Time and Frequency Analysis of Heart Rate Variability Data in Heart Failure Patients

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***Abstract*—The paper presents a mathematically based analysis of heart rate variability of two groups cardiology records: healthy individuals and patients diagnosed with heart failure. The main objective of the study is to perform a parametric evaluation of the cardiovascular system of the human body using time domain and frequency domain analysis of heart rate variability. Making distinguish between diseased individuals and healthy individuals is an interesting challenge that contemporary researchers are working on. Cardiologic records obtained through continuous Holter monitoring (24 hours) were used to address the issues in this study. The obtained results show significantly reduced values of most of the studied parameters in the time domain and the frequency domain in patients with heart failure compared to healthy individuals. The low values of the studied parameters indicate low variability of heart rate and poor overall health status. The graphical results of two study groups are shown when applying the modified Welch periodogram. These graphical results give a visual idea of the variability of time series in healthy and diseased individuals. The obtained numeric and graphical results show that heart failure patients can be distinguished from healthy individuals. The applied mathematical methods in heart rate variability studying can be used as an aid in the cardiology practice of doctors.**

Keywords*—Heart rate variability; time domain analysis; frequency domain analysis; Welch periodogram; heart failure

I. Introduction

Today's non-invasive methods for analyzing the functional activity of the human cardiovascular system are preferred methods of investigation because of the almost imperceptible nature of data capture. Today, the use of technological tools, methods of analysis and diagnostics that extract maximum information about the condition of the individual with minimal impact on his body is coming to the fore.

Electrocardiography (ECG) and Holter monitoring are the best methods for recording the electrical activity of the heart, providing data to measure the time intervals between heartbeats. The sampling rate of the data recording system is an important factor [1] in the accuracy in calculating cardiac parameters. Electrocardiographic data are very specific to each individual [2] and can be used in systems for analysis, diagnosis, treatment, and recognition.

The measure of the number of variations in the intervals between successive heartbeats (RR intervals) over time is known in the scientific literature as heart rate variability (HRV) [3]. An expression "RR interval variability" also is used to indicate these changes because it takes into account the variability in successive heart rate intervals. In healthy human organisms, high heart rate variability is normally reported. Even at rest, in healthy subjects have frequent changes in the length of consecutive cardiac intervals. The duration of cardiac intervals is influenced by the activity of the sympathetic nervous system, by the activity of the parasympathetic nervous system, and by the influence of various humoral factors. In healthy human organisms, the heart rhythm is regulated by the neurons of the autonomic nervous system (ANS) and is affected by the hormonal control balance. HRV takes into account the influence in the human body of many factors such as metabolism, respiratory process, hormones, nutrition, physical activity, emotional state, baroreceptor reflex, cycles day/ night and sleep-wake cycle, stress and others.

Heart rate variability is a very useful and essential method in the study of diseases that have cardiovascular, neurological, endocrine and other pathology. This method is used in the description of autonomic dysfunctions of patients, monitoring the natural fluctuations of the autonomic function of the nervous system, assessing changes occurring in the human body after various interventions, and to make a prognosis for the development of the disease. Heart rate variability parameters have diagnostic importance for diseases such as hypertension, thyroid pathology, neurological disorders, brain tumors, multiple sclerosis, and many other diseases.

HRV may be a predictor of death in patients with acute myocardial infarction [4]. Several researchers have studied the relationship between autonomic regulation of cardiac activity and cardiac mortality. A study by the North American Society of Pacing and Electrophysiology, including patients with past myocardial infarction (MI), found that low heart rate variability was more correlated with the risk of sudden death than other commonly accepted clinical indicators development of the patient's disease. This methodology gained popularity and in 1996 the Standards of measurement, physiological interpretation, and clinical use [5] were developed and adopted by the European Society of Cardiology and the North American Society of Pacing and Electrophysiology.

The rest of the paper is summarized as follows: Overview of heart failure research studies was presented in Section II. Research Background was shown in Section III. Heart Rate Variability Time Domain Analysis was presented in Section IV and Frequency Domain Analysis - in Sections V. Data Preprocessing was described in Section VI. The experimental results were presented and discussed in Section VII. Conclusions are presented in Section VIII.

