Poincaré plot of fingertip photoplethysmogram pulse amplitude suitable to assess diabetes status

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***Abstract*— Multiscale entropy (MSE), an estimate of the complexity of physiological signals has been used for assessing diabetes status. This method requires much computation effort. Our study aimed to examine the Poincaré plot, an easier method for computation to differentiate the diabetes status. We selected subjects and divided them into three groups including the non-diabetes (HbA1c ≤ 6.5%, n=22), diabetes with good control (6.5% < HbA1c < 8%, n=23), and diabetes with poor control (HbA1c ≥ 8%, n=17). Poincaré method used consecutive 250 data points of PPG pulse amplitudes from each subject's right index fingertip. This method resulted in SSR, the standard deviation of the original photoplethysmogram (PPG) pulse amplitude (SD1) and the standard deviation of the interval 1 PPG pulse amplitude (SD2) ratio. The SSR in the three groups of non-diabetes, diabetes with good control and diabetes with poor control were 0.50, 0.28, and 0.23, respectively and differed between groups (P < 0.05). Our findings suggested that the Poincaré plot of right-hand PPG pulse amplitude may be convenient to evaluate diabetes status.**

Keywords-- Poincaré plot; photoplethysmogram (PPG) pulse amplitudes; fingertip; diabetes;

I. INTRODUCTION

Multiscale entropy (MSE) analysis is useful for investigating the impact of diabetes on Pulse Wave Velocity (PWV). This method is important to reflect diabetes control [1]. The previous study exposed that the signal numbers measuring in MSE had to be larger than 750 data points to reduce an error, especially on large-scale factors [2]. In addition, collecting physiological signals of pulse rate to obtain available data in the MSE analysis require approximately 20 minutes. This requires more or less 60-100 beats pulse per minute.

Several studies have been employed the number of points data to get the optimal time for analyzing physiological signals. Choi applied of MSE using 1000 points signals from Electroencephalograph (EEG) (3). Whereas Chang et al compare the changes to the value of sample entropy using MSE and short MSE (sMSE) approaches with different scale factors on 600 successive white-noise signals (4). Furthermore, Yang et al evaluated the blood flow in the former and later acupuncture on 350-400 R-R interval signals in healthy patients (5).

The Poincaré plot is a famous method to visualize the non-linear system, such like autonomic nervous function in time series [6]. This plot can represent the complexity of cardiovascular such as diabetes. In the current study, we used the Poincaré plot to assist in the interpretation of 250 points data right finger PPG pulse amplitude to characterize discrepancies of diabetes status.

II. MATERIALS AND METHODS

A. Study Population

In this research, we selected subjects from a clinical program at the Hualien hospital and comprised in three different groups. The group 1 including patients who have HbA1c ≤ 6.5%, namely the non-diabetes subjects (n=22), whereas the group 2 (diabetes with good control, n=23) and the group 3 (diabetes without good control, n=17) who have 6.5% < HbA1c < 8% and HbA1c ≥ 8%, respectively. This program is conducted to examine both of healthy and diabetes status of patients. All the diabetes patients were registered from the Diabetes Outpatient Clinic at the Hualien hospital between July 2009 and March 2012 and admitted to having received regular treatment and clinic care for more than two years. In terms of treatment, there were no significant differences in the type of medicine, quantity, and regularity among the patients in good and poor control diabetes. The patients were also asked to restrain from caffeinated beverages and theophylline during the treatments for eight hours before visiting the hospital. Each subject provided an informed permission, completed feedback form on demographic data, medical history and went through blood sampling prior to data acquisition. Institutional Review Board of Hualien Hospital has permitted this research [7].

B. Experiment Procedure

All of the individuals visited the clinic in the morning between 08:30 and 10:30 to collect the data on medical records, demographic information, anthropometric data, and laboratory record for the analysis. We defined the body mass index (BMI) as the weight (kilogram) / height (meter) square. The concentration of high-density lipoprotein cholesterol, cholesterol, low-density lipoprotein cholesterol, and triglycerides was noted from the sample of blood acquired after a 12-hour fast. Unwanted signals arising from impulsive ambiances of the patients required to reduce, hence the subjects relaxed in a supine position in a control room (with the temperature at 26 ± 1 °C) in ten minutes. The blood pressure was acquired just the once from the left arm of patients (this procedure used a blood pressure monitor device producing by Microlife, Taiwan) [7].

