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Prediction of PAF Attacks using Time-Domain Measures of Heart Rate Variability

Kalp Hızı Değişkenliği Zaman Alanı Ölçümleri Kullanarak PAF Atağının Tahmini

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Abstract

Paroxysmal atrial fibrillation (PAF) is the mainly encountered type of arrhythmia and there is no validated method to predict a PAF attack before it occurs. In this study, predicting the PAF event was aimed using time-domain heart rate variability (HRV) measures in k- nearest neighbor (k-nn) classifier. Traditional time-domain HRV measures were analyzed in every 5-minute segments from 49 normal subjects, 25 patients with PAF attack and 25 patients with no attack within 45 minutes. All features were investigated whether they showed statistically significance. Significant features were classified by k-nn for odd numbers of neighbors between 1 and 19. This setup was run with two different configurations as study 1 to discriminate patients with PAF attack from normals and patients with no attack, and study 2 to discriminate patients with PAF attack from patients with no attack. SDNN, RMSSD and pNN50 measures were found to show statistically significant differences with p less than 0.05 in segments of 0-5 min, 2.5-7.5 min and 5-10 min intervals only. The maximum classification accuracy was obtained in the time interval of 2.5-7.5 minutes with %79 for Study 1 and just before attack with %80 for Study 2 in the time interval of 0-5 minutes. Results showed that the prediction of PAF events was possible when the classification between normal subjects from PAF patients was accurate. PAF attack can be determined 2.5 minutes earlier by simple classifier algorithms.

Keywords: Heart rate variability, K-nearest neighbor, Paroxysmal atrial fibrillation, Prediction

Öz

Paroksismal atriyal fibrilasyon (PAF), çoğunlukla rastlanan aritmi türüdür ve PAF atağı başlamadan önce öngörmek için geçerli bir yöntem yoktur. Bu çalışmada, k- en yakın komşu (k-nn) sınıflandırıcı algoritmasıyla kalp hızı değişkenliği (KHD) zaman alanı ölçümleri kullanılarak PAF olayının gerçekleşmeden önce tahmin edilmesi amaçlanmıştır. 49 normal, 25 PAF hastası olup atak geçirmeyen ve 25 PAF hastası olup verinin bitiminde atak geçiren 5 dakikalık veriler üzerinden geleneksel zaman alanı ölçümleri elde edilmiştir. Tüm bu ölçümlerin istatistiksel anlamlılık değerleri araştırılmıştır. İstatistiksel anlamlı olan öznitelikler kullanılarak k değerinin 1 ila 19 arasındaki tek değerleri için k-nn sınıflandırıcı algoritmasıyla sınıflandırılmıştır. Bu işlem hemen PAF atağı geçiren verilerin, normal ve atak geçirmeyen verilerin kontrol grubunda olduğu çalışma 1 ve hemen atak geçiren verilen, hemen atak geçirmeyen verilerin kontrol grubunda olduğu çalışma 2 için ayrı ayrı çalıştırılmıştır. Sonuç olarak, SDNN, RMSSD ve pNN50 ölçümlerinin istatistiksel anlamlılık değerlerinin 0-5 dakika, 2,5-7,5 dakika ve 5-10 dakika aralıklarında $p<0,05$ olduğu tespit edilmiştir. Maksimum sınıflandırıcı performansı 2,5-7,5 dakika aralığında çalışma 1 için %79 ve 0-5 dakika aralığında çalışma 2 için %80 dolaylarında elde edilmiştir. PAF atağının erken tahmini PAF hastalarının normallerden ayrılmasıyla daha da muhtemel olurken, PAF atağının gerçekleşmeden yaklaşık 2,5 dakika öncesinden basit bir sınıflandırıcı ile %80 oranında tahmin ediliyor olduğu gösterilmiştir.

Anahtar Kelimeler: Kalp hızı değişkenliği, K- en yakın komşu, Paroksismal atrial fibrilasyon, Tahmin

1. Introduction

Atrial fibrillation (AF) is the mainly encountered type of arrhythmia among heart diseases in clinics. More than 467,000 people are contracted AF and about more than 99,000 people are died on a yearly basis in the United States (January et al. 2014). Over six million Europeans suffer from are AF. Moreover, the number of patients with AF will increase at least twice depending on aging in 50 years (Camm et al. 2010). This is also probably true in other countries (Uyarel et al. 2008).