II. Review of Heart Failure Studies

Heart failure is a serious disease of a person's cardiovascular system, which has a close relationship with the condition of the individual's autonomic nervous system. Usually, heart failure corresponds to the presence of abnormal activity of the autonomic nervous system. In most cases, this disease is accompanied by increased activity of the sympathetic nervous system and decreased the activity of the parasympathetic nervous system. The normal variability of cardiac intervals corresponds to a good sympathetic balance in the human body. In patients with heart failure, the reduced or missing low-frequency spectral component is observed. According to [6], the missing low-frequency component in heart failure individuals reflects impaired baroreceptor function. Therefore, the ability to make a sufficiently accurate assessment of heart rate variability is important for the detection, monitoring, and prevention of heart failure. The non-invasive method, which studies the variability of the heart rate, can evaluate the activity of the two parts of the nervous system, the sympathetic activity of the nervous system and the activity of the parasympathetic part. These non-invasive studies are not complicated to administer; they may accompany the patient's treatment and be a means of monitoring the results of that treatment.

The heart failure disease is considered to be one of the most severe cardiac diseases that often have a poor prognosis for the patient. According to scientific research [7], up to 50% of individuals who have this disease die from sudden cardiac death. According to a study [8], the risk of sudden cardiac death in such individuals is five times higher than in healthy individuals. Author in [9] presents studies on patients with heart failure disease by determining the parameters of HRV.

III. Research Background

Frequency analysis of HRV is an effective tool for evaluating the cardiovascular autonomic activity of the heart. The following methods have been used in the scientific literature for frequency analysis of HRV data: Fast Fourier transform (the method is fast and with low computational cost); autoregressive method (performed on a small block of data and it does not need data interpolation [10] but is complex and in some cases produces erroneous results [11], [12]); wavelet analysis and other classical techniques.

The authors of [13] apply an autoregressive spectral approach to assess circadian modulation in hypertensive patients.

In research [14] to evaluate the spectral power in the cardiac data of newborn premature infants, the authors use Fast Fourier Transform.

The Burg method [15] is based on the idea of minimizing errors, has good resolution, and produces reliable spectral results and works well with different input series.

Lomb Periodogram Method - not a commonly used method, no need for input data series interpolation; but some authors [16] declare receiving insufficiently correct data.

The authors of [17] use the YuleWalker method and declare a distortion of the obtained results.

In the research [18], authors apply the Welch method to evaluate cardiac data in patients with insomnia and use a consistent estimator by averaging periodogram from overlapping intervals.

In their study [19] the authors use the classic and the Welch periodogram (implemented with Hann window) for spectral analysis of cardiac data.

The work [20] presents a temporal statistical analysis of changes in the duration of consecutive RR intervals originating from sinus rhythm.

In recent years, researchers have been developing new methods for spectral analysis. For example, trigonometric regressive spectral analysis [21] - uses trigonometric regression functions to examine variations in cardiac series.

IV. HRV Time Domain Analysis

Fig. 1 presents the model the input data recording, preprocessing, interpolation and mathematical estimation of cardiac time interval data.

Cardio data can be obtained by an electrocardiograph (5-20 minute) or Holter (long-term monitoring device - from 24/72 / 2 weeks). If the input data is in a compressed format, then it is decompressed. Performing preprocessing of cardio data: denoising [22], QRS complexes detection [23] and the RR interval obtained (R - a point corresponding to the peak cardio wave). The next step is to exclude the ectopic intervals in the resulting time series and formation of the normal-to-normal (NN) intervals. The NN time series is interpolated and downsampled. Analysis of the resulting HRV data included HRV Time Domain Estimation and Spectral Estimation.

Statistical parameters. The statistical time analysis of rhythmograms investigates two types of parameters: the duration of the NN intervals and the difference in the duration of the adjacent NN intervals.

The following indicators (Table I) are used to analyze the duration of NN intervals: SDNN, SDANN, SDNN index. To evaluate the variability of the adjacent NN intervals, the following parameters are calculated: NN50, pNN50, RMSSD. The SDNN (ms) parameter reflects the standard deviation of all NN intervals in cardiac monitoring; characterizes the state of regulation mechanisms; indicates the total effect of influence on the sinus node of sympathetic and parasympathetic parts of the autonomic nervous system. SDANN (ms) reflects the standard deviation of the duration of average NN intervals every 5 minutes from the record; SDNN index (ms) - mean of standard deviations for all 5-minute blocks of the observation period.

