International Journal of Research in Engineering and Applied Sciences (IJREAS)
Available online at http://euroasiapub.org/journals.php
Vol. 6 Issue 10, October - 2016, pp. 206~220
ISSN(O): 2249-3905, ISSN(P) : 2349-6525 | Impact Factor: 6.573 | Thomson Reuters ID: L-5236-2015

BIG PICTURE OF ECG SIGNAL PROCESSING AND MACHINE LEARNING BASED CARDIAC DISEASE RISK PREDICTION AND RESEARCH DIRECTIONS

Özlem Uçar[1],
Trakya University, Engineering Faculty, Computer Engineering Department
Edirne / TURKEY

Işıl GÜZEY[2]
Trakya University, Engineering Faculty, Computer Engineering Department
Edirne / TURKEY

ABSTRACT

Cardiac Health Problems are one of the top main causes of death all over the world. Though Electrocardiograpy (ECG) analysis, Imaging Technics and Blood Tests are the methods to diagnose the problem and detect probable risks, due to spontaneous and sudden progression nature of cardiac diseases, monitoring the status of the heart before and after hospitalisation of the patient is of great importance. Recent Signal Processing and Machine Learning studies on ECG, regarding arrhythmia classification and sudden cardiac death prediction are footsteps of a revolution on cardiology. With the attained risk prediction and disease classification accuracy rates, such as 96.7% for Sudden Cardiac Arrest Risk (Murukesan et al.,2014), 99,13% for Acute Chronary Syndrome diagnosis(Berikol et al., 2016), Cardiac Health problems and relevant sudden deaths seem to significantly diminish by means of preventive ECG monitoring in the future. Another medical domain which makes use of ECG Signal Processing and Machine Learning is the prediction of Sepsis like diseases, especially used in preterm neonatal disease prediction. Due to randomized control trails such as the one carried out on around 3000 patients in preterm neonatal infants (Moorman et al.,.2011), some of the academic studies started to be used in pediatric clinical routies. On the other hand, cardiac based studies are not prevalent in clinical routines yet due to lack of consensus regarding the most adequate methods. Features of ECG signal are significant clues regarding the prognosis of cardiac diseases. More effective research on ECG signal processing for feature extraction, with machine learning to extract the patterns relevant to cardiac diseases and randomized control trials seem to speed up this consensus.

Keywords: ECG, Signal Processing, Machine Learning, Medical Decision Support

Introduction

Current mostly used clinical applications of cardiac problem diagnoses are 12 lead ECG devices in hospitals and 24 hour Holter monitoring of patients out of hospital. The obtained records of the Holter are evaluated by a clinician after that period. Due to sudden progression nature of

cardiac diseases, this process risks the preventation of a fatal cardiac health problem.

Besides, compared to days and weeks, it was detected that just 24h monitoring pursued in Holter case, is insufficient duration for the detection of some arrhytmias. During a 2-3 weeks long study on 82 patients who had acute ischemic stroke, having normal resting sinus rithm ECG, paroximal atrial fibrilation was detected in just 1 patient in 24 hours, 2 in 48 h and 2 in 72h (Schuchert et al., 199). In another 21 days long study on 56 patients who had Cryptogenic TIA or stroke, the mean detection of atrial fibrilation was 7 days (Tayal et al. 2008). Longer period of monitoring is only possible with wearable device which are less intrusive to daily activities. Such devices are becoming commercially available and even included in clinical applications.
In last decade there have been many studies on cardiac health problems, such as arrhytmia classification and sudden cardiac risk prediction by making use of Signal Processing and Machine Learning methods. The high accuracy rates attained as the results of these studies are significantly promising. It is expected that these studies will give the opportunity to predict fatal risks in advance to prevent deaths from cardiac diseases, which is main cause of death all over world. Besides, the methods to classify the diseases form ECG data will assist cardiologist on the process of interpreting the ECG data, which needs considerable time and attention within their busy hospital schedules, especially in intensive care units.

Sepsis like disease prediction is another health domain making use of ECG Signal Processing and Machine Learning. Besides the comprehensive academic studies, after a randomized control trial on 2989 very low birth rate infants, 22% reduction (10.2% to 8.1%, p=0.04) in mortality rates was attained by means of Heart Rate Charecteristics monitoring (Moorman et al.,.2011).

There are plenty of comprehensive review articles regarding the studies in literature focused on ECG based signal processing and machine learning technologies (Luza et al., 2016: Gimeno-Blanes, et al., 2016: Jambukia et al., 2015: Acharya et al., 2006). The main contribution of our study will be to emphasize the importance ECG based features and future research requirements for cardiac disease classification and risk prediction.

Cardiovascular Diseases and ECG Signal

Electrocardiography (ECG) is a test to detect the electrical activity of the heart muscle. ECG signal of a healthy person has a certain characteristic morphology. In case of a Cardiovascular Disease, this morphology changes. Interpretation of an ECG by a cardiologist is one of the main diagnostic methods to understand heart abnormalities.

