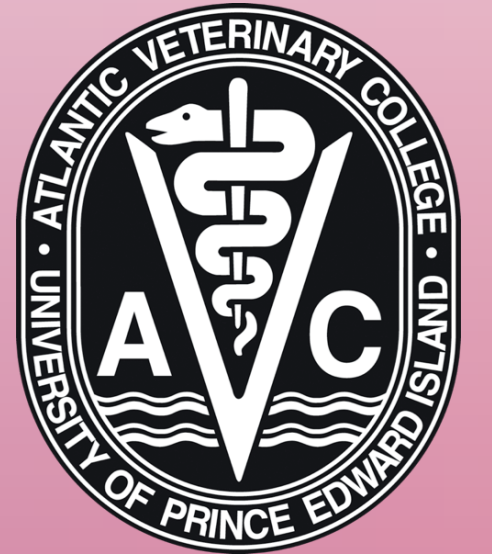


Retrospective Evaluation of Electrocardiographic T-wave Indices in

Doberman Pinschers with Dilated Cardiomyopathy

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Introduction

Dilated cardiomyopathy (DCM) is a common heart disease in dogs, especially Doberman pinchers, in which affected dogs are at high risk of congestive heart failure (CHF) and sudden cardiac death (SD). Arrhythmias associated with SD may be detectable on an electrocardiogram (ECG), but not all dogs with arrhythmias will experience SD. It can be challenging to predict which dogs are at higher risk for this outcome. Abnormal cardiac repolarization, the phase represented by the T-wave on an ECG, can lead to higher risk of arrhythmia and SD. In humans with heart disease and in dogs with mitral valve disease, T-wave indices have been shown to have utility in arrhythmia prediction and risk stratification. T-wave indices have not been examined in dogs with DCM.

Hypotheses and Objectives

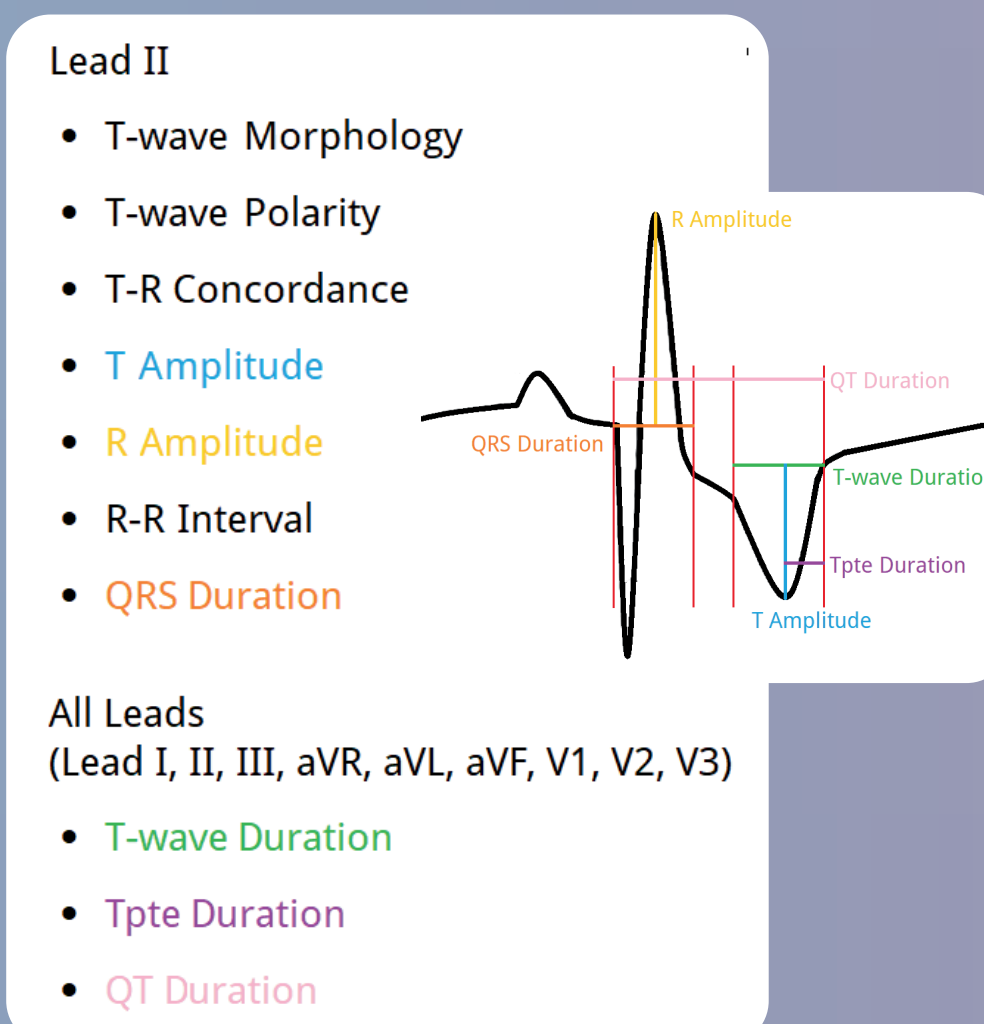
1. Dobermans with DCM will demonstrate repolarization (T-wave) abnormalities compared to normal dogs
2. T-wave indices will differ between Dobermans with and without arrhythmias
3. T-wave indices will differ between Dobermans with and without sudden death outcome