NN50 is a number of pairs of consecutive NN intervals that differ by more than 50 ms over the entire observation period; pNN50 (%) is a percentage of consecutive R – R intervals, the difference between which exceeds 50 ms; RMSSD (ms) - a square root of the sum of squares of differences in the values of consecutive pairs of NN intervals (the activity index of the parasympathetic system of autonomic regulation) [20].

TABLE. I. TIME DOMAIN PARAMETERS

Parameter [units]	Formula
SDNN [ms]	$SDNN = \sqrt{\frac{1}{N}\sum_{i=1}^{N}(RR_i - \overline{RR})}$
SDANN [ms]	$SDANN = \sqrt{\frac{1}{N}\sum_{i=1}^{N}(\overline{RR_i} - \overline{\overline{RR}})^2}$
RMSSD [ms]	$RMSSD = \sqrt{\frac{1}{N-1}\sum_{i=1}^{N-1}(RR_{i+1} - \overline{RR_i})^2}$
SDNNindex [ms]	$SDNN_{index} = \frac{1}{N}\sum_{i=N}^{N} SDNN_i$
pNN50 [%]	$pNN50 = \frac{NN50}{NN}.100\%$
HRVTi [-]	$HRVTi = \frac{\sum_{i=1}^{N_b} b(t_i)}{max_i b(t_i)} = \frac{N-1}{max_i b(t_i)}$

Geometric parameters: HRVTi - triangular index (the proportion of all accepted RR intervals to their modal measurement at a 1/128s bins discrete scale; TINN - triangular interpolation of cardio interval histogram.

V. HRV FREQUENCY DOMAIN ANALYSIS

Numerous methods for spectral analysis of HRV have been developed in the scientific literature, the most popular of which are based on traditional Fourier transform (e.g. fast Fourier transform) [24] and wavelet theory. The spectral analysis makes it possible to quantify the different frequencies contained in the investigated signal and to study the action of the regulatory systems of the human body.

HRV analysis is performed in four frequency bands - high frequency range (HF), low frequency (LF), very low frequency (VLF) and ultra low frequency (ULF) bands [25] (Table II). Usually, the analysis is performed on 5-minute segments, not on the entire cardiology record. Using a five-minute block for frequency analysis is one of the recommendations [5] of the Task Force (1996) heart rate variability standard.

Two of the ranges are important for cardiac clinical practice - LF and HF bands. The HF component in range 0.15-0.40 Hz is associated with respiratory sinus arrhythmia (RSA) and parasympathetic activity. Approximately 1 minute of cardiac recording is sufficient to evaluate the HF components of HRV. The LF component (0.04-0.15 Hz) is not yet sufficiently studied; it is related to the sympathetic activity of the nervous system and represents both sympathetic and vagal influences. It takes at least 4 minutes [26] to obtain correct values for the power in the LF range. For this reason, the determination of spectral power generally requires the use of a five-minute cardiac record.

