Comparative Analysis of Measuring Heart Rate Variability during Different Phases of Menstrual Cycle in Young Healthy Women

K. Rawal and I. Saini

Abstract—**Aim of this study is to investigate the effects of menstrual cycle on cardiac autonomic nerve function parameters in young healthy women by means of heart rate variability (HRV). Comparative analysis has been done using linear and non linear methods of HRV for analysis of real life stress during menstrual cycle. This study considers three phases of menstrual cycle i.e. menstrual phase, luteal phase, and follicular phase. Electrocardiograms (ECG) of twenty young healthy women were recorded in all the three phases of menstrual cycle and RR intervals were then obtained. Scaling exponent alpha (α) in detrended Fluctuation Analysis (DFA) successfully distinguish the stress in three phases of menstrual cycle based on their HRV's. In DFA mean values of scaling exponent alpha (α) are lowest in luteal phase (0.77) indicates maximum stress as compared to the menstrual phase (0.88) and follicular phase (0.86) of menstrual cycle. In contrast to DFA, linear methods of HRV i.e. standard deviation of all NN intervals (SDNN) and square root of the mean of the sum of the squares of differences between adjacent NN intervals (RMSSD) and low frequency (LF), high frequency (HF) and LF/HF ratio in frequency domain method of HRV failed to clearly distinguishes the HRV's in all phases of menstrual cycle. And also it has been concluded that the menstrual characteristics in young women vary with autonomic nerve function.**

Index Terms—**Autonomic nerve function, heart rate variability, menstrual cycle, phases.**

I. Introduction

Menstrual characteristics in women vary with different age groups, socioeconomic status and lifestyles. In women, HRV is related to many factors, including endogenous sex hormones [1], menstrual cycle [2], [3], menopause [4], hormone replacement therapy, [5], body mass index (BMI) [6], and physical conditioning [7]. In addition, the combined influence of age, BMI and menstrual cycle has been reported in young women, which indicated that age was an essential predictor of HRV, followed by BMI and menstrual cycle [8]. Menstrual cycle has three phases: the menstrual phase, follicular phase, and the luteal phase. Menstrual cycles started from the first day of menstrual bleeding. It is also called menses, menstrual bleeding, or a period. Two main hormones i.e. estrogen and progesterone are mainly affected during the entire menstrual cycle. Follicular phase is also called the proliferative phase because a hormone causes the lining of the uterus to grow, or proliferate, during this time. Through the influence of a rise in follicle stimulating hormone (FSH) during the first days of the cycle, a few ovarian follicles are stimulated. The luteal phase is also called the secretory phase. An important role is played by the corpus luteum, the solid body formed in an ovary after the egg has been released from the ovary into the fallopian tube. This body continues to grow for some time after ovulation and produces significant amounts of hormones, particularly progesterone. In the luteal phase of menstrual cycle, premenstrual syndrome (PMS) also describes various ranges of emotional, behavioral, and physical changes which decrease following menstruation [9]. Analysis of HRV provides another and more perceptive noninvasive measure of cardiac autonomic regulation than other measures of skin conductance. Beat-to-beat variability in the heart's rhythm is mainly caused by the autonomic nervous system's modulation of intrinsic cardiac pacemakers [10]. Analysis of HRV, therefore, can provide further information on the effective functioning of the heart and on autonomic control through sympathetic and parasympathetic regulation. HRV can be assessed in either the time domain or the spectral domain. The autonomic nervous system (ANS or visceral nervous system or involuntary nervous system) is the part of the peripheral nervous system that acts as a control system functioning largely below the level of consciousness, and controls visceral functions. It is the portion of the nervous system that controls visceral functions of the body. It is traditionally partitioned into the sympathetic (SNS) and parasympathetic (PNS) branches in reference to the neurotransmitters released at the nerve terminals (noradrenaline for the SNS, acetylcholine for the PNS) and to the region in which the nerves have their origin (the thoracic and lumbar segments of the spinal cord for the SNS, the brainstem via the cranial nerves or the sacral segments of the spinal cord for the PNS). The vagus (vagal nerve = 10th cranial nerve) is a major component of the ANS. The autonomic nervous system activity was thus noninvasively measured by HRV power spectral analysis, which decomposes the series of sequential R-R intervals into a sum of sinusoidal functions of different amplitudes and frequencies by the Fourier transform algorithm. The ANS affects heart rate, digestion, respiratory rate salivation, perspiration, ratepupillary dilation, micturition, and sexual arousal. Most autonomous functions are involuntary but a number of ANS actions can work alongside some degree