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A number of irregular electrical stimulations are traced from atria in addition to the normal stimulation from the SA node in patients with AF, which is resulted in very fast and irregular contractions through the atria. Therefore, increasing in the proportion of catastrophic problems such as death, stroke, thromboembolic events and heart failure is observed. That is the reason why AF must be handled carefully.

Paroxysmal Atrial Fibrillation (PAF) is the first step of AF that is lasting from 2 minutes to 7 days. PAF seriously affected the life quality by limiting daily activity of these patients. Patients with PAF give no sign before having an attack generally. On the other hand, there are some methods developed to predict PAF events in the literature including the frequency of atrial premature difference (Zong et al. 2001), the P-wave changes in 60-second segments of data (Schrier et al. 2001) atrial ectopic and ventricular ectopic numbers using RR intervals (Langley, et al. 2001), Heart Rate Variability (HRV) time domain measures (SDNN, pNN50, RMSSD), frequency domain (Wavelet Transform) and the number of atrial and ventricular ectopic beats on data segment of 1 min, 5 min and 30 minutes (Maier et al. 2001), time domain measurements (1-6 correlation coefficients, NN50, pNN50, RMSSD, SDSD), frequency domain measurements the Fast Fourier Transform (FFT) using RR interval, P-wave shape, a power spectral density of the P-wave (Chazal and Heneghan 2001), HRV measurements with two-level algorithm (Lynn and Chiang 2001), FFT using RR interval and calculate the RR interval dynamics (Krstacic et al. 2001) footprint analysis (Yang and Yin 2001), Spectrum, bispectrum and nonlinear measurements (Mohebbi and Ghassemian 2012), spectral changes of P wave (Alcaraz et al. 2015) and Poincare plot and based on Wavelet transform measurements from HRV (Park et al 2009), standard deviation and spectral entropy measures on RR interval data (Thuraisingham 2016), spectral analysis, approximate entropy (ApEn), sample entropy (SamEn) and multiscale complexity analysis using HRV signals (Chesnokov 2008) and time domain, frequency domain, non-linear and bispectrum measures from HRV data (Boon, et al. 2016), linear and non-linear HRV measurements (Narin et al. 2016, Narin et al. 2017, Narin et al. 2018).

This study is aimed to answer two major questions: (1) Is it possible to predict PAF episodes using HRV time domain measures? If it is possible, how many minutes ago it can be predicted? (2) Is it important to discriminate the patients with PAF from normal subjects for this prediction? Otherwise, may normal subjects be assumed non-attack PAF patients?

The study is organized in 4 sections. The following section covers methods used in the study including obtaining the data, time domain measures of HRV, k-nearest neighbor classifier, normalization and performance assessment. Third section presents the implementation details and results. Finally, the results are discussed.

2. Material and Methods

2.1. Data

In this study, the database of "PAF Challenge the MIT-BIH Database (afpdb)" is preferred since it is open to all researchers via the Internet and it has become a benchmark data (Moody et al. 2001). The database supplies 30-min ECG records from 3 groups:

- Normal: without any arrhythmia consists of 50 data in the control group (n1, n2, …, n50).
- Non-PAF: consists of 25 data. There is no PAF episode during 45 minutes just after or before these 30-min recordings (the odd numbers that belong to this group; for example, p1, p3, p5,…, p49).
- PAF consists of 25 data just before the occurrence of a PAF event (the even numbers that belong to this group; for example, p2, p4, p6,… , p50).

The data file of 'n27' was excluded from this study similar to other studies in the literature (Park et al 2009) because it has too much noise to detect heart beats and it is almost impossible to obtain time domain measures of HRV.

QRS wave structure is the most significant component having the biggest amplitudes in the ECG signal. RR interval data were extracted following to QRS detection (Isler and Kuntalp 2007). HRV data were defined difference between successive RR time intervals as ($RR_n=t_n-t_{n-1}$) (Narin et al. 2014). In this study, RR intervals were downloaded from the original website of the database (Moody et al. 2001).