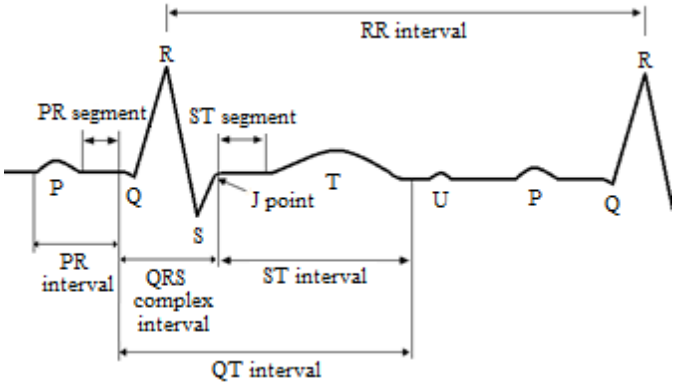

Fig. 1: ECG wave of a healthy person (Kumari et al., 2013)

The morphology of an ECG Signal varies depending on the cardiac issues of a patient. The main cardiac diseases studied within the context of ECG Signal variances in literature are:

Myocardial Infarction: Heartbeat of the patient is irregular. RR duration may be shorter or longer than standards.

Bundle Branch Block: It is the deviation of ventricular conduction. Electrical signal can not be conducted to both bundle branches simultaneously and blocked in one of them. One of the ventricules is activated with delay. Patients have bigger QRS (>0.12 ms) complex.

Dysrhythmia (Arrhythmia): Irregular heartbeats are seen. It may occur in upper and lower chambers of the heart or at the lower level of atrioventricüler junction. It is characterized by bigger than 100 or less than 60 beats per minutes. Therefore, RR interval is different than standard values. QT interval may also increase in case of ventricular arrhytmias. With the abnormal electric activity in the heart pumping efficiency decreases. Arrhytmias are named according to originated locations and speed of the pumping. Some of the arrhythmias have fatal risks and causes cardiac arrests.

Cardiac Failure: It is the inability of the heart to pump the oxygen and blood the body needs. Long QT interval is a sign of it.

Acute coronary syndrome (ACS): Supply and demand balance of myocardium's metabolic needs detoriates. Hyperacute T waves, negative T waves, ST segment elevation, pathological Q waves, or ST changes not specific to myocardial infarction are seen. As normal ECGs can also be encountered in some ACS patients, a normal ECG cannot rule out ACS diagnosis. Therefore serial ECGs or comparison of ECG changes with prior ECG changes are needed in diagnosis.

Cardiac Arrest: Preceded by Pulseless Electrical Activity and some asystole types, it is characterized by sudden ceasation of heart functions.

Sudden cardiac death (SCD): It is the rapid loss of cardiac function which does not show any specific clinical symptom. As a result of insufficient blood and oxygen pumping to organs, loss of conscience and cardiac arrest occurs.

Though, left ventricular ejection fraction (LVEF) is as the gold standard for SCD risk prediction, some other noninvasive techniques and measurements as late potentials, like heart rate variability (HRV), heart rate turbulence (HRT), T–wave alternans have been proposed lately. Ventricular Premature Beats (VPB) and left bundle-branch block like arrhythmic events have also been analyzed in the literature as a specific marker of SCD (Gimeno-Blanes, et al., 2016)

Another important point to consider during ECG analysis is to consider the age, gender and ethnic effects. In a relevant study, the obtained results demostrated that age and gender based criteria can improve sensitivity and specificity of diagnosing myocardial infarction (Macfarlane, et al., 2004). In another study, it was observed that QRS voltages tend to increase until early adulthood and subsequently decrease. Lower QRS amplitudes in females are probably caused by higher fat content and the influence of breast tissue. With regard to race, precordial voltages in young Chinese men and women are lower than for a corresponding Caucasian population(Macfarlane et al., 2004).

ECG Signal Processing and Machine Learning

Physiologic signals obtained from human body (ECG, EMG, etc) contain some type of noises such as powerline noise, baseline wander, muscle movement which negatively effect the analysis of the original signal. There are many studies in literature for the elimination of these noises and regarding their efficiencies.

With recursive digital filters of the finite impulse response (FIR) (Lynn, 1971), noises at certain frequencies may be eliminated but in case of insufficint information regarding the attenuation of the noise signal this process may distort the morphology of the main signal (ECG). In last decade there have been many wavelet based noise filtering applications which preserves the main features of ECG Signal. Sayadi and Shamsollahi (2007) added a modification called multi-adaptive bionic wavelet transform to standard wavelet transform and had very successful results regarding noise and baseline variation elimination. Methods focusing on QRS detection from ECG signal and automatic classification of arrhythmias requires different approaches. Though there are many studies regarding different arrhythmia classification method performances, there are still many unevaluated methods and this an important research requirement in this area.

