper interpretation of ventricular repolarization in the clinical setting, especially considering the role that repolarization alterations have in several canine cardiovascular conditions, such as myxomatous mitral valve disease, dilated cardiomyopathy, myocardial injury, familial QT prolongation, and heart failure [20,22–26]. Furthermore, such knowledge may be important for the early recognition of side effects of some frequently used drugs which have been demonstrated to be capable of altering ventricular repolarization and T wave features, both in humans and experimental canine models, such as sotalol [27,28].

Therefore, the purposes of this study were threefold: (1) to evaluate several qualitative and quantitative T wave variables in a large population of healthy dogs; (2) to assess the frequency distribution of selected T wave variables as well as their possible relationship with age, sex, body weight (BW) and somatotype; and (3) to provide reference intervals (RIs) for T wave quantitative variables.

Animals, Materials, and Methods

Study population

Medical records of healthy dogs that underwent an electrocardiogram as part of their diagnostic evaluation at the authors' institutions between January 2014 and June 2021 were retrospectively reviewed by a board-certified cardiologist (G.R.). Reasons for electrocardiographic analysis in an apparently healthy subject could include pre-operative evaluation before elective surgeries (e.g., castration, spaying) or screening for specific cardiac disorders in dogs from highly predisposed breeds. To be included, dogs had to be at least one year of age and have a complete case record, including signalment, history, clinical findings, a minimum laboratory database (including serum electrolytes) performed ≤six months from the examination, and cardiac investigation. The latter had to include at least a transthoracic echocardiography and one–two min six–lead electrocardiogram (leads I, II, III, aVR, aVL, and aVF) acquired at a paper speed of 50 mm/s and paper sensitivity of 10 mm/mV, which had to be performed on the same day according to standardized techniques [1,29]. Dogs were considered healthy based on an unremarkable clinical history and physical examination as well as on normal laboratory, electrocardiographic, and echocardiographic findings. Dogs were excluded if they had any cardiac or extra-cardiac disease as well as if they needed sedation or were receiving any therapy at the time of cardiovascular examination.

Electrocardiographic recording and measurements

In all dogs, an electrocardiogram was conducted with the dog positioned and manually restrained in right lateral recumbency, following the technique described by Tilley in 1992 [1]. All electrocardiograms were recorded in unsedated dogs using two commercially available machines[e,f]. For each animal, an effort was made to obtain an electrocardiographic tracing showing a clean baseline with easily recognizable waveforms. The same investigator (G.R.) manually measured intervals and amplitudes using a caliper and ruler with 0.5-mm graduations. Three representative consecutive beats were used to measure various electrocardiographic variables, and the results were averaged for each variable. Initially, the heart rhythm and conventional variables (i.e., heart rate; amplitude and duration of the P wave; PQ interval duration; R wave amplitude; duration and mean electrical axis in the frontal plane [MEA] of the QRS complex; and QT interval duration) were assessed according to the standard technique to evaluate if there were electrocardiographic abnormalities [2,3]. Such variables were judged to be normal/abnormal according to generic canine RIs [2]. Subsequently, according to the purposes of this study, particular attention was given to T wave qualitative and quantitative features. Qualitative variables were all assessed exclusively in lead II as previously described [2,14,17,20,26,30], and included:

(1) the T wave morphology (Fig. 1A–C): defined as “symmetrical” or “asymmetrical” if the T wave initial and terminal branches had a similar or clearly different slope, respectively. Moreover, it was noted whether the

asymmetricity was due to a gradual upstroke in the initial portion and a more rapid downstroke in the terminal portion, defined as “asymmetrical (slow/fast)”, or to an initial branch that was steeper than the terminal one, defined as “asymmetrical (fast/slow)”. Additional possible morphological patterns that were looked for included “biphasic” T waves (i.e., if T waves showed two peaks that moved in opposite directions in comparison to the baseline, one positive and one negative) and “bifid” (also known as “dome-and-dart”) T waves (i.e., if the ST segment and the first portion of the T wave formed a convex upward curve, followed by the terminal portion of the T wave, which formed a well-defined second positive peak separated from the first by a low amplitude negative deflection);

(2) the T wave polarity (Fig. 2A–C): T waves consisting of a single deflection could be classified as “positive” or “negative” according to the orientation of the wave’s peak in comparison to the baseline. In the case of biphasic T waves, three possible classifications were considered. Specifically, if the two peaks composing a biphasic T wave had different amplitudes, the T wave polarity was classified as positive when the positive peak’s amplitude was greater than the amplitude of the negative one, whereas it was classified as negative in the opposite case. Conversely, if the amplitudes of the two peaks moving in opposite directions were equal, the T wave polarity was classified as “neutral”;

(3) the concordance between the R and T waves (R/T concordance) (Fig. 2A–C): the term “concordant” was used when the R and T waves had the same polarity, while the term “discordant” was used in the opposite scenario. In the

case of a biphasic neutral T wave, the R/T concordance could not be evaluated.

