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EFFECT OF FASTING AND POSTPRANDIAL BLOOD GLUCOSE LEVEL ON TIME AND FREQUENCY DOMAIN HEART RATE VARIABILITY

Jitendra K Jain[1], Ranjan Maheshwari[2]

Abstract-The acute glucose ingestion causes autonomic alterations as well as increase in blood glucose level. The autonomic changes results into changes in heart rate variability (HRV). This study was carried out to identify the relationship between HRV and blood glucose level in young adults. The 46 young adults age ranging from 17 to 39 years participated in this study. 10 minutes Electrocardiogram (ECG), blood pressure and blood glucose level were recorded at minimum of 8 hours of fasting. The subjects were then given 75gm of glucose with water. The ECG and blood glucose level were again recorded at postprandial 1 hour (PP1H) and postprandial 2 hour (PP2H) intervals. Time and frequency domain short term measures of HRV were evaluated from 5 minute segment of ECG recording. The normalized low frequency (LF) power significantly increased at PP1H (r=.62, p=3.89x10-6) and PP2H (r=.30, p=0.045) intervals. The normalized high frequency (HF) power significantly decreased at PP1H (r=.66, p=5.24x10-7) and PP2H (r=.44, p=0.0023) response. The LF/HF ratio thereby increased at PP1H and PP2H response suggesting sympathetic dominance and parasympathetic withdrawal with glucose ingestion. The total power and time domain HRV parameters also decreased significantly at PP1H and PP2H response. Thus the changes in the HRV parameters were observed with changes in the blood glucose level. Their correlation may be used in the measurement of blood glucose level noninvasively which could be of great advantage over the present system.
Keywords-HRV, Fasting, Postprandial, Blood glucose level

1. INTRODUCTION

The all body parts require energy to work. The energy is obtained from food intake. The food may contain nutrients e.g. protein, fiber, vitamins, minerals, carbohydrates, fats etc. These nutrients mixed with acids and enzymes into stomach and breakdown into glucose and absorbed into the blood stream. The insulin, a hormone produced by β cells in the pancreas makes the cells to convert glucose into energy [1].

The food intake or glucose ingestion has been shown to affect autonomic nerve system in early 1980. The glucose ingestion reported to increase sympathetic nerve activity assessed by measurement of plasma norepinephrine level [2]. In another study of microneurography, the plasma glucose level was correlated with sympathetic response [3]. In addition to sympathetic response, increased blood flow in skeletal muscles was also reported with glucose infusion [4]. The physiological effect of insulin at the level of cardiovascular system to vasolidate skeletal muscles has been presented in further research study [5]. Another similar study revealed the sustained increased muscle nerve activity after a carbohydrate, fat, protein or mixed meal and the response was stronger with simultaneous stimulation of insulin secretion [6]. Several other studies also reported the higher postprandial plasma norepinephrine concentration after meal reflecting the increased sympathetic nerve system activity [7, 8, 9].

The quantitative and noninvasive measurement of sympathetic and parasympathetic activity of autonomic nerve system on cardiovascular control was presented in early 1981 [10]. In 1996, the task force presented the guidelines for standards of measurement, physiological interpretation and clinical use of heart rate variability (HRV) [11].

Since then various studies presented the use of HRV for identification of cardiovascular risk with blood glucose concentration level. The high blood glucose concentration level was shown as a risk factor for mortality in nondiabetic men [12]. Another study reported higher mortality rate from cardiovascular diseases with higher fasting blood glucose level [13]. The higher fasting plasma glucose level even within normoglycemic range is also associated with higher risk of insulin resistance and metabolic syndrome which further develops into type 2 diabetes and associated cardiovascular diseases. [14]

The increased glucose level in diabetic subjects showed cardiac autonomic impairment as reflected in reduced time and frequency domain HRV parameters [15]. The effect of oral glucose tolerance test (OGTT) on pregnant women with gestational diabetes mellitus (GDM) and without GDM was analyzed using HRV and the study revealed a impaired autonomic control of heart rate variability with GDM [16]. Similarly the blunted sympathetic response was reported in insulin resistant subjects as compared to insulin sensitive subjects [17]. In support of this, another study revealed the reduced HRV for type 1[18] and type 2[19] diabetes.

Therefore this study was designed to analyze the effect of fasting and postprandial blood glucose level on time and frequency domain HRV measures.