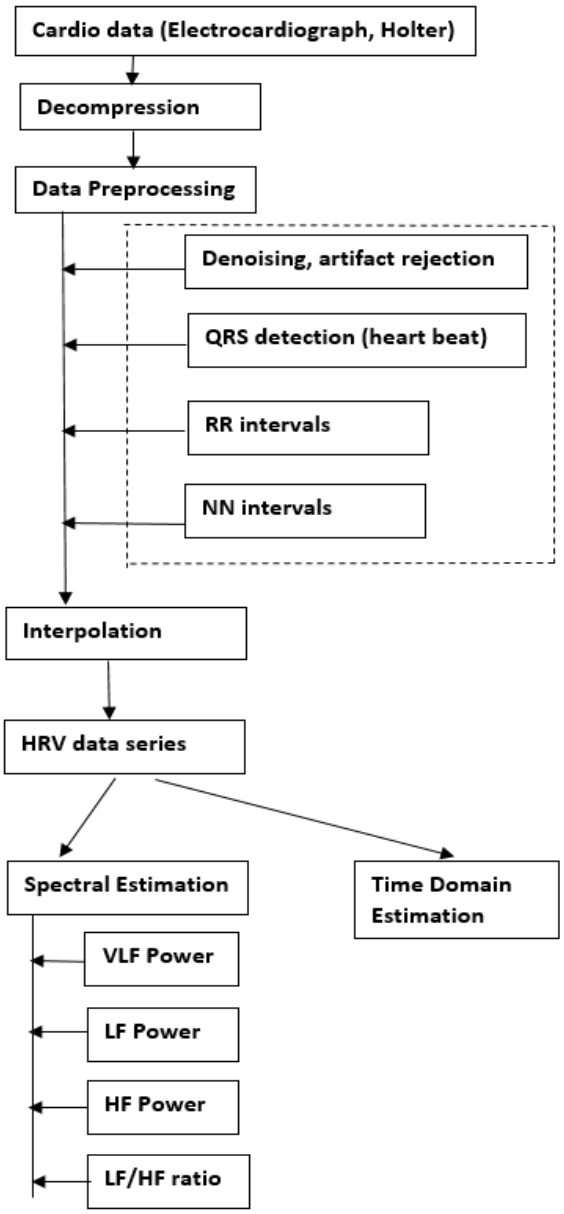

Fig. 1. Data Processing.

Spectral analysis parameters are used to evaluate the influence of the autonomic nervous system [27]. The parasympathetic branch of the autonomic nervous system is responsible for relaxation, rest, preservation of vital energy, lowers heart rate and lowers blood pressure.

The sympathetic branch of the autonomic nervous system is responsible for mobilizing the internal resources of the human body and manifests itself in conditions of physical activity, stress; it expresses acceleration of cardiac activity, increases blood pressure, accelerates breathing, raises the temperature and others.

Another important parameter - LF/HF ratio (known as sympathovagal balance) indicates the balance between sympathetic and vagal tones.

TABLE. II. FREQUENCY RANGE

Power [ms^2]	Frequency [Hz]	Cause
ULF - ultra low frequency	0-0.003	day/night cycle
VLF - very low frequency	0.003-0.04	sympathetic activity
LF - low frequency	0.04-0.15	sympathetic and parasympathetic activity
HF - high frequency	0.15-0.4	respiratory sinus arrhythmia; parasympathetic activity

A method with modified Welch Periodogram: With the Welch Periodogram method, the data series is split into blocks that can overlap. The data from each block is processed by the weighted window function and then the calculations are performed. The software calculates the periodograms in each Welch block [28], thereafter it starts to average for reducing variance.

The next step is to calculate the modified Welch Periodogram [29] in each block, using the following formula:

$$Welch_{ModifiedP}(f) = \frac{1}{U.K}.\left|\sum_{j=0}^{K-1} x_i\,(j).w(j).e^{-2j\pi fn}\right|^2,$$

Where:

U – Normalization factor;

K - Elements in each block;

N – Number of blocks that was overlap;

$w(j) -$ Window function;

$x_i(j)$ – input data;

f - frequency;

$n = 0{,}1 \ldots K - 1;$

$i = 0{,}1 \ldots N.$

The obtained average Periodogram for all blocks is determined by:

$$Welch_{Periodogram}(f) = \frac{1}{U.K.N}\sum_{i=0}^{N-1}\left|\sum_{j=0}^{K-1} x_i\,(j).w(j).e^{-2j\pi fn}\right|^2.$$

VI. DATA PREPROCESSING

Before performing time and spectral analysis, the input data is subjected to preprocessing. This treatment involves sampling, digitizing, artifact identification and rejection, input data editing, RR interval rejection. The device that captures the input data must be able to recorded data at a frequency greater than 200 Hz [10] for the cardiac complexes to be correctly identified in the next steps. In the artifact identification and rejection step, all artifacts (technical and other) and arrhythmic events must be removed for correct mathematical analysis.

Obtaining NN interval series. The NN interval sequence is derived from the RR interval sequence excluding the extrasystoles (the HRV studies are based on the normal sinus rhythm, and it excludes the involvement of extrasystoles). Extrasystoles are extraordinary cardiac contractions that do not originate from the sinus node. A healthy person can also have extrasystoles, but their amount is negligible (e.g. 30 per hour, which is 0.5 extrasystoles per minute). In case of abnormal occurrence, extrasystoles may reach one in each second.