Quantitative variables were assessed as previously described [2,14–16,18–21,26,27,31], and included:

(4) the T wave duration (Fig. 3A–C): measured from the beginning of the wave (i.e., the point where the initial branch of the T wave detached from the baseline) to its end (i.e., the intersection of a line tangential to the point of maximum slope of the terminal T wave with baseline level defined by the T-P segment) in lead II;

(5) the T wave amplitude (Fig. 3A–C): measured from the baseline to the peak of the wave in lead II. In the case of inconstant baseline associated with displacement of PQ interval relative to the TP one (e.g., PQ displacement due to atrial repolarization in patients with tall P waves), the latter interval was used as reference. In the case of a biphasic T wave, the amplitudes of both peaks were measured and noted separately;

(6) the ratio between the amplitude of the T wave and that of the R wave in lead II expressed in percentages (T/R %). Such a variable was not calculated in the case of biphasic T waves;

(7) the MEA of the T wave: calculated from leads I and aVF using the following equation: MEA axis = arctan (I_{amp}, aVF_{amp}) x 180/π (where lead I_{amp} is the amplitude of the T wave in lead I and aVF_{amp} is the amplitude of the T wave in lead aVF);

(8) the interval from the peak to the end of the T wave (Tpte) in lead II. In the case of a biphasic T wave, the interval between the nadir of the first component of the T wave and the end of the T wave was used (Fig. 4A–C);

(9) the ratio between the duration of the Tpte and that of the QT interval (Tpte/QT ratio).

Statistical analysis

All electrocardiographic data were collected into electronic spreadsheets[g] and then imported into a statistical software package[h] for further analysis. All continuous variables were tested for their distribution with a Shapiro–Wilk normality test. Initial descriptive statistics included mean ± standard deviation for normally distributed data and median and range (minimum to maximum) for data that were not normally distributed. For statistical analysis, when needed, dogs were divided according to their BW, age, and somatotype. Weight and age categories were adapted from previous literature [32,33], while somatotype categories were based on breed standards and conventional morphometric indices as previous done by other authors [12,34]. Specifically, dogs were purposefully classified as small (<15 kg) and medium-to-large dogs (≥15 kg), as adult (one–six years) and senior-to-geriatric dogs (≥seven years), and as brachymorphic and non-brachymorphic dogs (i.e., mesomorphic and dolichomorphic dogs grouped together). Continuous and categorical variables were compared between male and female dogs as well as between dogs of distinct BW, age, and somatotype categories using the Mann–Whitney U test and χ^2 test, respectively. To further investigate the role of age and BW on continuous variables, a correlation analysis was also performed. This had the aim of excluding the possibility that the subdivision into categories (i.e., small/medium-to-large dogs and adult/senior-to-geriatric dogs) could obscure a statistically significant relationship of such patient variables on continuous T wave variables. For this purpose, Spearman's correlation coefficients (r_s) between T wave quantitative variables and age as well as BW were calculated. For correlation analysis, age and

BW were not categorized but were used as continuous variables. All variables were evaluated for identification of outliers by visual inspection of histograms and box plots and by Tukey's method [35,36]. Lastly, the 95% RIs of quantitative T wave variables were determined in the overall population using the nonparametric percentile method as recommended by the Clinical and Laboratory Standards Institute when the reference sample exceeds 120 subjects [35]. The 2.5th and 97.5th percentiles were defined as the lower and upper reference limits, respectively. As recommended, 90% confidence intervals around these limits were also calculated using nonparametric methods based on integer ranks, following Clinical and Laboratory Standards Institute guidelines [35]. In contrast, for smaller sample sizes (i.e., less than 120), RIs were determined using the Robust method and confidence intervals about their limits were bootstrapped as recommended[h] [35]. A value of $P<0.05$ was considered significant.

Results

Of the 132 that were initially recruited, three were excluded as the amount of artifact precluded an accurate analysis of the electrocardiographic tracings. Accordingly, the definitive study population was composed by 129 dogs. Forty-eight were male (42 entire and six castrated) and 81 were female (of which 72 entire and nine spayed) with a median age of three years (one–14 years). One hundred and eight and 21 were classified as adult and senior-to-geriatric dogs, respectively. Median BW was 12.2 kg (1.8–47 kg). Ninety-one and 38 were classified as small and medium-to-large dogs, respectively. Sixty-eight dogs were French Bulldogs (FBs); 14 dogs were Doberman Pinschers; six dogs were Labrador Retrievers; five dogs each were Golden Retrievers, Maltese, and Pug; four dogs were German Shepherd dogs; three dogs were Jack Russell Terriers; two dogs each were Boxers and Yorkshire Terriers; and the remaining were an Akita, Argentine Dogo, Australian Shepherd dog, Dachshund, Boston Terrier, Breton, Cane Corso, Cavalier King Charles Spaniel, Giant Schnauzer, Maremma Sheepdog, Miniature Pinscher, Miniature Schnauzer, Nova Scotia Duck Tolling Retriever, Rottweiler, and Vizsla. Seventy-three and 56 were classified as brachymorphic and non-brachymorphic dogs, respectively. Mean heart rate was 124.6 ± 28.3 beats per minute. One hundred and four had a regular sinus rhythm, while 25 dogs showed sinus arrhythmia. In the majority of dogs, all standard electrographic variables were within the generic canine RIs. Only few exceptions have been identified, all in FBs and all concerning the QRS complex MEA. Specifically, such an electrocardiographic variable was documented to be slightly below the generic lower reference limit (+40° [2]) in 12 FBs (from +39° to +25°).

