Effect of Dyslipidemia on Photoplethysmography Flow Mediated Dilation

M. Zaheditochai, E. Zahedi, M.A. Mohd Ali

Abstract **Dyslipidemia (high level of cholesterol in blood) is considered as one of the main heart risk factors affecting the endothelial vascular function. This function can be non-invasively studied by ultrasound flow-mediated dilation (US-FMD), but with all disadvantages of a high-cost and operator-dependent technique. In this paper, the effect of dyslipidemia on the photoplethysmogram (PPG) signal recorded from the index finger is investigated, as it has been recently shown that FMD can also be studied using PPG. To this end, PPG signals were acquired from two groups: the first group consists of 31 healthy subjects free from any risk factors and the second group 31 subjects who have only one risk factor: dyslipidemia. The plot of AC (peak-to-peak) values versus time of the PPG after flow release following 4 minutes of brachial artery blockage was considered representative of the FMD. Results show that there is a significant difference between the time that the AC value remains above 35% of it's maximum in the two groups (p-value < 5%) pointing to a new index which could assist the physician assessing vascular risk in a non-invasive way.**

Keywords: **Vascular characterization, brachial artery blockage, vascular dilation.**

I. Introduction

Atherosclerosis is one of the main major causes of cardiovascular disease. Several risk factors such as smoking, high blood pressure, diabetes and high level of the cholesterol in the blood (dyslipidemia) may lead to developing atherosclerosis. It would be helpful to find an index which is capable to assess the atherosclerosis due to vascular endothelial dysfunction.

FMD measurement is known as an effective method to evaluate endothelial dysfunction to be used in early detection of atherosclerosis [1], [2]. This technique shows the ability of the vascular bed under study to self-regulate tone, control the blood flow and distribution in response to either physical or pharmacologic stimuli. Non-invasive methods have also been developed to measure FMD with the most popular one the ultrasound FMD [3], [4], [5], [6]. Unfortunately the latter method proves to be expensive due to the equipment involved, prone to errors requiring an experienced operator.

More recently, another non-invasive method based on photoplethysmography has been developed (PPG FMD) [7] where PPG pulse amplitude changes due to flow-mediated dilation in finger are recorded following a 4 minutes brachial artery occlusion.

Considering the effects of risk factors, it was found that photoplethysmography AC curves followed closely the US-FMD responses (good correlation) except for subjects who had more than one risk factor. The investigated risk factors were obesity, diabetes, hypertension and hypercholesterolemia [8].

This is why in the present study, the focus is on one risk factor only: dyslipidemia using the data recorded in [7]. We considered how PPG-FMD data can be influenced by this risk factor versus healthy subjects.

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II. Methods

A. Data Acquisition

The source of the raw database is from Universiti Kebangsaan Malaysia (UKM) [7]. As factors such as temperature, food, drug, caffeine and sympathetic stimuli that affect vascular flow-mediated vasodilation, each subject adhered to a strict diet protocol before experimentation.

Photoplethysmography signals were simultaneously recorded from fingers of both right and left hand without any blockage in order to establish the baseline.

The left hand PPG was the reference, and a blood-pressure cuff was used to create flow blockage (stimulus) in the brachial artery of the right arm. The cuff was inflated to the suprasystolic pressure (50 mmHg above the subject's systolic blood pressure) inducing total arterial occlusion. After 4 minutes occlusion the flow was established again by rapid cuff deflation, followed by reactive hyperemia in the brachial artery and subsequent dilation.

The artery diameter is increased to it's peak value and then decreases back to the baseline, as indicated in FMD. PPG signals are being recorded from both hands [7], [3] during the whole process at a final sampling rate of 50 Hz.

B. Signal Processing

MATLAB (The Math works, Inc.) was used for signal processing. PPG signals contain both DC and AC components: the DC is related to respiration, sympathetic nervous system activity and thermoregulation while AC parameter is referred to the cardiac synchronous changes with each heart beat in skin micro-vascular blood volume [9].

The DC of the signal was first removed and then the AC value was extracted. PPG AC refers to the difference between the amplitudes of the valley and the peak of the same heart cycle in the PPG signal. As the AC curves are subject dependent, the data were normalized as follows.

Given the 4 signals; 2 signals before blockage (for left and right hand) and 2 signals after cuff deflation (for left and right hand), the data before occlusion were used to normalize data after occlusion.

We assume that the difference between the mean value (M) of PPG AC of the left (L) and right (R) hands are equal before occlusion and after it. Therefore, the effect of hyperemia is removed from the baseline by Equation (1) which computes the new baseline (M (R_{after})).

$$M(L_{Before}) - M(R_{Before}) = M(L_{After}) - M(R_{After})$$
$$M(R_{After}) = new\ baseline \quad (1)$$

After the first step, Equation (2) shows the normalized value for each subject based on its new baseline.

$$T_{new} = \frac{T_{old} - new\ baseline}{new\ baseline} \times 100\% \quad (2)$$

III. RESULTS

Two groups of healthy and dyslipidemia subjects consisting of 31 subjects in each group are considered.

