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CLINICAL STUDY

Mathematical model presenting to assess variations in heart rate of different age groups

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ABSTRACT

OBJECTIVE: Recently, older people's cardiovascular systems have been affected by aging-related changes. An electrocardiogram (ECG) provides information about cardiac health. Analyzing ECG signals can help doctors and researchers diagnose many deaths. Besides direct ECG analysis, some measurements can be extracted from the ECG signals, and one of the most important measurements is heart rate variability (HRV). Research and clinical domains can benefit from HRV measurement and analysis as a potential noninvasive tool for assessing autonomic nervous system activity. The HRV describes the variation between an ECG signal's RR intervals over time and the change in that interval over time. An individual's heart rate (HR) is a non-stationary signal, and its variation can indicate a medical condition or impending cardiac disease. Many factors, such as stress, gender, disease, and age, influence HRV.

METHODS: The data for this study is taken from a standard database, the Fantasia Database, which contains 40 subjects, including two groups of 20 young subjects (21–34 years old) and 20 older subjects (68–85 years old). We used two non-linear methods, Poincare and Recurrence Quantification Analysis (RQA), to determine how different age groups affect HRV using Matlab and Kubios software.

RESULTS: By analyzing some features extracted from this non-linear method based on a mathematical model and making a comparison, the results indicate that the SD1, SD2, SD1/SD2, and area of an ellipse (S) in Poincare will be lower in old people than in young people, but %REC, %DET, Lmean and Lmax will recur more often in older people than in younger ones. Poincare Plot and RQA show opposite correlations with aging. In addition, Poincaré's plot showed that young people have a greater range of changes than the elderly.

CONCLUSION: According to the result of this study, heart rate changes can be reduced by aging, and ignoring this issue could lead to cardiovascular disease in the future *(Tab. 3, Fig. 7, Ref. 55)*. Text in PDF *www.elis.sk*

KEY WORDS: multidimensional model, heart rate variability, non-linear analysis, recurrence plot, fantasia.

Introduction

Nowadays, the number of cardiac patients is increasing with a warning rate. Heart diseases are the leading cause of death for men and women yearly. Each year, 17.9 million people die from cardiovascular disease (CVDs), an estimated 31 % of all deaths worldwide. According to the world health organization's (WHO) statistician, heart disease is one of the 17 million reasons for death (under the age of 70). For example, in 2015, CVDs caused 37 % of deaths worldwide. The number of mortalities from CVDs will increase to reach 23.3 million by 2030. About 610,000 people die of heart disease in the United States every year, that's 1 in every four deaths (1). A healthy heart has a regular characteristic pattern, but any abnormality or damage to the heart will show up differently from the normal heart pattern. The research of the Ferrari et al. showed that age-dependent parameters affected the heart, the blood vessels, and the reflex control of the cardiovascular system (2). Also, other dependent parameters are physiologic aging and complexity, such as heart rate (HR) and heart rate variability (HRV) process of reduction in elderly subjects (3). Also, this decline is evident in non-linear feedback loops on a range of time and length scales due to changes in physiologic dynamics (4).

The increasing age may include an increase in body functions (2). Aging affects the structures and functions of the cardiovascular system and causes change. Even the risk of cardiovascular disease increases (5, 6). Also, the other parameters affect the cardiovascular control system's function, including the HR and blood pressure (BP). The CVDs are disorders of the heart and blood vessels and include coronary heart disease, cerebrovascular disease, rheumatic heart disease, and other conditions. That is considered to be the result of increasing age.

Increasing age causes the blood vessels to lose their elasticity and become narrow. By narrowing the arteries, the heart works harder to pump blood into the veins. This leads to a decline in blood pressure and other cardiovascular problems in the elderly (7).

Biological measurement of age may help a better prediction of the age average in the population. It could be an important clinical tool for determining the medical risk related to diseases with

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advanced age (4, 8). Studies based on approximate non-linear dynamics show that biological markers of aging could be many older people produce conditions before death, and their biological age can be considered different from the period.

The Electrocardiogram signal has been widely used in cardiology to diagnose various heart diseases. Electrocardiography is a noninvasive tool, and the ECG signal can be measured to get important and valuable information about electrical activity related to the heart to doctors and researchers (9). This electrical activity can be recorded and analyzed by measuring the amplitudes, durations, and intervals in the ECG signals (10). ECG can show all the fluctuations of the heartbeat. Letters of the alphabet (P, R, Q, S, and T) identify the different peaks of the printout, and the doctor reads these to indicate problem areas in the heart rate. The highest peak of a normal QRS complex is at the peak of the R-wave, and the distance between two contiguous R-wave peaks is termed the R–R interval (11–13).

For HRV analysis, the necessity of filtering the signals can be performed, and this process requires the removal of all non-sinus-node originating beats. ECG parameters change during age and depend on the patient's age (14, 15). Rupali Sachin Khane et al studied increasing changes in ECG patterns with age (16). According to this study, the incidence of Q/QS patterns increases with age. Campbell et al observed a 15 % prevalence of ST-T wave abnormalities, especially T-wave flattening, and that infrequency increases with age (15). Several studies have been done on the effect of aging on electrocardiographic parameters in humans. Recognizing the standard electrocardiographic parameters can help evaluate cardiac healthiness or disease (14). The HRV shows variations of successive heartbeats, a physiological phenomenon / of the healthy sinus rhythm (17). Many studies pay more attention to the power of the heart rate. Hon and Lee were the first people to use HRV to evaluate fetal heart rate patterns preceding fetal death in 1965 (18). Many parameters affect HRV, like stress, age, gender, certain cardiac diseases, and other pathologic states.

The HRV analysis represents a noninvasive method for supervising the autonomic nervous system (ANS) control function. It is measured by diagnosing variations in beat-to-beat intervals sequential heartbeats (R–R intervals) (19). This interval regulation function balances the sympathetic and parasympathetic and causes R–R intervals with two branches of the ANS and polarization and depolarization process of the sinus node (20, 21). HRV is related to the measurement effects of SNS and PNS activity and other physiological regulatory affection on the heart (22, 23). Heartbeat regularity mechanism an increase in the parasympathetic activity means decreasing HR by the release of acetylcholine. However, an increase in HR directly results from an increase in sympathetic activity (24). There is conflicting evidence about parasympathetic control of cardiac function changes with age (25). Therefore, recognizing the effects of age on cardiac parameters can be helpful in preventing many diseases (26).