The objectives of this study were to examine ECGs in a group of Dobermans with DCM, measure T-wave variables, and determine whether these variables are associated with arrhythmia status or outcome.

Materials and Methods

This is a retrospective study of previously acquired ECGs in 59 Doberman pinchers with DCM and CHF. Data such as birth date, sex, death date and cause, and presence and frequency of premature ventricular complexes (PVC) were taken from the medical records.

ECGs were scanned into a digital format and measurements made using the application IC Measure. Each ECG was calibrated individually, and T-wave variables (shown in figure below) were measured in 3 consecutive sinus beats, where possible. Using the measured indices, T/R ratio, QTc interval, Tpte/QT ratio, QT dispersion, QTc dispersion, and Tpte dispersion were calculated. QTc was calculated using the formula $QT/(RR^{1/3})$. The QT dispersion, QTc dispersion, and Tpte dispersion were calculated by subtracting minimum value from maximum value in any lead, for each variable, respectively.



5 ECGs were initially used for training, and all ECG measurements were revised by the project supervisor.

Statistics were run using the applications JMP and GraphPad Prism. All variables were plotted to examine for outliers or errors. The data were tested for normality using the Shapiro-Wilk test. Data were reported as mean +/- standard deviation for normally distributed data and median [interquartile range] for non-normally distributed data. A one sample Wilcoxon Signed Rank test was used to compare data with available published normal reference values. T-wave indices were compared among groups of interest (SD vs non-SD, PVC vs no PVC) by t-tests for normally distributed data or Wilcoxon Rank Sum tests for non-normally distributed data.