Interpolation. The choice of the type of interpolation depends on the specific methods of data capture depends on, the selected methods of mathematical analysis, the quality of the input cardiology records, the type of extrasystoles, also the characteristics of the cardiac signal reflecting the type of disease. It is carried out when it is necessary to fulfill the requirement for uniformity of the studied interval time series.

VII. RESULTS

A. DataBase

Preprocessing and selection of records. The process of cardiac data recording is very sensitive to various factors: network disturbances, patient's respiratory process, quality of contact between the electrodes and the patient's skin, patient attention to the proper attachment of the electrodes to his body, etc. For this reason, the obtained data are carefully inspected for damage to the records and where such sections are found and the record is removed and it will be not an object of study (in case of major damage therein).

B. Subjects

The cardio data used in this paper were obtained with the help of Holter monitoring from the Varna Medical University, the Republic of Bulgaria. The cardio data is continuous electrocardiographic Holter monitoring records, second Lead. The control group of healthy people (volunteers) is in the same age group. All studied people provided informed written consent. Therefore all identified data were removed. All data used in this study is anonymous to protect the personal information of all Volunteers and Patients.

Two groups of HRV data records were chosen: 22 healthy individuals and 24 patients diagnosed with heart failure. Holter monitoring was performed on all for 24 hours.

C. Characteristics of the Subjects

Table III present the demographic characteristic (the age and gender distribution, the mean age of the individuals). The analyzed patient records are about 24 individuals aged 35-55 years including 13 males and 11 females. The analyzed healthy records are about 22 individuals aged 34-52 years including 12 males and 10 females. Values are expressed as mean ± standard deviation (SD) or in percent (%). No significant difference between the different groups according to demographic characteristics.

TABLE. III. DEMOGRAPHIC CHARACTERISTICS

Parameter	Heart failure N=24	Healthy N=22	P value
Gender, Men %	54.16	54.54	NS (0.9116)
Age ± SD	47.83± 4.37	47.50±4.64	NS (0.803)

Fig. 2 shows the RR intervals data series from a healthy individual. The data are distinguished by a wide amplitude of RR intervals values (from 0.38 to 1.6 seconds). Fig. 3 shows the RR intervals data series for a patient diagnosed with heart failure disease. The lengths of the time intervals are clustered/grouped around the value of 0.5 sec. This figure graphically presents a low variability in cardiac interval values.

D. Time Domain Results

Table IV presents the obtained results of the HRV analysis in Time Domain obtained from a study of two groups of Individuals (total number 46): Healthy Individuals and Heart Failure Individuals.

The calculations show that the main value of MainRR is 832.98 ms, which is much higher than the main value of MeanRR (632.44 ms) for patients with heart failure. The MeanHR of the healthy people (72.03 bpm) is much lower than the MeanHR (94.87 ms) in the studied patients' group. The assessments of the mean value of RR intervals and the mean heart rate (HR) indicate that these parameters have statistically significant ($p<0.005$ for Mean RR and $p<0.01$ for Mean HR).

The parameter SDNN for Heart failure patients (mean value 114.06 ms) is not that high that the SDNN calculated in the group of the healthy people (mean value 142.18 ms). The same thing is observed with the SDANN parameter (92.87 ms of heart failure group versus 122.16 of healthy). The parameter RMSSD is slightly reduced in heart failure people compared to healthy people (26.73 ms versus 30.41 ms). From time domain studied, the values of SDNN ($p<0.0001$), SDANN ($p=0.0013$), RMSSD ($p=0.0373$) and pNN50 ($p=0.0494$) have statistical significance ($p<0.05$). The SDindex (60.37 in sick versus 64.08 in healthy) hasn't statistical significance ($p>0.05$).

For geometric parameters, the mean value of HRVTi (18.31) is lower in sick people than in the healthy (24.11). This parameter has statistical significance ($p=0.0261$). The TINN (433.54 in sick versus 518.91 in healthy) hasn't statistical significance ($p>0.05$).

In conclusion in the group of patients diagnosed with heart failure, the values of almost all studied parameters in the time domain are significantly lower compared to the Healthy individuals.

