



Ventricular Tachyarrhythmias Prediction Methods and its Prognostic Features: A Review

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Abstract: This paper presents a literature review of ventricular tachyarrhythmias (VTAs) prediction methods and its prognostic features, as well as highlights the severity of the cardiovascular diseases in general population. This article provides the collective review of the short-term VTAs prediction based on the machine learning methods associated with the potential prognostics electrocardiogram (ECG) characteristics features that have been proposed in the recent literature. The basic morphology of the ECG waveform and its working principle is also briefly described for better understanding of the relationship between the ECG characteristics features and the occurrence of VTAs. In addition, the trend and future direction in the development of VTAs prediction system with machine learning are presented as well. It is desired that the progressive development of real-time, low computational cost and reliable short-term VTAs prediction algorithm in coming years could decrease the mortality rate of cardiovascular diseases within general populations. This article can be adopted as an initial idea and guidelines for beginners in this field to initiate their research.

Keywords: Electrocardiogram (ECG), ECG morphological features, heart rate variability (HRV), machine learning, prediction algorithm, ventricular tachyarrhythmias.

1. INTRODUCTION

Ventricular arrhythmia is the common problem met by the cardiologists in current clinical daily practice. The patient with ventricular arrhythmia may be apparent with a variety of signs and symptoms, such as palpitations, shortness of breath, chest pain, lightheadedness, weak pulse and syncope [1-3]. Yet, the most concerning issue is having the risk of sudden cardiac death (SCD). Based on the American Heart Association (AHA) statistical update-2016 [4], SCD is the leading cause of death in United States, causing about 350,000 deaths each year. SCD is a sudden, unexpected death due to the loss of heart function and is responsible for half of the heart disease deaths [5]. SCD may occur in healthy person with no previous symptoms of cardiovascular disease (CVDs) as well as patient with other medical conditions. However, most of the SCD events do occurs in the general population with the rate ranging from 50-100 per 100,000 population [6-8].

The main triggers of SCD are the occurrence of ventricular tachyarrhythmias (VTAs), namely ventricular tachycardia (VT) and ventricular fibrillation (VF) [9-10]. VT refer to the heart rate faster than 120 beats per minute,

out of sync with the upper chambers and with at least three irregular heartbeats in a row. If VT is left untreated, it may develop into VF. VF is a condition where a very rapid and disorganized electrical activities which is initialized in the ventricles, causing it to quiver instead of contract normally. A series of rapid and ineffective contractions of the ventricles results in immediate loss of cardiac output. This leads to insufficient blood supply to the brain, heart and other part of organs which can cause asystole and eventually ends with SCD within few minutes if no immediate treatments are taken.

This reflects the major challenge in current cardiology due to the absence of the powerful screening tool that is capable to predict the occurrence of VTAs for the general population [11]. Accurate short-term VTAs prediction prior to their onset initiation allows sufficient time for the preventive action to be taken to avoid its occurrence and further damage to the patients. Besides that, raising early awareness of clinicians of the possible occurrence will minimize the delay of medical care, thus enabling administration of preventive medication to help reduce mortality from SCD and increase the survival rate of the patient drastically [12, 13]. As a result, a reliable short-term

VTAs predictor is vital and essential in contributing to more lives saving and better healthcare for the general populations.

This article provides the readers a collective and comprehensive review of the short-term VTAs prediction methods, as well as the potential predictive electrocardiogram (ECG) characteristics features that have been reported in the recent literature. This article also briefly describes the basic morphology of the ECG waveform and its working principle. This article consists of five sections which begins with an introduction of VTAs in section one. Section two briefly describes the basic knowledge of the ECG morphology waveform. Section three presents the ECG characteristics features that have promising prognostic value to the occurrence of VTAs event reported by the recent literature, whereas section four presents the recent literatures related to the short-term VTAs prediction. Lastly, section five concludes the discussion on the future direction of the VTAs prediction.

2. ELECTROCARDIOGRAM

An electrocardiogram (ECG) is the most common screening tool used in clinical daily practice for cardiac performance assessment as it provides useful information on electrophysiological properties of the heart. ECG is a non-invasive measurement of the potential difference between pairs of electrodes attached on the surface of the body. The electrical potential is generated by the muscles in the heart which initiate the cardiac depolarization and repolarization process to cause contraction and hence pump the blood to whole body. In other words, ECG waveform is the representation of the electrical activity and mechanical event within the heart. It is useful to measure the heart rate, heart rhythm and its regularity as well as identifying the heart abnormality for potential CVDs. Figure 1 shows a normal ECG waveform which consists of P-wave, QRS complex, T-wave and U-wave [14].

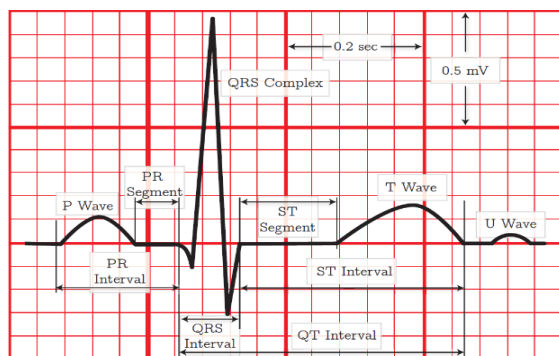


Figure 1. ECG waveform of an healthy adult [14].

Understanding the basic working principle of the cardiac conduction system is crucial in interpreting the ECG waveform. Cardiac conduction system is a result of atria and

ventricles who work coordinately to alternately contract and relax to pump blood throughout the whole body [15]. The heartbeats are initiated by a series of electrical impulses fired by a group of special cells located in the right atrium, known as sinus node or sinoatrial (SA) node, as the heart's natural pacemaker. A normal resting heart rate is ranging from 60 to 100 beats per minute.

