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Application of Photoplethysmography for Vascular Health Assessment in Healthy Individuals: A Novel Methodology

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Abstract

The research investigates using photoplethysmography (PPG) for assessing endothelial function, crucial in understanding cardiovascular diseases. Factors such as smoking, high blood pressure, cholesterol, obesity, and diabetes significantly affect cardiovascular health by damaging blood vessels and increasing heart strain. It measured HbAIc, FBG, Lipid profile, and calculation BMI. Using the Flow-Mediated Dilation (FMD) method, which requires complex equipment and expertise, PPG offers a simpler alternative. By analyzing Pulse Transit Time (PTT) and Digital Pulse Wave (DPW) amplitude after induced blood flow increase (reactive hyperemia), PPG serves as a non-invasive measure for evaluating vascular health, indicating early signs of cardiovascular problems. **Methods**: 30 Healthy Adhering to ethical standards, the cross-sectional study involved males, ensuring a baseline of metabolic health through measurement of HbA1c, FBG, lipid profile, and calculation of BMI. The measurements were within a normal range. The methodology entailed a standardized protocol for inducing and measuring RH, with signal analysis performed via Lab Chart Pro 7® software.

Results: Significant findings include increases in PTT and DPW amplitude during RH, indicating PPG's efficacy in detecting endothelial function changes comparable to FMD. These results validate PPG's potential for broader clinical and research applications, given its simplicity and non-invasiveness.

In conclusion, PPG emerges as a promising tool for non-invasively assessing endothelial function, offering insights into vascular health and the progression of cardiovascular diseases. The study underscores the importance of innovative methodologies in enhancing cardiovascular disease management and prevention strategies.

Keywords: Photoplethysmography, endothelial function, Flow-Mediated Dilation, reactive hyperemia, cardiovascular diseases, HbAIc, FBG, Lipid profile.

Introduction

Cardiovascular diseases represent the most prevalent communicable conditions globally, contributing to nearly one-third of all deaths worldwide **(1)**. Several modifiable risk factors, including body mass index, systolic blood pressure, low-density lipoprotein cholesterol levels, smoking, and diabetes, contribute to the incidence and prevalence of cardiovascular diseases. However, the degree of their impact varies depending on the population studied and the methodologies used. These risk factors are also incorporated into current risk models designed to estimate the 10-year likelihood of cardiovascular events, though they are assigned different levels of importance in such models **(2)**. Furthermore, these risk factors exhibit diverse relationships with

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cardiovascular and non-cardiovascular outcomes. For instance, tobacco use is highly associated with premature death, while elevated blood pressure and non-high-density lipoprotein cholesterol levels are more specifically linked to cardiovascular conditions **(3)**. Additionally, hyperglycemia can exacerbate endothelial dysfunction by promoting the peroxidation of low-density lipoprotein cholesterol, potentially leading to atherosclerotic plaque formation in arterial walls **(4,5)**.

Traditionally, Flow-Mediated Dilation (FMD) of the brachial artery has been the gold standard for the non-invasive evaluation of endothelial function. This technique measures the vasodilatory response to increased shear stress following temporary arterial occlusion and heavily depends on ultrasound imaging to assess changes in arterial diameter, which serves as a marker of endothelial health. However, despite its diagnostic utility, FMD is limited by the need for sophisticated imaging technology and considerable operator expertise, making it less feasible for widespread use, particularly in resource-limited settings or large-scale epidemiological studies **(6).**

In light of these limitations, this study suggests photoplethysmography (PPG) as a potential alternative for assessing endothelial function. PPG is a non-invasive, optically based technique that monitors variations in blood volume within the microvasculature of tissues. Its simplicity, cost-effectiveness, and ability to capture dynamic blood flow and vessel wall properties, such as Pulse Transit Time (PTT) and Digital Pulse Wave (DPW) amplitude, make it a promising tool for clinical and research applications. PTT measures the time it takes for a pulse wave to travel between two arterial sites, while DPW amplitude reflects the magnitude of the pulse wave. Both parameters are influenced by vascular tone and elasticity, which are closely related to endothelial function **(7)**.