Regarding T wave qualitative variables, the T wave morphology, the T wave polarity, and the R/T concordance were considered not appropriately interpretable only in 2/129 (1.6%), in 1/129 (0.8%), and in 3/129 (2.3%) dogs, respectively. Moreover, an additional seven cases were not included in the statistical analysis on R/T concordance as this qualitative variable could not be calculated according to the methodology employed herein (i.e., dogs with biphasic neutral T waves). Consequently, statistical analysis on T wave morphology, T wave polarity, and R/T concordance was available for 127/129 (98.4%), 128/129 (99.2%), and 119/129 (92.3%) dogs, respectively. In the overall population, T wave morphological patterns were distributed as follows: asymmetrical (slow/fast) in 67/127 (52.8%) dogs, symmetrical in 37/127 (29.1%) dogs, and biphasic in 23/127 (18.1%) dog; whereas no dog showed a symmetrical (fast/slow) or bifid pattern. Moreover, the T wave polarity patterns were distributed as follows: positive in 98/128 (76.6%) dogs, negative in 23/128 (18%) dogs, and neutral in 7/128 (5.5%) dogs. Lastly, T and R waves were more commonly concordant (in 97/119 [81.5%] dogs) than discordant (in 22/119 [18.5%] dogs). Interestingly, a similar frequency distribution was observed in each category (i.e., sex, age, BW and somatotype) for each qualitative variable (i.e., T wave morphology, T wave polarity and R/T concordance). This finding was explained by the lack of statistically relevant differences when comparing T wave morphology, T wave polarity, and R/T concordance between male and female, small and medium-to-large dogs, adult and senior-to-geriatric dogs, and brachymorphic and non-brachymorphic dogs (Tables 1–3).

Similar findings were found for T wave quantitative variables, as no statistically relevant difference was found when comparing T wave duration, T wave amplitude, T wave MEA, T/R %, Tpte, and Tpte/QT ratio between male and female, small and medium-to-large dogs, adult and senior-to-geriatric dogs, and brachymorphic and non-brachymorphic dogs (Table 4).

Spearman's correlation coefficients are presented in Table 5. No statistically significant correlations between T wave quantitative variables and age or BW were found.

Potential outliers were identified neither for T wave duration and MEA nor for T/R %. Identified outliers for remaining variables (i.e., T wave amplitude, Tpte and Tpte/QT ratio) were individually investigated and retained for RIs calculation (Table 6) because they were considered to be obtained from animals confirmed to be clinically healthy and not associated with errors in electrocardiographic measurements [36,37]. Reference intervals were generated using the entire study population (i.e., 129 dogs) in the case of T wave duration, T wave MEA, Tpte, and Tpte/QT ratio. Concerning T/R %, its RI was generated from 106/129 (82.2%) dogs as this quantitative variable could not be calculated in 23 subjects (i.e., dogs with biphasic T waves) according to the methodology employed herein. Among dogs that allowed T/R % calculation, 75/106 (70.8%) subjects had a T/R % <25%, while 31/106 (29.2%) subjects had a T/R % ≥25%. Even in the case of T wave amplitude, the RI was obtained from 106 dogs as the remaining 23 dogs had a biphasic morphological pattern. In these dogs, the amplitudes of two peaks composing their biphasic T waves were purposefully measured and noted separately. In dogs with biphasic T waves, the mean value of the positive peaks was +0.097 mV (± 0.043 mV); whereas, the median value of the negative peaks was -0.1 mV (from -0.5 to -0.05 mV).

Discussion

The T wave is one the most labile waves in the electrocardiogram and may change under several conditions, sometimes creating peculiar patterns that may suggest specific pathological states (e.g., deep/giant negative T waves secondary to myocardial injury [26], peaked T waves secondary to hyperkalemia [38]). Since an essential prerequisite to properly interpret T wave abnormalities is a thorough knowledge of its normal characteristics, we systematically analyzed several T wave features in a large population of healthy subjects, studying both qualitative and quantitative variables. Concerning qualitative variables, the main findings of the present study revealed that: (1) the asymmetrical (slow/fast) morphological pattern occurred most frequently, followed by the symmetrical and the biphasic ones, whereas no healthy dog showed either a symmetrical (fast/slow) or bifid pattern; (2) positive T waves occurred most frequently, followed by negative and neutral ones; and (3) T and R waves were frequently, but not always, concordant in lead II.