There are different methods for analyzing HRV. HRV analysis is a combination of linear and non-linear methods. The standard techniques for analyzing HRV are divided into statistical (time domain), power spectral (frequency domain), and non-linear geometrical analysis. The time-domain method calculated the standard deviation of R–R intervals (SDNN), root mean square differences of successive R–R intervals (rMSSD), for a stationary time series (SDSD) equals to the root mean square (RMS), and the percentage of differences between N–N intervals by more than 50 ms (pNN-50). Haber was the first person who introduced a non-linear autoregressive (NARMA) model. The non-linear method calculated the average value of instability directly by measuring the R–R interval. Aspects of heart rate dynamic information that can't elicit from the linear analysis can be shown by the non-linear analysis (19). Even an evaluation of the risk of the disease is available (20–22).

Even though time and frequency domain methods are related, representing the variability is done with different means, and the information obtained is not always the same. For this reason, both these families of methods are extensively used in clinical practice, but none has been used as the only standard. This method is spectral analysis. The spectral analysis of time series describes the techniques and theory of the frequency domain analysis of time series. This method interpolates the RR interval at a defined rate and changes this interval into the frequency domain. Frequency domain analysis includes fast Fourier transform (FFT) or AR-based power spectral density (PSD) analysis in systematic rhythms, representing information on how to divide as a function of frequency. Three main spectral components are distinct in a spectrum calculated from short-term recordings peaks: very low frequency (VLF) (≤ 0.04 Hz), low frequency (LF) (0.04–0.15 Hz), and high frequency (HF) (0.15–0.4 Hz) components.

The HRV changes with advanced age were first known in the 1980s (11). For better predicting and knowing how it changes, it's essential to understand the normal range of HRV at different ages. Umetani et al (23) showed that in normal subjects, the range of HRV (all time-domain measures except the SDNN index) in young people is wider than in old people, and the range of HRV narrows with aging. Also, Ken Umetani et al showed a significant negative correlation between HRV and increasing age. Boettger et al (24) worked on analyzing non-linear HRV parameters. There is a decreasing autonomic modulation with age increasing, which starts in childhood (25). However, increasing age does not cause considerable changes in resting heart rate. This reduction has been attributed to a decline in efferent vagal tone and reduced beta-adrenergic responsiveness (18). In rat models, clear aging shows increased and decreased sensitivity to vagal activity (26). Age often tends to change after the age of 50 years. The most changes (decrease) happen between the second and the third decades. The HRV decreases slowly with age increasing. However, HRV changes significantly at > 30 years (23).

Some studies worked on the relationship between age and heart rate based on traditional measurements (time and frequency domain analysis). Bonnemeier et al (27) worked on aging affection on HRV parameters by recording hour-by-hour in healthy subjects, but it limited time-domain HRV parameters. According to linear analysis, the previous studies didn't provide information about the dynamic properties of the heartbeat time series. The factors of the heartbeat time series are not dependent on traditional parameters such as mean and standard deviation and make additional informa-

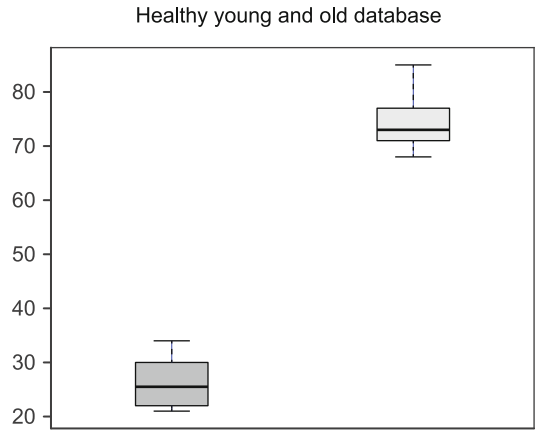

Fig. 1. Range of age among healthy young and old people.

tion about the underlying structure of the data (28–29). Mourot et al showed that the relation between linear parameters and HRV is weak. But there is a strong correlation between non-linear parameters and HRV (30). This paper explores the possibility of capturing the age-related influence on HRV changes using non-linear techniques to investigate heart rate variation in young and elder ages.

Material and method

Data collection

To analyze age's effect on HRV in this paper, we used data from the FANTASIA Physionet website (31). The database includes a lot of heart rates for different ages. This database contains two groups, F1 and F2. Each has ten young people (21–34 years old) and ten older people (68–85 years old). Each subgroup includes equal numbers of men and women. All the subjects were relaxing. During the ECG recording, they watched the movie Fantasia (Disney, 1940). Data set to help maintain wakefulness signals were collected. ECG was recorded for 120 minutes. The sampling frequency in this database is 250 Hz. The recordings were uncalibrated and transferred to a computer, and filtered. Figure 1 shows the age range of people in this paper. Also, Table 1 shows the complete characteristics of the participants in this study, including age and sex.

Tab. 1. Age and sex of all healthy young and old people.

Sl.No	Records	Age	Sex	Sl.No	Records	Age	Sex
1	F1y01	23	F	21	F1o01	77	F
2	F1y02	28	F	22	F1o02	73	F
3	F1y03	34	M	23	F1o03	73	M
4	F1y04	31	M	24	F1o04	81	M
5	F1y05	23	M	25	F1o05	76	M
6	F1y06	30	M	26	F1o06	74	F
7	F1y07	21	M	27	F1o07	68	M
8	F1y08	30	F	28	F1o08	73	F
9	F1y09	32	F	29	F1o09	71	M
10	F1y10	21	F	30	F1o10	71	F
11	F2y01	23	F	31	F2o01	73	F
12	F2y02	23	M	32	F2o02	75	F
13	F2y03	28	F	33	F2o03	85	F
14	F2y04	27	F	34	F2o04	70	F
15	F2y05	25	F	35	F2o05	83	M
16	F2y06	26	M	36	F2o06	70	M
17	F2y07	31	M	37	F2o07	77	M
18	F2y08	21	M	38	F2o08	71	M
19	F2y09	21	F	39	F2o09	77	M
20	F2y10	21	M	40	F2o10	73	F

Method

The theory of non-linear dynamics is widely used to analyze biosignals, which are non-linear (32). The following are non-linear methods for studying the effects of aging on cardiovascular dynamics. Each data of the subject was analyzed by Kubios software. Non-linear parameters like Poincare plot and recurrence quantification analysis were used in data analysis. Before using a Poincare plot, we used R–R intervals detection to avoid missing R–R intervals because Poincare is plotted according to R–R intervals. This paper used Poincare parameters like Standard Deviation (SD1, SD2) and calculated the ratio of SD1/SD2 and the area of Ellipse (s). In addition, we used RQA parameters like recurrence rate (REC) and determinism (DET) and mean line length (Lmean) and max line length (Lmax) to show what relationship between the variations of heart rate with increasing age. These methods are briefly explained in the following sub-sections.