This research aims to delve into the efficacy of PPG, focusing on PTT and DPW amplitude, as surrogates for the traditional FMD method in the assessment of endothelial function during reactive hyperemia (RH) a physiological response following arterial occlusion. By comparing these innovative PPG-derived metrics with established FMD outcomes, the study endeavors to underscore the potential of PPG in bridging the gap between the need for accurate endothelial function assessment and the limitations posed by current methodologies. Through this investigation, we aspire to enrich the scientific community's understanding of endothelial dynamics, contributing to the broader field of cardiovascular physiology and medical chemistry, and paving the way for improved preventive and therapeutic strategies against cardiovascular diseases **(8).**

Subjects and methods

Ethics statement

The Ethics Committee of the College of Medicine, Iraqi University, accepted the study protocol. The protocols for this study were fully following the 2013 Helsinki Declaration. All participants in the study gave their informed permission.

Participants

This cross-sectional study enrolled 30 healthy male subjects, aged approximately 22 years, without any history of major illnesses. Inclusion criteria necessitated participants to have normal cumulative sugar and lipid profiles, establishing a baseline of metabolic health. Before testing, subjects were instructed to fast for at least two hours, abstain from consuming tea, coffee, and tobacco, and avoid strenuous physical activities for 12 hours to minimize any confounding effects on the measurements.

Methodology:

Blood and Serum Collection:

Five milliliters of blood samples were collected from both patients and controls as follows:

1. Two milliliters of blood were collected in EDTA tubes for the HbA1c test.

2. Three milliliters of blood were collected in gel tubes and left at room temperature for 20 minutes. After coagulation, the serum was separated by centrifugation in 2000 xg for 10 minutes and then divided into small aliquots for:

- Immediate measurements of serum sugar and lipid profile.

Body Mass Index (BMI) Calculation:

BMI, a simple index of weight for height, was used to categorize participants as underweight, normal weight, overweight, or obese. It was calculated by dividing the weight in kilograms by the square of the height in meters (kg/m²) using the following formula:

$$BMI = \frac{Weight\ (KG)}{Height2(m2)}$$

Metabolic Assessments:

To explore the relationship between metabolic health and endothelial function, two key metabolic tests were conducted under fasting conditions:

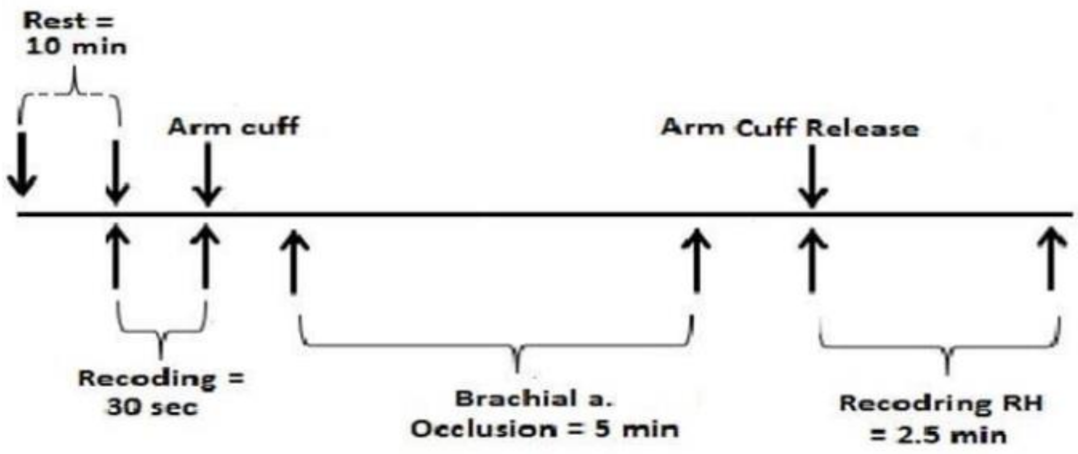
- **Cumulative Sugar Measurement:** Glycated hemoglobin (HbA1c) levels were measured to assess long-term glucose control, reflecting the average blood sugar levels over the preceding three months.
- **Lipid Profile:** A comprehensive lipid analysis was performed to determine serum concentrations of total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides. These measurements provided insights into the participants' lipid metabolism. All results from the metabolic tests were confirmed to be within normal reference ranges, affirming the metabolic health of the study population.