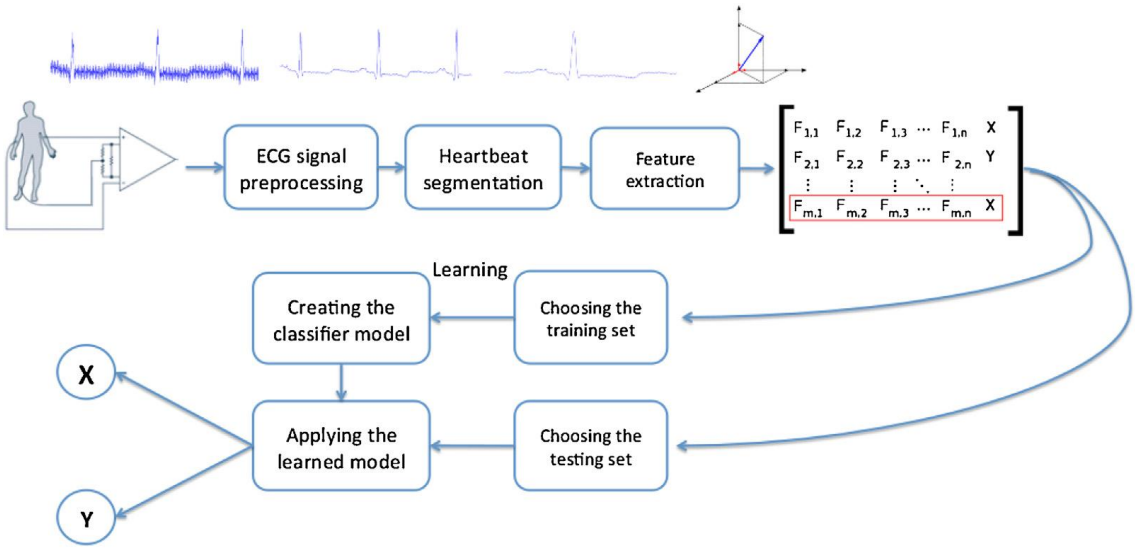

Figure 2: A diagram of the arrhythmia classification system (Luza et al, 2016)

Heartbeat segmentation, (i.e., detection of the R peak or the QRS complex) is the stage which has the highest effect on the results of ECG analysis as the errors here propagate to the following stages and have a strong impact in the final classification of the cardiovascular diseases

Any characteristic to differentiate the heartbeat types is named as feature. Features may be extracted from time, frequency, non linear domain structures or cardiac rhythym. It is important for the features to be representative, easily detected and high detection accuracy.

There are many studies on feature extraction in literature. Considering the frequency domain features representation of Fourier transform, the wavelet transform that represents both the time and frequency domain characteristics yielded significantly better results. Another frequently used method for feature extraction is Pan Tomkins, which is computationally simpler than wavelet transform.

In previous 'Cardiovascular Diseases and ECG Signal' section, we mentioned on the disease based abnormalities of ECG. Accordingly, some of time and amplitude based features used in disease classification and prognosis prediction are P,Q, R and S values mean/median/standard deviations and QRS, RR mean/median/standard deviations.

Another ECG based parameter ready for feature extraction is Heart Rate Variability (HRV), described as the variation in time between consecutive heart beats. Time, frequency and nonlinear domain analysis of HRV gives distinguishing information regarding the physiological status of the person.

Heart rate (HR) of a healty individual changes in accordance with bodily demands. On the contrary, decrease in HRV is linked to some diseases such as heart failure, diabetes and

inflammatory diseases (Acharya et al., 2006). Analysis of HRV provides a way to assess not only cardiac health, but the state of the autonomic nervous system, which is responsible for regulating cardiac activity. In a study, it was found that that the respiratory peak of HRV signals in SCD patients disappeared at night 1 week before the patient's death due to SCA(Ichimaru et al., 1988). In another study, it was reported that the standard deviation (SD) of the mean of sinus RR intervals (SDANN), and the mean 24 hour HRV was higher in young healthy people than in SCA patients (VanHoogenhuyze et al., 1989). Features from HRV signals were derived using time, frequency, and non-linear domains analysis.

In time domain analysis, most of the parameters (both short term and long term variation indices) are derived from the RR intervals and their statistical measures, calculated directly from the IBI(Inter Beat Interval) series, such as mean of IBI and standard deviation of NN (RR of 'normal' beats) interval series (SDNN). They reflect the combined influence of sympathetic and parasympathetic system contents (Gimeno-Blanes et al., 2016). In order to improve the robustness of HRV measurements, various approaches have been used to derive geometric measures. Two of them are triangular index and triangular interpolation. The triangular index is a measure, where the length of RR intervals serves as the x-axis of the plot and the number of each RR interval length serves as the y axis. The triangular interpolation of NN interval histogram (TINN) is the baseline width of the distribution measured as a base of a triangle, approximating the NN interval distribution (the minimum of HRV). The major advantage of geometric methods lies in their relative insensitivity to the analytical quality of the series of NN intervals (Acharya et al., 2006).