On the electrocardiogram, the T wave represents the electrical inhomogeneity in the ventricular repolarization [2,3,39,40]. It is mainly caused by the electrical field generated by the temporal and spatial sequence of repolarization during phase 3 of the membrane action potential [2,3,39,40]. In contrast to depolarization, this phase has a lower voltage, since some repolarization has already occurred during phases 1 and 2 (which correspond to the isoelectric ST segment on the electrocardiogram) and a much slower time course (as there is no specialized conduction system providing the pathway for repolarization) [3,39,40]. Furthermore, in normal conditions, repolarization is not a uniformly propagated phenomenon, but it occurs heterogeneously. Such heterogeneity, which may be found between the apex and the base and transmurally, is mainly due to differences in ion channel density (especially, I_{to}, I_{Kr}, and I_{Ks}) and action potential duration between epicardial, endocardial, and mid-myocardial cells (M cells) [3,39,40]. Given the above, ventricular repolarization normally proceeds from the epicardium to the endocardium as well as from the apex to the base, and repolarization velocity is slower in the subepicardial regions and faster in the subendocardial regions [2,3,36,37]. Such succession of electrical events determines the T wave configuration. In humans, the normal profile of the T wave is typically slightly asymmetric, with a slow ascending branch (the one associated with subepicardial repolarization) and faster descending branch (the one associated with subendocardial repolarization) [39,40]. Moreover, human T waves are normally concordant with the R waves as a consequence of the voltage gradient generated by opposing sequences of transmural depolarization and repolarization (as depolarization, contrary to repolarization, progresses from endocardium to epicardium) [39,40].

However, it is important to acknowledge that the human T wave may be variable in shape under physiological conditions. For example, the T wave polarity may be negative until the age of 12–14 years ("juvenile T wave") and then become positive after the age 16 years in many, but not all, adolescents [41]. Indeed, occasionally, negative T waves persist into adulthood, more frequently in women than in men [42,43]. Age and sex seem to influence even the human T wave morphology. For example, the incidence of bifid T waves may be relatively high in normal children [44]. In contrast, such a morphological pattern is infrequently encountered in adults, even more rarely if they are male [44,45]. Additional sources of variability are represented by ethnicity and levels of physical training [46]. Reasons for such variability are still a matter of debate in human medicine. Possible contributing factors may include differences in myocardial mass, myocardial tissue resistivity, extent of epicardial fat, endocrine status (especially concerning testosterone and estrogen levels), and chest conformation [46–48].

In light of the complexity of interpretation of human T waves, we felt it necessary not only to evaluate T wave qualitative variables in the entire study population, but also in selected categories. Interestingly, results from our overall population resembled those reported in the majority of healthy humans [39,40], as we frequently found asymmetrical (slow/fast) T waves that were positive and concordant with the R waves. Intriguingly, the higher prevalence of positive T waves, followed by that of negative and biphasic ones, were previously observed also by Vila et al. in 15 healthy dogs [20]. However, contrary to human literature, we were unable to demonstrate any apparent difference related to age, sex, BW, or somatotype. In light of the number of dogs enrolled herein, it seems unlikely that such a discrepancy may arise from a limited sample size, but it may rather be an expression of intrinsic species-related differences [49]. We also assume that some differences may become evident by investigating in future the effects on ventricular repolarization exerted by further possible influencing variables, such as the endocrine status (e.g., sex hormone levels), body condition score, respiration phase (e.g., inspiration versus expiration), and athletic level (e.g., working/sporting dogs versus companion dogs) of the enrolled subjects.

