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ALTERNATIVE METHOD TO PRE-DIAGNOSED CORONARY ARTERY DISEASE USING PHOTOPLETHYSMOGRAPHY: A LESSON FROM COVID-19 PANDEMIC

(Kaedah Alternatif untuk Diagnosis Awal Penyakit Arteri Koronari melalui Fotopletismografi: Satu Pengajaran daripada Pandemik COVID-19)

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ABSTRACT

Ischemic heart disease (IHD) is one of the underlying factors that contribute to mortality in COVID-19 infected patients. IHD or coronary artery disease (CAD) is commonly diagnosed using invasive coronary angiography (ICA) or computed tomography angiography (CTA). However, these imaging modalities are costly, operationally complex and hardly accessible, especially during the pandemic. Thus, researchers

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have great interest in using non-invasive techniques of electrocardiography (ECG) and photoplethysmography (PPG) as alternatives to pre-diagnose the disease. This study focused on the detection of the severity of stenosis in the coronary artery using PPG among newly diagnosed IHD patients. A total of 88 patients of Hospital Canselor Tuanku Muhriz were involved. They were grouped as having severe stenosis if their stenosis percentage are at 70% or more, based on ICA or CTA evidence. A total of 73 time-domain features were analyzed in this study. Five machine learning methods were investigated to categorize the patients using up to 15 selected features. Results showed that the Discriminant Analysis method performed the best with accuracy, sensitivity and specificity of 88.46%, 100% and 70%, respectively. In conclusion, the severity of stenosis in coronary arteries has a high potential of being detected using simple non-invasive tools of PPG.

Keywords: Coronary artery disease; photoplethysmography; stenosis detection

ABSTRAK

Penyakit jantung iskemik (IHD) merupakan salah satu faktor utama yang menyumbang kepada kematian pesakit yang dijangkiti COVID-19. IHD atau penyakit arteri koronari (CAD) biasanya didiagnosis menggunakan angiografi koronari invasif (ICA) atau angriografi pengkomputeran tomografi (CTA). Walau bagaimanapun, modaliti pengimejan ini mahal, kompleks dari segi operasi, dan sukar diakses terutamanya semasa wabak pandemik. Oleh itu, penyelidik lebih berminat dalam menggunakan teknik bukan invasif elektrokardiografi (ECG) dan fotopletismografi (PPG) sebagai alternatif untuk diagnosis awal CAD. Kajian ini memberi tumpuan kepada pengesanan keterukan penyempitan arteri koronari menggunakan PPG di kalangan pesakit IHD yang baru. Seramai 88 pesakit dari Hospital Canselor Tuanku Muhriz telah terlibat dalam kajian ini. Mereka dikelompokkan sebagai mengalami stenosis teruk jika peratusan stenosis mereka berada pada 70% atau lebih, berdasarkan bukti ICA atau CTA. Sebanyak 73 fitur domain masa telah dianalisis dalam kajian ini. Lima kaedah pembelajaran mesin telah digunakan untuk mengkategorikan pesakit dengan menggunakan sehingga 15 fitur pilihan. Kaedah Analisis Diskriminasi menunjukkan prestasi terbaik dengan ketepatan, kepekaan, dan kekhususan masing-masing pada 88.46%, 100%, dan 70%. Kesimpulannya, keterukan penyempitan arteri koronari mempunyai potensi tinggi untuk dikesan dengan menggunakan peranti PPG bukan invasif yang mudah.