The methodology for evaluating endothelial function in this study involves a standardized procedure starting with participants resting supinely for 10 minutes to establish baseline conditions. The evaluation protocol includes a 30-second baseline recording, followed by a 5-minute arterial occlusion achieved by inflating a cuff to 50 mmHg above the subject's baseline systolic blood pressure. This occlusion is monitored in the absence of a photoplethysmography (PPG) signal. After the occlusion period, the cuff pressure is released to induce reactive hyperemia, with subsequent changes in blood flow recorded over a 2.5-minute period at 30-second intervals. Throughout the procedure, participants maintain a supine position with closed eyes to minimize external influences. The combination of electrocardiography (ECG) and PPG measurements before, during, and after the occlusion phase provides insights into endothelial function by assessing the vascular response to induced hyperemia.

Recorded signals were analyzed offline using LabChart Pro 7® software for parameter extraction and calculation using peak detection algorithms for ECG and PPG signals. Baseline and reactive hyperemia (RH) beat-to-beat values for parameters like PPG pulse waveform amplitude and pulse transit time (PTT) were extracted. Mean values for these parameters were calculated for the baseline and every 30-second interval during RH. The analysis compared the time course of responses during RH to baseline averages. PPG amplitude is the difference between the maximum and baseline signal voltages. PTT is the time from each ECG R wave peak to the first significant peak in the SDDPW waveform, determined with LabChart's peak detection module.

Statistics

Results were reported as means ± standard deviations. The paired Student's t-test was employed for data comparisons, with correlations performed in Excel. A p-value of ≤ 0.05 was deemed statistically significant.



A schematic drawing that outlines the protocol that was followed for FMD.

Table 1: General Serum Biochemical Tests in the Study Groups:

Tested value	Control(n=30)
	Mean ±SD
Age (years)	45.63±8.81
BMI(kg/m²)	24.79±1.62
vLDL (mg/dl)	20.79±4.68
Cholesterol(mg/dl)	157.15±18.44
T.G(mg/dl)	105.71±25.46
HDL(mg/dl)	48.16±4.98
HbA1c (%)	4.84±0.29
Glucose (mg/dl)	92.03±6.75
LDL (mg/dl)	89.85±18.23
*: (p<0.05)	

P value is calculated relative to baseline value (C, before occlusion of brachial artery). NS = Not significantly different from baseline value (C, before occlusion of brachial artery).