R–R interval detection

R-peaks detection is not always precise and can have false or missed peaks. Algorithms need to increase detection sensitivity by processing the RR intervals were proposed (33–34). First, detecting each parameter of QRS complexes provides the fundamentals for almost all automated ECG analysis algorithms using derivative-based, Pan-Tompkins, wavelet transform-based algorithms. The Pan-Tompkins algorithm (35) is commonly used to detect QRS complexes in ECG signals. The QRS complex represents the ventricular depolarization and the main spike visible in an ECG signal. This feature makes it particularly suitable for measuring heart rate, the first way to assess the heart health state. In the first

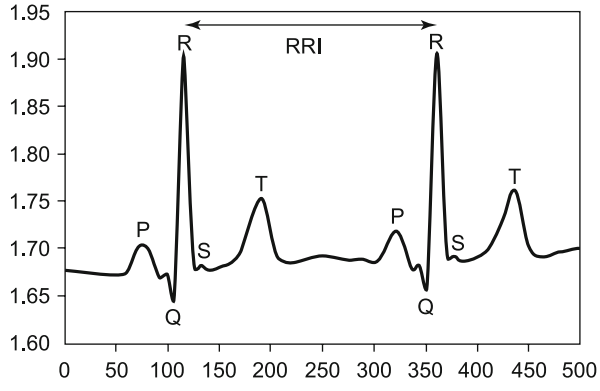

Fig. 2. Typical ECG trace with RR interval labeled.

derivation of Einthoven of a physiological heart, the QRS complex is composed of a downward deflection (Q wave), a high upward deflection (R wave), and a final downward deflection (S wave). This real-time QRS detection algorithm is based on digital analyses of the signal›s slope, amplitude, and width, as shown in Figure 2.

Some noise accompanies ECG signal recording. So, at the beginning of the HRV analysis it is necessary to eliminate and filter requirements for removing all non-sinus-node originating beats of the ECG. The Pan–Tompkins algorithm is divided into two different stages: preprocessing and decision. In the preprocessing stage, the signal is prepared for later detection. Therefore, the ECG signal is passed through a band-pass filter composed of a low pass and a high pass filter to highlight the frequency content of this rapid heart depolarization for smoothing and removing the background noise. After this, a derivative filter is a standard technique to get the high slopes that normally distinguish the QRS complexes from other ECG waves. The derivative procedure suppresses the low-frequency components of P and T waves and provides a large gain to the high-frequency components arising from the high slopes of the QRS Complex. Then, the non-linear squaring amplitude is done to amplify the QRS contribution, makes the output signal positive, and emphasizes large differences resulting; the small differences arising from P and T waves are suppressed. Then waveform feature information is obtained by the moving window integration along with the slope of the R wave. Finally, in the decision stage, adaptive thresholds are applied to detect and find the R-peak in which a maximum level helps detect R-peak. This paper used the algorithm for R–R interval extraction.

Non-linear phase space

Non-linear phase space is a non-linear graphical representation of the samples in a multidimensional phase, which plots the present sample according to a previous one (36). It is the plot between consecutive samples of the signals (37).

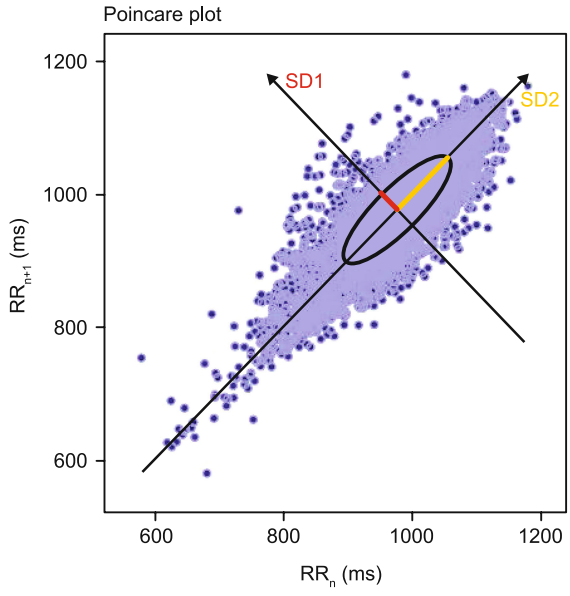

Fig. 3. Poincare Plot of RR intervals of F1Y08 young subject with its standard descriptor SD1 and SD2.

The Poincare plot is a technique taken from non-linear dynamics that portrays the nature of R–R interval fluctuations. It is a plot in which each R–R interval is plotted as a function of the previous R–R interval. Poincare plot analysis is an emerging quantitative-visual technique whereby the shape of the plot is categorized into functional classes that indicate the degree of heart failure in a subject (32). The plot provides a summary and detailed beat-to-beat information on the behavior of the heart (11). The geometry of the Poincare plot is essential and can be described by fitting an ellipse to the graph. The ellipse is fitted onto the so-called line-of-identity at 45° to the normal axis. The standard deviation of the point perpendicular to the line of identity denoted by SD1 describes short-term variability, which is mainly caused by respiratory sinus arrhythmia (RSA). The standard deviation along the line of identity denoted by SD2 describes long-term variability. SD1 and SD2 are the standard deviations of the distances of the points computed from two lines having the expression y = x and y = x + Rz, where Rm is the mean of the distances of the successive heartbeats, respectively. SD1 is the ellipse's width (short-term variability) (38). SD1 shows a level of rapid changes in R–R intervals. SD1 can be calculated mathematically as formula (1). But SD2 is the length of the ellipse (long-term variability) (38). Both sympathetic and parasympathetic effects on SD2.SD2 can be calculated as formula (2). The balance between short and long-term HRV can be measured by the ratio of SD1 to SD2 in formula (3). The area of the ellipse (S) is the area covered by the ellipse. S can be calculated as formula (4). Figure 3 shows the Poincaré diagram with the SD1 and SD2 parameters.

The variations of the biomedical signal for a short- time can be shown by phase space (39). Phase space can be used for analyzing HRV signals. Phase space shows the correlation between successive R–R intervals (RRi, RRi+1) (40). In HRV analysis by Poincare plot, every point in this plot defines one of the time series elements. Phase space reflects the non-linear features of the HRV.

$$\mathbf{SD1} = \sqrt{var(x1)} \tag{1}$$

$$\mathbf{SD2} = \sqrt{var(x2)} \tag{2}$$

$$\frac{\mathbf{SD1}}{\mathbf{SD2}} = \frac{\sqrt{var(x1)}}{\sqrt{var(x2)}} \tag{3}$$

$$\boldsymbol{S} = \pi \,.\, SD1.\, SD2 \tag{4}$$

A Poincare plot is a very powerful visual technique to assess hidden patterns in the dynamics of HRV and to gain more information about the entire RR interval time series. It has been used as a qualitative tool and a geometrical analysis by calculating HRV with the shape of the Poincaré plot (41). This method contains three items: A: The standard deviation of the instantaneous beat-to-beat RR interval variability (minor axis of the ellipse or SD1). B: The standard deviation of the continuous long-term RR interval variability (major axis of the ellipse or SD2) C: The axis ratio (SD1/SD2) (42).