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of control. To obtain a comprehensive view of cardiovascular autonomic responsiveness, each individual underwent the following well established tests for cardiovascular autonomic function before and at the end of the 6 month period of HT regimen.

During the entire menstrual cycle, women continually experience a wide fluctuation in estrogen and progesterone levels. Previous studies have suggested that respiratory function is affected by female sexual hormones, especially progesterone, which could increase ventilatory response during the luteal phase at rest and at exercise. Others studies have shown that progesterone and estradiol act together to produce increased ventilation by acting on receptor-mediated mechanisms in the central and peripheral regulation of respiratory function in rats. However, in humans, the results are contradictory [11]. The extent to which HRV is affected by the menstrual cycle has been a main subject of consideration [3]. Thus reduced heart rate variability (HRV) is important mechanism in the pathophysiology of cardiovascular disease [12]. The interpretation and quantification of HRV is a complex and sometimes contentious task.

The outline of this paper is as follows: section II consists of methods and experimental protocol used for this study. Section III consists of review of linear methods used for analysis of HRV during menstrual cycle. Section IV consists of review of nonlinear method used for analysis of HRV during menstrual cycle. Section V includes experimental results and discussion and section VI concludes the paper.

II. Materials And Methods

Twenty healthy female college students with a mean ± SD age of 22.7 ± 2.8 yr and body mass index of 20.9 ± 1.2 kg/m2 volunteered for this study. A detailed medical history was obtained from all participants, and they underwent a standard physiological examination. All subjects were confirmed to have no abnormalities on thyroid ultrasound and not having any heart disease. They were nondiabetic, and nonsmokers, and not having primary dysmenorrhea. Also subjects having regular menstrual cycle are included in the study. None of them had taken any oral contraceptives during the study and from previous two months. During luteal, menstrual and follicular phase, electrocardiograms (ECG) of all the subjects were recorded under lying position for 15 minutes in laboratory settings. Every subject comes three times for recording during its single menstrual cycle. The RR-intervals were then obtained using wavelet transform. All the HRV methods was validated on HRV dataset acquired using BIOPAC® MP 150 system having sampling frequency of 500Hz.

III. Linear Methods of HRV

Various methods are used for analysis of HRV but time domain measures are the most simplest to perform. Heart rate at any point in time or the intervals between successive normal complexes is determined by using time domain methods. Various spectral or frequency domain methods for the analysis of the HRV have been applied since the late 1960s. Power spectral density (PSD) analysis provides the basic information of how power (i.e. variance) is distributed as a function of frequency.

A. Time Domain Analysis of HRV

Various time-domain measures, which have been primarily used to assess effective cardiac functioning [9], includes the mean normal-to-normal (NN) interval (NN RR intervals), as well as statistical measures including SDNN, which is a measure of total variability in the interbeat interval. Mathematically SDNN is calculated as using (1)

$$SDNN = \sqrt{\frac{1}{M}\sum_{i=1}^{M}(RR(i) - RR)^2} \tag{1}$$

where $RR(i)$ is the mean value of RR intervals, RR denotes the value of i^{th} RR interval and M is total number of successive intervals. Changes in the value of SDNN are associated with the change of physiological balance between sympathetic and vagal activities. The other statistical measure is RMSSD, which is a measure of high-frequency (HF) activity. Mathematically RMSSD is calculated using (2)

$$RMSSD = \sqrt{\frac{1}{M}\sum_{i=1}^{M}(RR_{i+1} - RR_i)^2} \tag{2}$$

where $RR_{(i+1)}$ denotes the value of $i^{th}+1$ RR interval. Changes in the value of RMSSD are associated with the change of physiological balance between sympathetic and vagal activities.

