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Independent Association of Sudden Cardiac Death and the Tpeak-Tend Interval on Vectorcardiogram

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Independent Association of Sudden Cardiac Death and the Tpeak-Tend Interval on Vectorcardiogram

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by

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Abstract

The causes of Sudden Cardiac Death (SCD) are still uncertain in the field of electro-cardiology. Cardiac repolarization may be the instance in which fatal arrhythmias lead to SCD development. Cardiac disease has not been well treated, as it is the leading cause of death in industrialized nations. Correlation of the T wave length to Sudden Cardiac Death (SCD) has been demonstrated in recent studies, most notably in a meta-analysis published in 2017, (Tse, Gong, Wong, Georgopoulos, Letsas, Vassiliou, … Liu, 2017). However, this project is attempting to show independent association of the T wave and SCD. Independent association demonstrates some mechanism in the heart which is elongating the T wave and also causing SCD. Use of the Vectorcardiogram (VCG) is novel because of its consistency and accuracy over an Electrocardiogram (ECG). The VCG offers three independent orthogonal views of the electrical activity of the heart, thus limiting subjectivity, overlapping information, and noise. Each of the three views offer an X, Y, and Z axis; when plotted, the electrical activity is represented as loops in three dimensional space. The Tpeak-Tend interval (Tp-Te) is measured on these VCG loops via algorithms developed by the Tereshchenko laboratory (Alday, Hamilton, Li-Pershing, Thomas, Gonzales, Li … Tereshchenko, 2018). The data being analyzed was gathered from two prospective cohort studies, known as the Arteriosclerosis Risk In Communities (ARIC) and Cardiovascular Health Study (CHS), (Waks, Sitlani, Soliman, Kabir, Ghafoori, Biggs, …, Tereshchenko, 2016). These cohorts provide digital ECGs, large study sample (>102,000 ECG readings), and repeat visits. The ten second ECG readings are mathematically transformed with the Kors Transformation Matrix, in order to provide the VCG which is then analyzed. Independent association of the Tp-Te interval and SCD will provide better predictors of SCD and the possibility of risk score development.

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Introduction

The Heart

The heart is an extremely important organ in the human body. Its purpose is to cycle blood throughout the body. Without the heart, blood would not receive oxygen from the pulmonary system and the rest of the body could not be oxygenated. The heart continually supplies tissues with sufficient nutrients to maintain normal body function.

Anatomy & Physiology of the Heart

The heart receives unoxygenated blood from the rest of the body through the superior or inferior vena cava. The vena cava feeds into the right atrium. The atria are the two upper chambers of the heart (Dubin, 2000, p. 7). A normal human heart has four chambers (see Figure 1). The right atrium fills with blood, is activated, and then contracts thus sending the blood into the right ventricle. The right ventricle receives blood from the right atria through the tricuspid valve (Limmer, O' Keefe, Dickinson, 2012, pp. 112–113). The unoxygenated blood is then sent to the lungs through the pulmonary arteries. The left atria receives blood from the pulmonary veins once it has been oxygenated. The atria and ventricles are separated from each other by interatrial and interventricular septum (Tortora, 1991, p. 319). Once the blood is in the left atrium it is sent to the left ventricle through the mitral valve (Limmer et al., 2012, pp. 113–115). The left ventricle has the largest amount of cardiac tissue because its

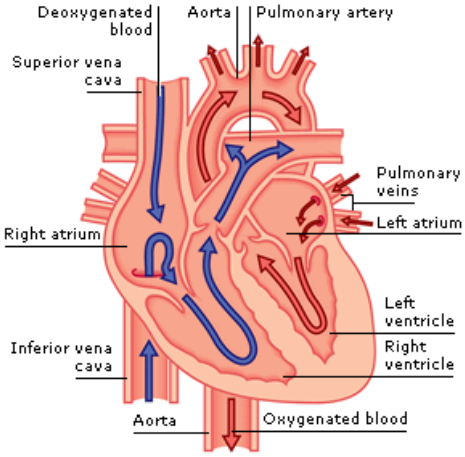

Figure 1. Diagram of the blood flow through the heart. Blue arrows indicate unoxygenated blood and red specifies oxygenated. (Aviva, 2018)

job is to send the newly oxygenated blood to the rest of the body through the large artery known as the aorta (Dubin, 2000, p. 18).

Cardiac Electrical Conduction System and Regulation of the Heartbeat

A normal heartbeat is initiated from the Sinoatrial node (SA node). A heart beat which is paced from this location in the heart is known as Sinus or Normal (Dubin, 2000, p. 98). Automaticity is the unique characteristic of cardiac tissue which allows it to generate its own electrical impulse (Dubin, 2000, p. 13). As the electrical activity is initiated for each heartbeat, each of these chambers are effected. This pulse, in a normal heartbeat, activates the atrial tissue which causes them to contract. Both atria contract simultaneously and send blood to the ventricles (Dubin, 2000, pp. 14–15). The electrical signal from the SA node is carried by Sodium ions which are small and quick moving (Dubin, 2000, p. 12). The atria and the ventricles are electrically isolated and connected only at the atrioventricular node (AV node). This node slows the movement of the impulse for approximately 0.09 seconds to allow the blood to fill the ventricles. The slowing of the electrical impulse is done using Calcium ions to carry the electrical current (Dubin, 2000, pp. 19–20). The impulse is then sent down the left and right bundle branches which spread towards the left and right ventricles. On the ends of the bundle branches are the Purkinje Fibers which complete the activation of the ventricles, allowing them to contract (Dubin, 2000, p. 21). This electrical activity is essential for our survival and each of these steps occurs between 60-100 times every minute (Dubin, 2000, p. 66).