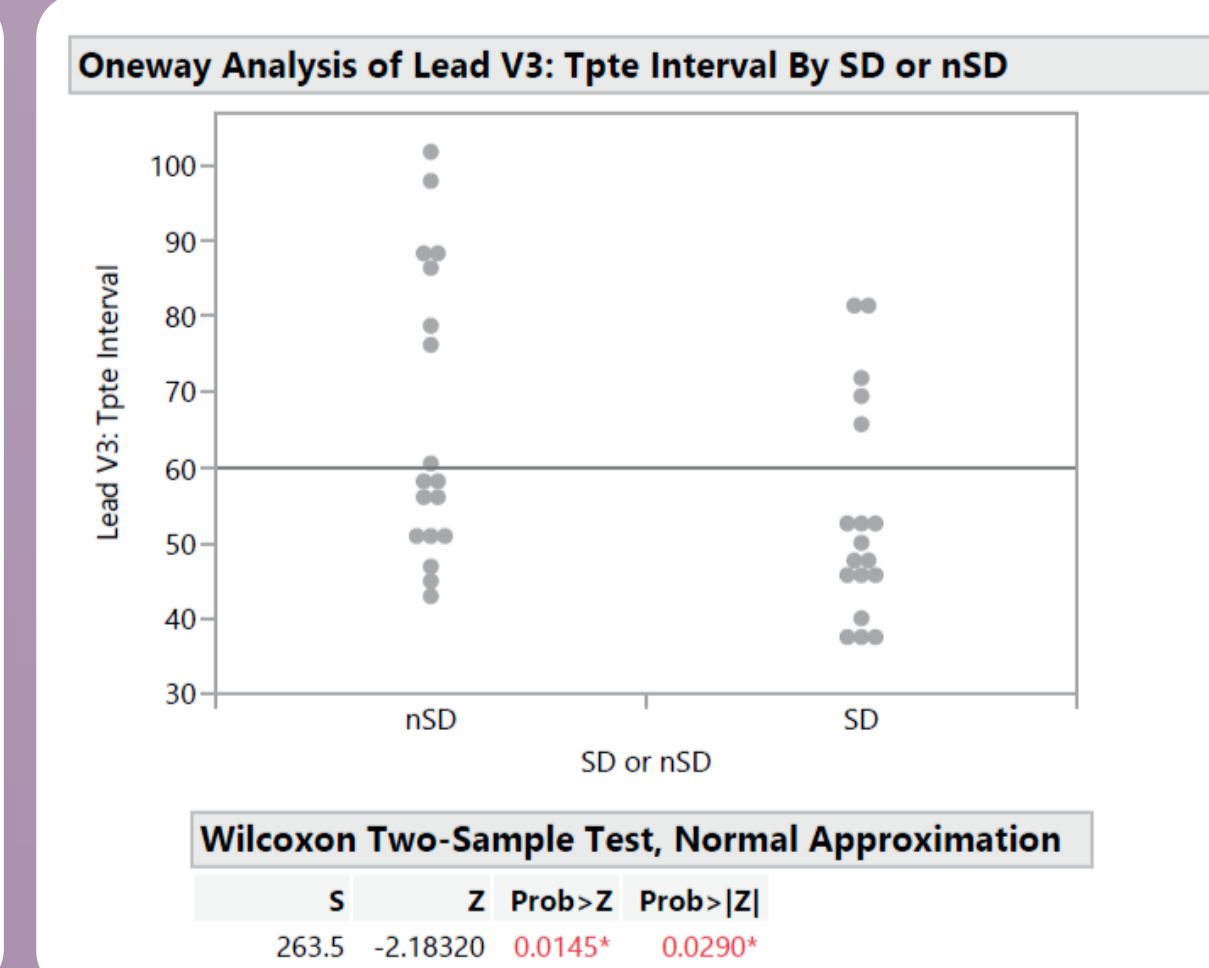
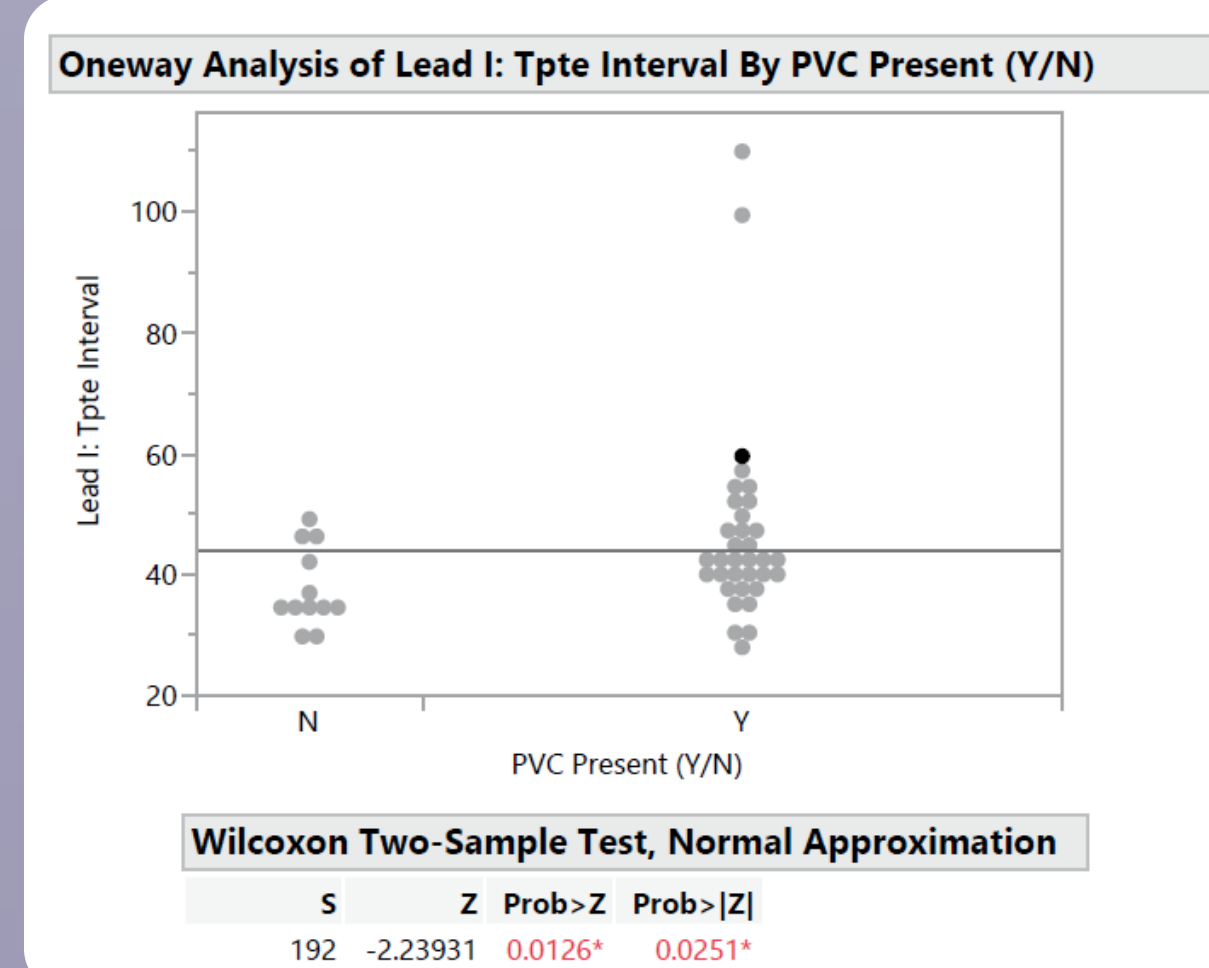
Results

