Minimization of Heart Rate Bias in the Estimation of Heart Rate Variability

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Abstract

Background: Heart Rate (HR) is a time varying signal indicating the beating activity of the heart, whereas Heart Rate Variability (HRV) is a noninvasive tool to evaluate the cardiac autonomic regulations. The HRV is widely used to evaluate cardiac/autonomic health in normal healthy as well as chronic diseased population. The HR and HRV are significantly connected with each other. HRV is dependent on the average HR as well on the Autonomic Nervous System (ANS) activity. To make the HRV a potential marker of ANS activity, the influence of HR must be reduced. The present study is designed to minimize the effect of HR on HRV by normalization of the RR interval tachogram.

Method: Forty six young adults participated in the non-invasive and benign study. 10 minutes of Electrocardiogram (ECG) lead II was recorded in each case in supine position. The electrocardiographic records of the subjects were divided into three groups based on their HR viz., slow, moderate and fast HR. The HRV indices were extracted at pre and post HR bias minimization.

Results: The improved HRV was observed with HR bias minimization in all three categories of HR. The reduced HRV was found with increasing heart rate even after HR bias minimization.

Conclusion: Significant impact of normalization was found on moderate and fast HR subjects. This suggests that the HRV studies would yield better results with HR bias reduced, thereby improving health monitoring systems based on HRV.

Keywords: *Heart rate; Heart rate variability; Normalization; HR bias.*

Introduction

Heart rate (HR) is a time varying signal and its variations may contain indications of various cardiac and non cardiac conditions[1]. The instantaneous HR can be calculated from the time between any two QRS complexes of the Electrocardiogram[2]. The Greek physicians were the first to measure the pulse rate and its variation with respiration was first observed by R. Stephen Hales[3]. Dyer et al. reported that high heart rate may be an independent risk factor from sudden death due to both cardiovascular and non-cardiovascular diseases[4]. The excess cardiovascular deaths with more rapid heart rates were also observed in a Framingham study of 5209 men and women for 30 years[5].

The HR is regulated by the natural pacemaker in the heart[6]. The HR is not constant but depends upon sinus node cycle length (CL) which is further under the control of autonomic nervous system (ANS)[7]. The CL variations result into beat to beat fluctuations in the HR which provides a noninvasive measure of cardiovascular control system; the sympathetic and parasympathetic systems[8]. Thus heart rate variability (HRV) is defined as the fluctuations of the RR intervals under the influence of ANS where short term variability mediated by parasympathetic system and long term variability by both sympathetic and parasympathetic pathways[9]. With the application of digital signal processing techniques, the HR and HRV and their relationship with health and diseases was explored[10-12]. The HRV has become a powerful and popular tool for the assessment of cardiovascular autonomic regulation. So far, more than 17000 PubMed listed HRV related articles have been published[13].

The HR and HRV both are strongly correlated. Their inverse correlation was reported by Ungi et al.[14]. The relationship between HR and HRV was further explored in various studies[15-16]. They demonstrated that the association between HR and HRV can be determined both physiologically and mathematically. The physiological association is manifested in ANS activity whereas mathematical association is observed by inverse relationship between HR and RR interval.

Monfredi et al. presented the increased HRV for slow HR (large RR interval) and decreased HRV for fast HR (small RR interval) and therefore concluded that HRV of two different average HR subjects cannot be compared[13]. In support to this, Kazmi et al. investigated the relationship between HR and linear/nonlinear HRV indices and concluded that HRV is dependent on HR and thus, HR should be considered while HRV analysis is performed in evaluation of cardiac ANS activity[17].

To overcome the influence of HR bias in HRV, Sacha et al. investigated the HRV relationship with HR by normalization of the RR interval with respect to the average value[18]. Their study revealed significant differences in the correlation between HR and HRV with normalization of the HR. Thus reducing the HR bias in HRV could metamorphose HRV in a significant manner for ANS activity. However the HR characterization in reducing HR bias is still to be explored. So, the present study was designed to investigate the effect of slow, moderate and fast HR bias minimization in HRV.

Materials and Methods

Study population

A number of college students were invited to take part in the study. Details of the study, procedure and objectives were given to the subjects prior to the data acquisition and written consent was obtained. Volunteers were examined for the following inclusion criteria:

1. Systolic blood pressure <140 mmHg and diastolic blood pressure <90 mmHg.

2. No history/treatment of any cardiovascular disease, diabetes or any other abnormality that would interfere with cardiac autonomic function.