Arrhythmias

Issues with these normal electrical workings are what can be fatal to a person. "Although arrhythmia literally means 'without rhythm,' generally it describes any rhythm disturbance, that is, any variance from a Normal Sinus Rhythm" (Dubin, 2000, p. 106). The heart has natural back-ups in terms of automaticity. For example, there are other points in the atria which can conduct electrical impulses other than the SA node, however these pace at a slower rate, these are called foci (focus singular) (Dubin, 2000, pp. 108–110). The AV node can conduct an impulse as well but it is even slower. This can be identified by the inversion of the P wave in an ECG (Dubin, 2000, p. 116). Then finally, in an emergency situation, the ventricles can pace about twenty to forty times a minute which is not viable for very long (Dubin, 2000, p. 117). If the heart is in this state for too long the ventricles can go into tachycardia or fibrillation. Tachycardia is the state of a rapid heartbeat either due to escape beats (atrial, junctional, or ventricular), an irritable focus point (paroxysmal atrial tachycardia), or the simultaneous firing of multiple foci (atrial fibrillation) (Dubin, 2000, pp. 110, 112, 149). Ventricular Tachycardia (VT) causes the body to not receive enough blood for sufficient oxygenation. This causes light-headedness, nausea, respiratory issues, and eventually the patient will become unresponsive (Dubin, 2000, pp. 167–170). SCD generally presents in the form of Ventricular Fibrillation (VF) or VT, requiring manual compressions, rescue breathing with the use of a Bag Valve Mask (BVM), supplemental oxygen, and most importantly, a defibrillation shock (Daniel Limmer et al., 2012, p. 484).

Healthcare professionals are trained to look for certain characteristics in a 12-lead ECG which have significant diagnostic implications. One such condition is Wolff-Parkinson-White Syndrome (WPW). WPW is characterized by a shortened PR interval and an elongated QRS, this is accompanied by the presence of the "Delta" wave (Dubin, 2000, p. 171) (see Figure 2). Physiologically this is caused by the electrical signal bypassing the delay in the AV node and passing freely through the Bundle of Kent. This can cause dangerously high ventricular rates, paroxysmal tachycardia, or a global re-entry loop of the electrical impulse (Dubin, 2000, p. 171). A particularly dangerous arrhythmia is Torsades de Pointes (TdR). TdR is a, "form of (very) rapid ventricular rhythm caused by low potassium, medications which block potassium channels, or congenital abnormalities" (Dubin, 2000, p. 158). TdR literally means "twisting of points" which can be seen in the ECG reading of this arrhythmia (Dubin, 2000, p. 158) (see Figure 3). This arrhythmia causes a heart rate of 250-350 beats per minute and if left untreated can result in a deadly arrhythmia (Dubin, 2000, p. 158). TdP is a life-threatening arrhythmia which has been shown to be correlated to an increase in the QT interval. The QT interval is a measurement of the time the Q wave begins to the time the T wave ends (Dubin, 2000, p. 158).

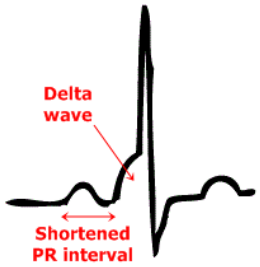

Figure 2. Example of WPW on an ECG, presence of the shortened PR interval and Delta wave are noted. (Stefanek Fajmon, 2014-2015)

Figure 3. Example of TdR, "twisting of points", on an ECG. (Medical Training and Simulation, LLC, 2013)

Sudden Cardiac Death

Sudden Cardiac Death (SCD) is an "unexpected cessation of circulation and breathing" (Tortora, 1991, p. 330). SCD is rampant in the world today and improved detection methods need to be developed. "Despite major advances in treatment and

prevention of CHD and implantable cardioverter defibrillators (ICDs) for SCD prevention in high-risk patients, SCD remains a major public health problem estimated to account for 15–20% of all deaths" (Hayashi, Shimizu, Albert, 2015, p. 2). SCD is responsible for 4-5 million deaths worldwide every year (Tse et al., 2017, p. 1132). "Approximately 44–52% of men and 59–69% of women who suffer SCD will not have had CVD diagnosed prior to the event; and therefore, SCD is the first manifestation of heart disease (Hayashi et al., 2015, p. 5–6). "The combination of late CPR (more than 4 minutes) and late advanced life support (more than 12 minutes) is particularly lethal" (Cummins, Ornato, Thies, Pepe, 1991, p. 1834). Due to the very nature of SCD, an asymptomatic individual will rarely receive Advanced Life Support (ALS) care prior to irreversible damage occurring to the body.