Frequency domain features are also highly efficient for distinguishing the sympathetic and parasympathetic contents of RR intervals. Frequency domain analysis is mainly done in four frequency bands: ultra-low frequency (ULF) (0–0.0033 Hz), very low frequency (VLF) (0.003–0.04 Hz), low frequency (LF) (0.04–0.15 Hz), and high frequency (HF) (0.15–0.4 Hz). These methods have the capability of distinguishing in the frequency domain the contribution of the sympathetic and the vagal branches, which are mostly confined in specific bands (Gimeno-Blanes et al., 2016). Some of the features to be extracted from frequency domain are absolute power of these bands (aVLF, aHF, etc.), ratio of band powers to each other and total power (ratio of LF/HF, pVLF=aVLF/aTotal, etc).

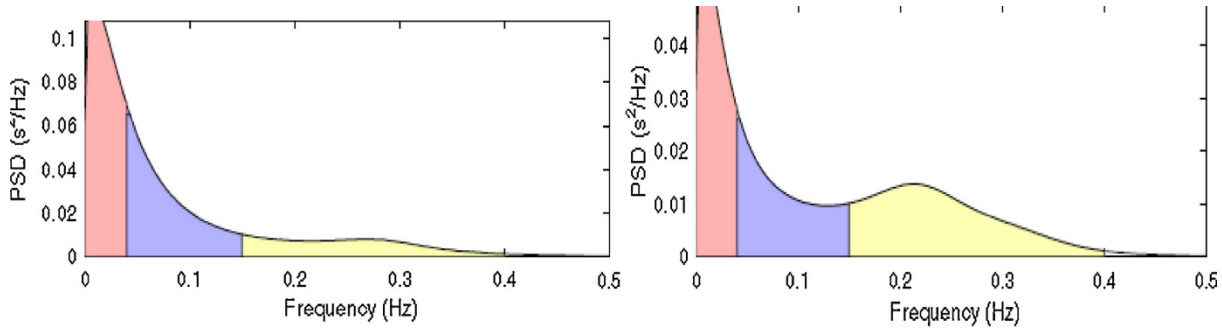

Figure 3: Typical Power Spectral Density of heart rate signal: a) normal subject b) CAD subject (Acharya et al., 2013)

Like the other biosignals, ECG is also has nonlinear nature. This nonlinearity contain important information suitable for feature extraction. Some of them measures of non linear domain are:

a) Poincaré plot is a plot of current IBI intervals versus previous IBI intervals. This plot is usually used to quantify selfsimilarity. It shows the correlation between consecutive intervals in graphical representation. The short term variability (SD1) of the heart signal is measured by the points that are perpendicular to the line-of-identity and long term variability by the points along the line-of-identity. By examining Poincare plot shapes, some diseases (CAD) can be discriminated. SD2 describes the long term variability of RR(n) (instantaneous RR),while SD1 indicates the shorter-term variability of RR(n). In theplot for CAD, SD2 and SD1 are very low compared to the normal plot.

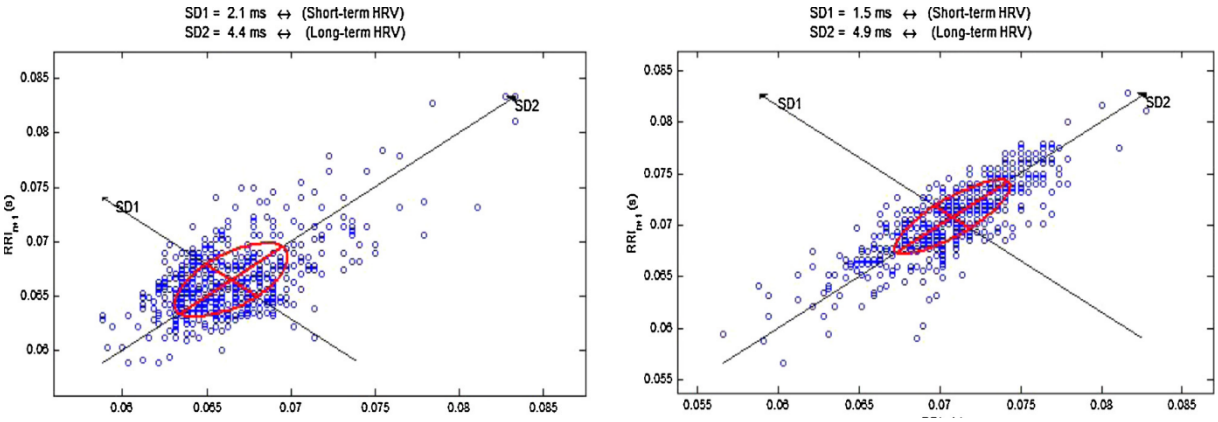

Figure 4: Poincare plots of HR signals a) normal b)CAD (Acharya et al., 2013)

b) Approximate entropy (ApEn): indicates the fluctuation in the time domain signal. The value of ApEn is higher for more varying data. Hence, morevarying time domain signals will have higher ApEn values,while regular and predictable time series signals will have lower ApEn values.

