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Research Article

Digital Volume Pulse Analysis to Differentiate Diabetic From Non-Diabetic Subjects

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Abstract. This paper aims to examine the validity of digital volume pulse waveform index namely the *diastolic pulse peak* (Dpp) in the evaluation of type II diabetics. In total, 153 participants (115 healthy participants and 48 diabetics type II patients) are recruited during the study. A customized algorithm for DVP waveform analysis is developed in MATLAB to analyze and calculate Dpp and b/a indices. The b/a index is found to be negatively correlated with both age and HbA1C test ($r = -83.8$ and $r = -66.7$, respectively), while Dpp index is found to be positively correlated with age and HbA1C test ($r = 65.7$ and $r = 63.3$, respectively). The DVP's Dpp index showed strong association with age and HbA1C test since it remains statistically significant based on the analysis of multi-linear regression. The model revealed that b/a, age, and Dpp contribute by 71.9% of the variance in HbA1C test. The findings showed that age, b/a, and Dpp indices are promising factors in diabetes type II assessment. These findings expand the potential utility of DVP signal in clinical settings.

Keywords. DVP; Diabetics type II; Age; HbA1C test; Arterial stiffness

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1. Introduction

The HbA1C test represents an important indicator of diabetic type II glucose level average during the last two to three months [1–3]. It was recognized by the ADA as a diabetes diagnostic test in 2009 [4]. It also used widely for the diagnosis, screening, and managing of diabetes patients [5]. However, its consequences can be disastrous to health [6]. This study used the HbA1C test as a reference method in diagnosis diabetes type II patients. The *digital volume pulse* (DVP) represents a circulatory waveform recorded non-invasively using the *photoplethysmogram* (PPG). The PPG is an optical method used for blood volume changes measurement in an organ[7]. The analysis of PPG waveform morphology has important clinical implications in noninvasive circulatory monitoring [8] and considered as important technology for the monitoring of unobtrusive physiological [9]. It is useful tool in examining changes in age associated atherosclerosis [10]. In addition, its waveform amplitude represents the most significant plethysmographic feature [7]. Several studies investigated the use of the non-invasive PPG technique in evaluating and detection of diabetics to investigate the association between PPG morphological changes and diabetics [9–11]. PPG is one of the most commonly displayed clinical waveforms [12]. Others highlighted the importance of using PPG waveform in the adoption of preventive measures that control different risk factors like hypertension and diabetes [13]. The evaluation of cutaneous circulation using PPG has been utilized by [14]. The second derivative of *PPG signal* (SDPTG) has been studied by several researchers seeking valuable information about cardiovascular system activities [15]. The analysis of PPG's derivatives facilitates the process of peaks and valleys detection on the original contour of PPG waveform. The present work aimed at investigating the analysis of PPG waveform application in diabetes type II patients utilizing the HbA1C test as a dependent variable in which it will be examined against the main independent variable (the predictor) PPG's Dpp index.

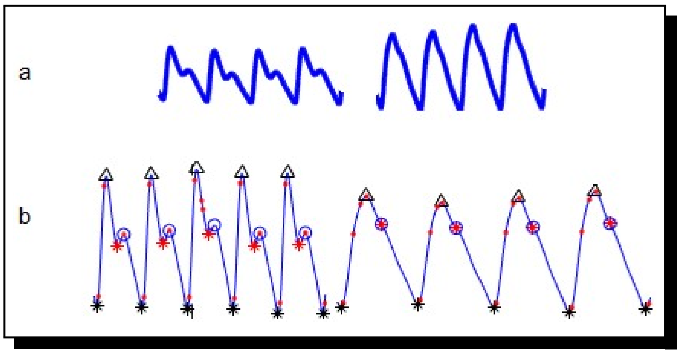

Figure 1. (a) PPG pulses for two different age group 26 and 65 years old; (b) PPG peak detection in two different age group 26 and 65 years old

2. Materials and Methods

2.1 Subjects and Methods

The study targeted the diabetic type II patients (patients with no hypertension or arrhythmia) from the internal medicine clinic in Al-Zulfi General Hospital from August to December 2018. Diabetes is determined as glycated hemoglobin (HbA1C>6.5%) [16]. At the same time lecturers, student, and staff from college of Science in Al-Zulfi (Majmaah University) are recruited as the control group after performing medical checkup and HbA1C test to ensure that they are healthy and have no diabetes. the subjects are given a questionnaire to obtain detailed information about their medical history and demographic data. Both diabetic patients and control group obtained a blood sample after 6-hours fasting to determine the glycated hemoglobin (HbA1C).