SCD is different than that of a myocardial infarction (MI), or heart attack. An MI is an issue with blood supply to the heart itself. This can be caused by high levels of cholesterol or some other foreign body which blocks blood flow through the coronary arteries (Tortora, 1991, p. 322). However, SCD is an issue with the electrical impulses of the heart. There is no issue of blood flow, but rather the heart is pumping too fast or too slow, tachycardia or bradycardia respectively. In either case the heart cannot sufficiently pump blood throughout the body.

Cardiac Repolarization

The purpose of this study is to determine if there is an independent association with the T wave of a VCG and SCD. This would determine that there is some mechanism in the heart which we do not fully understand that is elongating this specific interval and also causing SCD. The determination of independent association would allow researchers

to focus on cardiac repolarization for a possible cause of SCD, negative results of this study would be able to eliminate this as a possibility. Determination of independent association of the T wave and SCD would also aid in the development of risk factors associated with SCD. Preventive measures are the most effective means of countering SCD. These include use of an Implantable Cardioverter Defibrillator, controlling diabetes, lowering LDL cholesterol levels, lessening hypertension, and cessation of smoking.

The wave of specific interest to the Tereshchenko laboratory is the T-wave. This wave represents cardiac repolarization and has been shown to be a predictor of SCD. A meta-analysis released in 2017 compared a large number of studies which analyzed the Tp-Te interval and attempted to show correlation with SCD. Publications were taken from reputable databases: PubMed, Embase, Cochrane Library, and CINAHL Plus, there were no language restrictions on these papers (Tse et al., 2017, pp. 1132–1133). Exclusion criteria included: non-human studies, no Tp-Te recorded, no odds or hazard ratios or data necessary to calculate included (Tse et al., 2017, p. 1133). Thirty-three studies were reviewed in the meta-analysis, including 155,856 patients; the mean age was 62 +/- 11 years, patients were predominately male (69%), and all studies consistently reported a positive association between increased Tp-Te interval and an increased risk of VT/VF or SCD (Tse et al., 2017, p. 1133). The analysis found that “the Tpeak-Tend interval is a useful risk stratification tool in Brugada Syndrome, heart failure, ischemic heart disease, hypertension, and the general population” (Tse et al., 2017, p. 1136). The T wave is not well understood or well documented in the field of electro-cardiology.

A lab attempted to demonstrate this relationship using Cisapride to delay the transmural dispersion of repolarization. “Cisapride, a piperidinyl benzamide gastrointestinal prokinetic agent, was withdrawn from the market in the United States in July 2000 because of its propensity to prolong the QT interval and lead to life-threatening torsade de pointes (TdP) arrhythmias. Cisapride was the fifth drug to be withdrawn from the market in the span of 3 years, highlighting a growing problem and the need to better identify drugs with a proclivity to induce TdP” (Diego, Belardinelli, Antzelevitch, 2003, p. 1028). Prolongation of the QT interval would cause a delay in cardiac repolarization, due to the increase in cardiac action potential (Diego et al., 2003, p. 1028). The lethal arrhythmia known as Torsades de Pointes could only be initiated during elongation of the T wave. This demonstrates that there are dangers associated with the elongation of the repolarization interval.

The Electrocardiogram

The electrical activity of the heart is generally monitored with an Electrocardiogram (ECG). These are sometimes abbreviated as EKG but are, in fact, the same (Dubin, 2000, p. 6). “Transmission of action potentials through the conduction system generates electric currents that can be detected on the body’s surface” (Tortora, 1991, p. 322). ECGs are recorded by connecting unipolar electrodes to a person’s torso and limbs in specific areas. There are a total of ten electrodes needed to record a 12-lead ECG. Four of these are placed on

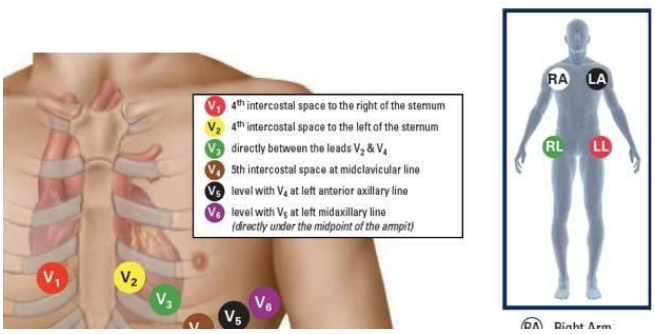

Figure 4. Proper placement of chest leads V1-V6. (Reading, 2016)