Recent advances in biological systems theory, HRV analysis, and complexity analysis, such as nonlinearity and determinism in a biomedical signal, are used as an index for risk stratification in many diseases. The non-linear analysis using Poincare plots is a geometrical and generally very powerful visual technique to assess hidden patterns in the dynamics of HRV and to gain more information about the entire RR interval time series. Also, a non-linear analysis is necessary because some information may be lost in linear methods (43, 44).

Recurrence plot (RP)

A recurrence plot (RP) is an advanced method of non-linear data analysis in a multidimensional phase. This method allows the recognition of system properties, which are useful for discovering hidden relations in highly complicated data periodicities and the non-stationary signal in the time domain, which is not easily found by linear and conventional techniques. Non-linear techniques usually approach Recurrence plots (RPs). RP is a basic feature of deterministic dynamical systems and is typical for non-linear or chaotic systems. RPs are used in non-linear dynamic analysis, and their quantification measures are based on the Poincare recurrence theorem (45). It is used to quantify the Recurrence plot of the ECG signal. RP is a visualization (or a graph) of a square matrix, in which the matrix elements correspond to those times at which a state of a dynamical system recurs (columns and rows correspond then to a certain pair of times). Technically, the RP reveals all the times when the phase space trajectory of the dynamical system visits roughly the same area in the phase space. These graphical tools were elaborated for the first time by Eckmann et al, which can visualize the periodic nature of a trajectory through $\vec{x_i}$ a phase space (46). Often, the phase space has a limited dimension (two or three), which allows it to be pictured since higher-dimensional phase spaces can just be visualized by projection into the two or three-dimensional sub-spaces, which displays the recurrences of states. However, Eckmann's tool for making a recurrence plot enables us to investigate certain aspects of the *m*-dimensional phase space trajectory through a two-dimensional representation. A recurrence is a situation happening when the distance between two states x_i, x_j, *is* less than the threshold ε value. Let x_i be the *i*th point on the orbit in *m*-dimensional space. Whenever x_j is sufficiently close to x_i, a dot is placed at (*i, j*). The plots are symmetric along the diagonal $i = j$ because if x_i is close to x_j, then x_j is close to x_i. Thus, the recurrence plot is an array of dots in an N ×N square. It can also be viewed as an N ×N matrix of black and white dots in time-related space. Here black dot means recurrence has occurred (47). This representation is called RP. Such an RP can be mathematically expressed as a formula (5).

$$R_{i,j} = \theta\left(\varepsilon_i - \left\|\underset{x_i}{\rightarrow} - \underset{x_j}{\rightarrow}\right\|\right), \underset{x_i}{\rightarrow} \in R^m, i, j = 1, \ldots, N, \qquad (5)$$

Where

– N is the number of considered states x_i
– ε_i is a threshold distance
– $\|.\|$ The neighborhood measure a norm
– $\theta(.)$ The unit step function and the Heaviside function.
– M is the embedding dimension.

Recurrence Quantification Analysis (RQA) is useful in analyzing dynamic systems from a time series. RPs were introduced to visually distinguish different dynamical behaviors in time series since periodic orbits and chaotic and random behaviors generate distinct structures in the RPs (48). Measures based on diagonal structures can find chaos-order transitions, and measures based on vertical or horizontal structures can find chaos-chaos transitions. These measures can be computed in windows along the main diagonal. This allows us to study their time dependence and can be used to detect transitions. Another possibility is to quantify the patterns, like parallel lines of RPs for each diagonal parallel to the main diagonal separately. This approach enables the study of time delays and unstable periodic orbits and, by applying to cross-recurrence plots, the assessment of similarities between processes (49).

Recurrence quantification analysis

The recurrence plot is a graphical "RQA plot" method based on the time delay method in a multidimensional space(50). RQA is the visual and non-linear data analysis of the RPs, which quantifies the number and duration of recurrences of a dynamical system presented by its state space trajectory. It is subjective and can lead to different interpretations. RQA uses pattern recognition algorithms to quantify the recurrence features depicted in RPs, which is more objective than the visual inspection of the graphs. RQA is an advanced tool that allows the study of chaos and complexity of a dynamical system with few parameters. It measures the dynamicity and subtle rhythmicity in the HR signal. Because graphical tools may be difficult to Figure out, RQA was developed to provide quantification of important aspects revealed by the plot. As RP, this methodology is independent of limiting constraints, like the data set size, and does not require stationarity, linearity, and any usual assumptions on the probability distribution of data. For these reasons RQA, as the RP, seems very useful for characterizing state changes.

Describe the analysis of the quantifying recurrences in the RPs leads to the generation of five variables, including the following: recurrence rate (REC), determinism (DET), maximum length of the diagonal lines (L_{max}), Mean diagonal line length (L_{mean}).

%REC

Indicates measure percent of recurrent points or global recurrence existing in the recurrent plot (RP); recall that a point (i, j) is recurrent if the distance between the vectors y(i) and y(j) is less than the threshold; in other words, %REC is the ratio of the number of recurrent states measured concerning all possible states.

The percentage of recurrence points in an RP is defined as:

$$\mathrm{REC} = \frac{1}{N^2}\sum_{i,j=1}^{N} R_{i,j} \qquad (6)$$

Here $R_{i,j}$ is the representation of the recurrence plot
N – Number of points $R_{i,j}$ on the phase space trajectory

%DET

Determinism describes the percentage of recurrent points forming line segments parallel to the main diagonal. The presence of these lines reveals the existence of a deterministic structure.

The determinism from the diagonal line in the RP is defined as:

$$\mathrm{DET} = \frac{\sum_{l=l\min}^{N} lP(l)}{\sum_{l=1}^{N} lP(l)} \quad (7)$$

Here $P(l)$ is the histogram of the lengths l of the diagonal lines.
$l_{\min}$ is the length of the minimum diagonal line.
N – Number of points on the phase space trajectory

L_{max}

Maximum diagonal lines (Maxline) represent the length value of the longest line diagonal, the two segments that remain with a similar pattern are determined by the time during which two segments evolve in parallel on a trajectory in the RP. Eckmann et al (51) and Trulla et al (52), have stated that this quantity is proportional to the inverse of the largest positive Lyapunov exponent. A periodic signal produces long line segments, while short lines indicate chaos.

The length of the longest diagonal line in the RP is defined as:

$$L_{max} = \max(\{l_i ;\ i = 1, \ldots, N_l\}) \quad (8)$$

Here N_l represents the number of diagonal lines in the RP.