Concerning quantitative variables, we investigated several variables with the aim of providing statistically reliable RIs either for those commonly assessed is small animal practice (e.g., T wave duration and amplitude) and those that, although less familiar among veterinarians, have been reported to have clinically-relevant implications in dogs (e.g., Tpte and Tpte/QT ratio have been demonstrated to be good markers to predict ventricular arrhythmias and all-cause mortality in dogs with myxomatous mitral valve disease [20]). Although some previous studies reported mean and median values for some of these variables, it is important to highlight that the majority of them did not enroll enough dogs to be able to provide RIs with adequate statistical power [14–20]. However, some similarities between previously documented mean/median values and our median values can be noted, including those related to the T wave duration [17,19], the Tpte, and the Tpte/QT ratio [20]. A further similarity regards the median of amplitude values measured in dogs with positive and negative T waves [14,17,18,21]. Concerning the amplitudes of positive and negative peaks composing biphasic T waves, comparison with previous literature is limited by the fact that, although such a morphological pattern has been identified even by many investigators [13,14,20], only one study reported specific measurements in this regard. Precisely, Hill [13], observed that the amplitude of both positive and negative peaks did not exceed 0.5 mV in dogs with biphasic T waves. Interestingly, this finding agrees with the results of our study. Concerning the T wave MEA, comparison is limited by the fact that, to our knowledge, only one previous study evaluated such a variable in healthy dogs [13]. Moreover, in that study, the author did not provide a RI representative of the entire study population, but presented results concerning T wave MEA distinguishing dogs with positive values from those with negative ones (i.e., they reported a MEA ranging from +26° to +180° in 35 dogs, and a MEA ranging from -45° to -147° in the remaining 35 dogs composing their study population) [13]. Nevertheless, it is intriguing to note that our minimum and maximum values (i.e., -146° and +180°) were almost identical to the lower negative and upper positive values previously documented [13]. A final consideration should be made concerning the T/R %. Although some veterinary textbooks state that the normal T wave should be <25% of the R wave amplitude in dogs [50–52], such a finding seems not to be supported by robust background evidence from original studies. Therefore, comparison between textbooks and our data should be made cautiously. Even if the majority (70.8%) of dogs enrolled herein had a T/R % <25% and the median T/R % value of our study population (i.e., 18%) fell into the cutoff mentioned by textbooks, it is interesting to note that some dogs (29.2%) had higher values and that the maximum value that we calculated (i.e., 71.4%) was remarkably beyond the aforesaid limit. Given the above, we believe that a T/R % <25% may represent an appropriate cutoff for many but not all dogs, and that a T/R % ≥25% should not be systematically interpreted as a certain pathological electrocardiographic finding, especially when this value is observed in healthy dogs with an otherwise normal electrocardiographic tracing. On the other hand, based on our results, we can hypothesize that a T wave approximately ≥75% of the R wave amplitude should always raise concern and prompt further investigations (e.g., assessment of serum potassium level to rule out hyperkalemia [38]).

As done for qualitative variables, we investigated the possible influence of age, sex, BW, and somatotype on quantitative variables. In line with the results from analysis on qualitative variables, we were unable to identify any statistically relevant influence of the aforesaid variables on T wave quantitative variables. Interestingly, this finding partially agreed with previous canine studies. Indeed, two studies found no effect of age and sex on T wave amplitude and duration [19,21], and another study demonstrated no statistically relevant differences in T wave amplitude among dogs of different sex and BW [17]. At the same time, it is important to underline that our results disagreed with human literature, as variables such as age, sex, and ethnicity have been demonstrated to influence T wave measurements in people [45,47,48,53]. As previously stated for qualitative variables, we do not know for certain whether this discrepancy may be due to intrinsic species-related differences or to the relatively limited number of variables investigated herein.

The results of the present study should be read in the context of certain limitations, first the retrospective design that prevented standardization of the time between electrocardiographic examinations and laboratory analysis. The fact that bloodwork was not systematically obtained on the day of electrocardiographic examination represents a limitation as it cannot be conclusively ruled out that some hematologic abnormality could have occurred at the time of the electrocardiogram. Nevertheless, it is unlikely that relevant laboratory changes may have arisen in the time between the blood tests and the electrocardiogram considering that all enrolled dogs appeared clinically healthy at the time of cardiological evaluation. The retrospective design also prevented a systematic and standardized acclimatation of dogs before electrocardiographic analysis. Second, our analysis was conducted exclusively on six–lead electrocardiograms, and almost all the T wave variables were assessed only in lead II as it represents the lead traditionally employed by veterinarians for electrocardiographic measurements [3,52]. Third, although the overall number of dogs enrolled was high, the number of subjects composing some categories was relatively low (e.g., the senior-to-geriatric dogs). Moreover, the sample size of groups composing each category was not always equally balanced (e.g., female and adult dogs were remarkably overrepresented compared to male and senior-to-geriatric dogs, respectively). Fourth, the high prevalence of FBs (likely caused by their recent exponential diffusion in our country [54, 55]) may have represented a source of bias; nevertheless, it was also useful, as it allowed us to create a wide group of brachymorphic dogs that almost proportionately counterbalanced the non-brachymorphic dogs. Concerning FBs, it should be also noticed that 12 dogs from this breed had a QRS complex MEA slightly below the generic RI provided by textbooks. Despite such a finding, we decided to maintain these dogs in our final analysis as they fulfilled all inclusion criteria (i.e., they were clinically healthy subjects with normal echocardiographic and laboratory findings) and their remaining electrocardiographic variables were within generic RIs. Our choice was also supported by data from a recent electrocardiographic survey in a large population of FBs demonstrating that a physiological left-shift of QRS complex MEA can be documented in healthy subjects from this breed, hypothetically due to their brachymorphic conformation rather than due to a true conduction disturbance [55].

Conclusions

In conclusion, a detailed description of several qualitative and quantitative features of the normal canine T waves is provided. Because our findings were obtained using a standardized electrocardiographic analysis in a large population of healthy dogs, they likely represent a reliable and broadly applicable guide for interpretation of the canine T wave.

Conflicts of interest

None of the authors has a conflict of interest.