When the SA node generates an electrical impulse, it spreads through the walls of the atria and causing them to contract. This process is represented by the P-wave of an ECG which is the result of atrial depolarization. The contraction forces the blood in the atria pool into ventricles. The electrical impulse is transmitted throughout the atria to the atrioventricular (AV) node, a cluster of cells in the center of the heart between atria and ventricles. The AV node delay the impulse by approximately 0.12s to ensure the ventricles have enough time to be fully filled with blood [15]. This delay is shown in an ECG waveform as the isoelectric line, PR segment just after the P-wave. The impulse is then transmitted from AV node to ventricles via the bundle branches causing the ventricles to contract and pump blood to the lungs and other parts of the body. This process is denoted by QRS complex, which represents the ventricular depolarization process.

Ventricular depolarization is then followed by an isoelectric line between the end of QRS complex, J point and beginning of T wave. It is known as ST segment which represents the interval between ventricular depolarization and repolarization. After that, the recovery of the ventricular, also known as ventricular repolarization is represented by the T wave signifying the relaxation of the cardiac muscle of the ventricles [15]. Additionally, U wave may appear or visible after the T wave, but not always. It is currently believed to be the mechano-electrical feedback or delayed repolarization of mid-myocardial or "M cells" [16-19]. However, the information underlying it remains unclear and certainly requires detailed further study. The cycle ends with the SA node firing another electrical impulse.

Ventricular tachyarrhythmias can be categorized into ventricular tachycardia and ventricular fibrillation with different ECG waveform characteristics. Ventricular tachycardia is a kind of cardiac arrhythmia characterized by heart rate more than 100 beats per minute, out of sync with the upper chambers and with at least three irregular heartbeats in a row. Other ECG key features of VT are absent of P-wave, unmeasurable PR interval and wide QRS complex with bizarre look as illustrated in Figure 2. The abnormal electrical impulses causing the rapid contraction that originate from lower chamber of the heart, ventricles. The rapid heartbeat does not allow the ventricles have sufficient time to fill with blood before contraction. Thus, the heart may not able to pump sufficient blood to the body. This is a very serious arrhythmia as it may deteriorate and lead to the life threatening events, such as ventricular fibrillation.

Ventricular fibrillation occurs when a very rapid and disorganized electrical activities initialized in ventricles and goes off on random paths around the ventricles instead of following its normal route. This cause the ventricles to quiver instead of pump normally. A series of rapid and ineffective contractions of the ventricles results immediate loss of cardiac output. VF usually ends with sudden cardiac death within few minutes unless immediate treatments are taken. Its ECG key features includes chaotic irregular deflections with varying amplitude, unidentifiable waves and its amplitude decrease with time duration as it develops from coarse VF to fine VF as illustrated in Figure 3. Hence, the right understanding and interpretation of ECG waveform is critical in assisting the clinicians to identify the abnormality and malfunction of the heart.

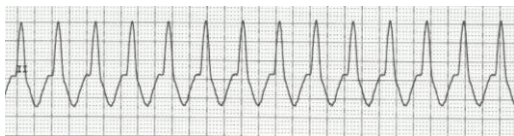


Figure 2. Ventricular tachycardia.



Figure 3. Ventricular fibrillation: (a) Coarse VF (b) Fine VF.

3. PROGNOSTIC VALUES OF ECG FEATURES

Recently, many researchers have revealed that the ECG characteristic features may reflect the underlying VTAs and have predictive value for the occurrence of VTAs event through the follow-up studies [20-24]. They offer the advantages of the availability of the long duration and high resolution ECG recordings prior to VTAs event that enable the possibility to investigate the mechanism that is responsible for the occurrence of VTAs. These identified ECG characteristic features have been used by the researchers to predict the onset of VTAs event before its occurrence. The prediction performance is then measured in terms of its accuracy, sensitivity and specificity.

As a result, this section presents the review of the identified ECG characteristic features which act as important input features of the short-term VTAs prediction based on machine learning. The identified ECG parameters that have prognostic value in predicting the occurrence of VTAs are, namely: QT interval, QT interval corrected with heart rate, QT dispersion, QT dynamicity, T-wave alternans and heart rate variability [24]. Each prognostic feature is further elaborated in detail in following subsection.

A. QT Interval

The measurement of the QT interval has become a standard practice in many ECG devices over past years. QT interval is the time interval between the onset of QRS complex to the offset of T-wave. It represents the duration of ventricular depolarization and repolarization. It is measured in lead II or V5 where it demonstrates the most measurable capability. The QT interval is below 400 to 440 ms for a healthy adult but female do have longer QT interval compared to male. Generally, QT interval is used to identify the arrhythmogenic syndromes such as Brugada Syndrome, long QT syndrome and short QT syndrome. These cardiac diseases can cause the shortening or lengthening of QT interval. Besides that, abnormal prolongation of QT interval is widely believed to be the maker of the increased risk for ventricular arrhythmias, especially Torsade's de Pontes and SCD in patient with or without structural heart disease [25-27]. However, there are few problems linked with the measurement of QT interval, which includes the estimation of the offset of T-wave and the variation of QT interval with the heart rate and gender. The most common solution is assuming the offset of the T-wave to be the intersection point between the tangent to the steepest down-slope of the T-wave and the isoelectric line [28]. However, it is very time consuming and involves heavy computation complexity.