L_{meann}

Mean diagonal line length is an indicator of the mean forecasting time of the system. This parameter measures the inverse of the divergence of the system.

The average length of the diagonal lines is defined as:

$$L_{mean} = \frac{\sum_{l=l\min}^{N} lP(l)}{\sum_{l=lmin}^{N} P(l)} \quad (9)$$

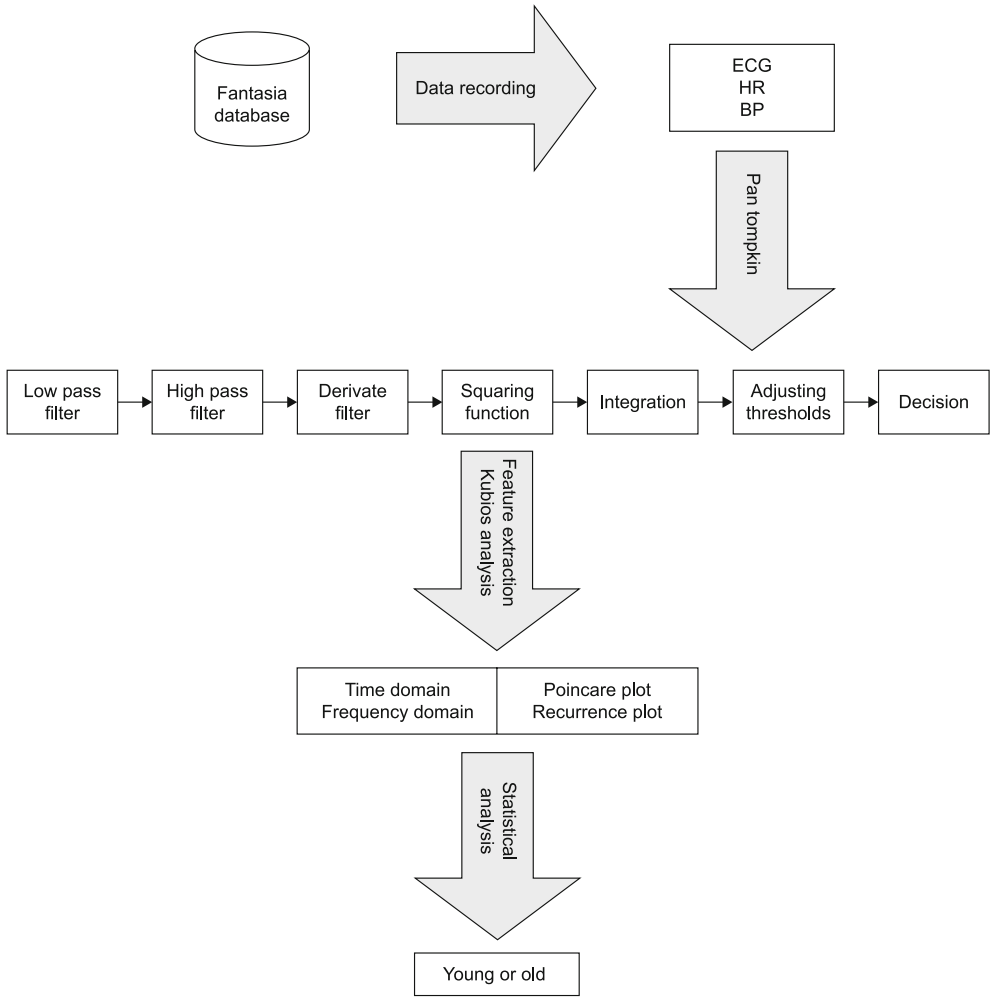

Fig. 4. Block diagram of Pan–Tompkins algorithm and detection processing.

Tab. 2. Mean and STD and Poincare and Recurrence Quantification parameters for young and old groups.

Record No.	SD1	SD2	SD1/SD2	S*10^{-3}	L_{mean}	L_{max}	DET	REC
F1y01	58.3	101.6	0.57	18.61	9.77	117	97.12	28.44
F1y02	49.3	128.9	0.38	19.96	15.33	221	98.57	43.59
F1y03	22.1	81.2	0.27	5.64	11.99	735	98.87	35.20
F1y04	83.3	135.9	0.61	35.56	9.20	106	96.40	30.42
F1y05	39.6	114.5	0.35	14.24	14.94	248	99.04	44.55
F1y06	50.4	127.0	0.40	20.11	12.75	431	99.00	39.21
F1y07	91.0	239.9	0.38	68.58	9.72	157	98.06	29.19
F1y08	33.8	109.6	0.31	11.64	12.48	546	98.97	38.65
F1y09	29.6	112.8	0.26	10.49	14.35	533	99.20	40.20
F1y10	39.6	104.6	0.38	13.01	11.75	266	98.37	35.44
F2y01	40.0	75.2	0.53	94.50	10.25	150	97.56	30.65
F2y02	77.8	185.9	0.42	45.44	10.76	232	98.16	31.43
F2y03	20.2	56.3	0.36	3.57	12.21	273	97.61	36.10
F2y04	29.6	75.9	0.39	7.06	21.62	769	99.46	53.21
F2y05	32.1	66.4	0.48	6.70	34.30	769	99.22	51.44
F2y06	21.8	81.0	0.27	5.55	12.16	909	98.82	37.44
F2y07	56.6	127.2	0.44	22.62	9.07	138	96.84	27.86
F2y08	75.3	124.3	0.61	29.40	10.16	110	96.76	28.52
F2y09	185.0	196.5	0.94	114.20	14.81	112	99.23	44.79
F2y10	550.0	545.1	1.01	9418.70	70.10	345	99.13	51.35
mean±STD	54.49	118.14	0.47	28.78	13.56	358.35	98.32	37.88
STD	38.26	46.92	0.20	531.2	5.83	260.88	0.95	8.11
Record No.	SD1	SD2	SD1/SD2	S*10^{-3}	L_{mean}	L_{max}	DET	REC
F1o01	18.8	66.6	0.28	3.93	21.49	911	99.71	49.45
F1o02	42.9	59.1	0.73	7.96	58.77	696	99.90	80.48
F1o03	23.0	51.0	0.45	3.68	17.92	530	99.43	49.19
F1o04	32.8	123.0	0.27	12.67	14.84	391	99.42	41.04
F1o05	12.5	57.5	0.22	2.26	17.78	917	99.72	46.36
F1o06	29.0	29.1	0.50	2.65	28.85	508	98.84	65.93
F1o07	46.7	69.1	0.68	10.14	19.98	260	99.38	55.83
F1o08	25.3	64.0	0.39	5.09	17.97	394	98.99	47.84
F1o09	103.5	146.8	0.70	47.73	12.88	204	98.95	42.01
F1o10	19.7	79.6	0.25	4.93	17.95	917	99.63	46.05
F2o01	93.3	116.5	0.80	34.15	20.10	347	98.88	51.23
F2o02	61.2	74.2	0.82	14.27	32.22	424	99.75	72.19
F2o03	34.0	54.0	0.63	5.77	19.70	313	98.83	50.16
F2o04	21.5	53.6	0.40	3.62	11.81	416	97.86	36.76
F2o05	33.7	60.0	0.56	6.35	33.58	418	99.91	69.30
F2o06	34.8	109.4	0.32	11.96	13.00	487	98.98	38.31
F2o07	21.7	57.2	0.38	3.90	13.82	505	98.98	41.36
F2o08	208.7	236.6	0.88	155.13	27.27	306	99.29	46.89
F2o09	33.0	78.9	0.42	8.18	22.85	738	99.77	57.26
F2o10	32.4	69.7	0.46	7.09	28.49	502	99.78	61.44
mean±STD	37.88	74.70	0.51	10.33	20.46	509.20	99.30	52.45
STD	24.12	29.19	0.21	11.55	6.62	217.05	0.51	11.97