Footnotes

[e] Cube ECG, Cardioline S.p.A., Caverano, Italy.

[f] ECG100S, Cardioline S.p.A., Italy.

[g] Microsoft Excel, version 2016, Microsoft Corporation, Redmond, Washington (USA).

[h] MedCalc Statistical Software version 19.5.1, Ostend, Belgium.

References

[1] Tilley LP. Principles of electrocardiographic recording. In: Tilley LP, editor. Essentials of Canine and Feline Electrocardiography: Interpretation and Treatment. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 1992, p. 21–39.

[2] Santilli RA, Moïse NS, Pariaut R, Perego M. Formation and interpretation of the electrocardiographic waves. In: Santilli RA, Moïse NS, Pariaut R, Perego M, editors.

Electrocardiography of the Dog and Cat – Diagnosis of Arrhythmia. 2nd ed. Milano: Edra; 2018, p. 35–70.

[3] Oliveira P. Cardiac vectors and the genesis of the electrocardiogram. In: Willis R, Oliveira P, Mavropoulou A, editors. Guide to Canine and Feline Electrocardiography. 1st ed. Oxford: John Wiley & Sons; 2018, p. 21–33.

[4] Zhu TG, Patel C, Martin S, Quan X, Wu Y, Burke JF, Chernick M, Kowey PR, Yan GX. Ventricular transmural repolarization sequence: its relationship with ventricular relaxation and role in ventricular diastolic function. Eur Heart J 2009;30:372–80.

[5] Osadchii OE. Role of abnormal repolarization in the mechanism of cardiac arrhythmia. Acta Physiol (Oxf) 2017;220:1–71.

[6] Patterson DF, Detweiler DK, Hubben K, Botts RP. Spontaneous abnormal cardiac arrhythmias and conduction disturbances in the dog. A clinical and pathologic study of 3000 dogs. Am J Vet Res 1961;22:355–69.

[7] Noszczyk-Nowak A, Michałek M, Kałuża E, Cepiel A, Pasławska U. Prevalence of arrhythmias in dogs examined between 2008 and 2014. J Vet Res 2017;61:103–10.

[8] Schneider HP, Truex RC, Knowles J. Comparative observations of the hearts of mongrel and Greyhound dogs. Anat Rec 1964;149:173–80.

[9] Eckenfels A, Trieb G. The normal electrocardiogram of the conscious Beagle dog. Toxicol Appl Pharmacol 1979;47:567–84.

[10] Hanton G, Rabemampianina Y. The electrocardiogram of the Beagle dog: reference values and effect of sex, genetic strain, body position and heart rate. Lab Anim 2006;40: 123–36.

[11] Carnabuci C, Tognetti R, Vezzosi T, Marchesotti F, Patata V, Domenech O. Left shift of the ventricular mean electrical axis in healthy Doberman Pinschers. J Vet Med Sci 2019;81:620–25.

[12] Santilli RA, Porteiro Vázquez DM, Gerou-Ferriani M, Lombardo SF, Perego M. Development and assessment of a novel precordial lead system for accurate detection of right atrial and ventricular depolarization in dogs with various thoracic conformations. Am J Vet Res 2019;80:358–68.

[13] Hill JD. The electrocardiogram in dogs with standardized body and limb positions. J Electrocardiol 1968;1:175–82.

[14] Rezakhani A, Atwell RB, Webster J. Electrocardiographic values of German Shepherd dogs. Aust Vet J 1990;67:307–9.

[15] Kanui T, Onyango E, Buoro I. The normal electrocardiogram in mongrel dogs in Kenya. Kenya Veterinarian 2000;19:27–9.

[16] Dijkstra M, Szatmári V. The T wave in the V10 precordial electrocardiographic lead is negative in healthy Chihuahua dogs. J Vet Cardiol 2009;11:123–7.

[17] Gugjoo MB, Hoque M, Saxena AC, Zama MM. Reference values of six-limb-lead electrocardiogram in conscious Labrador Retriever dogs. Pak J Biol Sci 2014;17:689–95.

[18] Mukherjee J, Das PK, Ghosh PR, Banerjee D, Sharma T, Basak D, Sanyal S. Electrocardiogram pattern of some exotic breeds of trained dogs: a variation study. Vet World 2020;8:1317–20.

[19] Lerdweeraphon W, Thanwongsa S, Youyod S, Imsopa S, Kenchaiwong W. The effects of breed, age, sex, and body weight on electrocardiographic parameters in military working dogs. Vet World 2020;13:1001–04.

[20] Vila BCP, Camacho AA, Sousa MG. T-wave peak-end interval and ratio of T-wave peak-end and QT intervals: novel arrhythmogenic and survival markers for dogs with myxomatous mitral valve disease. J Vet Cardiol 2021;35:25–41.

[21] Mukherjee J, Mohapatra SS, Jana S, Das PK, Ghosh PR, Banerjee KDAD. A study on the electrocardiography in dogs: reference values and their comparison among breeds, sex, and age groups. Vet World 2020;13:2216–20.