2.2 Data Collection

Participants are requested to rest in supine position in a quiet, temperature-controlled room (25±1°C) for 5 minutes, a written consent is taken from each subject declaring his agreement to participate in this work. A customized PPG device (National Instruments with data acquisition board (NI cDAQ-9172)) is used to obtain the infrared PPG waveform from the left index finger at 500 Hz sampling frequency. The recording ran for 1 minute and repeated twice to allow for the selection of best recording for each subject. The recorded signal is then de-trended to remove the outliers, drifts and offset, and any moving artifacts. Then the waveform is band-pass filtered (0.6-15 Hz) to remove any respiratory rhythm, involuntary vibrations from the examinee [17], and any disturbances from higher frequency. Distorted PPG signal and/or missing HbA1C test for any subject is excluded from the analysis. Digitized PPG signals are stored in a computer for further analysis. MATLAB software is used for PPG signal morphological analysis.

2.3 Measurement of Parameters

HbA1C test

The following methods are used commonly to measure HbA1C: immunoassay, enzymatic assays, ion-exchange high-performance liquid chromatography (HPLC), and boronate affinity HPLC [18, 19]. In this work, a blood sample for each patient is taken and checked with Diazyme, enzymatic assay method by a specialized nurse in Al Zulfi General Hospital.

The b/a index

The b/a index represents the ratio of PPG's second derivative b valley to PPG's second derivative a peak as shown in Figure 1. Many researchers, interestingly, examined the b/a index seeking relative information about cardiovascular activities. Early work by [20] has been conducted demonstrating that the b/a index reflects arterial stiffness and atherosclerosis. Moreover, [21] claimed that the value of b/a index is related to peripheral artery distensibility. The b/a index is important parameter in the diagnosis of the state of the arterial wall [2]. [15, 22–24] demonstrated that the value of b/a index is associated with atherosclerosis and aging.

The diastolic pulse peak (Dpp)

The Dpp represents the reflections of the pressure wave by arteries of the lower body back to peripherals. Dpp is calculated as the amplitude of PPG's diastolic peak. Dpp is the amplitude of inflection peak (second peak). PPG signals that have a clearly visualized second peak seem to be seen in healthy young subjects, while they tend to be less pronounced in old subjects [8]. In this work, PPG's second peak were less pronounced in diabetes patients.

2.4 Statistical Analysis

The average values of PPG indices are expressed as mean ±SD using the statistical package SPSS (version: IBM SPSS Statistics 25.0 for Windows). Pearson correlation is used to test the associations between dependent and independent variables. A P-value <0.05 was considered statistically significant. Multi-linear regression is used to investigate the contributions of *independent variables* (IVs) on the variance of the *dependent variable* (DV).

3. Results

A total of 153 subjects were participated for this study during a period of 3 months, including 115 healthy subjects (29.1±8.5) and 48 diabetics type II patients (62.1±6.8). All subjects are Saudis. Table 1 below illustrates the means and standard deviations of dependent and independent variables. In addition, Table 2 demonstrates the model summary in which the R-square value is 71.9% with a 3 degree of freedom indicating a great contribution in the variance of the dependent variable utilizing three predictors, age, b/a, and Dpp, respectively. However, ANOVA statistics as shown in Table 3 demonstrated the F ratio, which is the ratio of the Model Mean-Square to the Error Mean-Square, and since the F value (127.382) is large enough, the model rejected the null hypothesis.