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C. Calculation of PPG pulse amplitude

The optical transducers were assembled to the fingertips of the subjects, which was then being processed through an analog-to-digital converter (ADC). This operation includes the system of USB-6009 DAQ (National Instruments, Austin, TX, USA). It was applied at frequency sampling of 500 hertz. The computer held output signals and analyzed through the Matlab 7.7 designing by MathWorks on Massachusetts, USA [7].

The potential difference between the peak and the valley of PPG pulse amplitude was defined as the PPGA signals. We subsequently retrieved consecutive 250 PPGA only of the right fingertip as:

$$\text{PPGA}= \{\text{PPGA (1), PPGA (2), . . ., PPGA (250)}\} \quad (1)$$

Huang et al suggested the empirical mode decomposition (EMD) [8] which was extracted the {PPGA(i)} series. This regressed to the zero mean series after the unwanted signals are eliminated from data in non-linear and non-stationary processes. Thereby the {PPGA(i)} series was being normalized as nPPGA in (2). In these equations, SD_{PPGA} represents the standard deviations of series {PPGA(i)}, and $\overline{PPGA}$ represents the mean of series {PPGA(i)} in (2).

$$\text{nPPGA(i)}=\frac{\text{PPGA(i)}-\overline{\text{PPGA}}}{SD_{PPGA}} \quad (2)$$

D. Poincaré plot of PPG pulse amplitudes

Poincaré plot is one method to describe an indefinite pattern of the time series signal. This method is a famous approach to identify the complexity of nonlinear signals. It also has been successfully employed in the evaluation autonomic nervous function [9,10]. In this method, there are two parameters specifically short-term variability (SD1) and long-term variability (SD2). These parameters used to quantify the information from the plot. In this current study, we used the Poincaré method to plot sequence points of nPPGA time series (i.e. lag-1 plot). It is a representation of PPGA in phase space or Cartesian plane [9].

The time series from the finite sequence of nPPGA selected, then we define a set on the time interval which was computed from N-1 points of PPGA:

$$\text{nPPGA(i)} = \{\text{nPPGA(1)}, \text{nPPGA(2)}, \dots, \text{nPPGA(249)}\} \quad (3)$$

We used a lag of one pulse amplitude of PPG to decide a delay in another time series:

$$\text{nPPGA(i + 1)} = \{\text{nPPGA(2)}, \text{nPPGA(3)}, \dots, \text{nPPGA(250)}\} \quad (4)$$

Plotting is formed by sequences of nPPGA(i) vs nPPGA(i+1), those are (nPPGA (1) vs nPPGA(2)), (nPPGA(2) vs nPPGA(3) ….. (nPPGA(249) vs nPPGA(250)). Poincaré plot achieved three indices: the standard deviation (SD) of instantaneous originally pulse amplitude of PPG [minor axis of the ellipse or SD1 in (5)], the SD of the long term nPPGA [major axis of the ellipse or SD2 in (6)], and the SD1/SD2 ratio or SSR (7) [9, 10, 11].

In this study, the definition of SSR is the SD1/SD2 with a lag of 1. Calculating of SD1, SD2, and SSR is shown in (5), (6), (7), respectively.

$$\text{SD1} = \sqrt{\text{var}(\text{nPPGA(i)} - \text{nPPGA(i + 1)}/\sqrt{2})} \quad (5)$$

$$\text{SD2} = \sqrt{\text{var}(\text{nPPGA(i)} + \text{nPPGA(i + 1)}/\sqrt{2})} \quad (6)$$

Therefore, the SSR be able to define by

$$SSR = SD1/SD2 \quad (7)$$

E. Statistical Analysis

In this study, an independent sample t-test was used to determine the significant differences in age, height, weight, waist circumference, and body mass index (anthropometric), hemodynamic, and other parameters (i.e. SSR). The nonparametric Mann-Whitney analysis is applied when the data were normally distributed. Expressing values of average declared as the mean ± standard deviation. Statistical package for the social science (SPSS) in version 22.0 for Windows is used for all the analysis. A probability value, p, of ≤ 0.05 were denoted statistically significant.