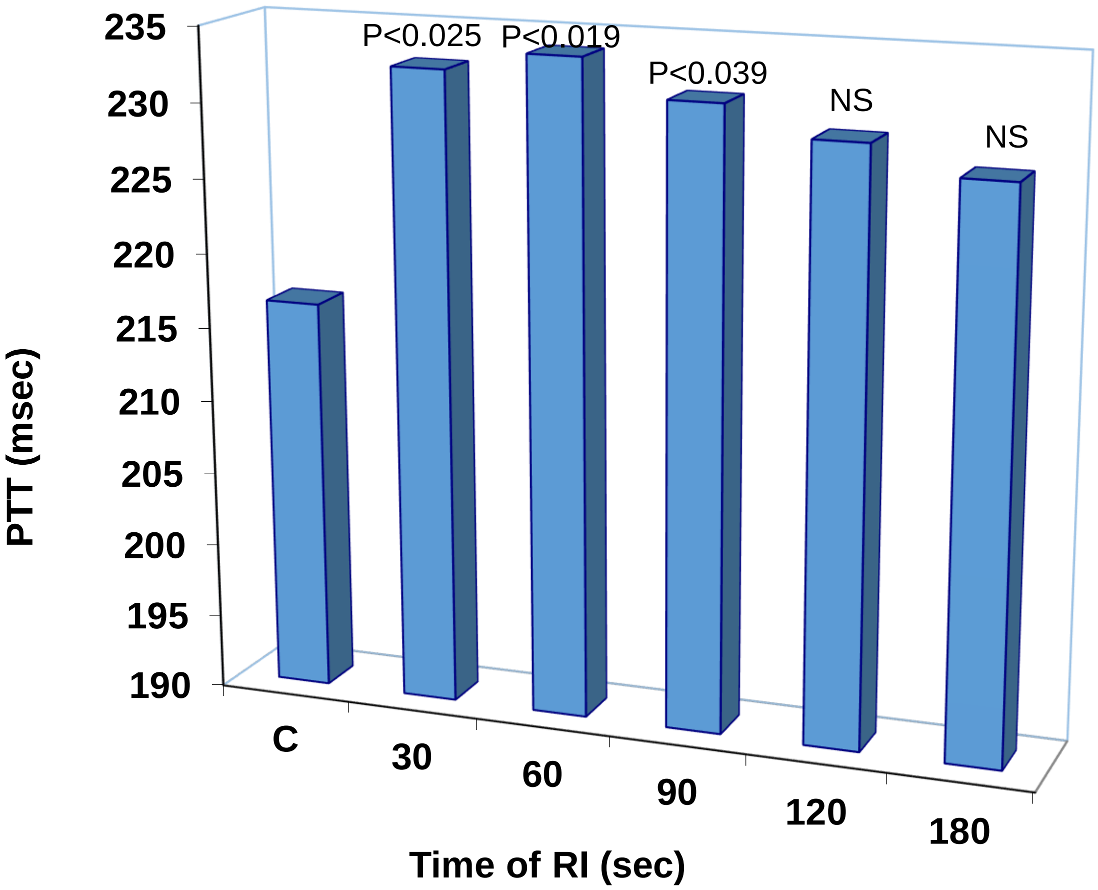


Figure 1: Pulse transit time (PTT) during reactive hypermemia (RI) after occlusion release of brachai artery . N = 20.

P value is calculated relative to baseline value (C, before occlusion of brachial artery).
NS = Not significantly different from baseline value (C, before occlusion of