[1] Govt. Engineering College Bikaner, Karni Industrial Area, Pugal Road, Bikaner
[2] Rajasthan Technical University, Kota, Rawatbhata Road, Kota

2. MATERIALS AND METHODS

2.1 Study population

46 healthy young adults, males and females, age ranging from 18 to 39 years were recruited to participate in this study. The subjects were students and academicians from Government Engineering College Bikaner, Rajasthan, India. A brief introduction about the study was given to the subject and then written consent was taken which included some basic information e.g. age, gender, height, weight, family history of diabetes, any serious cardiac or pulmonary disease, history of hypertension, any drug intake or illness. No case of cardiac diseases and hypertension (n=0) was found but two cases of drug intake (n=2) were excluded from the study. The body mass index (BMI) was derived by the weight by square of height (Kg/m2). The clinical characteristics of the study population are shown in Table 1.

Table 1: Characteristics of study population

N	46
Age (years)	23.46 ± 6.07
BMI (Kg/m2)	20.90 ± 3.15
Fasting Blood Glucose (mg/dl)	87.24 ± 9.92
Postprandial Blood Glucose (mg/dl)	107.87 ± 13.90
sBlood Pressure (mmHg)	111.54 ± 11.95
dBlood Pressure (mmHg)	73.35 ± 8.64

Data are represented as mean ± S.D.

2.2 Experimental Setup

The study was carried out at Applied Instrumentation Lab at Government Engineering College Bikaner between 8:00 am to 11:30 am. The Electrocardiogram (ECG) was recorded using a high performance data acquisition system Power Lab 26T® which is a 4 channel16 bit resolution recorder along with Lab Chart® 8.0. The Lab Chart software contains HRV module which uses a threshold detector to detect the R component from recorded ECG waveform and generate RR interval data.

2.3 Procedure

For data acquisition, 4 subjects were called in a day with 8 hrs minimum fasting. After reporting, subjects were asked to sit in relax position for 15 minutes. Then fasting blood glucose level was measured by glucometer. The blood pressure was measured as systolic and diastolic pressures with sitting in relax position. The ECG lead II was recorded for 10 min in supine position with Power Lab® data acquisition system. Then subjects were given 75 gm of glucose orally in 300ml of water. The ECG signal was again recorded after 1 hr of glucose ingestion. Then after 2 hr of glucose ingestion, blood glucose level, blood pressure and 10 minute ECG recorded for each subject.

2.4 Data Analysis

Out of 10 minute recording, smooth, noise free 5 minutes ECG was selected for short term HRV analysis. The time domain and frequency domain HRV parameters were extracted using HRV module of the Lab Chart software®. IBM SPSS Statistics24® and Microsoft Excel® software were used for statistical analysis of data.

3. METHODOLOGY

Heart rate variability is a marker of the autonomic index [21] so to analyze the effect of glucose load on autonomic system of the body, HRV analysis has been carried out for time domain and frequency domain parameters. Various HRV parameters are listed in Table 2.

Table 2: Time and frequency domain parameters

Parameters	Definition
SDNN	Standard deviation (SD) of normal to normal (NN) intervals (ms)
RMSSD	Root of mean of the sum of squares of differences of consecutive NN intervals (ms)
SDSD	SD of differences of consecutive NN intervals (ms)
pNN50	% of NN intervals greater than 50 ms divided by whole NN intervals
Total Power	Variance of all NN intervals (f ≤ 0.4 Hz) ms2
VLF	Very low frequency power (f ≤ 0.04 Hz) ms2
LF	Low frequency power (.04≤ f ≤0.15 Hz) ms2
LF norm (n.u.)	Normalized LF power (LF/(TP-VLF))*100
HF	High frequency power (0.15≤ f ≤0.4 Hz) ms2
HF norm (n.u.)	Normalized HF power (HF/(TP-VLF))*100
LF/HF	Ratio of LF to HF power

The SDNN reflects the total variability while RMSSD primarily reflects the short term components of HRV i.e. parasympathetic activity of the autonomic nervous system [15]. SDSD and pNN50 also reflected high frequency variation in

HRV. In frequency domain analysis, three bands are defined namely VLF, LF and HF. These components reflect the degree autonomic modulation rather than level of autonomic tone [11]. The LF power reflects the sympathetic dominance of cardiac function while HF power represents the parasympathetic measure of the HRV. The ratio LF/HF represents the sympathovagal balance of the ANS [18]. The total power is mathematically equal to the variance of the RR intervals.