Table 1. Descriptive statistics

	Mean	Std. deviation	N
HbA1C	5.8431	0.94352	153
b/a	0.6744	0.07409	153
Age	37.3268	16.42961	153
Dpp	0.5940	0.06004	153

Table 2. Model Summary[b]

Model	R	R square	Adjusted R square	Std. error of the estimate	Change statistics				
					R square change	F change	df1	df2	Sig. F change
1	0.848[a]	0.719	0.714	0.50474	0.719	127.382	3	149	0.000

[a]: Predictors: (Constant), Dpp, b/a, Age   [b]: Dependent Variable: HbA1C

Table 3. ANOVA[a]

	Model	Sum of squares	Df	Mean square	F	Sig.
1	Regression	97.356	3	32.452	127.382	0.000[b]
	Residual	37.959	149	0.255		
	Total	135.315	152			

[a]: Dependent Variable: HbA1C   [b]: Predictors: (Constant), Dpp, ba, Age

Table 4. Coefficients[a]

		Unstandardized coefficients		Standardized coefficients			Correlations		
	Model	B	Std. error	Beta	T	Sig.	Zero-order	Partial	Part
1	(Constant)	1.567	0.963		1.627	0.106			
	ba	1.598	1.013	0.125	1.578	0.117	–0.667	0.128	0.068
	Age	0.049	0.005	0.846	9.722	0.000	0.838	0.623	0.422
	Dpp	2.333	0.905	0.148	2.577	0.011	0.633	0.207	0.112

[a]: Dependent Variable: HbA1C

The interpretation of the coefficients in this model can be explained as the following:

- For every additional unit of b/a index, the expected value of HbA1C test increases by 1.598 on average, holding all other variables constant.
- For every additional year of age, the expected value of HbA1C test increases by 0.049 on average, holding all other variables constant.
- For every additional unit of Dpp, the expected value of HbA1C test increases by 2.333 on average, holding all other variables constant.

Therefore, the model generates the following equation in which it represents the contribution of the predictor variables to the dependent variable (HbA1C test):

$$\text{Expected HbA1C test value} = 1.567 + 1.598(\text{ba}) + 0.049(\text{Age}) + 2.333(\text{Dpp}). \tag{3.1}$$

4. Discussion

As several studies reported the ability of PPG waveform indices in evaluating diabetes type II [10], this research is the first one in establishing a reliable and significant diagnostic screen tool for diabetes type II using the PPG's diastolic pulse amplitude (Dpp) index. The study showed that age is the most contributor factor in the development of diabetes type II. The more we age, the more the possibility of getting diabetes type II. Figure 2 illustrates the line chart of age by HbA1C test. Still, this study aimed at investigating the Dpp index as a predictor to the variance in diabetes type II. The strong positive correlation between HbA1C test and the Dpp index introduces a new possibility of utilizing the non-invasive PPG signal in the pre-detection and diagnosis of diabetes type II.