the wrists and ankles (Limmer, O'Keefe, Dickinson, 2012, pp. 1140–1141). The other six are known as nodes V1-V6. V1 and V2 are placed on either side of the sternum in the fourth intercostal space, below the fourth ribs. V4 is placed in line with the first two directly under the left nipple. V3 splits the difference between V2 and V4. V5 is placed on the same linear line just before the left underarm. V6 is placed in the medial underarm in the same linear line (Dubin, 2000, pp. 48–52) (see Figure 4). This arrangement is known as a 12-lead ECG because it provides medical professionals with twelve different views of the heart (Dubin, 2000, p. 53). An ECG presents the movement of the electrical impulse as waves. A normal ECG has three waves (see Figure 5). The first wave of an ECG is known as the P wave. This wave represents the activation of the atria (Dubin, 2000, pp. 14–15). The second wave is actually a complex of three waves known as the QRS complex. The Q wave is the first downward deflection following the P wave. The R wave is normally a very large spike following the Q wave. The S wave is another negative deflection following the R peak wave. The QRS complex represents the activation of the ventricles (Dubin, 2000, pp. 21–24). The PR interval—the time between the P wave and the R wave—is representative of the slowing of the electrical impulse by the AV node (Dubin, 2000, p. 19). There really is no deflections for the repolarization of the atria because this occurs during the QRS complex (Dubin, 2000, p. 29). The final wave is the T wave which represents ventricular repolarization.

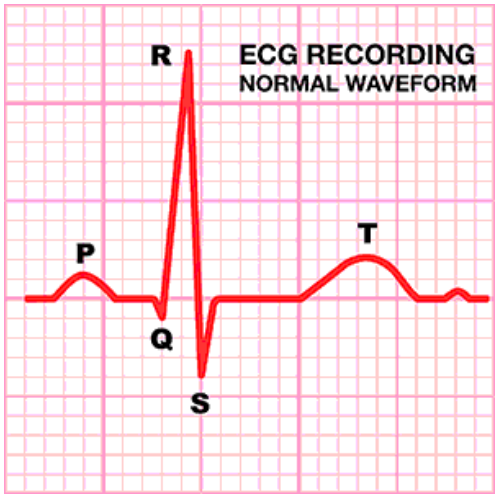

Figure 5. P, Q, R, S, and T waves as read on a normal ECG. (2015)

Repolarization is achieved by Potassium ions leaving the myocardial tissue (Dubin, 2000, p. 27). There, then, is a moment of electrical silence, approximately 0.8 seconds, and then another wave is initiated by the SA node.

Clinical Problems Associated with the ECG

The ECG has been shown to have diagnostic implications for the medical field. Some possible complications include long QT syndrome, P wave inversion, and other wave abnormalities. Long QT syndrome is an issue with the action potential of the cardiac tissue. P wave inversion would indicate the pacing of the heart is coming from the AV node (Dubin, 2000). Ischemia can be a cause of T wave inversion, and Beta-blockers can cause the T wave to appear flat. These are just a small number of the clinical uses of the ECG. The electrical activity of the heart is not well documented as a predictor of SCD.

Problems with Electrocardiogram Accuracy

"QT interval measurements from electrocardiograms (ECGs) are routinely used in clinical medicine. These measurements are usually done by expert readers using calipers

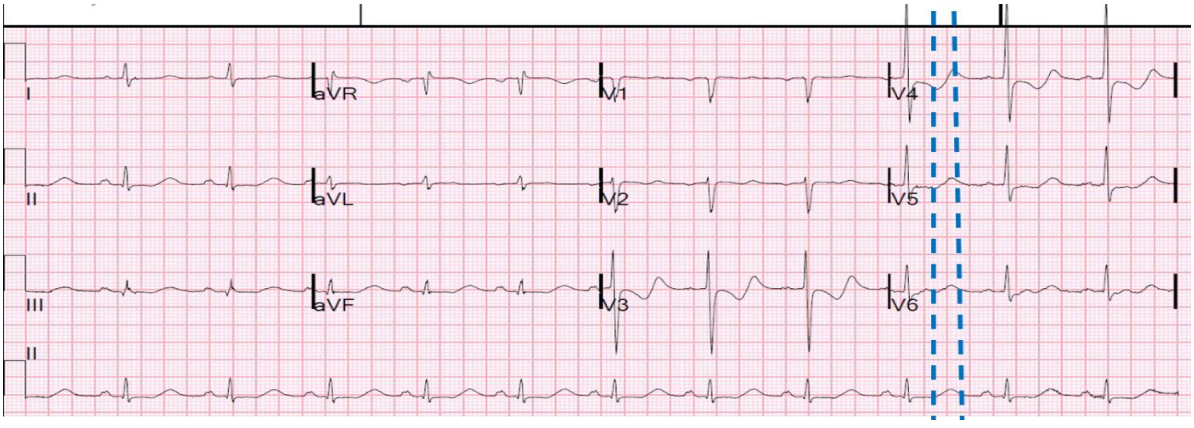

Figure 6. Example of the differences of interval lengths on different leads of an ECG. The vertical dotted lines are showing the two different possible points which could represent Tp.

on paper or e-calipers on computer screens" (Zong, Saeed, Heldt, 2006b, p. 1). The ECG provides 12 different views of the heart, each of these leads represent a different perspective of the heart's electrical activity. The leads called Lead I, II, and AVL are commonly used for diagnostic purposes. However, each of these three would provide slightly different measurements in terms of interval length (see Figure 6).