Based on these inclusion criteria, forty six young individuals with age ranging from 18 to 39 years were chosen who met the criteria to participate in this study. The distribution of the population is shown in Table 1.

Table 1 Distribution of population

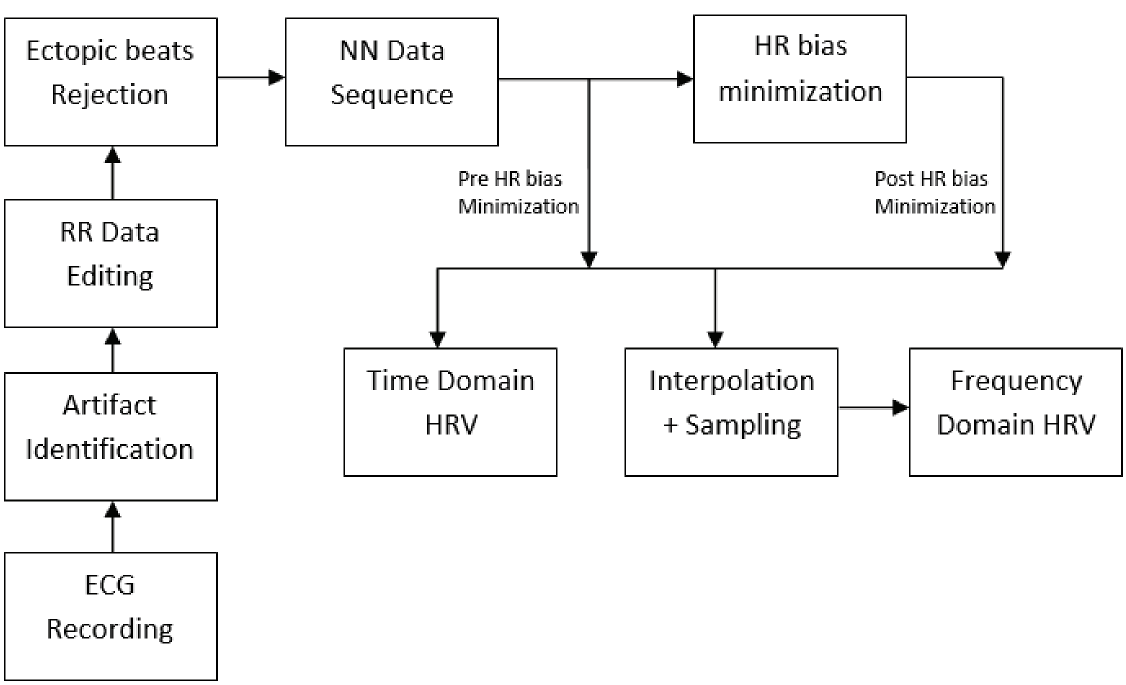
Parameters	HR (BPM)		
	Slow (HR<65)	**Moderate (65≤HR≤85)**	**Fast (HR>85)**
N	16	15	15
Age(years)	23.4±6.09	22.4±5.4	24.5±6.9
HR(BPM)	61.1±3.6	74.9±3.1	88.8±2.6
SBP(mmHg)	119.12 ± 5.75	120.31± 5.92	118.92±9.51
DBP(mmHg)	75 ± 3.18	79.1±4.92	77.1±5.99

Values are shown as mean±SD.
Abbreviations: N, No. of subjects; HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure

Procedure

The ECG lead II was recorded in supine position for 10 minutes duration with a PowerLab26® and LabChart8.0® software (AD Instruments, Australia). The ECG data acquisition system along with flow chart of the study is shown in Fig. 1.

Fig. 1 Experimental setup and flow chart of the study



Data processing

Out of 10 minutes of ECG recording; smooth, 5 minutes duration of ECG was selected. The HRV module detected beats by detecting R waves in the ECG signal. The beats were classified as normal or ectopic beat based on preset limit. The ectopic beats were identified if the inter beat interval (IBI) differs more than ±30% from mean[19]. The cubic spline interpolation method was used to replace the ectopic beats with interpolated values based on weighted average of nearby accepted values.