B. Heart rate Corrected QT Interval

Heart rate corrected QT interval (QTc) is proposed to overcome the variation of QT interval with the heart rate as mentioned previously. As the QT interval is inversely correlated with the heart rate which it shortens at fast heart rates and vice versa, the QTc is able to minimize the impact of the heart rate on QT interval. It recalculates the QT interval according to heart rate, which allows the comparison of QT interval between different heart rates. Several formulas for QTc calculation have been proposed as shown in Table I [29]. The most commonly used methods are Bazett's formula [30] and Fridericia's formula [31]. Based on the AHA/ACCF/HRS recommendations [32], the proposed abnormal prolongation QTc values for adults are ≥ 450 ms in male and ≥ 460 ms in female, while the $QTc \leq 390$ ms is considered abnormally short. In addition, Straus *et al.* [33] assessed the QTc value into three categories know as normal, borderline and prolonged. $QTc \leq 430$ ms considered as normal, between 431- 450 ms considered as borderline and >450 ms considered as prolonged for adult male. While for female, $QTc \leq 450$ ms considered as normal, between 451- 470 ms considered as borderline and >470 ms considered as prolonged. Different opinions exist due to the lack of standardization and the evidences remain contrasting for the selection of the QTc formulas which cause the determination of the abnormal QT values to be different [34]. Yet, the QT and heart rate corrected QT interval remains a prognostic in predisposing

CVDs and as a marker for increased risk of ventricular arrhythmias [35].

TABLE I. FORMULAS FOR QTc CALCULATION [29].

QTc Measurements	Formulas
Bazzet	$QTc = QT / (RR)^{(1/2)}$
Fridericia	$QTc = QT / (RR)^{(1/3)}$
Framingham	$QTc = QT + 0.154 \times (1 - RR)$
Hodges	$QTc = QT + 1.75 \times (HR - 60)$
Sarma	$QTc = QT - B1 \text{Exp}(-k1 \times RR)$ $QTc = QT [1 - \text{Exp}(-k2 \times RR)]$ $QTc = QT (RR)^{(1/2)} + B3$ $QTc = QT (RR)^{(1/2)}$
Ecuación de fuerza	$QTc = 453.65 \times RR^{1/3.02}$
Van de Water	$QTc = QT - 0.087 (RR - 1000)$
Matsunaga	$QTc = \log(600) QT / (\log RR)$
Kawataki	$QTc = QT/RR \times 0.25$
Mayeda	$QTc = QT/RR \times 0.604$
Larsen y Skulason	$QTc = QT + 0.125 \times (1 - RR)$
Schlamowitz	$QTc = QT + 0.205 \times (1 - RR)$
Wohlfart	$QTc = QT + 1.23 \times (HR - 60)$
Boudolas	$QTc = QT + 2.0 \times (HR - 60)$
Sagie	$QTc = QT + 0.154 \times (1 - RR)$
Malik	$QTc = QT/RR \times 0.371$
Lecocq	$QTc = QT/RR (0.314)$

C. QT Dispersion

Another prognostic marker used to measure the non-uniformity and heterogeneity state of the ventricular repolarization is known as QT dispersion (QTd). QTd is the measurement of the variability of the QT interval. It is defined as the difference between the maximum and minimum QT interval measured on standard 12-lead ECG [36]. QTd measurement can be troublesome due to the difficulties in estimating the offset of the T-wave on 12 different leads precisely. From the literatures, the QTd for the healthy subject mostly ranging from 10 to 71 ms [37-39]. However, most of the researchers have reported different QTd upper normal limit for healthy subject as well as a wide overlap values between the healthy and patient groups [38-39]. Moreover, there are different conclusion made by the different researchers about the gender related difference. From the published works [40-41], it shows that there is no significant difference of QTd between male and female, while some [42-43] reported that QTd is greater in male population. Nevertheless, most of the literatures shows QTd is significantly increased in the patient with cardiac diseases or those with susceptibility to ventricular arrhythmias, although the QTd value largely overlapped with the healthy subject [44-45]. The conclusion made regarding the QTd remains conflicting and controversial

[39]. Thus, further detailed study is required to affirm the significance of the QTd in quantifying the abnormality of ventricular repolarization in predicting ventricular arrhythmias.

D. QT Dynamicity

As the QT intervals and its dispersion failed to play a significant role in predicting arrhythmic events [46], the QT dynamicity is proposed as an alternate feature used to analyze the relationship of the QT interval and heart rate change. It visualizes the effect of the autonomic nervous system (ANS) on both components, reflecting the vulnerability of the myocardium and the change in autonomic heart rate control which is associated to increased risk of SCD [47]. QT dynamicity can be assessed by plotting the QT apex, QTa or QT end, QTe corresponding to the R-R interval. QTa is the interval begin with the onset of QRS complex to the apex of T-wave, while QTe is the interval begin with the onset of QRS complex to the offset of T-wave. The apex of the T wave is determined by fitting a parabola through the peak of the T wave. The slopes of the linear regressions between the QTa or QTe and the corresponding R-R intervals (QTa/RR or QTe/RR) is then computed as shown in Figure 4 [48].

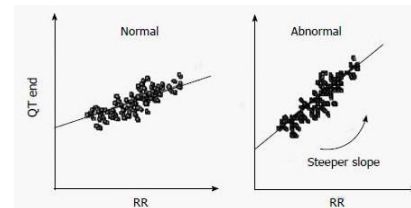


Figure 4. QT dynamicity analysis [48].

The steeper slopes indicate QT interval with greater variation for change in R-R intervals associated with abnormalities in ventricular repolarization [48-49]. A steeper QTe/RR slope may be due to the excessive shortening of QT with fast rate or excessive lengthening of QT interval with slower heart rates, which reflects greater arrhythmic risk [47, 49]. The QT/RR slope appeared to be steeper in female than male and during the day than night [50]. Iacoviello *et al.* [51] suggested that the QTe/RR slope value greater than 0.19 has a high risk of arrhythmic events, while the QTa/RR slope failed to demonstrate the predictive value of major arrhythmic events, similar to the results obtained from previous works [52-53]. Besides that, Chevalier *et al.* [54] demonstrated that the slope of QTe/RR slope has prognostic significance in predicting both total mortality and SCD in 265 post-infarction patients during 7-year follow-up with the steeper slope (>0.18) highly correlated with the increased risk of mortality.