There is subjectivity on what lead someone decides to use, or if all leads are averaged, etc. The electrical impulses on the ECG are measured both in a positive and negative fashion (Dubin, 2000, p. 33). For example, there is a type of T-wave which has a peak in the positive direction, crosses the origin, has a peak in the negative direction, and then returns to the origin. This type of wave is called biphasic (Goldenberg, Moss, Zareba, 2006, p. 333). Another abnormal T wave is one which only is present in the positive direction but have two different peaks. This wave is called bifid (Watanabe, Toda, Nishimura, 1984, p. 208). When dealing with these waves, there is much subjectivity. Biphasic T waves have two possible points to represent T-peak and two possible points to represent T-end. In a bifid T wave there are two possible points which can represent T-peak. Subjectivity comes from deciding whether the first peak is always T-peak, or the largest wave is always T-peak (see Figure 7). These issues raise concerns on the accuracy of intervals measured on the ECG. In order to reduce subjectivity the Tereshchenko laboratory is utilizing what is known as a vectorcardiogram (VCG).

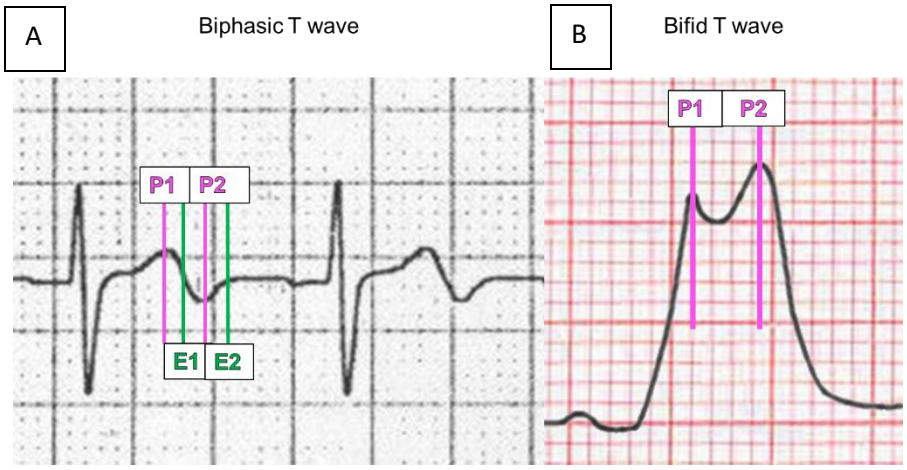

Figure 7. Example of biphasic and bifid T waves respectively. The vertical lines in figure 7A the two possible points of Tp and Te are shown. In figure 7B the two possible points of Tpeak are shown.

The Vectorcardiogram

An ECG records, on the body surface, the continuous dynamic details of cardiac functioning (Yang, Bukkapatnam, Komanduri, 2012, p. 1). It also provides what is essentially a twelve dimensional view of the heart. Twelve different views of the same electrical signal (Dubin, 2000, p. 53). In each lead there is some overlap with the preceding lead which can cause confusion (Yang et al., 2012, p. 2). A VCG provides three independent and orthogonal views of the heart's electrical activity (Yang et al., 2012, p. 2). This eliminates overlap of the signals. These three leads provide an X-axis, Y-axis, and a Z-axis which can be plotted to form vector loops (see Figure 8). When measuring interval lengths on the vector loops, there is substantially less subjectivity. All of the points are in a circular fashion, therefore, the peak of each wave is simply the furthest point away from the origin, "Each heart cycle consists of three loops corresponding to P, QRS, and T wave activities" (Yang et al., 2012, p. 2). The loops

begin and end at the electrical origin point. The peak-to-end interval is simply the remainder of the loop back to the origin.

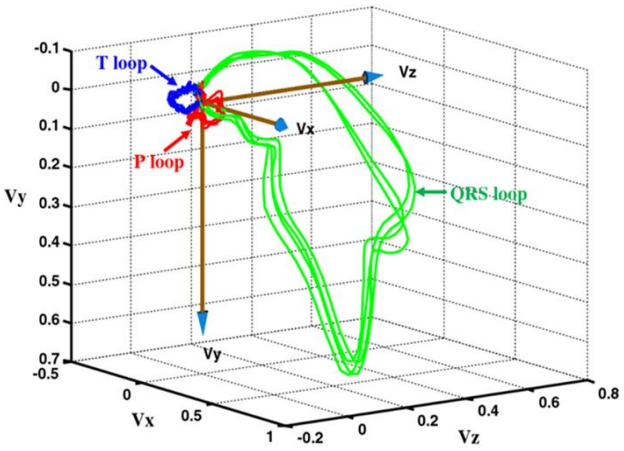

Figure 8. Example of a VCG and the corresponding loops which track the dynamic cycle of the cardiac conduction system. (Yang et al., 2012, p. 2)