Many of the time domain parameters in patients have larger SD (Table IV). This is most likely due to the larger variations in these parameters in different patients, depending on the degree of their disease.

E. Frequency Domain Results

Spectral method realization. In this study, the Welch periodogram was implemented using a Hamming window function, overlapping at 50% was performed. RR intervals data is interpolated with a cubic spline basis and then sampled at 4 Hz.

Table V presents the results of the HRV analysis in Frequency Domain obtained from the study of two groups studied. Signal power values in the low frequency range (absolute and normal values) and the high frequency range (absolute and normal values) were investigated and LF/HF ratio. The results show that all spectral parameters are significantly lower in patients diagnosed with heart failure. When examining the spectrum in absolute value in LF and HF range Pvalue has values <0.0001. When examining the spectrum in normal units in the LF and HF range Pvalue has values <0.05. The sympathetic balance index has a value of 1.16, which is significantly lower ($p<0.05$) in the heart failure group than the value of this index 1.56 (included in the normal values recommended by the standard for variability) in healthy individuals.

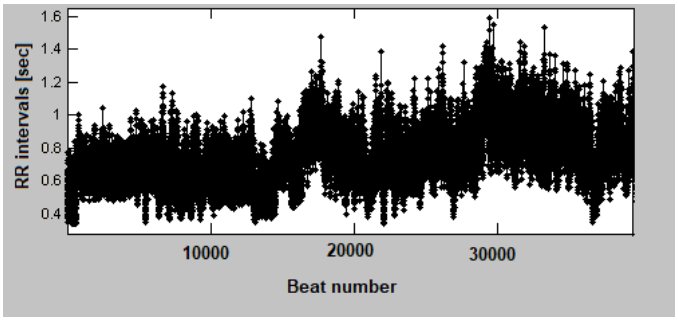

Fig. 2. RR Intervals of a Healthy Individual.

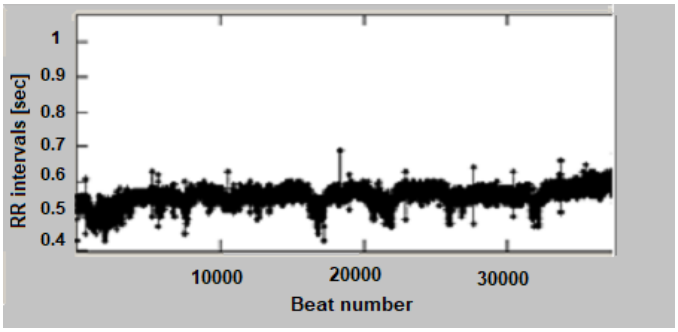

Fig. 3. RR Intervals of Heart Failure Individual.

TABLE. IV. PARAMETERS IN THE TIME DOMAIN

Para-meter	Heart failure N=24	Healthy N=22 (mean± sd)	P value mean± sd
MeanRR [ms]	632.44 ± 263.71	832.98± 144.32	<0.005 (0.0029)
MeanHR [bpm]	94.87± 36.29	72.03± 8.91	<0.01 (0.0063)
SDNN [ms]	114.06± 18.12	142.18± 20.31	<0.0001
SDANN [ms]	92.71± 26.84	122.16± 31.08	<0.005 (0.0013)
SDindex [ms]	60.37± 28.94	64.08± 15.62	NS (0.5961)
RMSSD [ms]	26.73± 10.95	30.41± 6.08	<0.05 (0.0373)
pNN50 [%]	11.04± 8.33	14.92± 3.56	<0.05 (0.0494)
HRVTi	18.31±9.62	24.11± 7.16	<0.05 (0.0261)
TINN [ms]	433.54± 172.98	518.91± 131.47	NS 0.068

TABLE. V. PARAMETERS IN THE FREQUENCY DOMAIN

Para-meter	Heart failure N=24	Healthy N=22 (mean± sd)	P value mean± sd
LF [ms^2]	663.83± 102.03	1204.67± 247.53	<0.0001
LF (nu)	0.5379± 0.1108	0.6094± 0.1207	<0.05 (0.042)
HF [ms^2]	570.31± 108.12	772.18± 209.31	<0.0001
HF (nu)	0.4621± 0.1084	0.3906± 0.1108	<0.05 (0.0323)
LF/HF	1.16±0.62	1.56±0.47	<0.05 (0.0184)

The studied groups were also compared using a graphical method of the Welch periodogram.