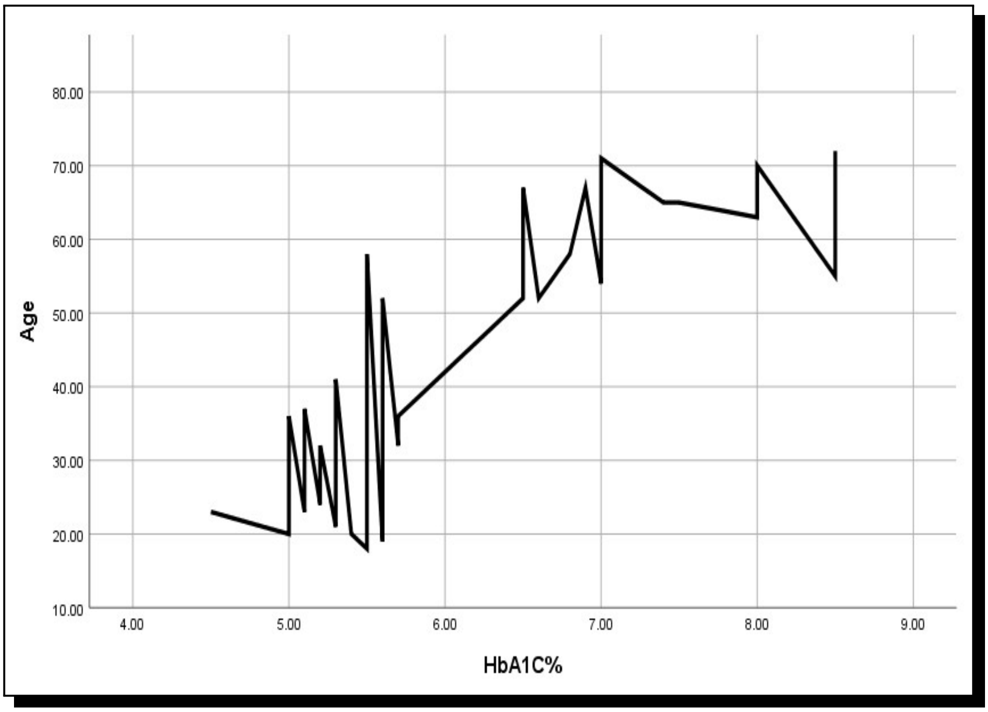

Figure 2. Line chart of Age by HbA1C%

Although the correlation between PPG's b/a index was very high, it is moved out from the multi-linear regression since it comes with no statistically significant value. However, b/a index remains a very important factor in the prediction of diabetes type II and atherosclerosis. The boxplot of Dpp by HbA1C% is shown in Figure 3 below. It illustrates that the more the amplitude of Dpp, the more the possibility of getting diabetes type II. The Dpp index remains statistically significant in the multi-linear regression which in turn strengthen the contribution of Dpp as a predictor of diabetes type II.

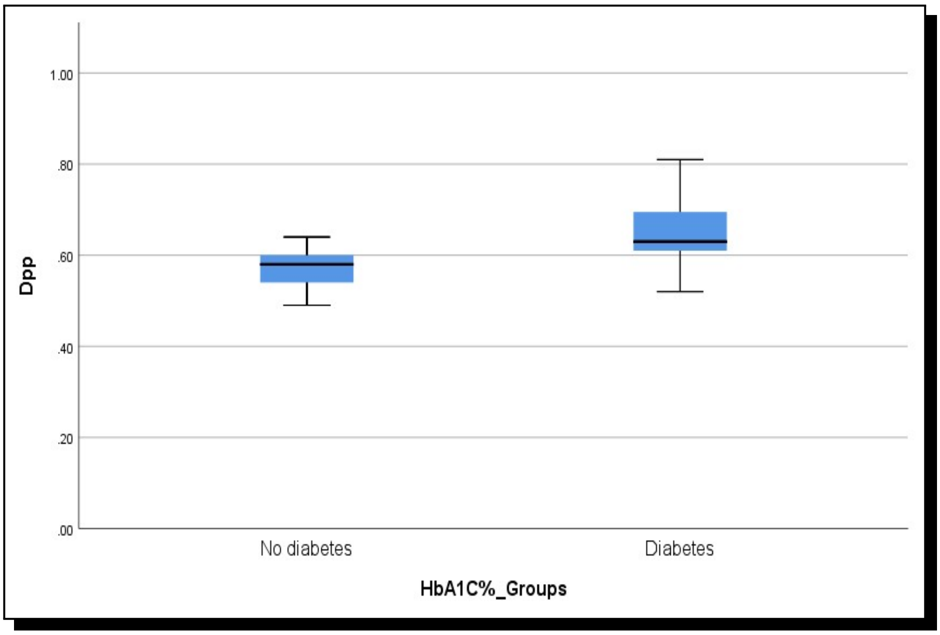

Figure 3. Boxplot of Dpp by HbA1C% groups

Moreover, to check for normal distribution and for homoscedasticity, the normal P-P plot of regression standardized residual and the scatterplot of regression standardized residual vs regression standardized predicted value were conducted. Figure 4 showed the normal P-P plot of regression standardized residual. The plot explains that the data follows the normal (diagonal) line and has no strong deviations, which in turn indicates that the residuals are normally distributed.

The *receiver operating characteristics* (ROC) is used to interpret the sensitivity and the specificity levels and to determine the related cut-off scores. In addition, it is used to explain a common scale for investigating different independent variables (predictors). ROC analysis has a very useful tool for indicating the overall diagnostic accuracy of the curve named the *area under the curve* (AUC). As the AUC gets closer to 1, the more the reliability of screening measure to distinguish subjects of being healthy with no diabetes or being patients with diabetes type II. The model obtained a very strong AUC value of 85.7 which in turn reflects the high reliability of Dpp index to distinguish between health and diabetic subjects. In addition, the model revealed 76.9 sensitivity and 83.3% specificity in classifying true positives and true negatives. Thus, the ROC and the AUC showed a reliable model that could be used as a screening measure for diabetes type II. Figure 5 shows the ROC curve for identifying HbA1C using Dpp index.