Methodology

Study Sample

The Tereshchenko laboratory conducts ancillary study of two prospective cohort studies, with the goal to study mechanism and predictors of sudden cardiac death. They are known as the Arteriosclerosis Risk in Communities (ARIC) study and the Cardiovascular Health Study (CHS). “SCD was similarly defined in both ARIC and CHS: a sudden pulseless condition presumed due to a ventricular tachyarrhythmia in a previously stable individual without evidence of a non-cardiac cause of cardiac arrest” (Chen, Sotoodehnia, Buzkova, Lopez, Yee, Heckbert, … Alonso 2013, p. 3). ARIC and CHS are, “2 large, biracial, prospective, community-dwelling adult cohorts. The Atherosclerosis Risk in Communities (ARIC) study is an ongoing, prospective cohort study assessing risk factors, progression, and outcomes of atherosclerosis in 15792

community participants (45% male, 74% white) 45 to 64 years of age recruited from 4 US communities between 1987 and 1989" (Waks et al., 2016, p. 2223). "The final ARIC study population included 14 609 participants. The Cardiovascular Health Study (CHS) is an ongoing, prospective cohort study assessing risk factors, progression, and outcomes of CHD and stroke in 5888 community participants 65 to 100 years of age (42% male, 85% white) recruited from 4 US communities. During 1989 to 1990, 5201 participants were enrolled, and in 1992 to 1993, a second cohort of 687 blacks was recruited" (Waks et al., 2016, p. 2223). "The final CHS study population included 5568 participants. Together, the 2 cohorts included 20 177 adults (mean age, 59.3±10.1 years; range, 44–100 years; 44.1% male; 77.3% white). Both studies were approved by the institutional review boards of all participating institutions, and all participants gave informed consent" (Waks et al., 2016, p. 2223)

These studies are significant due to the fact that they provide digital ECG's, a large data set, and repeat visits from each individual. These studies were observation only, and a ten second digital ECG reading was taken for each person. ARIC collected follow-up visits every three years and have accumulated five visits. CHS followed up every year and has collected ten visits. The Tereshchenko laboratory excluded individual's samples which included Premature Ventricular Contraction (PVC), Atrial Fibrillation (AF), artifacts, Bundle Branch Blocks, or Ventricular pacing at baseline.

Automatic Algorithmic Detection

The origin point or, "the electrophysiological definition of the baseline is the interval of time where there is no cardiac electrical activation" (Alday et al., 2018, p. 1). There has been some disagreement as to whether the origin point should be located in the

PR interval or the TP interval (Alday et al., 2018, p. 1). After investigation by the Tereshchenko laboratory, the TP interval was chosen as the region where the origin point is located. With the vectorcardiogram, the Tereshchenko laboratory is developing algorithms to automatically measure the fiducial points—the beginning, peak, and end, of each wave. In order for the ECG's to be analyzed by computer algorithms in the form of a VCG, the data must be mathematically transformed. Ten-second 12-lead ECG's were collected from each individual from the ARIC and CHS studies every visit. The normal beats were collected and averaged. A normal beat means it was originated from the SA node of the cardiac conductive system. The averaged normal beats then underwent a mathematical transformation to take the ECG 12-leads down to three, using the Kors Transformation matrix (Man, Maan, Schalij, Swenne, 2015). These three new leads are independent, orthogonal views of the heart forming an X, Y, and Z axis. These XYZ's are what form the VCG. The VCG required shifting and scaling of the vector loops to account for respiration. Origin points needed to be chosen for the VCG. The point before the P wave was chosen to represent the electrical origin point because it is the point of electrical silence. Once the origin points were accurate, automatic fiducial point selection was done via algorithms developed by the Tereshchenko laboratory (Alday et al., 2018). Intervals were calculated with vector magnitude measurements.

Results

Due to the controversy surrounding the alignment of origin points on VCG, many trials needed to be completed in order to assure accuracy (Alday et al., 2018). Repeat trials were required in order to correct algorithmic accuracy and automatic fiducial point detection. Both of these algorithms have been created and edited by the Tereshchenko

laboratory (Alday et al., 2018). The goal of these repeat trials is to standardize evaluation methods of VCG and the algorithms.

Review of electrical origin point accuracy and fiducial point accuracy were done separately. Origin points were analyzed by comparing the X, Y and Z axes of the VCG and the vector magnitude graph (see Figure 9). While reviewing algorithmic accuracy, there were certain exclusion criteria which need to be considered. Contact of the vector magnitude graph just before the P wave was required. Some issues arose from the algorithm making the PR interval the origin point. Noise interference was another exclusion factor to be evaluated. If the reading was so noisy that the waves could not be positively distinguished, the sample was removed. Noise can be accumulated due to fat/muscle tissue in the individual, incorrect electrode placement, or electrical interference with the ECG monitor. The VCG readings were corrected if a clearer, more accurate, origin point could be detected. This was done so that the lab could better correct the issues of the algorithm. Altered data will not be used in any statistical analysis. The figures were sorted in terms of accuracy. Questionable figures were reviewed by Erick Alday, Postdoctoral Fellow; *Tereshchenko Laboratory, Knight Cardiovascular Institute*, and Larisa Tereshchenko; *Tereshchenko Laboratory, Knight Cardiovascular Institute*. During the time of my involvement with the study, 102,447 VCG samples were reviewed for origin point detection. This is the complete data set collected by the ARIC and CHS cohort studies. After complete review we had concluded that the algorithmic accuracy for origin point detection was 87%.