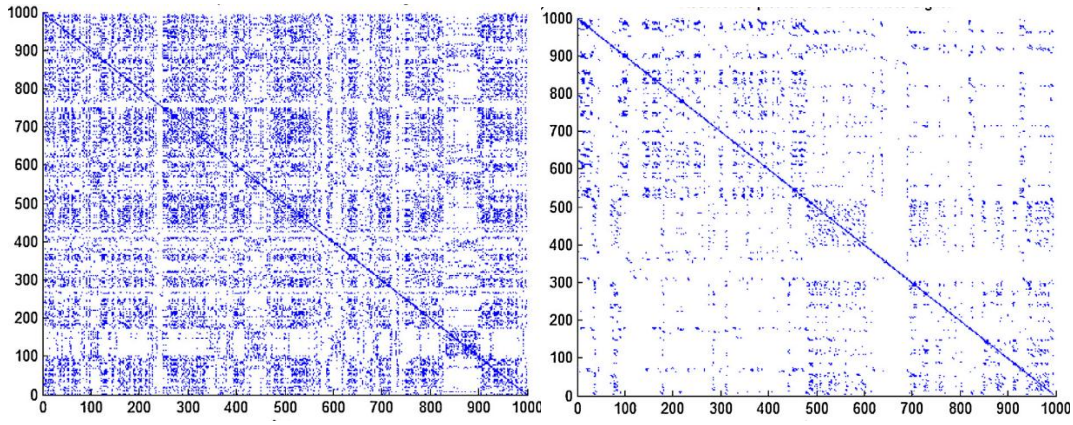

Figure 5: Typical recurrence plot of HR signal: (a) normal (b) CAD (Acharya et al., 2013)

c) Sample Entropy (sampen) is the embedded entropy that attempts to quantify a signal's complexity or rate of generation of new information. If the consecutive sequences are identical, then the value of sample entropy is zero. Higher values of SampEn describes more irregularities in the time series. It is more refined than ApEn.

d) Detrended fluctuation analysis (DFA) quantifies the fractal correlation properties of non-stationary time series data. It is used to calculate the root-mean-square fluctuation of integrated and detrended time series, permits the detection of intrinsic self-similarity embedded in a non-stationary time series, and also avoids the spurious detection of apparent selfsimilarity (Signorini et al., 2006)

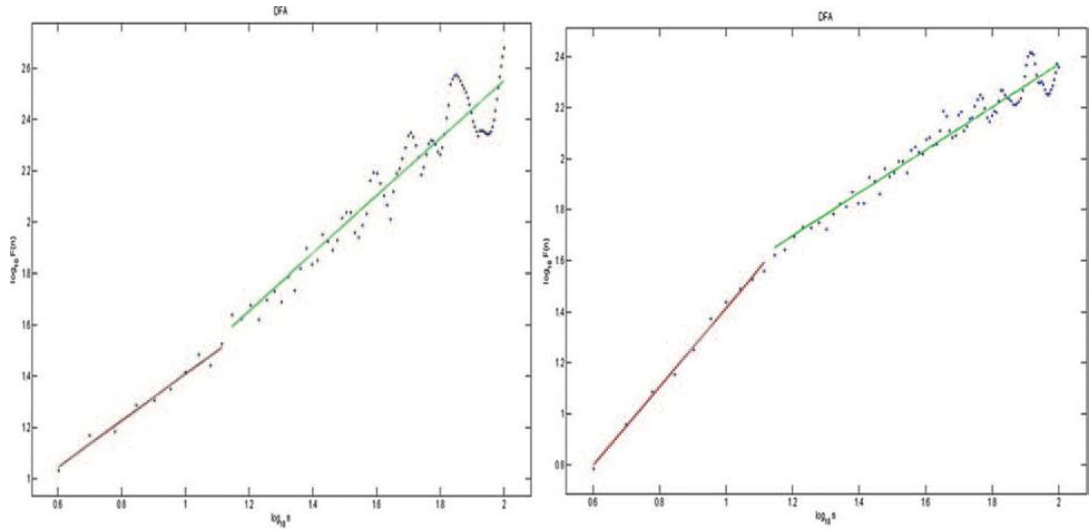

Figure 6: DFA of (a) SCD and (b) normal patient (Murukesan et al., 2014)

e) Correlation Dimension (D2): D2 is a useful measure of self-similarity of a signal, D2 will have higher value, if the RR variations are more and vice versa. The value will be high for the chaotic

data and it decreases as the variation of RR signal becomes less or rhythmic. The CD is more for NSR and it decreases for different cardiac diseases (Acharya et al., 2013)

f) Higher Order Spectrum (HOS): Most of the biomedical signals are non-linear, non-stationary and non-Gaussian in nature. By means of HOS, the non-Gaussian and non-stationary bio-signals may be evaluated. It identifies diversions from Gaussianity and phase correlations among frequency components of the signal. HOS is more immune to noise and can retain the actual phase information of the signal(Ichimaru et al., 1988).