[22] Koyama H, Yoshii H, Yabu H, Kumada H, Fukuda K, Mitani S, Rousselot JF, Hirose H, Uchino T. Evaluation of QT interval prolongation in dogs with heart failure. J Vet Med Sci 2004;66:1107–11.

[23] Noszczyk-Nowak A. QTc dispersion and T-wave alternans as predictors of mortality in dogs with dilated cardiomyopathy and ventricular tachycardia in Holter monitoring. A retrospective study. Bull Vet Inst Pulawy 2012;56:189–92.

[24] Ware WA, Reina-Doreste Y, Stern JA, Meurs KM. Sudden death associated with QT interval prolongation and KCNQ1 gene mutation in a family of English Springer Spaniels. J Vet Intern Med 2015;29:561–8.

[25] Brüler BC, Jojima FS, Dittrich G, Giannico AT, Sousa MG. QT instability, an indicator of augmented arrhythmogenesis, increases with the progression of myxomatous mitral valve disease in dogs. J Vet Cardiol 2018;20:254–66.

[26] Romito G, Cipone M. Transient deep and giant negative T waves in dogs with myocardial injury. J Vet Cardiol 2021;36:131–40.

[27] Emori T, Antzelevitch C. Cellular basis for complex T waves and arrhythmic activity following combined I(Kr) and I(Ks) block. J Cardiovasc Electrophysiol 2001;12:1369–78.

[28] Malik M. Drug-induced changes in the T-wave morphology. Drug Saf 2009;32:613–7.

[29] Thomas WP, Gaber CE, Jacobs GJ, Kaplan PM, Lombard CW, Moise NS, Moses BL. Recommendations for standards in transthoracic two-dimensional echocardiography in the dog and cat. Echocardiography Committee of the Specialty of Cardiology, American College of Veterinary Internal Medicine. J Vet Intern Med 1993;7:247–52.

[30] Romito G, Côté E, Domenech O. ECG of the month. Sinus tachycardia due to albuterol-induced hypokalemia. J Am Vet Med Assoc 2013;243:1108–10.

[31] Xia Y, Liang Y, Kongstad O, Holm M, Olsson B, Yuan S. Tpeak-Tend interval as an index of global dispersion of ventricular repolarization: evaluations using monophasic action potential mapping of the epi- and endocardium in swine. J Intervent Card Electrophysiol 2005;14:79–87.

[32] Wallis C, Saito EK, Salt C, Holcombe LJ, Desforges NG. Association of periodontal disease with breed size, breed, weight, and age in pure-bred client-owned dogs in the United States. Vet J 2021;275:105717.

[33] Harvey ND. How old is my dog? Identification of rational age groupings in pet dogs based upon normative age-linked processes. Front Vet Sci 2021;8:643085.

[34] Groppetti D, Pecile A, Palestrini C, Marelli SP, Boracchi P. A national census of birth weight in purebred dogs in Italy. Animals (Basel) 2017;7:43.

[35] CLSI. Defining, establishing, and verifying reference intervals in the clinical laboratory; approved guideline – third edition. CLSI document EP28-A3c. Wayne, PA: Clinical Laboratory Standards Institute; 2008.

[36] Friedrichs KR, Harr KE, Freeman KP, Szladovits B, Walton RM, Barnhart KF, Blanco-Chavez J; American Society for Veterinary Clinical Pathology. ASVCP reference interval guidelines: determination of de novo reference intervals in veterinary species and other related topics. Vet Clin Pathol 2012;41:441–53.

[37] Dunlop MM, Sanchez-Vazquez MJ, Freeman KP, Gibson G, Sacchini F, Lewis F. Determination of serum biochemistry reference intervals in a large sample of adult greyhounds. J Small Anim Pract 2011;52:4–10.

[38] Tag TL, Day TK. Electrocardiographic assessment of hyperkalemia in dogs and cats. J Vet Emerg Crit Care 2008;18:61–7.

[39] Hlaing T, DiMino T, Kowey PR, Yan GX. ECG repolarization waves: their genesis and clinical implications. Ann Noninvasive Electrocardiol 2005;10:211–23.

[40] Conrath CE, Opthof T. Ventricular repolarization: an overview of (patho)physiology, sympathetic effects and genetic aspects. Prog Biophys Mol Biol 2006;92:269–307.

[41] Onat T, Onat A, Can G. Negative T wave in chest lead V1: relation to sex and future cardiovascular risk factors. Turk Kardiyol Dern Ars 2008;36:513–8.

[42] Hiss RG, Averill KH, Lamb LE. Electrocardiographic findings in 67,375 asymptomatic subjects. VIII. Nonspecific T wave changes. Am J Cardiol 1960;6:178–89.