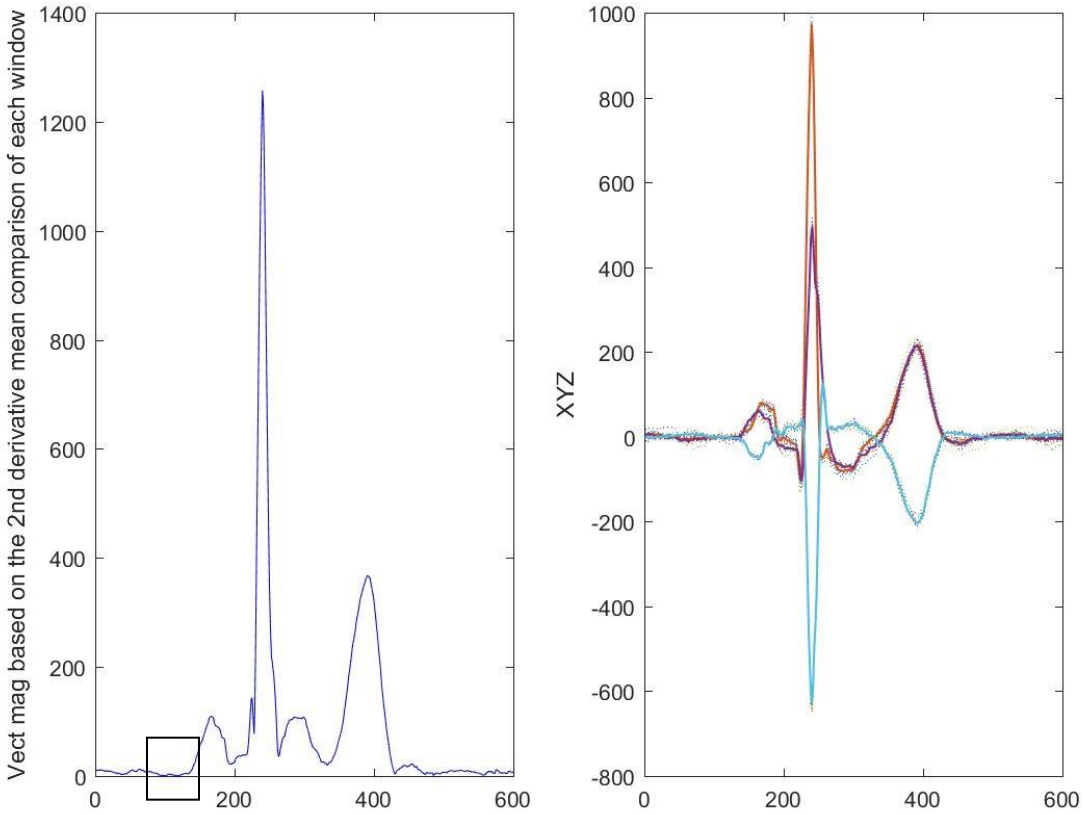

Figure 9. Vector magnitude reading of a VCG (left) and the superimposed XYZ axes of the same VCG (right). The origin point has been identified.

The fiducial points, which measure the beginning, peak, and end of each wave were also reviewed for algorithmic accuracy (see Figure 10) (Murray, Institute of Electrical and Electronics Engineers, 2006; Pan & Tompkins, 1985). These images are also presented as the X, Y, and Z axes superimposed as well as the vector magnitude graph. Fiducial point images were corrected for analysis by the lab to assure algorithmic accuracy. Again, the altered data will not be statistically analyzed. A total of 65,329 fiducial point readings were analyzed providing an algorithmic accuracy of 82%.