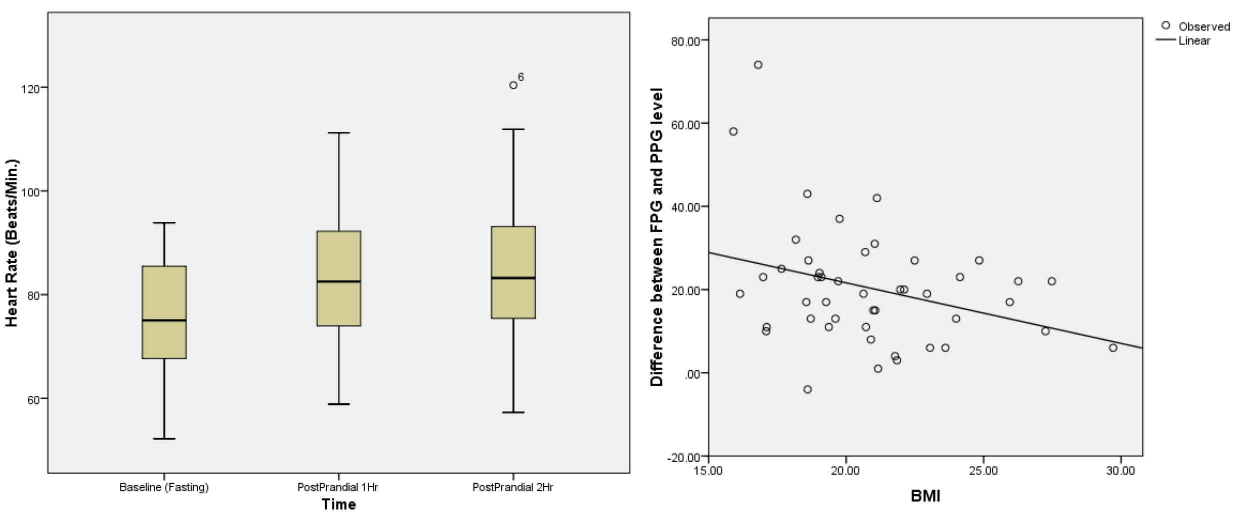
Table 3: Time and frequency domain HRV measures during fasting and postprandial glucose ingestion

Parameters	Fasting	Postprandial 1Hr	Postprandial 2Hr
Heart Rate (Beats/min.)	74.83 ± 10.38	83.57 ± 11.97 (r=.81, p=9.17x10-12)	84.79 ± 13.30 (r=.80, p=2.02x10-11)
SDNN (ms)	55.50 ± 18.31	42.93 ± 18.08 (r=.79, p=6.27x10-11)	42.98 ± 16.78 (r=.73, p=1.05x10-8)
RMSSD (ms)	49.81 ± 23.53	34.95 ± 18.79 (r=.78, p=2.27x10-10)	35.79 ± 18.96 (r=.68, p=2.18x10-7)
SDSD (ms)	49.89 ± 23.59	35.44 ± 19.71 (r=.78, p=2.51x10-10)	36.56 ± 20.24 (r=.69, p=1.14x10-7)
pRR50 (%)	26.32 ± 20.00	15.21 ± 15.77 (r=.81, p=9.21x10-12)	15.67 ± 16.24 (r=.77, p=3.81x10-10)
L.F. Power (n.u.)	50.70 ± 17.85	54.67 ± 16.84 (r=.62, p=3.89x10-6)	56.14 ± 17.89 (r=.30, p=0.045)
H.F. Power (n.u.)	44.31 ± 16.47	40.07 ± 16.26 (r=.66, p=5.24x10-7)	38.84 ± 16.79 (r=.44, p=0.0023)
Total Power (μs2)	3032.9 ± 1722.6	1749.2 ± 1302(r=.62, p=3.97x10-6)	1701 ± 1212 (r=.52, p=0.00023)
LF/HF	1.40 ± 0.9	1.66 ± 0.92 (r=.56, p=5.28x10-5)	1.83 ± 1.13 (r=.26, p=0.081)