Tab. 3. Comparison of the results of Poincaré parameters and RQA parameters.

Sbject	SD1	SD2	SD1/SD2	S	L_{mean}	L_{max}	DET	REC
Young(F1Y01)	58.3	101.6	0.57	18.61	9.77	117	97.12	28.44
old (F1O01)	18.8	66.6	0.28	3.93	21.49	911	99.71	49.45

Statistical analysis

Non-linear regressions were performed using the Matlab and Kubios software to determine the effect of age on SD1 and SD2, and the ratio SD1 to SD2 and S as Poincare parameters and L_{mean} and L_{max} and DET and REC as Recurrence parameters were reported for all extracted features in Table 1. The results are presented as mean ± standard deviation. All these parameters for both young and old groups are compared with each other in box plots. The Block diagram of the proposed method is shown in Figure 4.

Result

Poincare plot analysis

First, we test the Poincare Plot Analysis that has been done on the R–R intervals, which are taken from ECG signals to show the variation of HRV behavior effect on young and old people in the Fantasia database. Poincare Plot analysis has provided us with both the quantitative and qualitative analysis of ECG signals using the non-linear methodology. The Poincare plot analysis statistics values are shown in Table 2. Also, the variation between the statistics of old and young groups can be seen in boxplots, which are plotted based on Poincare parameters represented separately for left- and right-sided seizures in young and old, as shown in Figure 5. The results are summarized in Table 2 and Table 3 (Poincare plot quantification measures for young), we found evidence of mean and standard deviation along a line of identity (SD1) for the young group with an average range of 54.49 ms and SD1 for the elderly group is with an average range of 37.88 ms (Fig. 5a). The standard deviation perpendicular to the line of Identity (SD2) for young and elderly groups is 118.14 ms and 74.70 ms, respectively (Fig. 5b); the mean SD1/SD2 ratio for young and elderly groups is 0.47 ms and 0.51 ms, respectively (Fig. 5c) and overall variability represented by ellipse area (S) for young and elderly groups 28.78 ms2 and S10.33 ms2 (Fig. 5d). There is a reduction of % in SD1, % in SD2, % in SD1/SD2, and % in the ellipse area in the elderly group compared to the young group. These results indicate for all parameters higher variability in younger subjects. Reflect approximately % higher variability in the old age group.

Recurrence quantification analysis

Next, we test the Recurrence Quantification Analysis on the same R–R intervals used in Poincare Plot Analysis as another method to show the variation of HRV behavior effect on young and old subjects. Recurrence Quantification Analysis has provided us with the quantitative analysis of ECG signals using

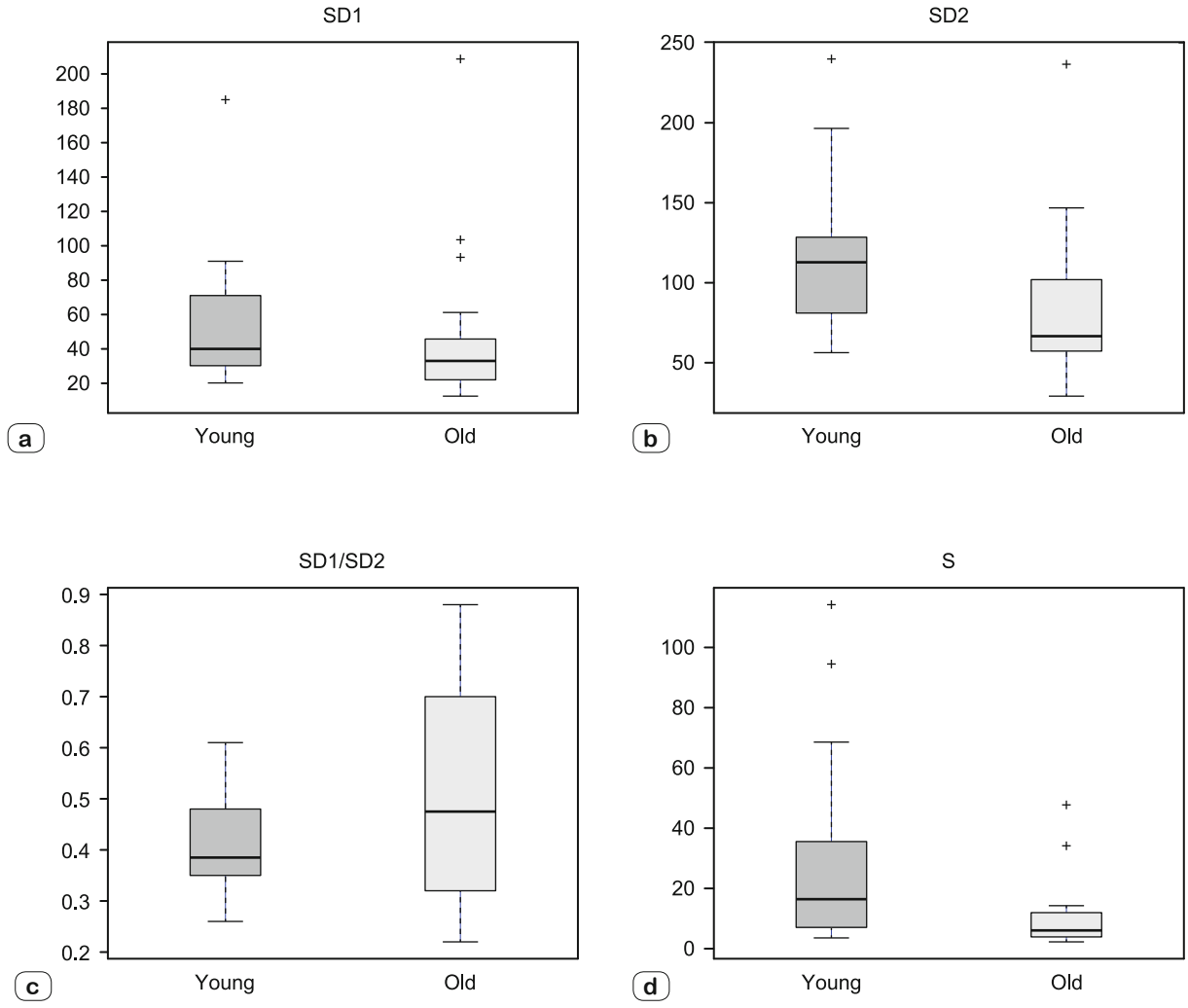

Fig. 5. (a) standard deviation along the line of identity (SD1); (b) standard deviation along the line of identity (SD2); (c) SD1/SD2 ratio; (d) ellipse area (S).