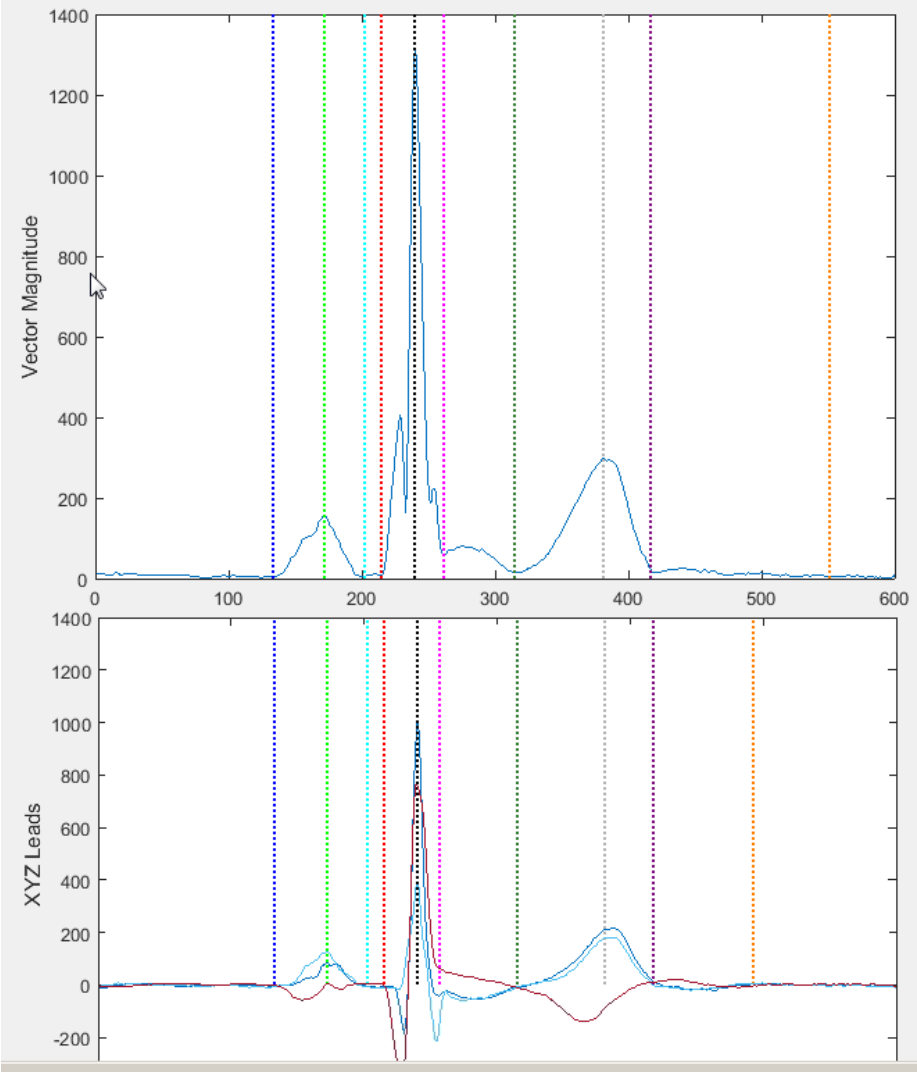

Figure 10. Fiducial point readings with the vector magnitude graph (top) and the superimposed XYZ axes of the corresponding VCG (bottom).

Conclusion

Review of the algorithmic accuracy will have a significant impact on the validity of automatic VCG interpretation. Due to the VCG's three-dimensional nature and the complexity of the electrical activity of the heart, automatic detection is very difficult. Once the algorithm of the Tereshchenko laboratory is completed and effective, the complete ARIC and CHS data can be measured and statistically analyzed (Alday et al.,

2018). The computer algorithms and VCG's developed by the Tereshchenko laboratory in association with the ARIC and CHS data propose a completely objective method of measuring this data (Alday et al., 2018). Historically ECG analysis has been highly subjective.

Results of this completed study will impact the way we understand the function of the T wave. If the results of our statistical analysis on the data shows an independent association of SCD and the Tp-Te interval, this will demonstrate that there is something mechanistically in the heart which is elongating the T wave and also causing SCD which we do not yet understand. If the results do not support our alternate hypothesis, then researchers can look to other possible causes of SCD not related to the specific lengthening of the Tp-Te interval.

Future Direction

If there is shown to be an independent association between the Tp-Te interval and SCD then this will allow electro-cardiologists to narrow their search for what causes SCD. This would lead research to understanding cardiac repolarization; there would be some mechanism in the heart which is elongating the Tp-Te interval and also causing SCD that we do not yet understand. If there is no independent association, then this will also narrow the search. There are many researchers which look to the mechanisms of repolarization for an answer to why SCD occurs. A negative association between Tp-Te could show that we do not need to study the repolarization of cardiac tissue (Alday et al., 2018).

Once corrected for accuracy, the VCG data will undergo statistical analysis. One of the statistical tests will include the Cox-Regression Survival Analysis. This test will be ran against three models. The models account for other variables which have some inherent risk of SCD, making the only outlier the Tp-Te interval. The models are as follows: Model 1: Age, Race, and Gender. Model 2: model 1, diabetes, CHD, heart failure, hypertension, smoking, obesity, cholesterol, hypertension medications, stroke, Afib, exercise, alcohol, creatine, and Beta-Blockers. Model 3: model 1, model 2, heart rate (V1), QRS (V1), QT (V1), and Bundle Branch Blocks.

Currently in the Tereshchenko laboratory, the first visit of ARIC have been analyzed and corrected for accuracy: 95% fiducial point accuracy and 98% origin point accuracy. The next step will be statistical analysis of this first set of data. This will be utilized to demonstrate alignment accuracy and validity. Then, progress can be made on the other visits of ARIC and CHS.

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