Heart Rate Turbulence describes the short–term fluctuation in ECG cycle length that follows a VPB(Ventricular Premature Beat). The turbulence can be very well identified in RR interval time series and its regular pattern exhibits an initial sinus rhythm acceleration after the VPB, followed by a subsequent deceleration to finally return to preectopic levels (Gimeno-Blanes et al., 2016). Any deviation from normal pattern may reflect anomalous autonomic function, thus, patients at risk show an attenuated or even entirely missing HRT, and this difference on the HRT response has been proven to be an informative predictor of mortality and SCD .

The measurement of HRT is carried out by means of two parameters, namely, Turbulence Onset (TO) and Turbulence Slope (TS), which quantify the two phases described above. The early acceleration is characterized by

$$TO = [(RR_1 + RR_2) - (RR_{-3} + RR_{-2})] \div [(RR_{-3} + RR_{-2})] \times 100$$

where RR−3 and RR−2 are the two RR intervals preceding the coupling interval, while RR1 and RR2 are the two RR intervals immediately following the compensatory pause. The spots used for calculating TO are identified in Figure 7.

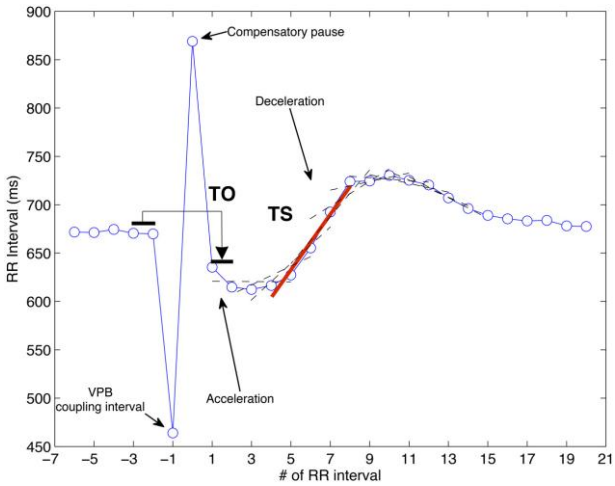

Figure 7: Biphasic response after a VPB in an RR interval time series (Gimeno-Blanes, et al.,2016)

TWA is a particular type of ECG alternans that is related to changes in amplitude, waveform, and duration of the ST–T complex occurring on an every other beat basis. Also known as repolarization alternans, it has been shown to be a clinical marker for stratifying risk in SCD patients). Figure 8 depicts an example of a severe TWA where the periodic pattern of two beats is clearly observed on the ECG of the left panel.

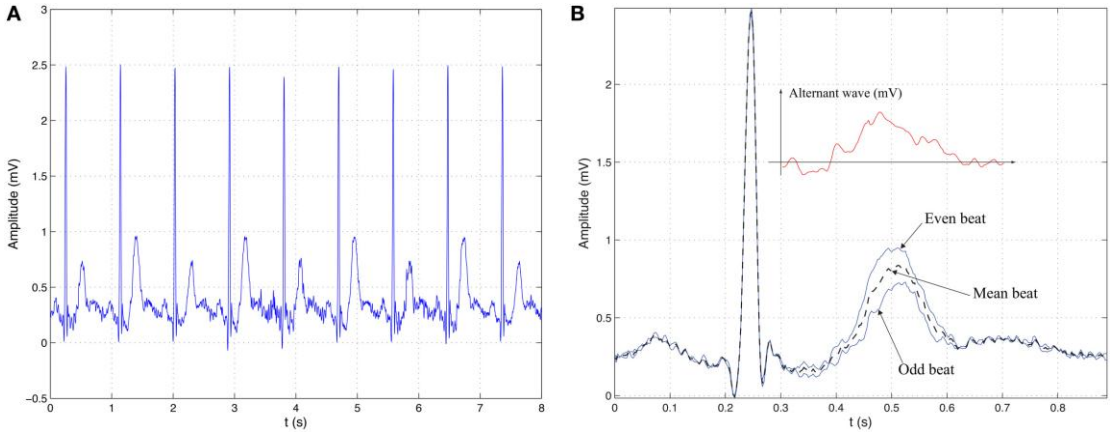

Figure 8: a) ECG signal with periodic pattern alternation in the repolarization segment with a period of two beats. b) Visual interpretation of TWA as the difference between the averaged event beat and the averaged odd beat (Gimeno-Blanes, et al.,2016).

Due to difficulty of visualizing TWA, Spectral Method (SM) and Modified Moving Avarage (MMA) approaches have been proposed. SM estimates the power spectrum density function P(f) of each beat series through the periodogram. With MMA a measure of the alternant wave is achieved as the difference between even and odd estimates. maximum alternans magnitude Vl, is computed as the maximum of the absolute value of the difference.