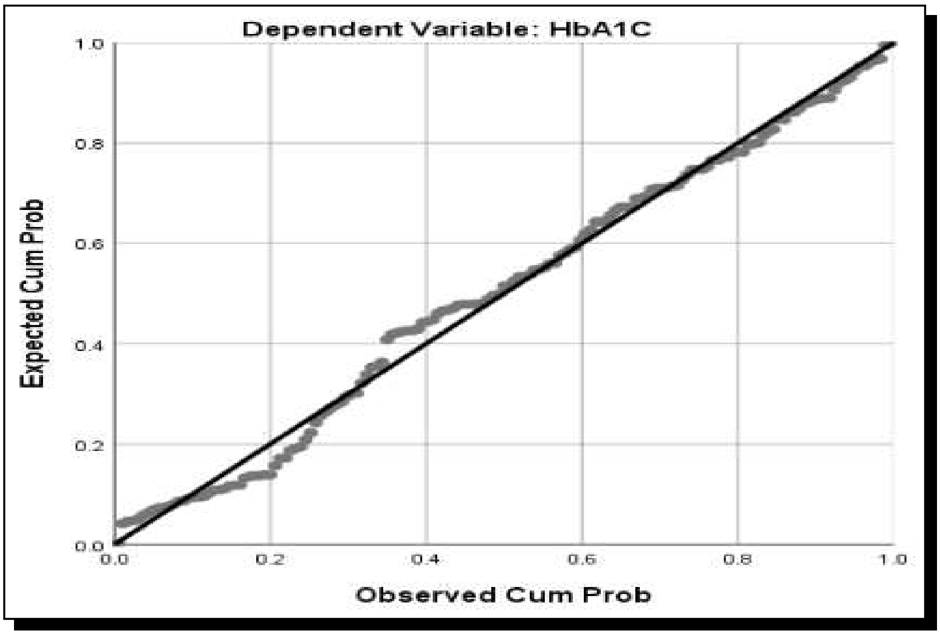

Figure 4. The normal P-P plot of regression standardized residual

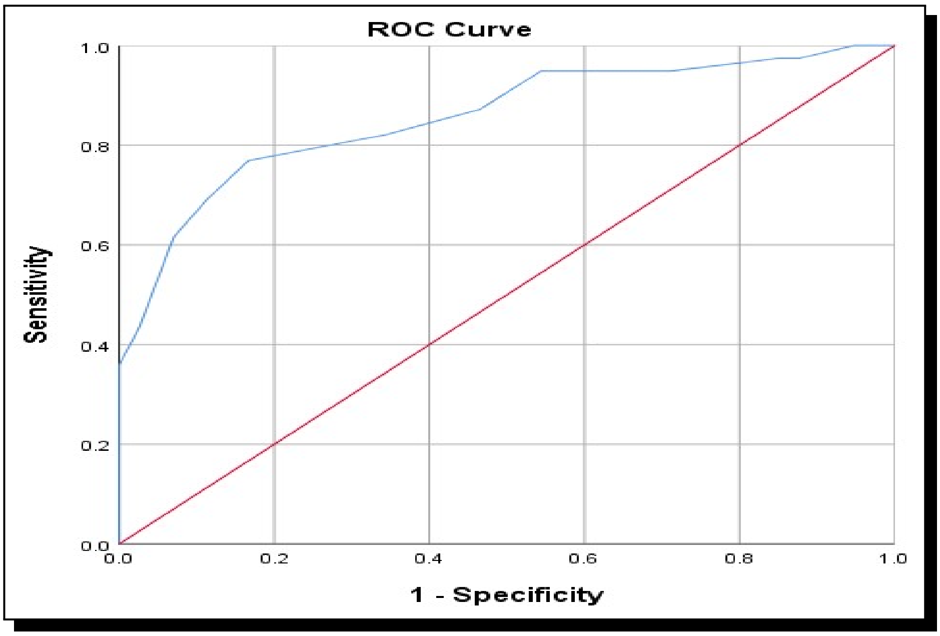

Figure 5. The receiver operating characteristics (ROC) curve for identifying diabetes type II (HbA1C>5.7%) using the *diastolic pulse peak* (Dpp) of PPG waveform, with an area *under the curve* (AUC) of 85.7%, sensitivity of 76.9%, and specificity of 83.3% at (0.6) cut-off value of Dpp