E. QT Variability Index

Another parameter used to assess the stability of the ventricular repolarization by the measurement of beat-to-beat QT interval is the QT variability index (QTVI), as



proposed by Berger *et al.* [55]. It is a non-invasive measurement of repolarization lability that measures the beat-to-beat QT interval variation against heart rate variability, normalized by both mean QT duration and the magnitude of the heart rate variation. In other words, QTVI is the log ratio between the normalized QT interval and normalized heart rate variability. In mathematical definition, QTVI is defined as $\log_{10}[(QTv/QTm^2)/(RRv/HRm^2)]$, where QTv is the QT interval variance, QTm is the mean of the QT interval, RRv is the R-R interval variance and HRm is the mean of the heart rate where $HR = 1/RR$ [55]. Thus, the QTVI measurement involves the assessment of the ANS tone. Berger *et al.* [55] proposed a semi-automated template matching algorithm that compares and fits every continuous beat to the template. The template is stretched or compressed to fit with the ECG input. Then, the QT interval value is derived from the templates instead of estimating the offset of the T-wave by the intersection point between the tangent and isoelectric lines. In this way, the QTVI value can be updated depending on the length of the template and the duration of ECG recording that can reflect the gradual change in the ECG morphology over time.

For a healthy subject, the QTVI value is usually less than -1 [56]. Several studies have reported that the QTVI values in healthy subject range from -0.97 to -2.23, with mean value of -1.53 [55-60]. The QTVI value does vary with the lowest at night time [61], increase with age [62], and higher in female compared to male [56]. As proven by previous studies, the QTVI values are significantly higher for patients with cardiac disease and VF history as well as linked with cardiac disease mortality [63-65]. Dobson *et al.* [64] reported that the QTVI >-0.84 increases the risk of cardiovascular mortality in heterogeneous heart failure population. Picirillo *et al.* [65] suggested that the cutoff value for QTVI is >-0.47 in predicting mortality among the post-infarct patient with moderately reduced left ventricular ejection fraction. Hence, QTVI can be evaluated to assess the cardiac electrical instability and cardiovascular mortality risk.

F. T-wave Alternans

T-wave alternans (TWA), also known as microvolt T-wave alternans (MTWA) describes the periodic beat-to-beat fluctuations or variations in the amplitude, shape and phase of the T-wave, where the alternans defined as the change of the ECG morphology that repeating itself at alternate heartbeats. In order words, TWA is an ECG phenomenon that repeating ABAB pattern in the T-wave morphology [66]. TWA reflects the cardiac electrical instability and spatiotemporal heterogeneity of the ventricular repolarization. Besides that, electrical conduction block that occurs at every-other-beat can alternate the conduction pattern as well as the alternating of the excited cardiac muscle's size could produce the TWA [67]. Hence, TWA are believed to be a precursor and strong predictor to life-threatening ventricular arrhythmias and SCD [68-70].

TWA can either be spatially concordant or discordant. Concordant alternans occurs when the action potentials in neighboring cell regions are alternating in phase, while the discordant alternans occurs when they are out of phase. Both concordant and discordant alternans are visualized in Figure 5 [71]. Discordant alternans alters the spatial organization of repolarization across the ventricles and increases its heterogeneities. Thus, producing substrate that blocks the electrical conduction and initiating reentrant excitation that cause VF [69, 72].

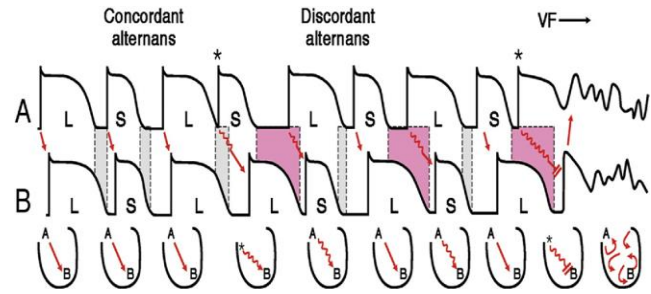


Figure 5. Action potential of two ventricular site A and B developed from concordant alternans, discordant alternans into ventricular fibrillation [71]. *Shaded area: dispersion of repolarization between sites; L: long action potential; S: short action potential.

There are two techniques commonly used to compute the TWA namely, spectral method and modified moving average method (MMA). For the spectral method, the sequential ECG waveforms are aligned based on their QRS complex [73-74]. Then, the amplitude of the T-wave at 128 pre-defined points are measured. Each beat-to-beat variation is processed with Fast-Fourier Transform to compute the spectrum for each pre-defined point [73]. The alternans voltage is defined as the square root of the alternans power at 0.5 cycle/beat. The spectral TWA method is illustrated on Figure 6 [74]. Besides that, the significance of TWA can be expressed by the K score, ratio of the alternans power at 0.5 cycle/beat divided by the standard deviation of spectral noise [75]. However, this method must be conducted during treadmill exercise to optimum heart rate [76]. The positive test result is defined as TWA level $>1.9 \mu V$, cutoff point with the K score >3 and continuous for more than 2 mins [75, 77].

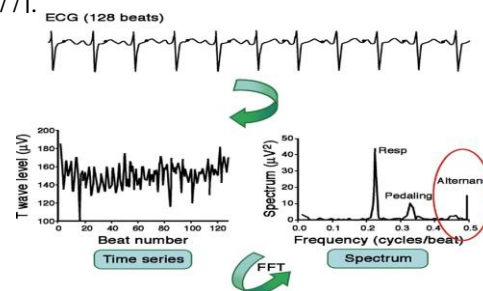


Figure 6. TWA spectral analysis [74]

Next, modified moving average method is the alternative approach used to measure the TWA. It acquires the ECG signal with the Holter ECG device and employs the



recursive averaging algorithm [78]. The odd and even heartbeats are separated into different bins and create the median complexes for each bin [79]. Both complexes are then superimposed and the maximum difference between both complexes at any points within JT segment is averaged for every 10 to 15 seconds, where its average value is the TWA value [78-79]. MMA based TWA analysis can be measured from the standard precordial ECG leads with standard electrode as well as ambulatory ECG recording [80-82]. The higher the value of the TWA indicates greater risk for SCD and cardiovascular mortality where $TWA \geq 47\mu V$ is believed to be the cutoff points [83, 84]. However, the main drawback of the TWA analysis is it requires elevating the heart rate ≥ 105 bpm. The TWA analysis can be impractical for patients whom cannot achieve targeted heart rate due to the cardiac diseases [71].