Heart Rate Parameters	Domains	Analysis Method	Sample Features	Clinical Relevance
Time and Amplitude			P, Q, R, S values mean / median / standard deviations and QRS, RR mean / median / standard deviations	In case of many cardiac diseases Time and Amplitude based features show abnormalities.
HRV	Time	Statistical	SDNN, pNN50, r – MSSD, HRVindex, and LoadIndex	The greater HRV, the healthier cardiovascular system. SDNN and HRVindex are absolute measures of HRV (influenced both by the sympathetic and the parasympathetic branches), whereas pNN50, r – MSSD reflect vagal activity.
		Geometric	HRVti, TINN	Improves robustness of HRV measurements. The major advantage of geometric methods lies in their relative insensitivity to the analytical quality of the series of NN intervals.
	Frequency		aVLF, aLF, aHF, Ratio LF/HF	Highly efficient for indiscriminating between the sympathetic and parasympathetic contents of RR intervals, which could be exploited for predicting SCA

	Non Linear	Poincare Geometry	SD1, SD2	Shows the comprehensive every beat to beat variation. for CAD patients have much lower SD2 and SD1 compared to the healty ones.
		Recurrence quantification analysis	Lmean, Lmean, Lmean	It measures the dynamicity and subtle rhythmicity in the HRsignal. More variation (dots) is predominantin the normal signal compared to the CAD class, there is more rhythmicity with respect to normal subjects
		Approximate entropy	ApEn value	Indicates the fluctuation in the time domain signal.
		Sample entropy	SampEn value	Quantifies the complexity in signal
		Detrended fluctuation analysis	Roughness of the signal	Assesses the self-similar properties of short term HR signals
		Correlation dimension (D2)	D2	Measure of self-similarity of a signal. higher value, if the RR variations are more andvice versa
HRT			TO, TS	Patients at risk of SCD show an attenuated or even entirely missing HRT. This difference on the HRT response has been proven to be an informative predictor of mortality and SCD.

TWA	P(f), V_1	A clinical marker of SCD

Table 2: Several features to be extracted from ECG data and their correlation with Cardiac Diseases.

As explained in previous section, ECG signal presents plenty of features for classification and risk prediction for many cardiac diseases which may be used in machine learning algorithms in case of an investigation. Though the high number of alternatives to be used, too many features do not guarantee a better prediction rate, due to risk of overfitting or too much processing requirement. In order to avoid these risks, significant features must be selected. Principle Component Analysis (PCA), Independent Component Analysis (ICA), SOM (Self Organising Maps), Statistical feature reduction was performed using the inter quartile range (IQR) and standard deviation (STD) are some of the methods used in previous studies.

The ECG data of patients having cardiac problems presents a voluminous and high dimensional big data structre having certain patterns within. These patterns may be extracted by means of Machine Learning methods with a certain accuracy. Depending on the amount and correctness of the data used in learning stage, the accuracy increases accordingly.The relevancy of a new patient data to the extracted patterns gives the opportunity to classify the underlying disease and health risk.

Several machine learning methods used in previous studies are; Artificial neural networks (ANNs), Multilayer perceptron (MLP), Decision Trees (DT), Support Vcetor Machine, k-Nearest Neighbour and Reservoir Computing With Logistic Regression (RC) methods.

Conclusion and Research Requirements

As stated in the beginning of the article; though attained high accuracies in ECG based cardiac risk prediction with mentioned signal processing and machine learning methods, they are not yet prevalently used in clinical and monitoring based ambulatory routines due to lack of consensus on the most appropriate methods. Here are several approaches to foster this consensus.

In most of the studies, ECG data of databases like Physionet were used. Considering the age, gender and even ethnic origin based effects on ECG data, comprehensive enlargement of these databases is necessary. Cardiac disease relevant patterns extracted from this big data shall be validated by means of randomized control trials.

Due to multidisciplinary nature of studies, inclusion of cardiology practioners in the studies in order to confirm clinical meaningfulness of the highly accurate results is of utmost importance.

Our emphasize in this study was mostly on features to be extracted form ECG data. We

mentioned on the correlation of these features with cardiac disease specific issues. Extraction of common hidden patterns specific to certain diseseas from ECG data by means of machine learning methods will give the opportunity to pinpoint the fatal risks in advance and prevent cardiac disease based deaths.