III. ANALYSIS AND RESULTS

The baseline characteristics of each group were shown in Table I. All of the groups namely, non-diabetes (Group 1), diabetes with good control (Group 2) and diabetes without good control (Group 3) was relatively similar in height, weight, waist circumference, Body Mass Index (BMI), Diastolic Blood Pressure (DBP), and triglycerides. The comparison between the diabetes subjects with good control and those without good control revealed that control had higher Systolic Blood Pressure (SBP), cholesterol, triglycerides HbA1c levels, Low-Density Lipoprotein (LDL), and blood sugar.

Furthermore, The SSR in three different groups, i.e. group 1, group 2, and group 3 (non-diabetes, diabetes with good control, and diabetes without good control) are highly different from the highest to the lowest respectively. In addition, the concentration of HbA1c is a significant difference between all of the different groups as well. This result could have supported the statement in the previous findings that the larger SSR stands for more active autonomic activities [9,10].

TABLE I. DEMOGRAPHIC, ANTHROPOMETRIC, HEMODYNAMIC, BIOCHEMICAL AND ANALYTICAL PARAMETERS

	Group 1	***Group 2***	***Group 3***
Subjects number	*N=22*	*N=23*	*N=17*
M/F	10/12	15/8	10/7
Age (years)	59.86 ± 12.32	66.00 ± 7.64	58.00 ± 7.70
Height (cm)	160.45 ± 8.08	162.77 ± 8.40	161.47 ± 8.14
Weight (kg)	66.25 ± 9.99	70.33 ± 15.25	72.24 ± 14.06‡
Waist circumference (cm)	87.39 ± 9.91	91.77 ± 11.07	92.50 ± 12.20
BMI (kg/m^2)	25.74 ± 3.51	26.39 ± 4.51	27.78 ± 5.45

SBP (mmHg)	124.60 ± 20.03	119.36 ± 13.12	128.19 ± 18.18
DBP (mmHg)	71.60 ± 9.52	71.55 ± 10.06	76.94 ± 10.48
Pulse pressure (mmHg)	71.25 ± 10.75	75.64 ± 10.58	81.76 ± 11.14‡
HbA1c (%)	5.97 ± 0.35**	7.27 ± 0.69††	9.50 ± 1.80‡‡
HDL (mg/dL)	48.82 ± 18.76*	42.47 ± 17.07	42.44 ± 17.24
Cholesterol (mg/dL)	195.14 ± 35.85*	168.61 ± 26.21	179.88 ± 34.56
Triglyceride (mg/dL)	104.57 ± 45.60	117.06 ± 49.76	153.60 ± 78.09
LDL (mg/dL)	113.62 ± 26.99*	94.06 ± 23.07†	109.81 ± 29.40
Blood Sugar AC (mg/dL)	111.38 ± 29.43	129.56 ± 8.64†	188.81 ± 49.52‡
SSR	0.50 ± 0.16**	0.28 ± 0.08†	0.23 ± 0.12‡‡

Age: Group 1 range 38-81; Group 2 range 51-80; Group 3 range 44-71
*$P < 0.05$ Group 1 vs. Group 2,
**$P < 0.001$ Group 1 vs. Group 2
†$P < 0.05$ Group 2 vs Group 3
‡‡$P < 0.001$ Group 1 vs Group 3
Abbreviations: BMI, body mass index; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; HbA1c, hemoglobin A1c; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SSR, SD1 SD2 ratio;

Fig. 1, shows the correlation between HbA1c and SSR in all of the groups. The correlation (r) and p-value between HbA1c and SSR are –0.254 and 0.047 respectively. This result indicates that HbA1c and SSR have a statistically significant linear relationship ($p < 0.05$). This also describes that the SSR has the ability to determine diabetes status.