G. Heart Rate Variability

Heart rate variability (HRV) is a noninvasive electrocardiographic marker reflecting the activity of the sympathetic and parasympathetic components of the ANS on the sinus node of the heart [85]. It is expressed by the variation or oscillation of the instantaneous heart rate and interval between successive normal heart beats, R-R intervals (N-N intervals) to identify different pathological condition related to the ANS. The conditions such as physical stress, mental stress and exercise can cause the augmentation of sympathetic tone. On the other hand, parasympathetic tone is high during the resting condition. Both sympathetic and parasympathetic tone fluctuates throughout the day in healthy adults [86]. In other words, HRV analysis is used to assess the cardiac autonomic regulation through quantification of sinus rhythm variability.

Thus, the abnormality of the heart that cause sympatho-vagal imbalance is reflected by a diminished HRV. HRV analysis can be categorized into long term HRV analysis which analyses the ECG signal with long duration (up to 24 hours) and short term HRV analysis uses to analyses only 2-30mins ECG recording. HRV can be analyzed using time domain, frequency domain and non-linear methods. Each of them will be briefly described in the following subsections.

1) Time Domain Analysis

HRV time domain analysis is the simplest to perform as the value of the N-N interval can be easily obtained from the ECG signal with good accuracy using the Pan-Tompkins algorithm [87]. Pan-Tompkins algorithm is a well-established method used to detect the QRS complexes from where the N-N interval can be determined. The time domain features are derived from the N-N interval and its statistical measure. They can be categorized into two groups [88]. First, the features that derived directly from the measurements of the N-N interval of the ECG signal such as Mean NN, SDNN, SDANN and ASDNN. Second, the features that derived from the differences between the adjacent N-N interval such as SDDSD, rMSSD, NN50 and pNN50. The HRV time domain features are summarized in

Table II [88]. As the time domain analysis is dependent on the ECG duration, it should be standardized to ensure the fair and accurate comparison. Besides that, the N-N interval values are prone to unwanted artifacts and outliers which certainly requires proper and effective ECG pre-processing before analyzing the HRV signal.

TABLE II. DESCRIPTION OF THE HRV TIME DOMAIN FEATURES [88].

Feature	Description	Unit
Mean NN	Mean of the N-N intervals	ms
SDNN	Standard deviation of the N-N intervals	ms
SDDSD	Standard deviation of the difference between adjacent N-N intervals	ms
SDANN	Standard deviation of the average N-N interval of 5-min segment	ms
ASDNN	Average standard deviation of the N-N interval of 5-min segment	ms
rMSSD	Root mean square of the differences of adjacent N-N intervals	ms
NN50	Number of adjacent N-N intervals differs by more than 50ms	-
pNN50	NN50 divided by total number of N-N intervals	%

In addition, a series of N-N interval can be constructed and expressed in geometrical form. There are different geometrical methods used to interpret the HRV signal such as the histogram, HRV triangular index and triangular interpolation of NN interval histogram (TINN) [87]. This has advantage as the geometrical methods are relatively insensitive to the quality of the series of N-N interval [89]. However, the main drawback of the HRV geometrical interpretation is it requires certain quantity of N-N intervals, at least 20 mins and up to 24 hours ECG recording to ensure the construction of the accurate geometrical representation. Hence, restrict the applicability of the geometrical based HRV features in short-term HRV analysis [88].

2) Frequency Domain Analysis

Power spectral density (PSD) is the method used to analyze the HRV in frequency domain. PSD provides basic information on the power distribution across various frequency range. In other words, it describes the periodic oscillations of the heart rate signal, decomposed at different frequency range and amplitudes [90-91]. PSD analysis can be performed by using non-parametric and parametric methods. The non-parametric methods such as fast fourier transformation (FFT) is characterized by peaks for the frequency components. It has advantages in term of algorithm simplicity and processing speed. It also makes no assumption on the model, thus more robust. Whilst, the parametric methods such as autoregressive model estimation results in continuous smooth spectral components, improved frequency resolution with easy pre-processing and easy



identification of the central frequency for each component. Besides that, the parametric methods can estimate the PSD accurately even for small number of samples. However, the drawback of the parametric methods is its complexity and required verification on the suitability of the chosen model.

The power spectrum of HRV signal consists of four frequency bands ranging from 0-0.4Hz which can be classified into ultra-low frequency band (ULF), very low frequency band (VLF), low frequency band (LF) and high frequency band (HF) [88]. The frequency domain analysis for the short term HRV are characterized by the VLF, LF and HF components, while for long term HRV analysis includes ULF, in addition to VLF, LF and HF components [88]. The detailed description of the HRV frequency domain features and its frequency range are shown in Table III [86, 88].

Different power spectrum components have different information underlying it [92-93]. The main power spectrum components that represent the ANS activity are LF and HF components. HF component provides the information about the cardiac parasympathetic activity and is respiration mediated. While, LF component represents the combination of sympathetic and parasympathetic activity. The VLF components is a major determinant of physical activity and was proposed by Frenneaux *et al.* [94] as the marker of sympathetic activity. Lastly, ULF components reflect circadian and neuroendocrine rhythms as introduced by Bigger *et al.* [95]. Besides that, the LF/HF ratio is used to describe sympathovagal balance and normally is between 1 and 2 for a resting adult. The total power is the variance of all N-N intervals and corresponds to the sum of all frequencies bands which indicates the sympathetic and parasympathetic balance of the system. Furthermore, the features extracted from 24-hours ECG recording using both time domain and frequency domain methods are highly correlated due to their mathematical and physiological relationships [88]. The approximate correspondence of the time domain and frequency domain features are shown in Table IV.