The study population was divided into three categories based on the HR viz., slow HR (HR<65 BPM), moderate HR (65 BPM ≤HR≤ 85 BPM) and fast HR (HR>85 BPM). Time domain and frequency domain HRV indices were obtained from HRV module of the LabChart8.0® software[20-21]. For HR bias minimization, the RR interval tachogram was normalized with average RR interval for each subject. The normalization process neutralizes the mathematical inverse relationship between HR and HRV. The HRV parameters were extracted at pre and post HR bias minimization states from recorded Electrocardiographic data.

The data are expressed as mean±SD. Student paired t test was used to compare the difference between HRV parameters of slow, moderate and fast HR cases. Differences were considered significant at the level $p<0.05$.

Results

The time and frequency domain HRV parameters were obtained with LabChart8.0® software. The average values of HRV measures were obtained for slow, moderate and fast HR at pre and post HR bias minimization and presented in Table 2. The improved HRV was observed for all three HR categories with HR bias minimization. However, the impact was more significant in moderate and fast HR cases.

Table 2 HRV measures during pre and post HR bias minimization

HR bias minimization		**HRV Parameters**					
		SDNN (ms)	**RMSSD (ms)**	**pNN50 (%)**	**LF (ms2)**	**HF (ms2)**	**TP (ms2)**
Slow HR	Pre	63.95±20.63	81.16±28.54	51.68±14.33	1450.13±1308.74	2266.94±2007.02	3808.13±3207.70
	Post	65.65±18.51	83.83±26.33	53.88±13.29	1453.13±1077.92	2405.56±1810.92	3964.25±2693.76
	% Δ	+2.7	+2.8	+4.3	+0.2	+6.1	+4.1
	t stat	1.26	1.49	1.78	-0.02	1.5	-0.65
	p value	0.23	0.16	0.09	0.98	0.16	0.53
Moderate HR	Pre	43.7±13.97	43.25±15.16	19.13±12.04	961.24±622.94	861.8±718.06	1897.2±1181.04
	Post	52.36±16.77	53.08±18.76	27.97±13.68	1627.13±1255.31	994±778.38	2721.13±1964.52
	% Δ	+19.8	+22.7	+46.2	+69.3	+15.3	+43.4
	t stat	8.53	8.36	9.80	3.35	1.81	3.47
	p value	<0.05*	<0.05*	<0.05*	<0.05*	0.09	<0.05*
Fast HR	Pre	35.03±19.53	32.45±22.85	10.45±13.31	566.6±365.07	491.2±610.36	1149.27±982.79
	Post	46.21±26.04	44.78±31.18	19.17±16.96	1067.4±642.06	793.6±885.85	1974.67±1417.06
	% Δ	+31.9	+37.9	+83.4	+88.4	+61.6	+71.8
	t stat	5.51	5.12	5.82	5.55	3.89	5.78
	p value	<0.05*	<0.05*	<0.05*	<0.05*	<0.05*	<0.05*