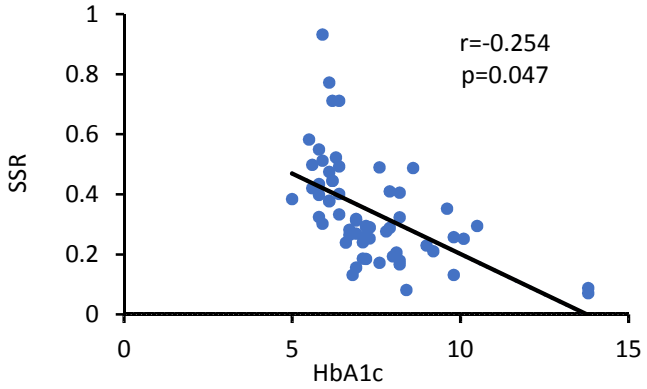

Fig. 1. Comparison between HbA1c status and SSR in all of the groups

The example of plotting between nPPGA (left side) and the Poincaré plot (right side) in three different groups from one subject is shown in Fig. 2. On the left side, showing the relationship between the number of points from PPG signal and the amplitude. As it is shown, the figure of non-diabetes and diabetes with good control is highly similar, therefore, it is difficult to determine the discrepancies between the two groups. However, it can clearly be seen from the right side of Fig. 2, that there were differences in the size of scatering plot between the three different groups. In addition, the SSR in the three different groups is significantly different with the highest value being reached by non-diabetes subjects (0.52) followed by diabetes with good control and diabetes without good control, which was recorded at 0.31 and 0.23, respectively.

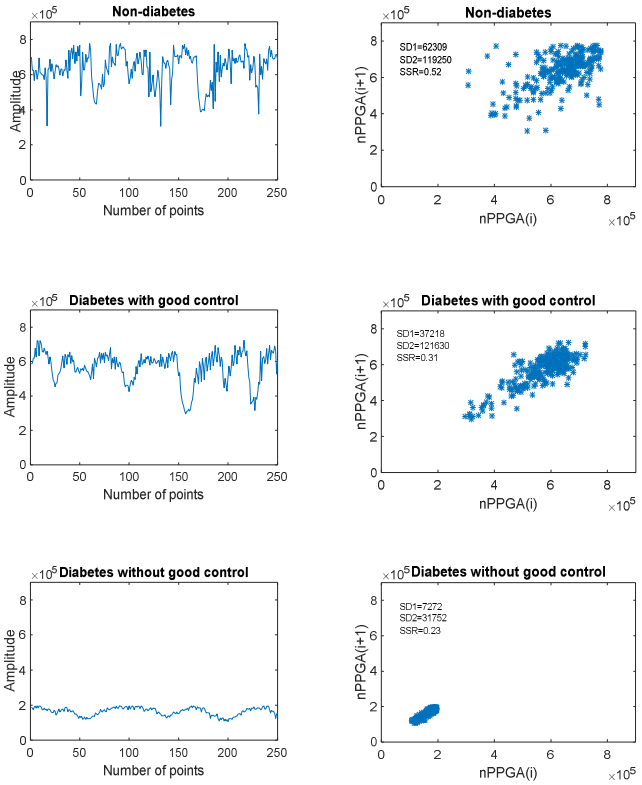

Fig. 2. nPPGA and Poincaré plots of right fingers in non-diabetes subjects, diabetes with good control, and diabetes without good control.

IV. DISCUSSION AND STUDY LIMITATIONS

In the previously study, we used multiscale cross approximately entropy (MCAE) to analyze the PPG pulse amplitudes of bilateral index fingertip (left and right) in the middle-to-old individuals and revealed that the signal from the right finger was more challenging for analysis than the left finger [12]. Therefore, in this present study, we used only PPG pulse amplitude from the right finger.

In this study, we used only the 250 points PPG pulse amplitude. Meaning that the SSR poses a serious challenge to assess the PPG signal within a short period. In addition, when compared with the simultaneous blood pressure measurement using sphygmomanometer cuffs on upper arms, the PPG has the advantages of being more comfortable, economical, and it also can allow continuous measurement without the need for repeated pressure cuff inflations.

Our result indicates that SSR did show significant differences between the groups. SD1 indicates short term variability, which has been shown to correlate to the high-frequency component as shown in the left figure in Fig. 2. Therefore, indicates a decreasing in the effect of the parasympathetic component of autonomic nervous system. SSR also reduced which reflect the change in modulation of the heart rate as SD2 increased. This result is similar with previous study conducting by Hanin, et al [13].

Poincaré plot is an obviously effective method to identify significant difference among study groups, however, we still have limitations. First, we used fewer data in this study, therefore we need more subject to investigate. Second, the medicine treatments such antihypertensive, hypoglycemic, may also affect autonomic nervous activity. Nevertheless, it is hard to assess these influences in the statistical analysis, hence the impact of medication was not considered.

V. CONCLUSIONS

The main finding of this study was that the right fingertip PPGA could be used for SSR analysis to evaluate subjects controlling by HbA1c ≤ 6.5%, 6.5% < HbA1c < 8%, and HbA1c ≥ 8%, respectively. In conclusion, our findings suggested that the Poincaré plot of the right fingertip could be a practical non-invasive approach to reflecting the diabetes status.

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