TABLE III. DESCRIPTION OF THE HRV FREQUENCY DOMAIN FEATURES [86,88]

Features	Description	Frequency Range	Units
ULF	Total number of N-N interval with spectral power up to 0.003Hz	<0.003Hz	ms^2
VLF	Total number of N-N interval with spectral power between 0.003 and 0.04Hz	0.003-0.04Hz	ms^2
LF	Total number of N-N interval with spectral power between 0.04 and 0.15Hz	0.04-0.15Hz	ms^2
HF	Total number of N-N interval with spectral power between 0.15 and 0.4Hz	0.15-0.4Hz	ms^2

Total power	Total number of N-N intervals with spectral power up to 0.4Hz	$\leq 0.4Hz$	ms^2
LF/HF	Ratio of low-high frequency power	-	-

TABLE IV. CORRELATION BETWEEN TIME AND FREQUENCY DOMAIN FEATURES [88].

Time Domain Features	Frequency Domain Features
SDNN	Total power
HRV triangular index	Total power
TINN	Total power
ASDNN	Mean of 5-mins total power
SDANN	ULF
rMSSD	HF
SDSD	HF
NN50	HF
pNN50	HF

3) Non-linear Domain Analysis

The linear or conventional HRV analysis such as time domain and frequency domain analysis are often inadequate to interpret all aspects of cardiac performance. The cardiac system is dynamic, non-linear and non-stationary due to the intricate interactions of haemodynamic, electrophysiological, humoral variables, autonomic and central nervous regulations. Thus, the HRV analysis in non-linear domain is able to provide useful information by accessing the quality, scaling and correlation properties of the signal [96]. They are related to the unpredictability, fractability and complexity of the signal [97]. The non-linear dynamical theory is based on the concept of chaos and have been proposed by Cohen *et al.* [98] to analyze the HRV signal and to predict the arrhythmia events. Numerous non-linear analysis techniques exist, however only several commonly used techniques such as Poincare Plot, Approximate Entropy (ApEn), Sample Entropy (SampEn) and Detrended Fluctuation Analysis (DFA) are briefly discussed.

Poincare plot is a graphical and quantitative presentation of the correlation between adjacent R-R intervals, for instance the plot of RR_{n+1} versus RR_n . In other words, each R-R interval is plotted as a function of previous R-R interval. In this way, it provides detailed and summary information about the heartbeat variation [99]. A frequently used method to analyze the Poincare plot is fitting an ellipse oriented according to the line-of-identity and compute the standard deviation of the points perpendicular to and along to the line-of-identity which referred as SD1 and SD2 respectively [100]. SD1 is the standard deviation of points from $y = x$ axis that reflect the short-term R-R interval variability. SD2 is the standard deviation of the distances of points from $y = -x + \overline{RR}$ axis that reflect the long-term R-R interval variability. The ratio of SD1/SD2 are used to describe the relationship between short-term variation and

long-term variation [101-102]. The Poincare plot with fitted ellipse to the plotted shape are shown in Figure 7 [103].

The approximate entropy represents an index for overall signal complexity and predictability [104]. It was first introduced by Pincus to quantify the likelihood of patterns, which are close or remain similar for the subsequent incremental comparison [104]. In other words, it is used to measure the irregularity and unpredictability of fluctuations of the R-R intervals [105]. The more irregular, more complex and less predictable the R-R interval, the higher value yield of ApEn, while the repetitive patterns of R-R intervals have relatively small ApEn value. For healthy subjects, the values of ApEn is approximately between 1.0 and 1.2 [106-107]. Besides that, sample entropy introduced by Richman and Moorman [108], an improved ApEn which highlight the signal complexity and regularity by computing the conditional probability that two sequences of data that are similar to each other. The small computational difference is that the SampEn does not includes self-matches in calculating the probability. However, both face several limitations such as evaluating the signal regularity on one scale only, and they are easily affected by the artefacts and outliers.

The detrended fluctuation analysis is used to quantify the presence of fractal correlation in non-stationary signal. This method is based on a modified root mean square analysis of random walk, which was proposed and applied in physiological signal by Peng *et al.* [109]. DFA is developed to measure the fluctuations on multi-length scales. Short-term scaling exponent α_1 is used over the range of $4 \leq n \leq 16$ heartbeats, while long-term scaling exponent α_2 is used over the range of $16 \leq n \leq 64$ heartbeats [109]. For healthy adults, scaling exponent is approximately 1, signifying fractal-like behavior. For patients with cardiovascular disease this results in reducing scaling exponents ($\alpha_1 < 0.85$ [110]; $\alpha_1 < 0.75$ [111]) which demonstrates the loss of fractal-like heart rate dynamics. This method is only applicable on the recording with at least 2000 R-R interval and requires editing on ectopic beats.

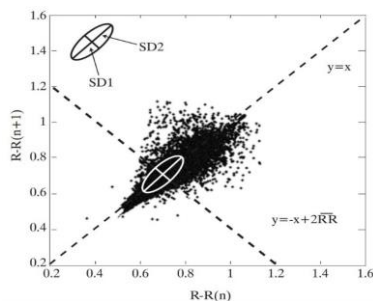


Figure 7. Poincare plot with fitted ellipse to the plotted shape [103].