Data are represented as mean± SD

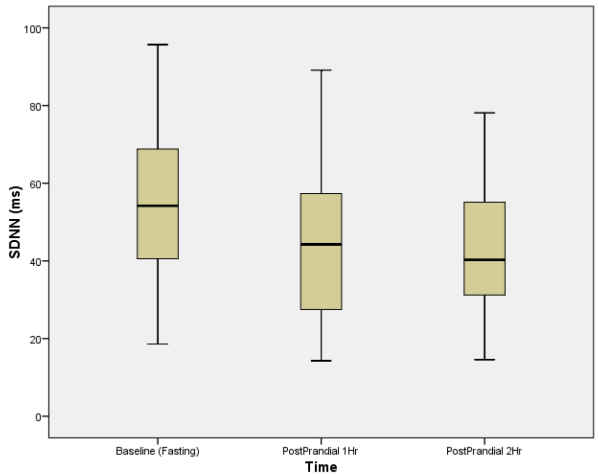
4. RESULTS

The response to glucose load on HRV measures is presented in Table 3. The mean heart rate during fasting was 74.83 ± 10.38 and significantly increased to 83.57 ± 11.97 (r=.81, p=9.17x10-12) during PP1H response and further increased to 84.79 ± 13.30 (r=.80, p=2.02x10-11) during PP2H response. The box plot for the heart rate is shown in Fig. 1(a). The blood glucose response was also affected by the BMI. The higher BMI subjects showed less change in blood glucose level (r=.27, p=0.07) as shown in Fig. 1(b).

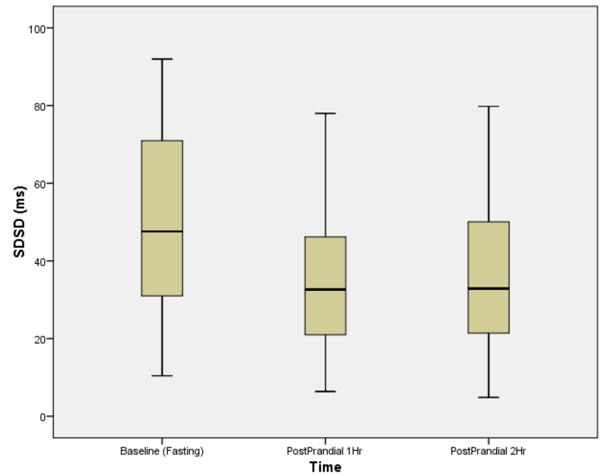


Heart rate (b) Blood glucose level

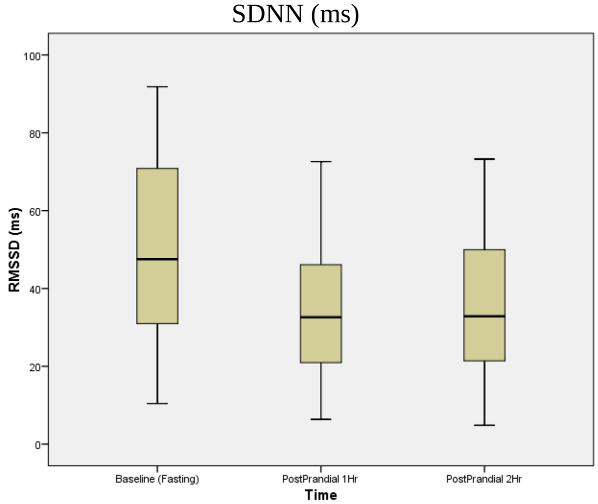
Fig.1: Response of glucose ingestion on heart rate and blood glucose level



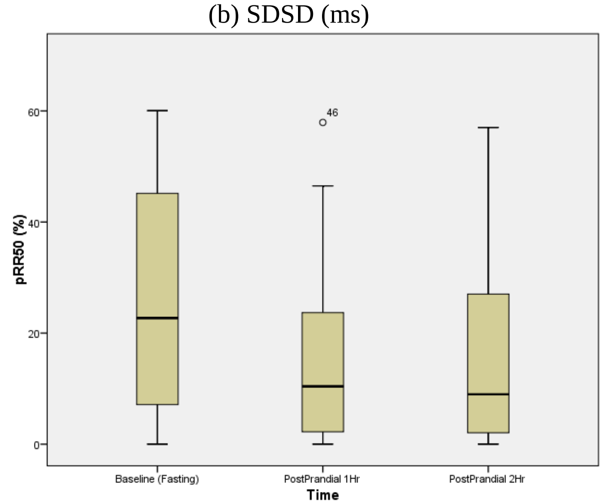
SDNN (ms)