A typical PPG %AC change from a subject in the healthy group is shown in Fig. 1 where the curve reaches it's peak value and decreases to the baseline. In other words, after hyperemia the diameter of the micro vascular blood bed volume is first increased and then decreased to its normal size.

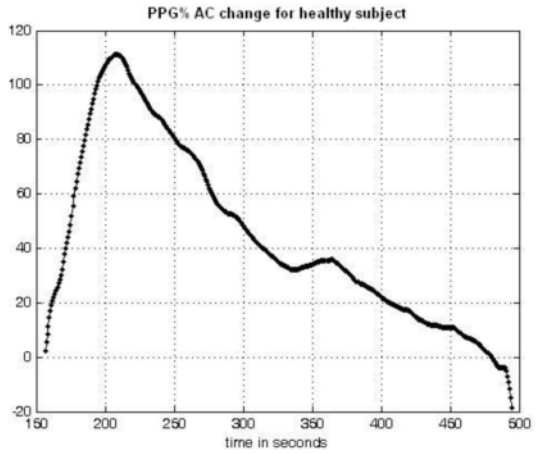

Fig. 1: PPG %AC change for a typical healthy subject after cuff deflation.

Fig. 2 shows the same data for a subject who has dyslipidemia. As it can be seen, the curve reaches the peak but goes down with some delay compared to the healthy subject (Fig. 1). It was observed that in some subjects the plot did not even reach the baseline again. This means that the diameter of the vascular bed increases due to hyperemia but it cannot return to its normal size as sharply as it occurred in healthy subjects.

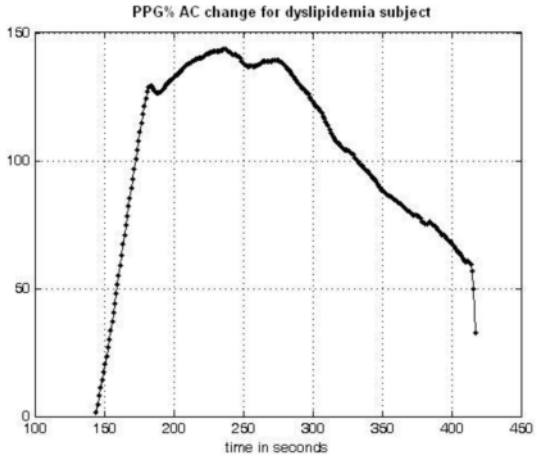

Fig. 2: PPG %AC change for a typical dyslipidemia subject after cuff deflation.

To make a quantitative analysis, a feature is needed to show that vascular diameter of dyslipidemia subjects stays on its dilated size longer than healthy subject.

To this end, the duration for which data points were higher than 35% of maximum value of the peak PPG %AC value were extracted (Fig. 3). This feature is referred to as "Time" in the following graphs.

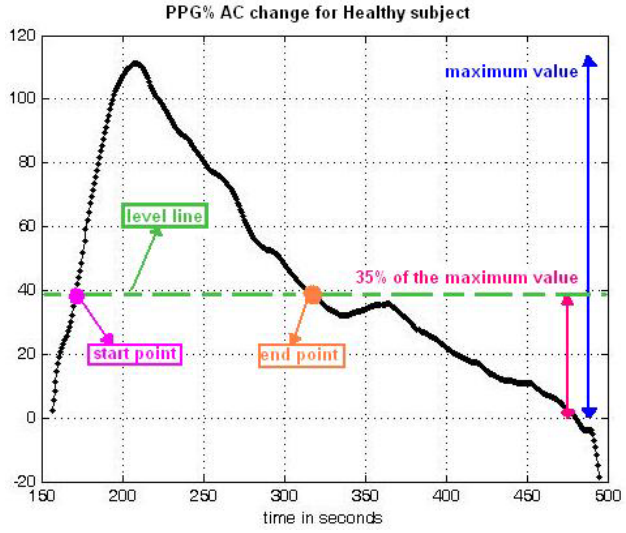

Fig. 3: Determination of the feature of interest ("Time" = duration data points remain > 35% maximum) in a healthy subject

The value of 35% was found through experimentation to be the threshold.

Fig. 4 shows the distribution of the feature defined above for the 2 groups of healthy and pathologic subjects whereas the bold line shows a fitted Gaussian distribution. The histogram hints to a difference between these groups.