B. Frequency Domain Analysis of HRV

Power spectrum analysis of HRV provides information on how power is distributed as a function of frequency. It was conducted to determine activity in the HF and LF bands according to published guidelines [11]. Due to its broad applications as a functional indicator of the autonomic nervous system, frequency-domain analysis of HRV has gained popularity as compare to time domain analysis of HRV [13]. The main spectral components which are distinguished in a spectrum calculated from short term recordings of 2 to 5 min [14]–[19]: very low frequency (VLF), low frequency (LF), and high frequency (HF) components. In the frequency domain we analyzed spectral data as total power (TP) in the overall signal from 0.04/to 0.40 Hz, low frequency (LF) power from 0.04 to 0.15 Hz, reflects combined parasympathetic and sympathetic function, and high frequency (HF) power from 0.15 to 0.40 Hz which is an index of the vagal activity and reflects parasympathetic nervous system (PNS) activity [9]. The spectral power in each frequency is stated in absolute values (ms^2/Hz), which were then transformed into normalized units (NUs). NUs were calculated as follows: LF NUs = LF power / (TP − VLF power) × 100. HF NUs =/HF power / (TP − VLF power) ×/100. The ratio of LF to HF (LF/HF) was calculated [14]. LF/HF is a useful parameter that reflects cardiac sympathetic modulations or sympathovagal balances [20], [21]. Higher LF/HF is a predictor of higher sympathetic activity and lower parasympathetic activity.

IV. Nonlinear Methods of HRV

To study the nonlinear dynamics through a new approach, many nonlinear signal processing methods are developed in the last decades. Linear methods in time and frequency domain [22]–[24] have been most commonly used to measure the fluctuation in heart rate. But there is increasing evidence to suggest that the heart is not a periodic oscillator under normal physiologic conditions [25] and linear parameters of HRV are not giving much adequate information on the complexity that lies inside beat-to-beat variability, so the application of nonlinear techniques is appropriate. Many efforts were made to explain the complex behavior of deterministic systems with the presence of nonlinear features instead of the usual stochastic models. The most direct link between chaos theory and the real world is the analysis of time series from real systems in terms of nonlinear dynamics. Recently, interest in nonlinear measures of HRV has emerged. The two nonlinear techniques which are used in this paper to assess the variations in HRV during menstrual cycle are detrended fluctuation analysis (DFA) and Poincare plot.

A. *Detrended Fluctuation Analysis*

DFA is a technique used to determine the correlations within the signal. It also quantifies the fractal scaling properties of RR interval time series. The concept of a fractal is most often associated with irregular geometric objects that display self-similarity or self affinity. Fractal forms are composed of subunits (and sub-sub-units, etc.) that resembles or show correlation with the structure of the overall object. Similarly, times series extracted from physical or biological systems contain hidden long-range correlation that can provide interesting and useful information on the structure and evolution of the dynamical system. Thus DFA which developed by Peng *et al*. (1994) is a simple and efficient scaling method commonly used for detecting long-range correlations. This technique is a modification of root-mean-square analysis of random walks applied to nonstationary signals [26]-[27]. The root-mean-square fluctuation of an integrated and detrended time series is measured at different observation windows and plotted against the size of the observation window on a log–log scale.

The main steps of DFA algorithm are following:

1) First, the RR interval series (of total length k) is integrated using (3):

$$y(k) = \sum_{i=1}^{k} RR(i) - RR_{av} \tag{3}$$

where $y(k)$ is the k^{th} value of the integrated series, $RR(i)$ is the i^{th} inter beat interval, and the RR_{av} is the average inter beat interval over the entire series.

2) Then, the integrated time series is divided into windows of equal length, n.

3) In each window of length n, a least-squares line is fitted to the RR interval data (representing the trend in that window). The y coordinate of the straight line segments are denoted by $y_n(k)$.