DCM study group medians compared to available published normal reference medians.

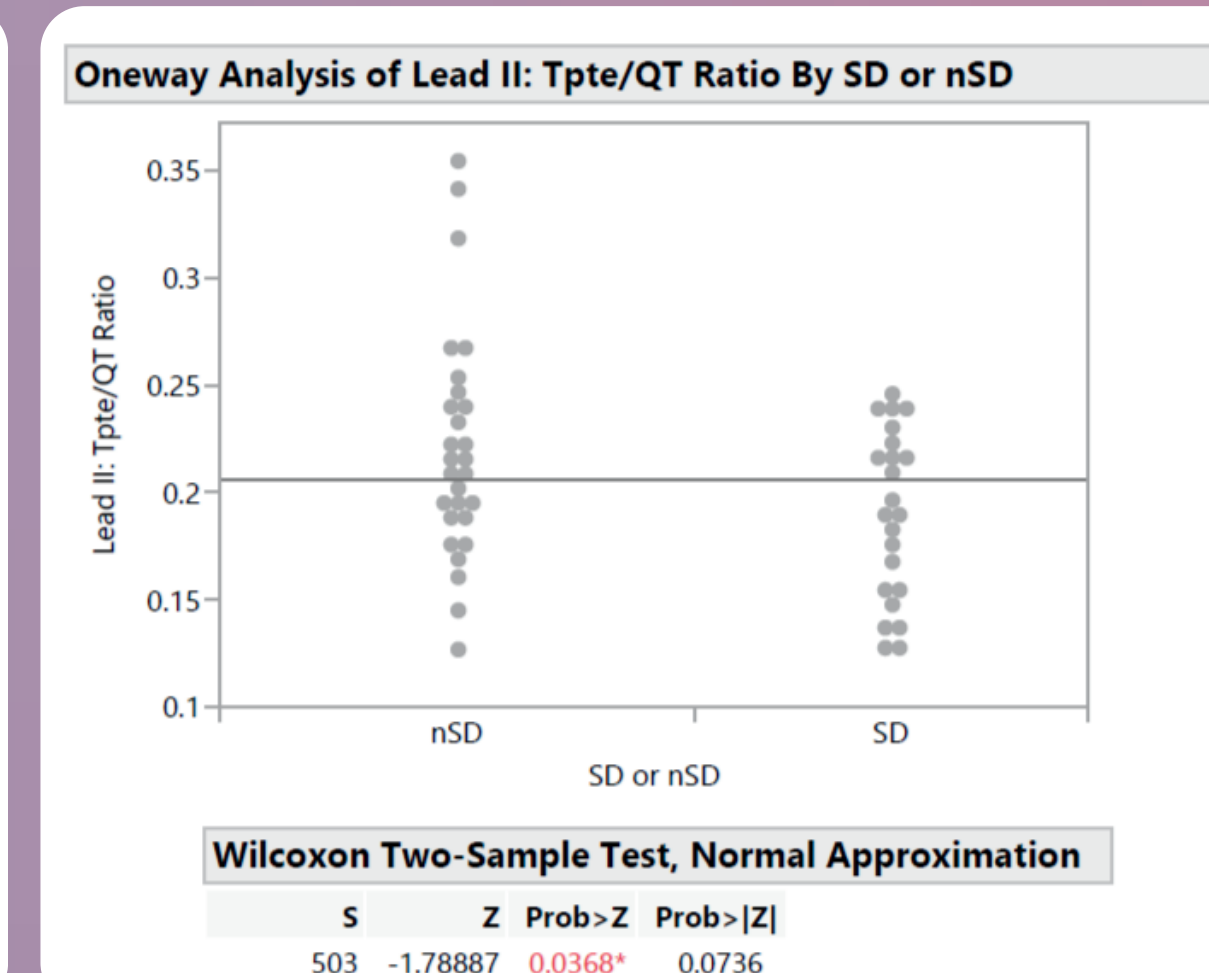
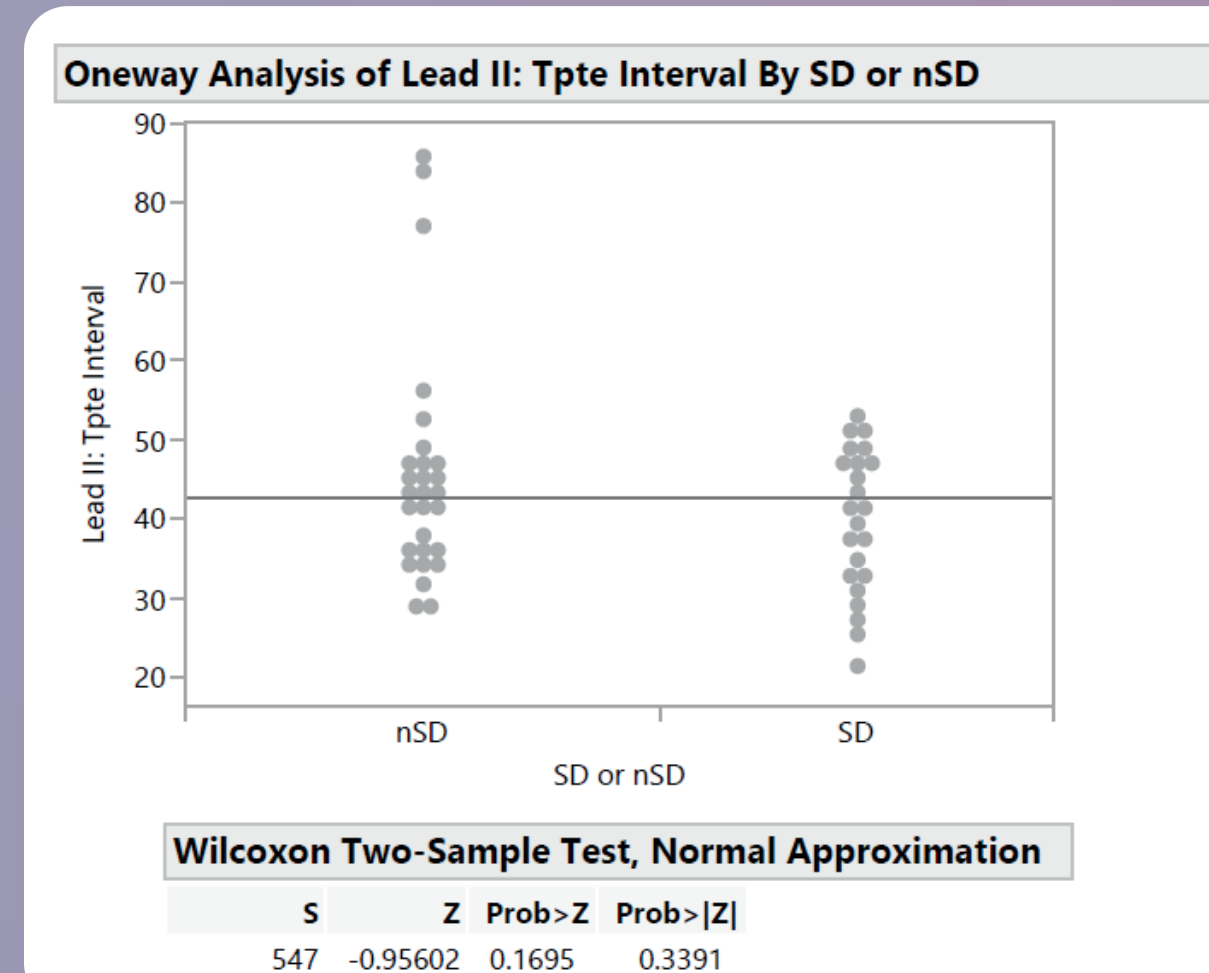
| | Normal Reference Medians | DCM Median | P-value (two tailed) |
|-------------------------------|--------------------------|------------|----------------------|
| Lead II T-wave Duration (ms) | 60 | 94.13 | <0.0001 |
| Lead II T-wave Amplitude (mV) | 0.15 | 0.50 | <0.0001 |
| Lead II T/R % | 0.18 | 0.43 | <0.0001 |
| Lead II QTc (ms) | 230.3 (212.6-245.6) | 263.6 | <0.0001 |
| Lead II Tpte (ms) | 25 | 42.07 | <0.0001 |
| Lead II Tpte/QT | 0.13 | 0.20 | <0.0001 |