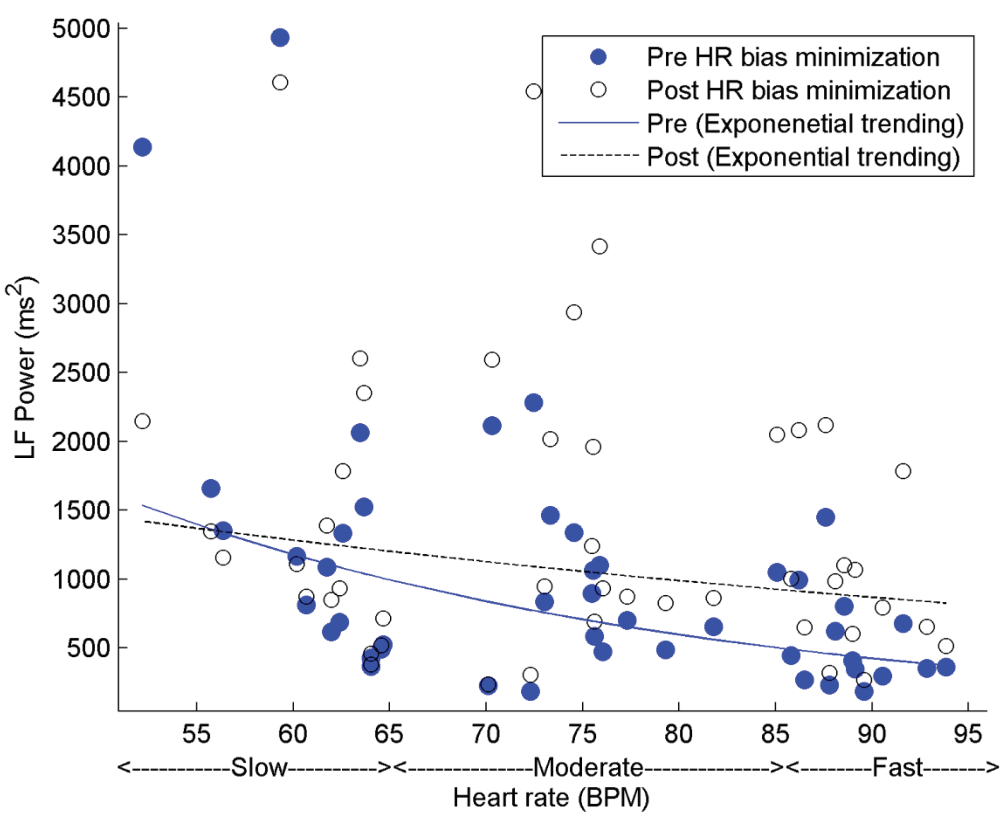
Values are shown as mean±SD. *Statistically significant at $p<0.05$

Abbreviations: t stat, student t test statistics; SDNN, standard deviation of NN intervals; RMSSD, root mean square of differences of successive RR intervals; pNN50, percentage of RR intervals greater than 50 ms; LF (ms2), low frequency power; HF (ms2), high frequency power; TP, total power.

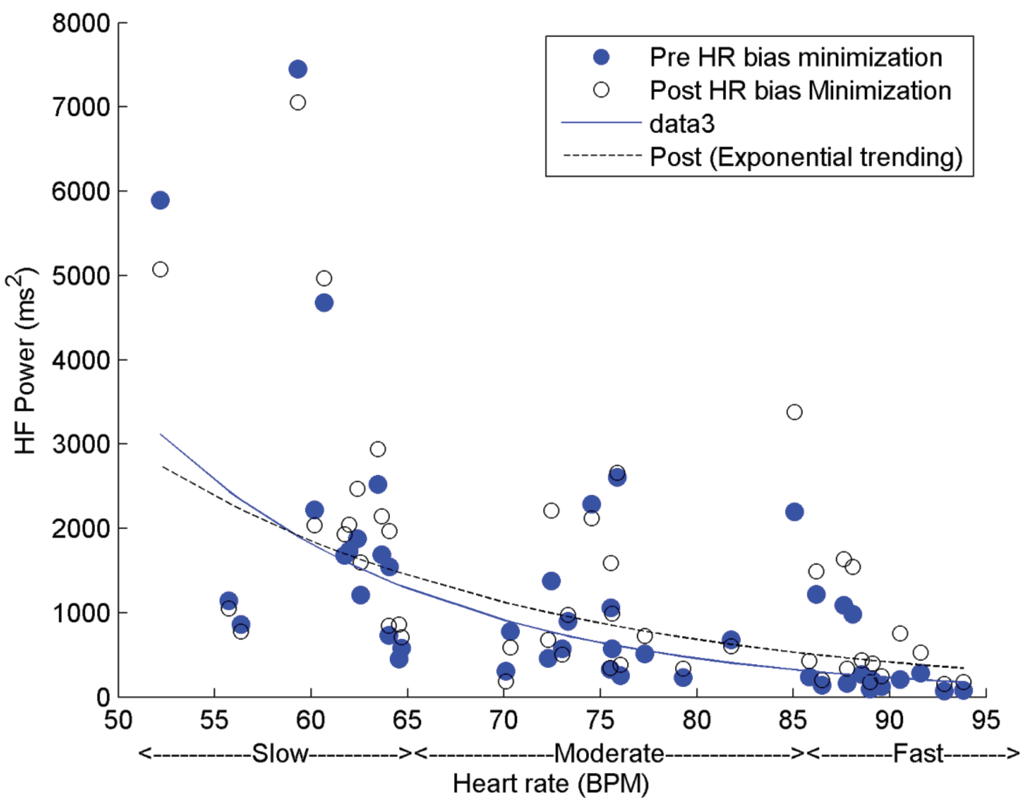
The SDNN was increased at post HR bias minimization. The changes were not statistically significant for slow HR subjects (+2.7%, p=0.23) whereas statistically significant changes were observed for moderate and fast HR subjects (+19.8%, 31.9%, p<0.05) respectively. The RMSSD also increased with HR bias minimization. However the changes were significant only for moderate and fast HR subjects (+22.7 %, 37.9, p<0.05) respectively whereas changes were not significant for slow HR subjects (+2.8%, p=0.16). The pNN50 count also had similar trends. It increased significantly with HR bias minimization in moderate and fast HR subjects (+46.2%, +83.4%, p<0.05) respectively whereas insignificant variation was observed for slow HR subjects (+4.3%, p=0.09).