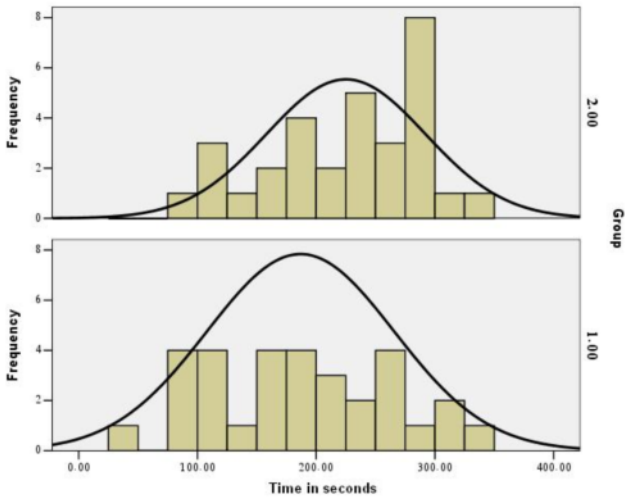

Fig. 4: Histogram of 2 groups. (a): Pathological group. (b): Healthy group.

Fig. 5 illustrates the probability-probability (P-P) plot, checked here to ascertain applicability of statistical tests such as T-Test.

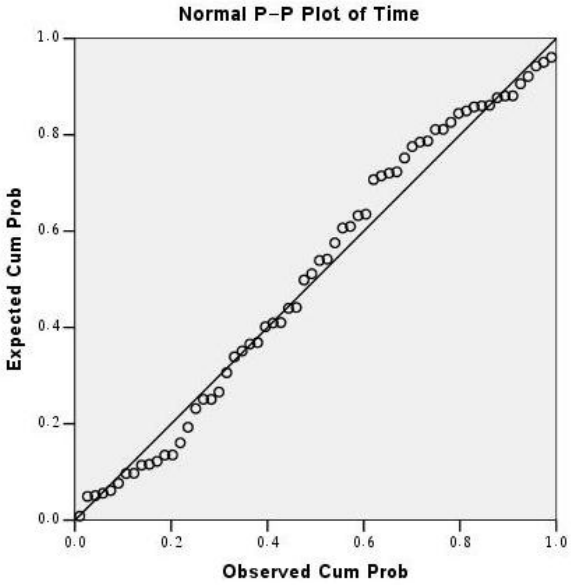

Fig. 5: P-P Plot of the data.

Results of t-test show that the mean of the 2 groups are significantly different (p-value of 4.4%) and that the 95% confidence interval of the difference for means is from -75.4 to -1.0.

The box-and-whisker diagram and error plots are illustrated in Fig. 6 and Fig. 7 respectively.

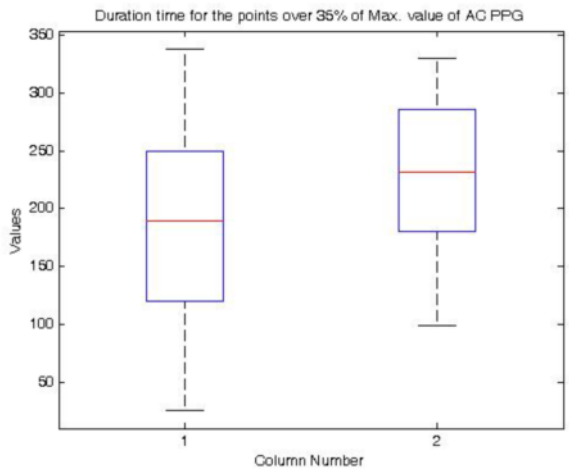

Fig. 6: Box-and-whisker diagram of two groups. First column is for healthy subjects and second column is for the dyslipidemia subject.

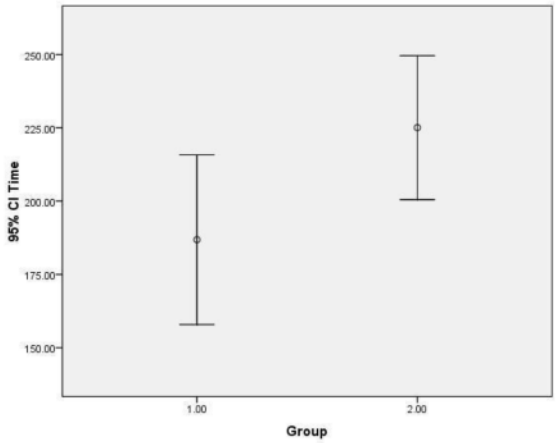

Fig. 7: Error plot of two groups. First group is for healthy subjects and second group is for the dyslipidemia subject.

CONCLUSION

A significant difference between healthy and dyslipidemia groups does exist for the specific PPG-related feature hereby defined.

The physiological reason for this observed phenomenon is still under study: it may be that in healthy subjects, the vascular function is better controlled affecting the behavior of its diameter after hyperemia, but in pathologic subjects this function is altered.

Another area to be explored is to study a larger population and other risk factors to eventually reach a useful index assisting physicians in their diagnostic of the vascular health.

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