| | Normal Reference Medians | DCM Median | P-value (two tailed) |
|--------------------|--------------------------|------------|----------------------|
| Lead I QTc (ms) | 226.4 (210.9-233.3) | 266.7 | <0.0001 |
| Lead I Tpte (ms) | 24.5 (21-29.5) | 40.53 | <0.0001 |
| Lead I Tpte/QT | 0.1378 (0.1198-0.1714) | 0.20 | <0.0001 |
| Lead III QTc (ms) | 227.9 (216.9-239.7) | 269.2 | <0.0001 |
| Lead aVR QTc (ms) | 231.4 (214.9-237.6) | 261.9 | <0.0001 |
| Lead aVL QTc (ms) | 230 (223.1-236.5) | 267 | <0.0001 |
| Lead aVL Tpte (ms) | 25 (23-27) | 44.00 | <0.0001 |
| Lead aVL Tpte/QT | 0.1405 (0.1327-0.1535) | 0.21 | <0.0001 |
| Lead aVF QTc (ms) | 226.9 (217.8-236.6) | 267.9 | <0.0001 |
| Lead aVF Tpte (ms) | 27 (20.75-28.75) | 44.87 | <0.0001 |
| Lead aVF Tpte/QT | 0.1489 (0.1202-0.175) | 0.22 | <0.0001 |
| Lead V2 QTc (ms) | 231.1 (222.4-246.4) | 293.9 | <0.0001 |
| Lead V2 Tpte (ms) | 32 (30-35) | 59.87 | <0.0001 |
| Lead V2 Tpte/QT | 0.177 (0.154-0.1849) | 0.24 | <0.0001 |