The HR bias minimization also improved frequency domain HRV measures. The LF power increased with HR bias minimization. The statistically significant changes were observed for moderate and fast HR subjects (+69.3%, 88.4%, p<0.05) respectively. The impact of HR bias minimization on HF power was also significant for fast HR subjects (+61.6%, p<0.05). However the changes were substantial for moderate subjects as compared to slow HR subjects. The TP also increased with HR bias minimization. It increased significantly for moderate and fast HR subjects (+43.4%, +71.8%, p<0.05) respectively.

The scatter plot between HRV indices and HR at pre and post HR bias minimization is presented in Fig. 2. An exponential trending was estimated on the scatter plot. It can be observed a less exponential decay for post HR bias minimization indicating an improved HRV with HR bias minimization. Negative decay of the exponent indicates that HRV decreases with increasing HR, even after HR bias minimization. The similar trends can be observed for all time and frequency domain HRV indices with HR. The two exponent curves are in close proximity at slow HR region depicting less impact of HR bias minimization on slow HR subjects. As HR increases, both the exponent curves moves apart depicting significant impact of HR bias minimization on moderate and fast HR subjects.



(A)



(B)

Fig. 2 HRV measures during pre and post HR bias minimization (A) LF power (B) HF power

Discussion

In this study, the effect of HR bias minimization on HRV measures was presented. The HR bias is present due to inverse mathematical relationship between HR and HRV. To minimize the HR bias, the RR interval was normalized with average RR interval. The normalization procedure do not changes information about signal oscillations. It just changes the oscillations relative to signal average value.

The HR bias has also effect on the QT interval i.e. faster the HR, shorter the QT interval and vice versa. HR dependency on the QT interval has been presented early in 1920 by Bazett and Fridericia and established HR correction formulae[22]. These formulae adjust the QT interval for HR, if it is deviated from 60 beats per minute. The adjustment of the QT to varying HR is a dynamic phenomenon consisting of slow and fast adaptation phases and depends upon nature of HR changes. Repolarization adapts faster to increasing HR than it does to decreasing HR[23]. As the QT prolongation is associated with risk of cardiac arrhythmias and mortality, a correction for HR is warranted for QT interval[24].

Similar to this, correction for HR is also needed in HRV analysis. In this study, the HR bias minimization by RR interval normalization with average RR interval also sets the HRV measures for HR at 60 beats per minute. The HRV measures were improved after HR bias minimization. The HRV measures were found lower at higher HR even after HR bias minimization. This indicates a strong correlation between HR and HRV and the results obtained are in line with numerous studies[13,17,25]. Reduced HRV may be a natural response of ANS in higher HR; however reduced HRV has been also reported in many cardiovascular diseases. Therefore the HRV of two subjects with different average HR cannot be compared. It may lead to draw inappropriate inferences.

In this study, the HR was further characterized as slow, moderate and fast HR. It is proposed that,

(1) The heart rate has significant effect on HRV, particularly in moderate and fast heart rate cases. So, the

effect of heart rate bias minimization is more significant on moderate and fast HR as compared to slow HR.

(2) HRV has inverse relationship with heart rate even after HR bias minimization. It can be attributed to the natural response of ANS at increased heart rate.

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Ethical Clearance: The study was approved by the institutional ethical committee of Government Engineering College Bikaner, Rajasthan, India (Ref. no. F1B(93)/Estt/ECB/226/2007/207, dated 03-02-2018).

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