2.2. Time-Domain Heart Rate Variability Measurements

Time domain measures are the most simple and easy to calculate HRV measures. Therefore, 8 different commonly used time-domain measures were calculated as follows.

$$AVRR = \frac{1}{N}\sum_{i=1}^{N} RR_i \qquad (1)$$

$$SDNN = \sqrt{\frac{1}{N-1}\sum_{i=1}^{N}(RR_i - AVRR)} \quad (2)$$

$$RMSSD = \sqrt{\frac{1}{N-1}\sum_{i=1}^{N-1}(RR_{i+1} - RR_i)^2} \quad (3)$$

$$SDSD = \sqrt{\frac{1}{N-1}\sum_{i=1}^{N-1}(|RR_{i+1} - RR_i| - ARR)^2} \quad (4)$$

$$ARR = \frac{1}{N-1}\sum_{i=1}^{N-1}|RR_{i+1} - RR_i| \quad (5)$$

$$NN50 = \sum_{i=1}^{N-1}\{|RR_{i+1} - RR_i| > 50ms\} \quad (6)$$

$$pNN50 = \frac{NN50}{N}.100 \quad (7)$$

$$NN20 = \sum_{i=1}^{N-1}\{|RR_{i+1} - RR_i| > 20ms\} \quad (8)$$

$$pNN20 = \frac{NN20}{N}.100 \quad (9)$$

where N is the number of RR intervals, RR_i is the i-th RR interval, AVRR is the mean value RR intervals, SDNN is the standard deviation of RR intervals, SDSD is the standard deviation of differences between successive RR intervals, RMSSD is the root mean square of successive differences between RR intervals, NN50 is the absolute number of differences between successive RR intervals that are greater than 50 ms, NN20 is the absolute number of differences between successive RR intervals that are greater than 20 ms, pNN50 is the percent of NN50, and pNN20 is the percent of NN20 (Task Force et al. 1996).

2.3. Feature Selection

The independent t-test, which is commonly used to show significance of differences between measures of two distinct groups (Ashcroft and Pereira 2003), was used as a feature selection method in this study (Isler et al. 2015, Isler et al. 2019) "IBM SPSS Statistics 22" software package, which is possibly the most common program in statistical analysis, is used to find p-values that show statistical significances. Then, the features that have statistical evidence values of %5 (p=0,05) were selected and applied to the input of a classifier in this study.

2.4. Normalization

The measures must be equalized on the same scale to eliminate the effect of units, which is called as normalization (Duda et al 2001). In this study, the MIN-MAX normalization method, in which all measures are scaled into the range between 0 and 1, was preferred.

$$X_i^{normalized} = \frac{X_i - Min\{X_i\}}{Max\{X_i\} - Min\{X_i\}} \quad (10)$$

where X_i is the i-th measure, min{X_i} and max{X_i} show the smallest and the largest values of these measures, respectively.

2.5. Classification Algorithm

K-nearest neighbors (k-nn) is a sample-based classifier. When a new sample is tested, the sample is classified as the class of the majority of classes from its k nearest neighbors (Isler et al 2015). K-nn does not have a training step because it uses examples with known classes (Duda et a 2001). Euclidean distance is commonly used in order to determine the distance as follows:

$$dis\tan ce(X_i - X_j) = \sqrt{\sum_{k=1}^{D}(X_i^k - X_j^k)^2} \quad (11)$$

where D is the number of measures, k is the k-th measure in both samples of X_i and X_j.

2.6. Performance Assessment

The performance of a classifier is given by means of SEN (sensitivity), SPE (specificity) and ACC (accuracy) as follows (Duda et al 2001):

$$SEN = \frac{TP}{TP+FN} \quad (12)$$

$$SPE = \frac{TN}{TN+FP} \quad (13)$$

$$ACC = \frac{TP+TN}{TP+FN+FP+TN} \quad (14)$$

where TP is the number of patients correctly identified as patients, FP is the number of normal misidentified as patients, TN is the number of normal correctly identified as normal, FN is the number of patients misidentified as normal.