4. RECENT WORKS RELATED TO SHORT-TERM VENTRICULAR TACHYARRHYTHMIAS PREDICTION

Numerous research related to cardiac arrhythmia have been reported recently. They can be grouped into two categories known as arrhythmia detection and arrhythmia prediction. Arrhythmia detection is to detect and classify the type of the arrhythmia after it occurs. While, the arrhythmia prediction is to predict the onset of the arrhythmia before its occurrence. In this section, we will present and discuss about the previous works related to short-term ventricular tachyarrhythmias prediction algorithm. It is critical and crucial to predict the onset of VTAs before its occurrence as this allows enough time for the preventive action to be taken to avoid life-threatening cardiac event and decrease the likelihood of SCD. Lastly, these recent works are summarized in Table V at the end of this section.

Thong and Raitt [112] proposed an algorithm using the acceleration pattern of the R-R interval to predict an imminent episode of VTAs. A total number of 208 set of R-R interval that acquired from 90 subjects were taken from the Biotronik European HRV database and used in this study. The pattern of prolonged, slow and monotonous acceleration were used as the short-term indicator of VTAs [112]. The proposed predictor based on the heart rate acceleration pattern achieved sensitivity of 53-69% and specificity of up to 91%, with average false positive rate of 0.8 event/day across the patient population [112]. However, the accuracy of the proposed method was not reported.

Joo *et al.* [113] proposed an artificial neural networks (ANNs) based classifier that was able to predict the occurrence of the VTAs using short-term heart rate variability. The datasets used in this study was the Spontaneous Ventricular Tachyarrhythmia Database (Medtronic Version 1.0) obtained from PhysioNet [114]. It comprised of 106 pre-VT records, 29 pre-VF records and 126 control datasets. The HRV analysis were performed on R-R intervals in 5 minutes' window prior to the VTAs event [113]. The ANNs based classifier were then trained with the HRV features extracted using time domain, frequency domain and nonlinear methods. There were total 11 HRV feature which consisted of Mean NN, SDNN, rMSSD, pNN50, VLF, LF, HF, LF/HF, SD1, SD2 and SD1/SD2. The ANNs topology with 11 input nodes, 26 neurons in the first hidden layers, 26 neurons in the second hidden layers and one output node were chosen [113]. The ANNs classifier was trained with two-thirds of the datasets, while the remaining one-thirds of the datasets were used to evaluate the performance of the ANNs classifier. In this study, the proposed ANNs classifier achieved 75.6% accuracy, 77.3% sensitivity and 73.8% specificity in predicting the occurrence of short-term VTAs [113].

Rozen *et al.* [115] proposed and evaluated a novel multipole based HRV analysis method as a predictor of imminent VTAs. 64 pre-event R-R interval recording acquired from 28 patients were analyzed and compared with the event-free recording of the same patients. These



recordings were taken from the HAWAII Registry and recorded 4,500-9,000 R-R intervals prior to the onset of VTAs. The multipole method extracted and used both time domain and frequency domain features in predicting the occurrence of VTAs event. In this preliminary study, multipole based HRV analysis method achieved 50% sensitivity and 91.6% specificity [115]. However, the accuracy of the multipole method was not reported as well.

Riasi *et al.* [116] proposed a support vector machine (SVM) based algorithm to predict the occurrence of VT event using ECG morphological features such as change in QT intervals, T-wave, ST segment and number of premature ventricular complexes. The dataset used in this study consisted of 40 pre-VT recording and 40 control recording obtained from MIT-BIH arrhythmia database. The proposed algorithm comprised of five steps; preprocessing and noise removal, ECG signal fiducial point detection, extraction and selection of morphological features of ventricular activity and SVM based classifier [116]. The ECG morphological features were extracted from within the last 20 seconds of the pre-VT and control recordings. From total 80 datasets, 60 of datasets were selected to train the SVM based classifier and the remaining 20 datasets were used to evaluate the performance of the trained classifier. The proposed method achieved 94% accuracy, 88% sensitivity and 100% specificity. However, the further validation and experiment are required to affirm the role of ECG morphological features in short-term VTAs prediction.

Lee *et al.* [117] proposed an early prediction ANNs based model that trained with HRV and respiratory rate variability (RRV) features to predict the VT event one hour before its occurrence. The datasets used were obtained from the cardiovascular intensive care unit at the Asian Medical Center. It consisted 52 recordings obtained one hour before VT events and 52 control recordings. The features used in

predicting the VT event consisted of 11 HRV parameters extracted from time domain, frequency domain and nonlinear domain and 3 RRV parameters. They were Mean NN, SDNN, rMSSD, pNN50, VLF, LF, HF, LF/HF, SD1, SD2, SD1/SD2, respiratory period mean (RPdM), respiratory period standard deviation (RPdSD) and respiratory period variability (RPdV). Two-thirds of the randomly selected datasets were utilized for ANNs training purpose, while the remaining datasets were used to evaluate the performance of the trained ANNs model. The ANNs model trained with the selected HRV and RRV features was able to achieve 85.3% accuracy, 88.2% sensitivity and 82.4% specificity [117].

Boon *et al.* [118] proposed an improved VTAs prediction method based on HRV and Support Vector Machine (SVM) classifier. The dataset used was the Spontaneous Ventricular Tachyarrhythmia Database (Medtronic Version 1.0) obtained from the PhysioNet [114]. These were collected from 78 patients with 106 pre-VT records, 29 pre-VF record and 135 control records of R-R intervals. Half of the datasets were used to train the classifier and the remaining half were used to evaluate the classifier performance. The HRV analysis was performed on 5 minutes HRV signal before the onset of VTAs events. A total of 53 HRV features consisted of 5 time-domain, 6 frequency-domain, 5 non-linear-domain and 37 bi-spectrum features were extracted. The genetic algorithm was then implemented to perform the features selection and optimize the feature subset [119]. Thus, optimising the SVM based classifier's performance. In this study, the proposed method achieved 79.41% accuracy, 77.94% sensitivity and 80.88% specificity [118]. However, this study is yet limited by the small sample size used in predicting the VTAs event although it used the highest number of sample size compared to the method aforementioned.