the non-linear methodology. The RQA statistics values of both groups are showed in Table 1. Also, the variation between the statistics of old and young groups can be seen in boxplots, which are plotted based on recurrence parameters represented separately for left- and right-sided seizures in young and old as shown in Figure 6. The results are summarized in Table 2. Table 2 shows the Poincaré plots measure for both age groups. Table 2 describes the meaning of diagonal line length (L_{mean} (for the young group, with an average range of 13.56, and L_{mean} for the elderly group, with an average range of 22.25 (Fig. 6a). The average of Maximum diagonal lines (L_{max}) for young and elderly groups is 358.35 and 509.20, respectively (Fig. 6b). The mean value of Determinism (DET) for young and elderly groups is 98.32 and 99.30, respectively (Fig. 6c). Also, the mean value of recurrent points (REC) for young and elderly groups is 37.88 and 52.45, respectively (Fig. 6d).

In Table 3, it is obvious that $L_{mean,}$ L_{max}, DET, and REC in young persons have smaller values than in older ones. These results indicate for all parameters higher variability in older subjects. Reflect approximately % higher variability in the old age group.

Comparison of Poincare plot and RQA

Finally, we compare these two analyses with non-linear techniques, which are shown in Table 3. Table 2 shows two subjects from old and young groups for comparison between Poincare Plot and RQA analysis. By making the comparison, it has been observed that in the case of patient persons, the Poincare value of SD1, SD2, SD1/SD2, and the area of the ellipse (S) in old subjects will be less than in young ones, but the recurrence value of % REC, %DET, L_{mean} and L_{max} in old subjects will be higher than young ones. It meant that there is an opposite correlation between Poincare Plot and RQA to aging. Also, obtaining information about

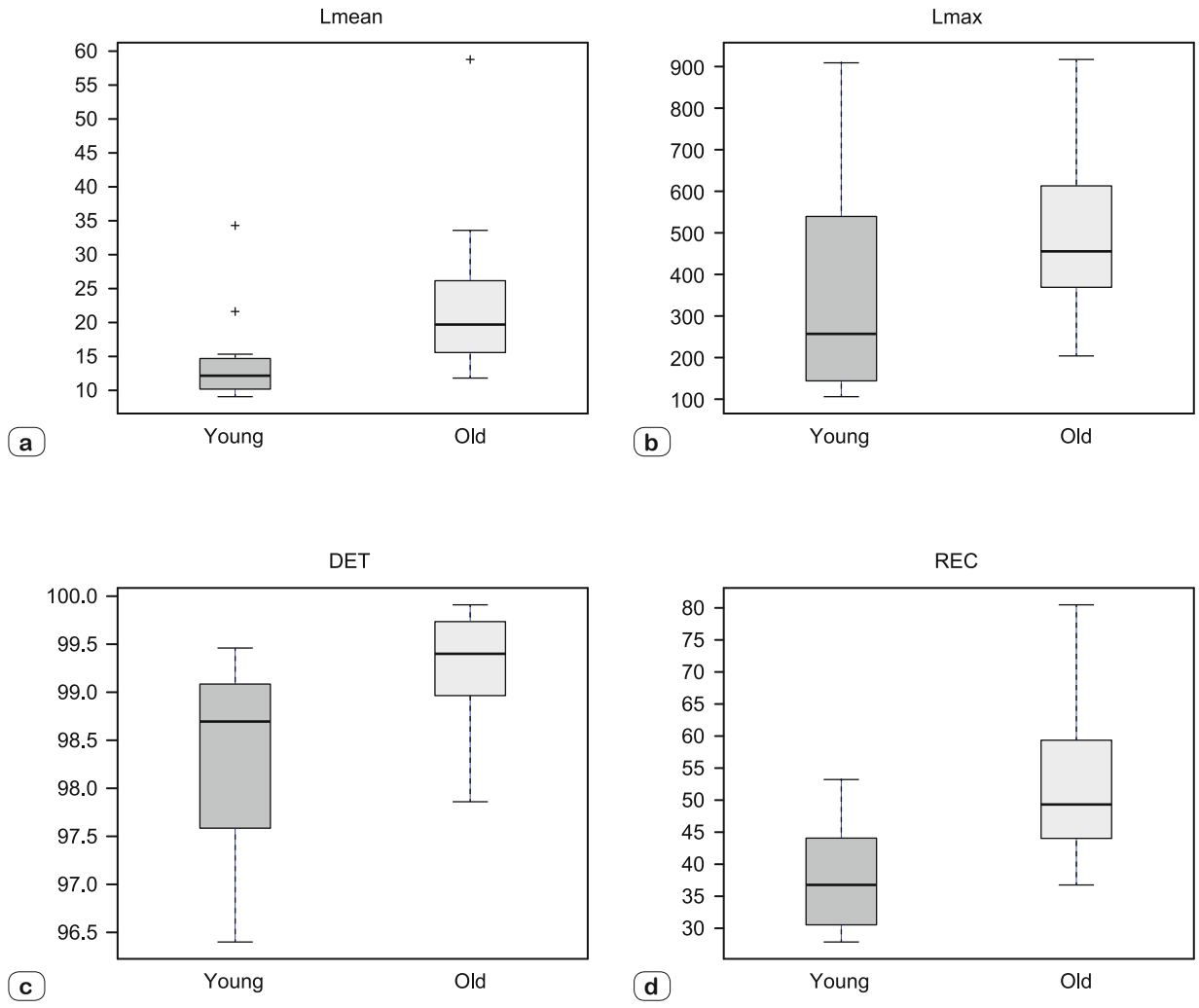

Fig. 6. (a) mean diagonal line length (L_{mean}); (b) Maximum diagonal lines (L_{max}); (c) Determinism (DET); (d) recurrent points (REC).

all subjects of male and female gender with age change between the old and young subject Poincaré plots according to Figure 7 that Poincaré cloud is spread over a wider area for the young age group as compared to the elderly, which shows more power in the young group. Old subjects have smaller values of SD1 and SD2 and area ellipses than young subjects.