[43] Aro AL, Anttonen O, Tikkanen JT, Junttila MJ, Kerola T, Rissanen HA, Reunanen A, Huikuri HV. Prevalence and prognostic significance of T-wave inversions in right precordial leads of a 12-lead electrocardiogram in the middle-aged subjects. Circulation 2012;125:2572–7.

[44] Calabrò MP, Barberi I, La Mazza A, Todaro MC, De Luca FL, Oreto L, Russo MS, Cerrito M, Bruno L, Oreto G. Bifid T waves in leads V2 and V3 in children: a normal variant. Ital J Pediatr 2009;35:17.

[45] Mansi IA, Nash IS. Ethnic differences in electrocardiographic amplitude measurements. Ann Saudi Med 2004;24:459–64.

[46] McClean G, Riding NR, Pieles G, Sharma S, Watt V, Adamuz C, Johnson A, Tramullas A, George KP, Oxborough D, Wilson MG. Prevalence and significance of T-wave inversion in Arab and Black paediatric athletes: should anterior T-wave inversion interpretation be governed by biological or chronological age? Eur J Prev Cardiol 2019;26:641–52.

[47] Blackburn H; Vasquez CL; Keys A. The aging electrocardiogram: a common aging process or latent coronary artery disease? Am J Cardiol 1967;20:618–27.

[48] Carbone V, Guarnaccia F, Carbone G, Zito GB, Oliviero U, Soreca S, Carbone F. Gender differences in the 12-lead electrocardiogram: clinical implications and prospects. Ital J Gender-Specific Med 2020;6:126–41.

[49] Lepeschkin E. The configuration of the T wave and the ventricular action potential in different species of mammals. Ann N Y Acad Sci 1965;127:170–8.

[50] Tilley LP. Analysis of canine P-QRS-T deflections. Principles of electrocardiographic recording. In: Tilley LP, editor. Essentials of Canine and Feline

Electrocardiography: Interpretation and Treatment. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 1992, p. 59–99

[51] Anderson E. Electrocardiography. In: Ettinger SJ, Feldman EC, Côté E, editors. Textbook of Veterinary Internal Medicine. 8th ed. St. Louis, Missouri: Elsevier; 2017, p. 390–2.

[52] Willis R. Electrocardiography. In: Willis R, Oliveira P, Mavropoulou A, editors. Guide to Canine and Feline Electrocardiography. 1st ed. Oxford: John Wiley & Sons; 2018, p. 35–56.

[53] Xie Z, Wang C, Li M. Electrocardiographic T-wave amplitude of normal population and its correlation with age, sex and race. Hunan Yi Ke Da Xue Xue Bao 1999;24:335–40.

[54] [Internet] Ente Nazionale Cinofilia Italiana. 2021. [cited October 6, 2021]. Available from: https://www.enci.it/libro-genealogico/razze/bouledogue-francese

[55] Romito G, Castagna P, Sabetti MC, Cipone M. Physiological shift of the ventricular mean electrical axis in healthy French Bulldogs: a retrospective electrocardiographic analysis of 80 healthy dogs. J Vet Cardiol 2022 [In Press]. doi: https://doi.org/10.1016/j.jvc.2022.05.001.

Figure legends

Figure 1. Selected close-ups of electrocardiographic tracings obtained in three healthy dogs. In all cases, a single complex recorded in lead II has been selected to illustrate in detail distinct T wave morphological patterns. A. Asymmetrical (slow/fast) T wave. B. Symmetrical T wave. C. Biphasic T wave.

Figure 2. Selected close-ups of electrocardiographic tracings obtained in three healthy dogs. In all cases, a single complex recorded in lead II has been selected to illustrate in detail distinct T wave polarity patterns as well as the concordance between the T wave and the R wave. A. Positive T wave that is concordant with the R wave. B. Negative T wave that is discordant with the R wave. C. Neutral T wave. Note that the T wave morphology is biphasic and the two opposite peaks have an almost identical amplitude. In this case, concordance between the T wave and the R wave cannot be established.

Figure 3. Selected close-ups of electrocardiographic tracings obtained in three healthy dogs. In all cases, a single complex recorded in lead II has been selected to illustrate in detail how T wave amplitude and duration have been measured. A. Measurements in a dog with a positive T wave. B. Measurements in a dog with a negative T wave. C. Measurements in a dog with a biphasic T wave. In each panel, the blue dotted lines help to identify the baseline, the red dotted lines the start and the end of the T waves, and the green dotted lines the T wave amplitudes.

Figure 4. Selected close-ups of electrocardiographic tracings obtained in the same three healthy dogs from Figure 3. In all cases, a single complex recorded in lead II has been selected to illustrate in detail how Tpte has been measured according to previous indications [20]. A. Measurement in a dog with a positive T wave. B. Measurement in a dog with a negative T wave. C. Measurement in a dog with a biphasic T wave. In each panel, the blue dotted lines help to identify the baseline, while the red dotted lines the reference points for the measurement of Tpte. Tpte: T wave peak-end interval duration.