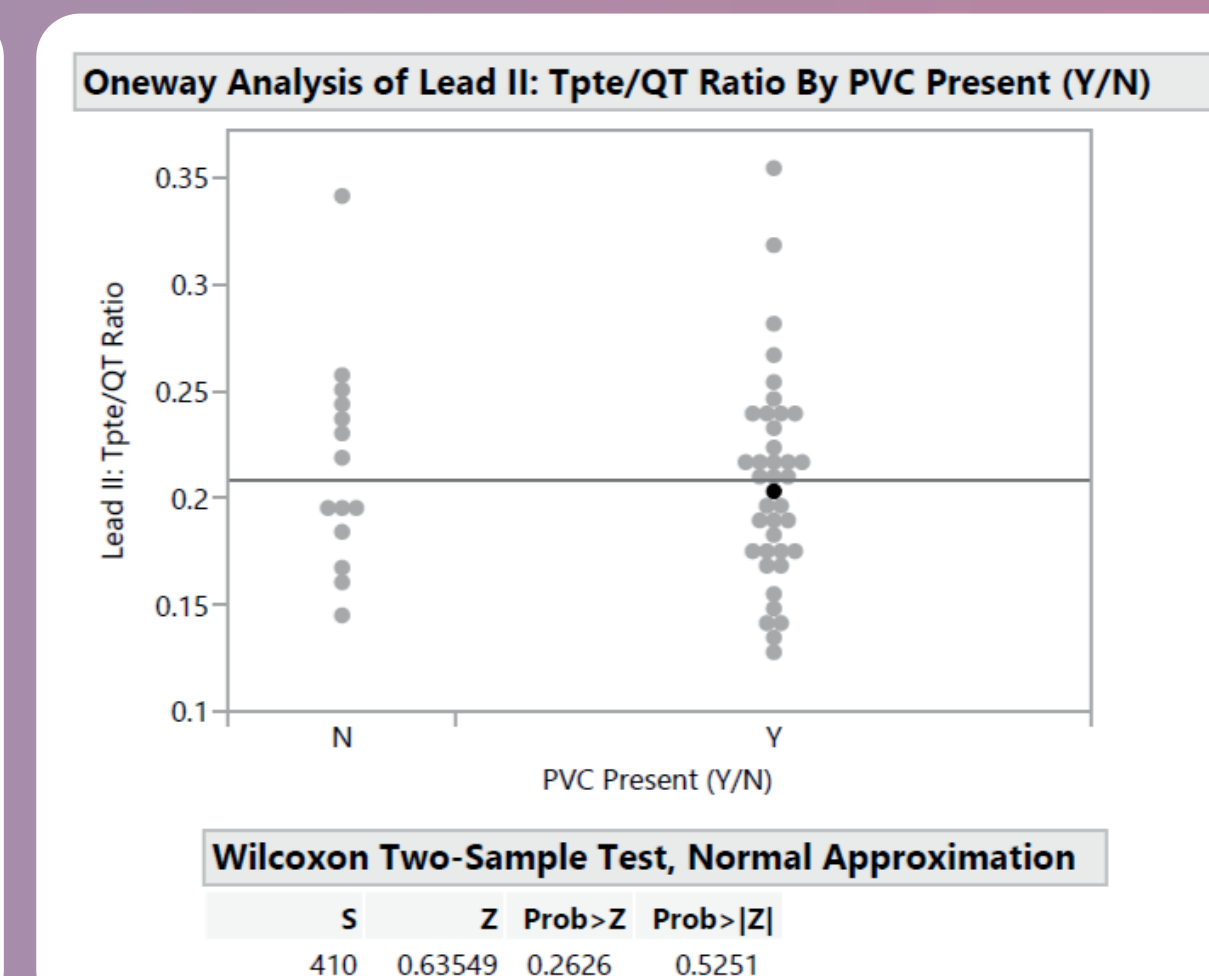
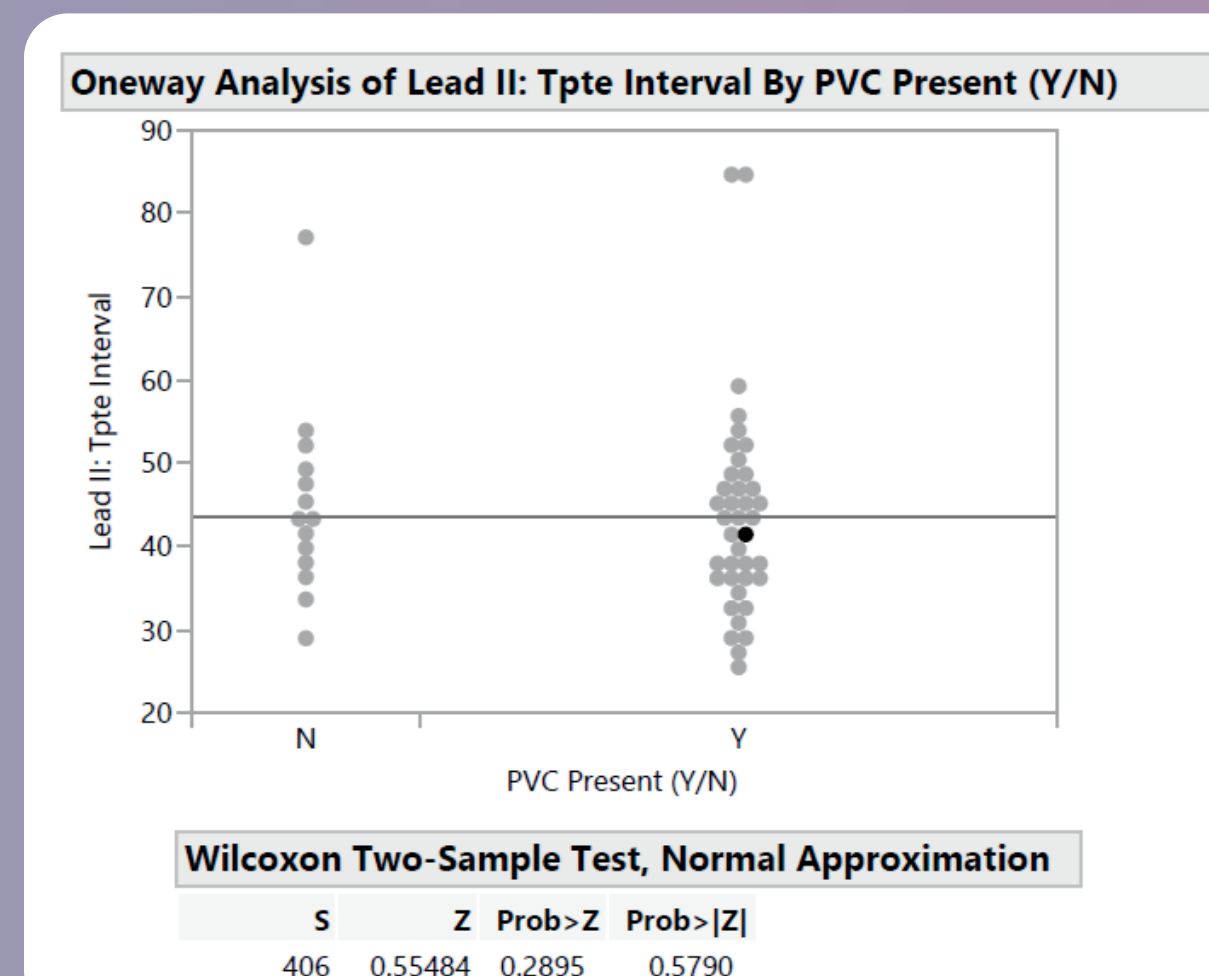
Out of 109 group comparisons made (56 for SD, 53 for PVC), only 2 were significant.