5. Conclusions

The current results supported the previous findings in the potential of PPG waveform in the detection and prediction of arterial wall elasticity changes, atherosclerosis, and diabetes type II. Age, b/a index, and Dpp index were statistically significant contributors to the variance of the dependent variable (HbA1C). The results showed that patients with diabetes type II showed a rounded PPG with loss of dicrotic notch and high diastolic pulse peak amplitude. The more the amplitude of the Dpp, the more the vulnerability of having diabetes type II. It would be of interest to study and investigate more on the associations between atherosclerosis, diabetes type II, and PPG waveform morphological changes. The research provided a reliable tool (Dpp) for the prediction of diabetes type II in comparison with HbA1C test. The findings expand the potential utility of PPG signal in clinical settings due to the simplicity in data acquisition and computation of PPG's morphological indices.

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Competing Interests

The author declares that he has no competing interests.

Authors' Contributions

The author wrote, read and approved the final manuscript.

References

[1] S. I. Sherwani, H. A. Khan, A. Ekhzaimy, A. Masood and M. K. Sakharkar, Significance of HbA1c test in diagnosis and prognosis of diabetic patients, *Biomarker Insights* **11** (2016), 95 – 104, DOI: 10.4137/BMI.S38440.

[2] J. Wang, S. Tu, I. Lee, S. Lin, S. Lin, S. Su, W. Lee and W. H. Sheu, Contribution of postprandial glucose to excess hyperglycaemia in Asian type 2 diabetic patients using continuous glucose monitoring, *Diabetes Metab. Res. Rev.* **27** (2011), 79 – 84, DOI: 10.1002/dmrr.1149.

[3] E. B. Ketema and K. T. Kibret, Correlation of fasting and postprandial plasma glucose with HbA1c in assessing glycemic control; systematic review and meta-analysis, *Archives of Public Health, Archives belges de santepublique* **73** (2015), 43, DOI: 10.1186/s13690-015-0088-6.

[4] D. M. Nathan, P. A. Cleary and J. Y. Backlund, Diabetes control and complications trial/epidemiology of diabetes interventions and complications (DCCT/EDIC) study research group, Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes, *N. Engl. J. Med.* **353** (2005), 2643 – 2653, DOI: 10.2337/dc13-2112.

[5] C. Sandler and M. McDonnell, The role of hemoglobin A1c in the assessment of diabetes and cardiovascular risk, *Cleveland Clinic Journal of Medicine* **83** (Supplement 1) (2016), S4 – S10.

[6] V. Vaidya, N. Gangan and J. Sheehan, Impact of cardiovascular complications among patients with Type 2 diabetes mellitus: a systematic review, *Expert Rev. Pharmacoecon. Outcomes Res.* **15**(3) (2015), 487 – 497, DOI: 10.1586/14737167.2015.1024661.

[7] J. M. Ahn, New aging index using signal features of both photoplethysmograms and acceleration plethysmograms, *Healthcare Informatics Research* **23**(1) (2017), 53 – 59.

[8] Q. Yousef, M. B. I. Reaz and M. A. M. Ali, The analysis of PPG morphology: investigating the effects of aging on arterial compliance, *Meas. Sci. Rev*. **12** (2012), 266 – 271, DOI: 10.2478/v10048-012-0036-3.

[9] B. G. Papini, P. Fonseca, L. X. Aubert, S. Overeem, W. J. Bergmans and R. Vullings, Photoplethysmography beat detection and pulse morphology quality assessment for signal reliability estimation, *39th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)*, Seogwipo, 2017, pp. 117 – 120, DOI: 10.1109/EMBC.2017.8036776.

[10] P. C. Hsu, H. T. Wu and C. K. Sun, *J. Med. Syst.* **42** (2018), 43, DOI: 10.1007/s10916-018-0901-1.