(b) SDSD (ms)



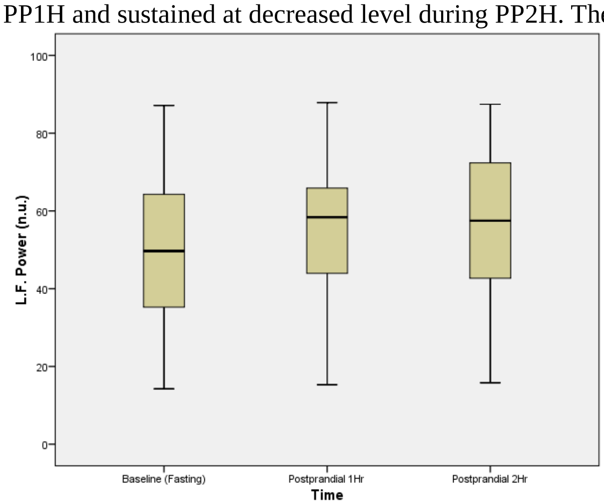
(c) RMSSD (ms)



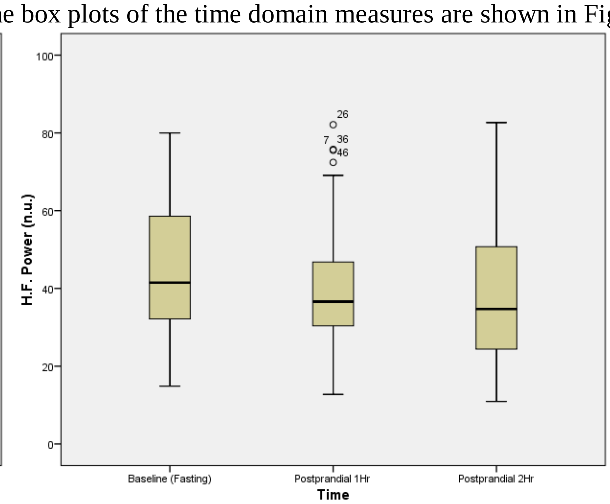
(d) pRR50 (%)

Fig. 2: Box plot of time domain measures of HRV during fasting, PP1H 1and PP2H

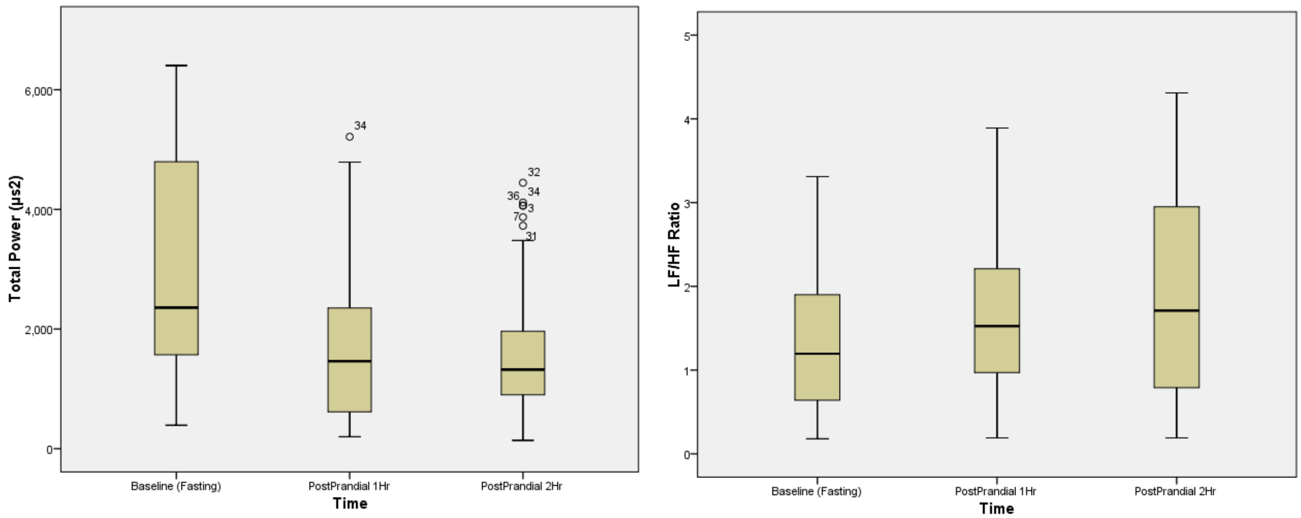
The SDNN, the square root of the variance reduced from 55.50 ± 18.31 to 42.93 ± 18.08 (r=.79, p=6.27x10-11) during PP1H and sustained at decreased level during PP2H. The mean RMSSD decreased significantly (r=.78, p=2.27x10-10) during PP1H and sustained at decreased level during PP2H (r=.73, p=1.05x10-8). The SDSD also responded in the same way as RMSSD. The mean pRR50 also decreased significantly from 26.32 ± 20.00 to 15.21 ± 15.77 (r=.81, p=9.21x10-12) during PP1H and sustained at decreased level during PP2H. The box plots of the time domain measures are shown in Fig. 2.