References

Acharya U. R., Joseph K. P., Kannathal N. Lim C. M., Suri J. S., 2006, Heart rate variability: a review, Medical and Biological Engineering and Computing, 44(12), pp. 1031–1051

Acharya, U. R., Fausta, O., Sreec, V., Swapnae, G., Martisa, R. J., Kadrib, N. A., Surif, J. S., 2013, Linear and nonlinear analysis of normal and CAD-affected heart rate signals, Computer Methods and Programs in Biomedicine, 113(1), pp. 55–68

Berikol, G. B., Yildiz, O., Ozcan, A. T., 2016, Diagnosis of Acute Coronary Syndrome with a Support Vector Machine, Journal of Medical Systems, 40 (4), pp.1-8

Gimeno-Blanes, F.J., Blanco-Velasco, M., Barquero-Pérez, Ó., Rojo-álvarez, J.L., García-Alberola, A., 2016, Sudden Cardiac Risk Stratification with Electrocardiographic Indices - A
Review on Computational Processing, Technology Transfer, and Scientific Evidence, Frontiers in Physiology, 7, Article 82

Ichimaru Y., Kodama Y., Yanaga T.,1988, Circadian Changes of Heart Rate Variability. Proceedings of Computers in Cardiology, pp.315–318.
Jambukia, S.H., Dabhi, V.K., Prajapati, H.B., 2015, Classification of ECG signals using Machine Learning Techniques: A Survey, Conference Proceeding International Conference on Advances in Computer Engineering and Applications, pp.714-721
Kleiger, R. E., Miller, J. M., J.Thomas Bigger J. T., J. A., 1987, Decreased heart rate variability and its association with increased mortality after acute myocardial infarction Decreased heart rate variability and its association with increased mortality after acute myocardial infarction, , The American Journal of Cardiology, 59(4), pp. 256-262

Kumari, V., P. Kumar, R., 2013, Cardiac Arrhythmia Prediction Using Improved Multilayer Perceptron Neural Network, International Journal of Electronics, Communication & Instrumentation Engineering Research and Development (IJECIERD), 3(4), pp. 73-80

Luza, E. J. S., Schwartzb, W. R., Cámara-Cháveza, G., Menottia, D., 2016, ECG-based heartbeat classification for arrhythmiadetection: A survey, Computer Methods and Programs in Biomedicine, 127, pp.144–164

Lynn, P. A., Recursive digital filters for biological signals, 1971, Medical and Biological Engineering and Computing, 9, pp. 37-43
Macfarlane, P.W., Chen, C.Y., Chiang, B.N., Comparison of the ECG in healthy Chinese and

Caucasians, 1987, Computers in Cardiology, pp. 143-146

Macfarlane, P.W., Devine, B., Clark, E., Miller, E., Seyal, J., Browne, D., Hampton, D, 2004, Effect of Age and Gender on Diagnostic Accuracy of ECG Diagnosis of Acute Myocardial Infarction , Computers in Cardiology, 31, pp.165-168

Moorman J. R., Carlo, W. A., Kattwinkel J., Schelonka, Robert L., Porcelli, P. J., Navarrete, C. T., Bancalari, E., Aschner, J. L., Whit W. M., Perez, Jose A., Palmer, C., Stukenborg, G. J., Lake, D. E., Michael O. T., 2011, Mortality Reduction by Heart Rate Characteristic Monitoring in Very Low Birth Weight Neonates: A Randomized Trial, The Journal of Pediatrics, pp.900-906

Murukesan, L., Murugappan M., Iqbal M., and Saravanan K., 2014, Machine Learning Approach for Sudden Cardiac Arrest Prediction Based on Optimal Heart Rate Variability Features, Journal of Medical Imaging and Health Informatics, 4(4), pp.521-532.

Schuchert, M., Behrenz, G., Meinertz, T., 1999, Impact of Long-Term ECG Recording on the Detection of Paroxysmal Atrial Fibrillation in Patients After an Acute Ischemic Stroke, PACE - Pacing and Clinical Electrophysiology, 22(7), pp. 1082-1084

Signorini, M. G., Ferrario, M., Marchetti, M., Marseglia, A., 2006, Nonlinear analysis of heart rate variability signal for the characterization of cardiac heart failure patients, 28th Annual International Conference of the IEEE Engineering in Medicine and Biology Society 1, pp. 3431–3434.

Tayal, A.H., Tian M., Kelly, K.M., Jones S.C., Wright D.G., Singh D., Jarouse J., Brillman J., Murali, S., Gupta, R., 2008, Atrial fibrillation detected by mobile cardiac outpatient telemetry in cryptogenic TIA or stroke, Neurology, 71(21), pp.1696-1701

Sayadi, O., Shamsollahi, M. B., 2007, Multiadaptive Bionic Wavelet Transform: Application to ECG Denoising and Baseline Wandering Reduction, EURASIP Journal on Advances in Signal Processing, 2007(1), p 041274

Signorini, M. G., Ferrario, M., Marchetti, M., Marseglia, A., 2006, Nonlinear analysis of heart rate variability signal for the characterization of cardiac heart failure patients, 28th Annual International Conference of the IEEE Engineering in Medicine and Biology Society 1, pp. 3431–3434.

VanHoogenhuyze, D., Martin, G., Weiss, J., Schaad, J., Singer, D., 1989, Spectrum of heart rate variability, Proceedings - Computers in Cardiology, pp.65