Fig. 4 shows a PSD of a healthy individual obtained by the Welch Periodogram method. The PSD values are with high values in the three tested ranges: VLF, LF, and HF.

Fig. 5 shows the PSD graphical presentation of heart failure individuals. The PSD in VLF, LF and HF area are with small values. This shows a low heart rate variability of RR interval series, the predictor of serious cardiac disease.

The use of the Welch Periodogram method shows significant differences between the spectral parameters in healthy people and heart failure individuals.

F. Statistical Analysis

Descriptive statistics of data are presented as mean ± standard deviation (SD). For statistical analysis, the T-test has been used. The p-value of <0.05 was considered as statistically significant.

There are some limitations to performing with the analysis above. First, the study included a limited number of patients and healthy people (22 healthy individuals and 24 patients with heart failure). Secondly, the study uses time and frequency domain analysis. These limitations are imposed by the stage of work on the study of heart rate variability in healthy people and patients with heart disease. This study demonstrates the ability to distinguish the diseased patients from healthy individuals by using time domain and frequency domain heart rate variability analysis.

G. Discussion

Differentiating healthy people from diseased individuals is extremely useful in the treatment of cardiac diseases. The use of interdisciplinary approaches to addressing health problems would lead to an improvement in the quality of healthcare and an increase in the health status of the population. For these reasons, the in-depth penetration of mathematical technologies into the study of phenomena such as heart rate variability may prove particularly useful and may enter clinical practice soon.

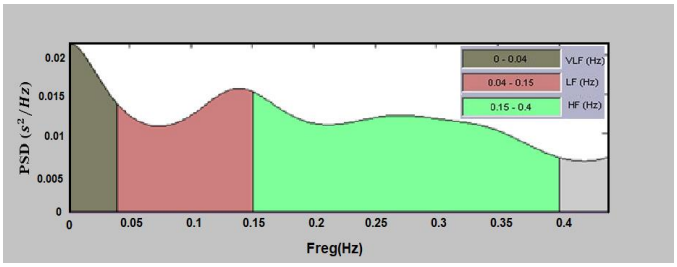

Fig. 4. PSD of a Healthy Individual.

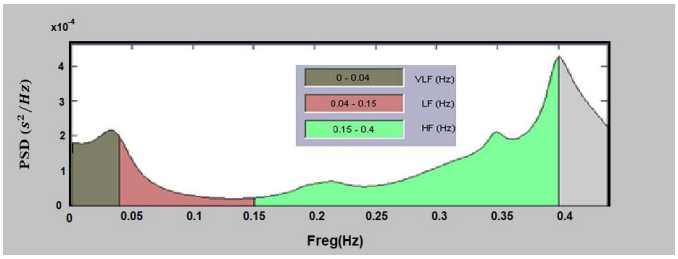

Fig. 5. PSD of Heart Failure Individual.

VIII. CONCLUSION

The paper presents effective mathematical methods for studying the parameters of heart rate variability in the time and frequency domain. Examination of cardiac record parameters of patients diagnosed with heart failure shows significant differences from certain values of the same parameters in healthy individuals. HRV parameters in the time domain and frequency domain are significantly reduced in heart failure people, and in some cases parameters (such as the LF frequency parameter) are times smaller than in healthy people. This shows extremely low variability in the time series of cardiac intervals, risky low health status and in some cases risk to the patient's life. The parameters studied can be determined during the treatment of patients and the change (in a positive or negative direction) of their values can be monitored. This method can be used for predictive purposes to determine the course of disease development during the treatment of patients.

IX. FUTURE WORK

Analysis of the parameters of HRV will be performed with other mathematical methods: nonlinear methods, fractal and wavelet analysis. It is planned to investigate the parameters in patients with other cardiac diseases and to evaluate the impact of these diseases on values of heart rate variability.

ACKNOWLEDGMENT

This research work was carried out as part of the scientific project “Investigation of the application of new mathematical methods for the analysis of cardiac data” No KP-06-N22/5, date 07.12.2018, funded by the National Science Fund of Bulgaria (BNSF).

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