[11] H. Karimipour, H. Shandiz and E. Zahedi, Diabetic diagnose test based on PPG signal and identification system, *JBiSE* **2**(6) (2009), 465 – 469.

[12] A. Aymen and K. H. Shelley, Photoplethysmography, *Best Pract Res Clin Anaesthesiol*. **28**(4) (2014), 395 – 406, DOI: 10.1016/j.bpa.2014.08.006.

[13] J. L. Moraes, M. X. Rocha, G. G. Vasconcelos, F. J. E. Vasconcelos, V. H. C. de Albuquerque, A. R. Alexandria, Advances in photopletysmography signal analysis for biomedical applications, *Sensors* **18** (2018), 1894, 2 – 26, DOI: 10.3390/s18061894.

[14] A. J. Flammer, T. Anderson, D. S. Celermajer, M. A. Creager, J. Deanfield, P. Ganz, N. M. Hamburg, T. F. Luscher, M. Shechter and S. Taddei, The assessment of endothelial function from research into clinical practice, *Circulation* **126**(6) (2012), 753 – 767.

[15] Y. Qawqzeh, U. Rubins and M. Alharbi, Photoplethysmogram second derivative review: Analysis and applications, *Scientific Research and Essays* **10**(21) (2015), 633 – 639, DOI: 10.5897/SRE2015.6322.

[16] L. Aaron and W. Eleanor, Genetics of HbA1c: a case study in clinical translation, *Current Opinion in Genetics & Development* **50** (2018), 79 – 85, DOI: 10.1016/j.gde.2018.02.008.

[17] H.-T. Wu, C.-C. Liu, P.-H. Lin, H.-M. Chung, M.-C. Liu, H.-K. Yip, A.-B. Liu and C.-K. Sun, Novel application of parameters in waveform contour analysis for assessing arterial stiffness in aged and atherosclerotic subjects, *Atherosclerosis* **213**(1) (2010), 173 – 177, DOI: 10.1016/j.atherosclerosis.2010.08.075.

[18] R. R. Little and W. L. A. Roberts, A review of variant hemoglobins interfering with hemoglobin A1c measurement, *Journal of Diabetes Science and Technology* **3**(3) (2009), 446 – 451, DOI: 10.1177/193229680900300307.

[19] A. Karami and A. Baradaran, Comparative evaluation of three different methods for HbA1c measurement with High-performance liquid chromatography in diabetic patients, *Advanced Biomedical Research* **3** (2014), 94, DOI: 10.4103/2277-9175.129364.

[20] K. T. N. Takazawa, M. Fujita, O. Matsuoka, T. Saiki, M. Aikawa, S. Tamura and C. Ibukiyama, Assessment of vasocative agents and vascular aging by the second derivative of photoplethysmogram waveform, *Hypertension*. **32** (1998), 365 – 370, DOI: 10.1161/01.HYP.32.2.365.

[21] I. Imanaga, H. Hara, S. Koyanagi and K. Tanaka, Correlation between wave components of the second derivative of plethysmogram and arterial distensibility, *Jpn. Heart J.* **39** (1998), 775 – 784., `https://www.ncbi.nlm.nih.gov/pubmed/10089939`.

[22] M. Reguig, F. Med and F. Reguig, Photoplethysmogram signal processing and analysis in evaluating arterial stiffness, *International Journal of Biomedical Engineering and Technology* **23** (2017), 363, DOI: 10.1504/IJBET.2017.10003507.

[23] B. Peskin and R. Rowen, Breakthrough in clinical cardiology: InOffice Assessment with Pulse Wave Velocity (PWV) and Digital Pulse Analysis (DPA), *Clin. Cardiol*, 2010, pp. 80 – 86, https://www.semanticscholar.org/paper/Breakthrough-in-Clinical-Cardiology%3A-In-Office-with-Peskin-Rowen/374273d6383cb2cfa66e7945aa54ceb53274d7e1.

[24] A. Alberto, The finger volume pulse and the assessment of arterial properties, *J. Hypertens.* **20** (2002), 2341 – 2343, DOI: 10.1097/00004872-200212000-00007.