In this study, k- fold cross validation method is used for calculation of the performance evaluation. Data is divided into k segments in this method. One of these segments is used for testing whereas other segments are used for training. This process is repeated until all segments are used for test purpose. TP, TN, FP and FN values are obtained as average of obtained performance values from these processes (Task Force et al. 1996).

3. Results

Data used in the study were divided into two main study groups (Table 1). First study was named as Study 1 to discriminate patients with PAF attack from normal subjects and patients with no attack; whereas the second study was named as Study 2 to discriminate patients with PAF attack from patients with no attack.

Table 1. Study groups of data

Study 1	74 (Normal + non- PAF) versus 25 (PAF)
Study 2	25 (non-PAF) versus 25 (PAF)

For these groups, each data was divided into 10 segments of 5 minutes with 50\% overlapping (Segment #1: 0-5 minutes, Segment #2: 2.5-7.5 minutes, …, Segment #10: 22.5-27.5 minutes ago). Eight HRV time domain measures (AVRR, SDNN, RMSSD, SDSD, NN50, NN20, pNN50, and pNN20) were obtained for each 5-minute segment. Statistical significance values of these measures were determined using independent samples t-test for these segments (Table 2 and Table 3). This tables show that there are statistical significances, which are less than or equal to %5, in measures of SDNN, RMSSD, and pNN50 in both studies between discrimination groups. In addition, three time segments, showing these statistical significances, are Segment #1 (0-5 min), Segment #2 (2.5 -7.5 min) and Segment #3 (5-10 min). These three measures were applied to k-nn classifier with different k values of 1, 3, 5, 7, 9, 11, 13, 15, 17 and 19.

All algorithms were conducted 100 times to find the best discrimination performance. The 10-fold cross-validation method was preferred to determine classifier performances. Classification performances were given in Table 4 for both studies in all segments. In addition, values of k for that show the maximum discrimination performances were also given for each classification study.

4. Discussion

In this study, it has been investigated in which 5 minute interval the PAF attack can be predicted. Similar studies using short-term data in the literature examined about early PAF attacks: Chazal and Henegham obtained %81 SEN, % 69 SPE and % 75,6 ACC using P-wave power spectral densities measurements on the 5 minute immediately

Table 2. Statistical significance values for study 1.

	0-5 min	2,5-7,5 min	5-10 min	7,5-12,5 min	10-15 min	12,5-17,5 min	15-20 min	17,5-22,5 min	20-25 min	22,5-27,5 min
AVRR	0,538	0,487	0,348	0,429	0,539	0,559	0,548	0,523	0,646	0,702
SDNN	**0,003**	**0,001**	**0,005**	0,527	0,446	0,630	0,712	0,714	0,969	0,958
RMSSD	**0,000**	**0,000**	**0,001**	0,151	0,098	0,154	0,322	0,445	0,640	0,499
SDSD	0,976	0,988	0,565	0,509	0,650	0,674	0,658	0,569	0,618	0,724
NN50	**0,011**	**0,009**	**0,029**	0,228	0,204	0,219	0,245	0,498	0,946	0,995
NN20	0,062	0,081	0,222	0,788	0,635	0,446	0,413	0,747	0,831	0,736
pNN50	**0,032**	**0,039**	0,127	0,529	0,341	0,271	0,369	0,609	0,891	0,962
pNN20	0,168	0,232	0,593	0,779	0,978	,750	0,768	0,938	0,757	0,662

Table 3. Statistical significance values for study 2.