Group comparisons of lead II Tpte interval and Tpte/QT ratio for SD vs non-SD.



Group comparisons of lead II Tpte interval and Tpte/QT ratio for PVC presence (Y/N).



Discussion

- Comparing available published normal reference medians to the study DCM group, significant differences were detected, suggesting evidence that Dobermans with DCM had repolarization abnormalities. This makes clinical sense, as cardiomyopathies have been associated with ionic and structural remodeling of the ventricles, leading to electrical dysregulation.
- Only 1/56 variables (lead V3 Tpte interval) for outcome and 1/53 variables (lead I Tpte interval) for arrhythmia presence were significant. This was unexpected, as Tpte interval and Tpte/QT ratio have been well recognized in the medical literature for their use as indices of arrhythmogenesis and mortality in humans with DCM. Only Tpte in lead I was significantly longer in Dobermans with PVC compared to those without.
- Lead V3 Tpte interval data were unexpected, as logically Tpte interval should become longer in dogs at risk for sudden death. This finding could be due to many missing data points for lead V3 due to artifact.
- Additional statistical modelling and survival analyses may provide further insight into the data.
- Project limitations: retrospective evaluations are more prone to selection bias, confounding data, and missing data; euthanasia was considered a non-SD endpoint, but the presence of euthanasia confounds natural death outcomes; all Dobermans in this study were in active CHF, thus our results are only applicable to this specific subset of dogs with DCM; some dogs with DCM may die before entering CHF, and the value of risk assessment may be earlier in the disease; diagnosis of arrhythmias was based solely on the interpretation of 3-5 min ECG recordings, which reduces sensitivity for detection of rhythm disorders; there wasn't control for anti-arrhythmic medications, which could alter arrhythmia status.
- Future studies could include prospective evaluation, more dogs, dogs with preclinical DCM (not yet in CHF), controls for medications and other confounding variables, and longer term ECG for more sensitive arrhythmia diagnosis.

Key Research Findings

- Dobermans with DCM have evidence of repolarization abnormalities compared to normal dogs.
- T-wave variables were not different between Dobermans that experienced sudden death and those that did not.
- Only T peak-to-end interval in Lead I was longer between Dobermans that had ventricular arrhythmias on 3 min ECGs compared to those that did not.
- This study may benefit from additional modelling and survival analyses to provide further insight.



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Acknowledgements

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