Discussion

Many parameters affect HRV, like stress, age, gender, certain cardiac diseases, and other pathologic states. Therefore, recognizing the effects of age on cardiac parameters can be useful in preventing many diseases. Age effects on both linear and non-linear parameters of HRV.

It's obvious that HRV analysis, according to non-linear methods, elicits valuable information for the physiological interpretation of HRV. This study used non-linear indexes (SD1, SD2, SD1/SD2, S, L_{mean}, Lmax, DET, and REC) examined in a population of 40 healthy subjects between the age of 21 and 85 yr. We found a decrease in the variable of the Poincare plot and an increase in the variable of the recurrence plot with advancing age.

Many studies worked on the correlation between non-linear and linear parameters of HRV and aging. For example, Frank Beckers et al (50) worked on the relation between non-linear parameters like Approximate entropy (ApEn) and detrended fluctuations analysis (DFA) a1 and Detrended fluctuations analysis (DFA) a2 and aging. They studied healthy groups that included 135 women and 141men between the age of 18 and 71 years during 24 hours. Their study approved a relation between these non-linear indexes of HRV and aging. But this correlation is significant during the day. And the relation with age disappeared in some indexes during the night, especially in the male population. The other problem in this study is that these non-linear indexes are more pronounced in the female population. Pikkuja¨msa¨ et

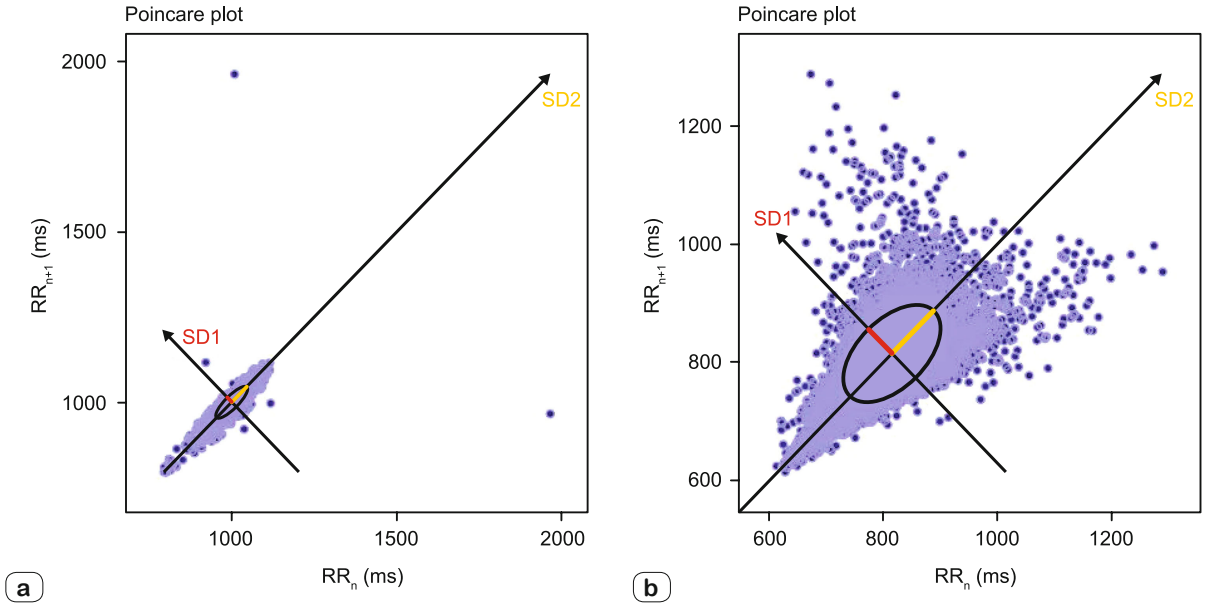

Fig. 7. (a) Poincare Plot for F1o01 elderly subject; (b) Poincare Plot for F1Y01 young subject.

al (53) worked on non-linear indexes (ApEn and DFA a1) but couldn't find a relation with age, and the range of age that they studied was very limited (40–59 yr). KEN UMETANI et al (54) worked on non-linear parameters of HRV and aging. One of these parameters that they studied was the standard deviation. This study showed that HRV decreased with advancing age, but this change is gradual, and this decrease was not very clear by the tenth decade. In frequency domain analysis, Krishan Pal Singh Yadav et al (55) showed that the peak frequencies, low frequency (LF), and high frequency (HF) are not much affected by aging. They compared Poincaré plots and Frequency−Domains (LF, HF, LF/HF) and showed a difference between young and elderly subjects in Poincaré plots' parameters (SD1, SD2, SD1*SD2), but the ratio LF/HF is the same for both age groups. This study used Recurrence Quantification Analysis and Poincare plot as non-linear methods for extracting HRV features. We found a decrease in the variable of the Poincare plot and an increase in the variable of the recurrence plot with advancing age. Poincare Analysis is easy to implement and interpret in comparison to RQA. The quantity of subjects in this study is not too much.

Study limitations

The number of subjects is not evenly distributed between the various genders and the nine decades. Women 40 to 49 years old are oveR–Represented, and old men 70-year-old are underrepresented. To solve this, each group should have an adequate gender number of subjects. Second is the definition of a "healthy subject."Just pay attention to the terms of medical history. It was needed that subjects did not take any medications except for non-steroidal anti-inflammatory agents and oral contraceptives. The third is that subjects didn't do special activities during the ECG recording and were relaxed and just watching, so there weren't any possible information differences between the young and the elderly population.

Forth is that this paper used non-linear methods, but linear methods are more advantageous and more suitable when shorter data sets are used. The interpretation of spectral components is more intuitive and easier to understand.

Conclusion

Investigate the plots and the results; extracted features from the lagged Poincare plot of RR intervals and Recurrence Quantification Analysis parameters can evaluate and differentiate young and elderly subjects' impact of age on HRV Parameters. And also, it is concluded that age is an important factor to be considered for the prognosis and diagnosis of HRV.

This study showed that HRV (by all measures) decreases with aging. These parameters can be used as early indicators of cardiovascular disease and other disease detection. There is a considerable change in the degree of nonlinearity with aging. It can also be concluded that the results indicated by both techniques are the same, but Poincare Analysis is more convenient to implement and interpret than RQA. In the future, these methods can be used to develop a biomarker for understanding advancing personal health care to prevent disease and telemedicine – the involvement of the autonomic nervous system in generating non-linear fluctuations in healthy human subjects.

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