	0-5 min	2,5-7,5 min	5-10 min	7,5-12,5 min	10-15 min	12,5-17,5 min	15-20 min	17,5-22,5 min	20-25 min	22,5-27,5 min
AVRR	0,883	0,869	0,785	0,817	0,922	0,941	0,950	0,835	0,723	0,630
SDNN	**0,012**	**0,008**	**0,014**	0,600	0,376	0,502	0,777	0,466	0,888	0,871
RMSSD	**0,013**	**0,005**	**0,010**	0,537	0,349	0,542	0,742	0,588	0,982	0,946
SDSD	0,702	0,620	0,965	0,860	0,988	0,988	0,869	0,777	0,816	0,691
NN50	0,059	**0,029**	0,057	0,380	0,690	0,769	0,769	0,956	0,825	0,998
NN20	0,119	0,103	0,205	0,769	0,941	0,863	0,811	0,995	0,822	0,968
pNN50	**0,028**	**0,018**	**0,044**	0,375	0,513	0,504	0,581	0,672	0,696	0,692
pNN20	0,088	0,090	0,215	0,855	0,862	0,683	0,662	0,744	0,738	0,664

Table 4. K-nn classification performance of all segments for study 1 and study 2.

Time İntervals	Study 1				Study 2			
	k	SEN(%)	SPE(%)	ACC(%)	k	SEN(%)	SPE(%)	ACC(%)
0.0- 5.0 min	5-NN	40	90	77	5-NN	88	72	80
2.5- 7.5 min	5-NN	36	94	79	11-NN	64	80	72
5.0-10.0 min	9-NN	44	89	77	9-NN	76	68	72
7.5-12.5 min	13-NN	4	100	75	11-NN	60	56	58
10.0-15.0 min	9-NN	24	94	76	5-NN	72	64	68
12.5-17.5 min	11-NN	4	100	75	11-NN	84	48	66
15.0-20.0 min	11-NN	8	98	75	9-NN	76	64	70
17.5-22.5 min	11-NN	4	100	75	3-NN	52	68	60
20.0-25.0 min	11-NN	20	98	78	5-NN	64	64	64
22.5-27.5 min	13-NN	8	98	75	11-NN	76	44	60

preceding the PAF attack, obtained %90 SEN, %59 SPE and %77,6 ACC using time domain measures on RR interval data on the 10 minute immediately preceding the PAF attack, similarly, obtained % 91 SEN, % 84 SPE and % 86,6 ACC with FFT power spectral density measurements over 10 minutes of data (Chazal and Heneghan 2001). Hickey and Henegham obtained % 51 SEN, % 79 SPE and % 68 ACC using HRV-power spectral density and premature atrial complex measurements using data from the 5 min immediately preceding PAF attacks (Hickey and Heneghan 2002). Boon and colleagues obtained % 58.5 SEN, % 81.1 SPE and %68.9 ACC using HRV linear and nonlinear measurements on the 10 minute before the PAF attack while they obtained % 77.4 SEN, % 81.1 SPE and % 79.3 ACC over the 15 minute data (Boon, et al. 2016).

Since time-domain measures are the easiest methods to calculate among HRV measures, time-domain measures must be used in order to achieve a computational cheap prediction method. Therefore, it may be possible to implement real-time applications in the near future by using the outcomes of this study.

One of the most important steps of this paper is to divide into 10 parts of 5 minutes with 50\% overlapping since it has been examined which of the five minute piece or pieces have the distinctiveness. 5-minute HRV data is recommended by the most famous guideline for HRV studies (Task Force et al 1996).

In this study, it was determined that the first three segments before the PAF were separated statistically in RMSSD, SDNN and pNN50 measurements to the other segments. In the literature, RMSSD shows statistically significant difference (Segerson et al. 2008, Shin et al 2006, Vincenti et al. 2006} similar to this study. Nonetheless, SDNN (Segerson et al. 2008, Vikman et al. 1999), AVRR (Vikman et al. 1999) and pNN50 (Segerson et al. 2008) don't show statistically significant difference where whole 30-minute data are used in the prediction. In this study, SDNN and pNN50 also showed statistically significant difference where 5-minute data were used. Maybe, this shows that using long-term HRV measures may not be used in prediction, but short-term variability can reflect the changes in these measures.

Table 4 shows that Study 1 has lower discrimination performances of SEN values. This means that classifiers were not able to detect PAF attacks. On the other hand, Study 2 has the maximum discrimination performance of % 80. According to these results, eliminating the normal subjects from patients with PAF has very big effect on predicting PAF events. Otherwise, performances of SEN decrease drastically.

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