TABLE V. PREVIOUS WORKS RELATED TO SHORT-TERM VTAS PREDICTION ALGORITHM

Authors	Performance	Methodology	Pros and Cons
Thong and Raitt [112]	<ul style="list-style-type: none"> ❖ Accuracy = Unknown ❖ Sensitivity = 91% ❖ Specificity = 53-69% 	<ul style="list-style-type: none"> ❖ Heart rate acceleration pattern ❖ Decision rule based on threshold value ❖ 208 R-R intervals from 90 subjects ❖ Biotronik European HRV database ❖ Pattern of prolonged, slow and mostly monotonous acceleration during sinus rhythm used as the predictor of imminent VTAs 	<ul style="list-style-type: none"> ❖ Unknown accuracy ❖ Poor performance ❖ Heterogeneous data used
Joo <i>et al.</i> [113]	<ul style="list-style-type: none"> ❖ Accuracy = 75.6% ❖ Sensitivity = 77.3% ❖ Specificity = 73.8% 	<ul style="list-style-type: none"> ❖ ANNs classifier used ❖ Spontaneous Ventricular Tachyarrhythmia database (78 patients, 106 pre-VT, 29 pre-VF and 126 control datasets) ❖ HRV based time domain, frequency domain and nonlinear features 	<ul style="list-style-type: none"> ❖ Short-term HRV data analysis (5mins) ❖ 2/3 datasets used to train the classifier ❖ Remaining 1/3 datasets used to evaluate the performance of the classifier



Rozen <i>et al.</i> [115]	<ul style="list-style-type: none"> ❖ Accuracy = Unknown ❖ Sensitivity = 50% ❖ Specificity = 91.6% 	<ul style="list-style-type: none"> ❖ Multipole Analysis on HRV ❖ Decision rule based on threshold value ❖ 64 pre-event and 60 event-free recording obtained from 28 patients (HAWAI Registry) ❖ New HRV parameter, Dyx is proposed as feature for prediction 	<ul style="list-style-type: none"> ❖ 4500 R-R intervals ~75mins HRV data used ❖ Poor performance
Riasi <i>et al.</i> [116]	<ul style="list-style-type: none"> ❖ Accuracy = 94% ❖ Sensitivity = 88% ❖ Specificity = 100% 	<ul style="list-style-type: none"> ❖ SVM classifier used ❖ MIT-BIH arrhythmias database (40 pre-VT and 40 control datasets) ❖ ECG morphological features are extracted ❖ Feature selection using cross correlation method 	<ul style="list-style-type: none"> ❖ 20 sec ECG analysis ❖ 60 sets data used for classifier training ❖ Remaining 20 sets data used for performance evaluation
Lee <i>et al.</i> [117]	<ul style="list-style-type: none"> ❖ Accuracy = 85.3% ❖ Sensitivity = 88.2% ❖ Specificity = 82.4% 	<ul style="list-style-type: none"> ❖ ANNs classifier used ❖ Datasets acquired from cardiovascular intensive care unit at Asan Medical Center ❖ 15 patients, 52 pre-VT and 52 control recordings ❖ HRV and RRV features are extracted 	<ul style="list-style-type: none"> ❖ Predict the occurrence one hour before onset ❖ 2/3 datasets used to train the classifier ❖ Remaining 1/3 datasets used for performance evaluation
Boon <i>et al.</i> [118]	<ul style="list-style-type: none"> ❖ Accuracy = 79.41% ❖ Sensitivity = 77.94% ❖ Specificity = 80.88% 	<ul style="list-style-type: none"> ❖ SVM classifier used ❖ Spontaneous Ventricular Tachyarrhythmia database (78 patients, 106 pre-VT, 29 pre-VF and 135 control datasets) ❖ HRV features used: Time domain, frequency domain and nonlinear parameters ❖ Feature selection based on Genetic algorithm 	<ul style="list-style-type: none"> ❖ Short-term HRV analysis (5min) ❖ 1/2 datasets used to train the classifier ❖ Remaining 1/2 datasets used for performance evaluation

5. CONCLUSION AND RESEARCH DIRECTION

In conclusion, this article has discussed thoroughly the morphology of the ECG waveform, ECG characteristics and HRV features that demonstrated its prognostic value as well as the recent works related to VTAs prediction. Accurate and precise VTAs prediction algorithm would provide early alert to the clinicians prior to the occurrence of the life-threatening ventricular arrhythmias. This allows enough time for the preventive action to be taken to avoid its initiation and further damage to the patients. However, it remains an open and challenging research area since there is yet to be a standard methodology that exists to handle various targeted groups and clinical settings.

From the literature review, most of the previous works used HRV features in predicting the onset of the VTAs events, while the ECG morphological features are excluded mainly due to the delineation of the ECG characteristics features have yet to achieve sufficient performance. This limited application encourages more investigation and research on the delineation of ECG morphological characteristics points which is the direction of our research team. Thus, a better understanding and exploration on both ECG morphological features and HRV features would validate and affirm its role in the VTAs prediction system

and further contribute to the development of the reliable short-term VTAs prediction. In addition, the use of machine learning techniques such as ANNs and SVM in recognizing and differentiating the fluctuating pattern of the selected features just before the occurrence of VTAs event between control and patient groups is a promising methodology in short-term VTAs prediction field. Our research team aims to develop a machine learning based VTAs prediction algorithm with both ECG morphological and HRV features to enhance the performance of the short term VTAs prediction system. It is hoped that the progressive development in real-time, low computational cost and reliable short-term VTAs predictor in coming years will contribute to reduction in mortality from cardiovascular diseases and more saving of lives within general populations.

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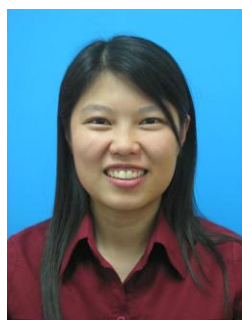
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