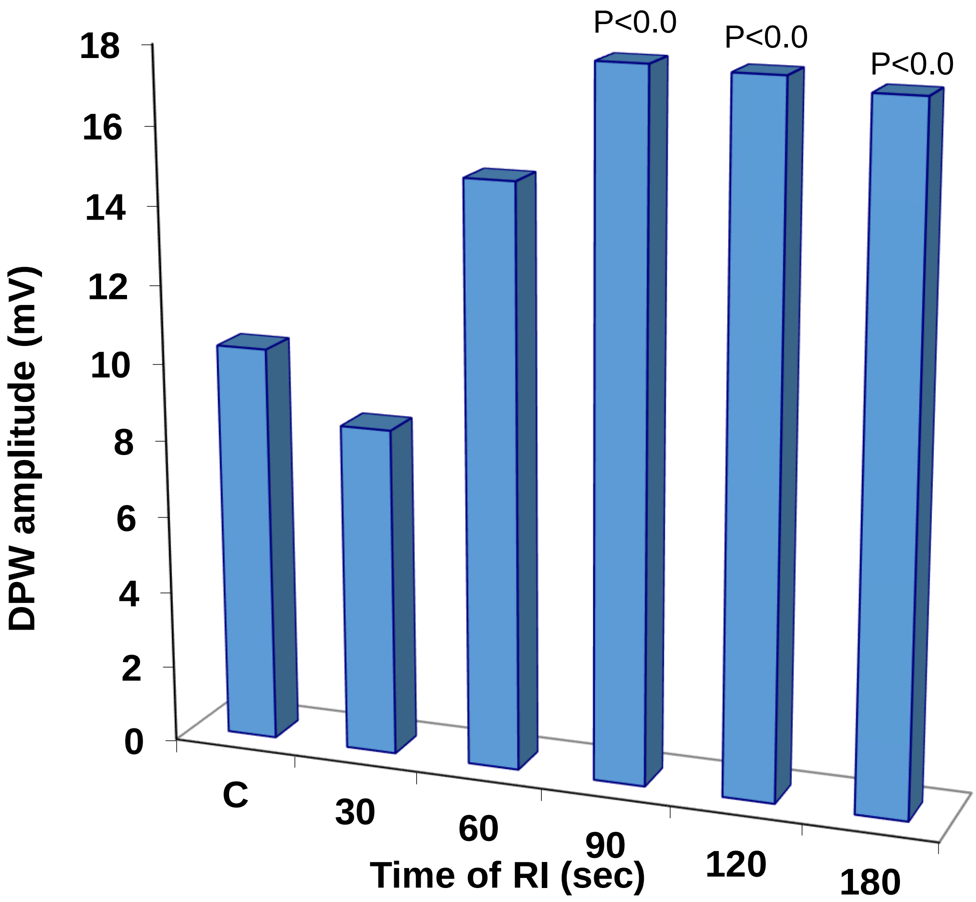


Figure 2: Digital pulse wave (DPW) amplitude during reactive hypermemia (RI) after occlusion release of brachai artery . N = 20.

Discussion:

In this study, the data presented in Table 1 reveals significant findings, primarily attributed to the healthy status of the participants, which influenced the absence of conditions such as diabetes mellitus, hyperglycemia, and related metabolic syndromes like hypertension, obesity, and dyslipidemia. These conditions are known to exacerbate the production of free radicals and diminish the body's antioxidant defense mechanisms, leading to oxidative stress. Dyslipidemia, in particular, plays a critical role in the development of atherosclerosis, a condition closely associated with an increased risk of cardiovascular diseases (CVD). The findings align with previous studies that have demonstrated similar associations between these risk factors and vascular health **(9)**.

The study group, consisting of 30 second-year medical students with a mean age of 22±0 years and an average body mass index (BMI) of 25.7±4.8 kg/m², showed notable results in terms of systolic (SBP) and diastolic blood pressure (DBP), averaging 128.5±14.2 mmHg and 74.1±16.2 mmHg, respectively. These values fall within the normal range, further confirming the health status of the participants.

During reactive hyperemia (RH), the study observed a significant increase in Pulse Transit Time (PTT), with the digital pulse wave (DPW) amplitude rising by 7.1% at 30 seconds post-occlusion, followed by increases of 8.2% and 7% at 60 and 90 seconds, respectively, compared to pre-occlusion values. These findings suggest an enhanced vascular response during RH. However, the changes in PTT at 120 and 180 seconds did not reach statistical significance, though a trend toward significance was noted at 120 seconds. In contrast, DPW amplitude demonstrated a significant rise, with a 74.4% increase at 90 seconds and sustained elevations of 73.9% and 70.6% at 120 and 180 seconds, respectively, relative to baseline measurements. The increase at 60 seconds was near significant ($P = 0.066$), indicating a robust vascular response post-occlusion.

The evolution of endothelial function assessment methods has seen a shift from invasive techniques, such as venous occlusion plethysmography, which requires arterial catheterization, to non-invasive options like ultrasound-based flow-mediated dilation (FMD) and photoplethysmography (PPG). PPG, in particular, offers a more accessible, operator-independent method of assessing endothelial dysfunction (ED) by evaluating changes in vascular tone through PTT and peripheral pulse waveform alterations during RH. This approach aligns with methodologies proposed by Nohria et al. (2006) **(10)**. The current study sought to determine whether the experimental setup could effectively detect changes in blood vessel stiffness and DPW amplitude under both normal endothelial conditions and experimentally induced dysfunction. Unlike previous studies **(11- 13)**, this study did not normalize RH indices against flow in the contralateral, non-occluded limb, thereby eliminating potential systemic influences on FMD results. Consistent with findings from **(14,15)**, the results demonstrated that maximal brachial artery dilation occurred within the first 60 seconds post-cuff release, highlighting the responsiveness of the vascular system to RH. The sustained increase in DPW amplitude further supports the utility of PPG in assessing vascular health and endothelial function.

Conclusions

Pulse Transit Time (PTT) and Digital Pulse Wave (DPW) amplitude, as measured by Photo plethysmography (PPG), have demonstrated significant potential in detecting variations in vessel wall diameter and tone during the reactive hyperemia (RH) process. These measures offer a promising non-invasive methodology for evaluating vascular aging and stiffness, providing valuable insights into the underlying health of the vascular system.

Conflict of interest: NIL

Funding: NIL

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