Low frequency power



(b) High frequency power



(c) Total power (d) LF/HF ratio

Fig. 3: Box plot of frequency domain measures of HRV during fasting, PP1H and PP2H

In the frequency domain, the mean normalized LF power significantly increased from 50.70 ± 17.85 to 54.67 ± 16.84 (r=.62, p=3.89x10-6) during PP1H and further increased to 56.14 ± 17.89 (r=.30, p=0.045) during PP2H. Similar trend was obtained for mean LF/HF ratio which significantly increased from 1.40 ± 0.9 to 1.66 ± 0.92 (r=.56, p=5.28x10-5) during PP1H and further increased to 1.83 ± 1.13 (r=.26, p=0.081) during PP2H. The normalized HF power and TP showed reduced response with glucose ingestion. The mean HF power significantly decreased from 44.31 ± 16.47 to 40.07 ± 16.26 (r=.66, p=5.24x10-7) during PP1H and further decreased to 38.84 ± 16.79 (r=.44, p<.05) during PP2H. Similarly the TP reduced from 3032.9 ± 1722.6 to 1749.2 ± 1302 (r=.62, p=3.97x10-6) during PP1H and further reduced to 1701 ± 1212 (r=.52, p<.001) during PP2H response. The box plots for frequency domain measures are shown in Fig. 3.

Thus the study suggests that the HRV may be related to the blood glucose level even in healthy young adults. Since the HRV measurement is noninvasive method, it can be helpful in determining the blood glucose level noninvasively which could be a great advantage over the present system.

5. DISCUSSION

The present study analyzed the effect of glucose load on autonomic nervous system. The changes are characterized as stimulating response of sympathetic activity and attenuation of parasympathetic activity.

The effect of glucose ingestion with time on sympathetic nervous system has been reported in many studies. Wang R et al25 compared OGTT response on normal and obese subject, Fagius J et al22 analyzed muscle nerve sympathetic activity after glucose intake, Matsuda M et al23 found insulin sensitivity during OGTT, Scott EM et al24 reported sympathetic activation and vasodilatation with carbohydrate ingestion. In these studies, the peak blood glucose and insulin level in normal healthy adults found maximum after 60 minutes of glucose ingestion and thereafter decreased slightly. In consistent with these studies, our study also showed increased heart rate at PP1H and further increased PP2H response due to increased sympathetic modulation of the sinoatrial node of the heart.

Similar response was obtained for LF Power and LF/HF ratio which were also in support with earlier research studies by Weissman A et al16 in power spectral analysis of HRV during OGTT in pregnant women, Straznicky NE et al17 in the study of insulin resistant and insulin sensitive subjects, Jaiswal M18 et al in the study of reduced HRV in type 1 diabetes. The increased LF power and LF/HF ratio implicates the sympathetic overdrive on HRV by autonomic nervous system. The increased LF/HF ratio implies decrease in HF power with increase in LF power depicting parasympathetic withdrawal with glucose ingestion.

The other HRV parameters e.g. HF power, Total power, SDNN, RMSSD, SDSD, pRR50 showed decreased PP1H and PP2H response which are marker of parasympathetic loss [18]. Few subjects showed outliers in the box plot for HF power and total power. This may be due to the involvement of the subjects in the physical or mental activities during PP1H and PP2H measurements.

Conflict of interest:The authors have no conflict of interest.

6. References

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