4) Next, as in (2) we detrended the integrated time series, $y_n(k)$, in each window. The detrended profile is obtained by subtracting the y coordinate of straight line i.e. trend $y_n(k)$ from the integrated signal $y(k)$ as in (4)

$$y(k) - yn(k) \tag{4}$$

5) The root-mean-square fluctuation of this integrated and detrended series is calculated using (5)

$$F(n) = \sqrt{\frac{1}{N}\sum_{k=1}^{N}\left[y(k) - y_n(k)\right]^2} \tag{5}$$

6) The procedure is repeated for different boxes size or time scales. Finally, the relationship on a double-log graph between fluctuations $F(n)$ and time scales n can be approximately evaluated by a linear model that provides the scaling exponent α given in (6)

$$F(n) \approx n^{\alpha} \tag{6}$$

White Gaussian noise (totally random signal) results in a exponent value of 0.5, and a Brownian noise signal with spectrum rapidly decreasing power in the higher frequencies results in an value of 1.5 [28], [29]. The scaling exponent α can be viewed as an indicator of the ‘‘roughness’’ of the original time series: the larger the value of the scaling exponent α smoother the time series. The fractal scaling (α) for the normal subjects (healthy young) is closer to 1, and this value falls in different ranges for various types of cardiac abnormalities.

V. Results and Discussion

Results indicates that the values of DFA scaling exponent (α) segregate three phases of menstrual cycle as compare to SDNN, RMSSD and frequency domain parameters i.e. LF,HF and LF/HF ratio. Mean values of DFA scaling exponent (α) are lowest in luteal phase (0.77) as compare to follicular phase (0.86) and menstrual phase (0.88) (Table I). This study hence adds further supports to the notion that reduced HRV is a feature shared by number of related psychiatric disorders that are characterized by symptoms such as depressed mood, tension, and/or irritability and anger. Thus all the results in table I clearly demonstrate that the autonomic regulation of the heart in normal women fluctuates during the menstrual cycle, HRV being lower in the luteal phase than in the follicular phase and menstrual phase. In contrast to SDNN, RMSSD and frequency domain parameters i.e. LF,HF and LF/HF ratio, there are difference in values of DFA scaling exponent (α) in three phases of menstrual cycle demonstrated that HRV decreases in luteal phase which leads to more stress and higher sympathetic activity as compared to follicular and menstrual phase of menstrual cycle.

VI. Conclusion

The results of this study have confirmed that linear methods i.e. SDNN, RMSSD and frequency domain parameters i.e. LF,HF and LF/HF ratio are failed to investigate the stress during luteal, menstrual, and follicular phase of menstrual cycle. Thus it is concluded that a nonlinear complexity measure DFA is more useful to classify the stress in three phases of menstrual cycle based on their HRVs.

TABLE I: RESULTS DURING THREE PHASES OF MENSTRUAL CYCLE

		Linear methods					Nonlinear method
		Time domain		Frequency domain			
S.No.	Menstrual Cycle Phases (20 Subjects)	SDNN (ms)	RMSSD (ms)	LF (ms)	HF (ms)	LF/HF	DFA Scaling Exponent (α)
1.	Luteal phase	46.58	42.43	33.94	43.66	1.22	0.77
2.	Menstrual phase	48.24	43.74	29.64	42.335	0.96	0.88
3.	Follicular phase	45.05	38.67	31.22	41.515	0.93	0.86

Higher mean value of scaling exponent (α) in DFA indicates less stress in follicular phase as compare to lower values of (α) in the luteal and menstrual phase of menstrual cycle. Results shown above clearly demonstrates that DFA has low scaling exponent value (α) during luteal and menstrual phase means the subjects experiencing more stress, in contrast to follicular phase. Also SDNN, RMSSD and frequency domain parameters i.e. LF,HF and LF/HF ratio do not clearly distinguishes the HRV's of three phases of menstrual cycle. Thus non linear properties in HRV are altered during the regular menstrual cycle. All these observations may enrich the physiological interpretations of complexity measures.

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