Kata Kunci: *Penyakit arteri koronari; fotopletismografi; pengesanan penyempitan arteri*

INTRODUCTION

Ischemic heart disease (IHD) remains as the number one killer in the world with an estimated 16% of total deaths in 2019 (World Health Organization 2020). The Department of Statistics Malaysia (DOSM) also reported that the disease is the main leading cause of death in Malaysia with a mortality rate of 16.1% until 2022 (Department of Statistics Malaysia 2023). However, the IHD or its common form coronary artery disease (CAD), is a type of heart problem caused by narrowed heart arteries. It is normally caused by atherosclerosis, where blood flow in the coronary arteries is restricted by the build-up of fatty deposits or plaque. The non-invasive procedure of computed tomography angiography (CTA) has been increasingly utilized in clinical practice to diagnose CAD. Nevertheless, invasive coronary angiography (ICA) remains as the gold standard procedure to diagnose CAD (Paradkar and Roy Chowdhury 2017). Angioplasty is performed during ICA to open the blocked arteries and restore the blood flow without open-heart surgery.

Early diagnosis of CAD disease is difficult as symptoms such as chest pain or angina, light-headedness, nausea, or shortness of breath might appear long after a person acquired the disease. In most cases, CAD is known after a person experienced a heart attack, which indicates the narrowing of the artery (stenosis) is already severe. Pre-diagnosis of CAD using non-invasive 12-lead ECG analysis or exercise stress test is often inconclusive, where ECG might be normal in patients at rest during angina (Tantimongcolwat et al. 2008; Kumar, Pachori & Acharya 2017). Moreover, stenosis severity cannot be determined. This issue is further complicated by the presence of COVID-19, where CAD patients have a higher risk of serious illness or death (Ng et al. 2022). The COVID-19 pandemic also restricted access to ICA or CTA for CAD diagnosis (Núñez, Sreeganga & Ramaprasad 2021). Thus, this study aims to provide an alternative non-invasive method to detect the severity of stenosis in coronary arteries using non-invasive physiological signal of photoplethysmography. Eighty-eight newly diagnosed IHD patients were studied to find the correlation between PPG features and the severity of stenosis in the coronary arteries. Angiogram evidence of ICA and CTA are used as benchmarks to classify subjects into case group (with severe stenosis) and control group (with non-severe stenosis).

LITERATURE REVIEW

The used of non-invasive signals such as electrocardiogram (ECG), phonocardiogram (PCG) and photoplethysmogram (PPG) to detect IHD or CAD has become an important research topic. ECG is well known as a clinical routine to detect any type of heart diseases including CAD (Singla, Azeemuddin & Sistla 2020). However, accurate analysis on ECG waveforms involves the usage of 10 electrodes to view 12 ECG channels. Thus, researchers are more interested in PPG. PPG is a pulse waveform that measures the volume of blood in the vascular tissue at the peripheral sites of the body, such as the finger, thumb and earlobe. PPG can be recorded simply using a small and portable sensor module that emits red and infrared lights to the tissue. The reflected or transmitted light are detected by a photodiode, where the reading is directly proportional to the variation of blood volume that carries the oxygen in each heart cycle (Castaneda et al. 2018).

PPG has been explored to detect multiple types of heart disease, which includes arrhythmias, atrial fibrillation and CAD (Banerjee, Bhattacharya & Alam 2018). In CAD detection, narrowed coronary arteries could changes the PPG waveform, where capability of myocardium to pump blood with proper volume is disturbed (Pal & Mahadevappa 2022). PPG are normally analyzed with velocity plethysmogram (VPG) and acceleration plethysmogram (APG), which represents the first and second PPG derivatives, respectively. Figure 1 shows the diagram of PPG, VPG and APG, with their fiducial points. These points are commonly used to extract variation of features in distinguishing subject with normal and narrowed coronary arteries. Paradkar and Roy Chowdhury (2017) have used the time domain information from PPG and its derivatives signal to classify CAD and healthy subjects with accuracy of 18%. Then, Banerjee et al. (2016) and Ihsan, Mandala & Pramudyo (2022) have successfully analyzed heart rate variability features in time and frequency domain from PPG waveforms to differentiate CAD and non-CAD subjects with more than 90% accuracy. These results show the potential PPG to be used as alternative tool to detect CAD, despite its simplicity.

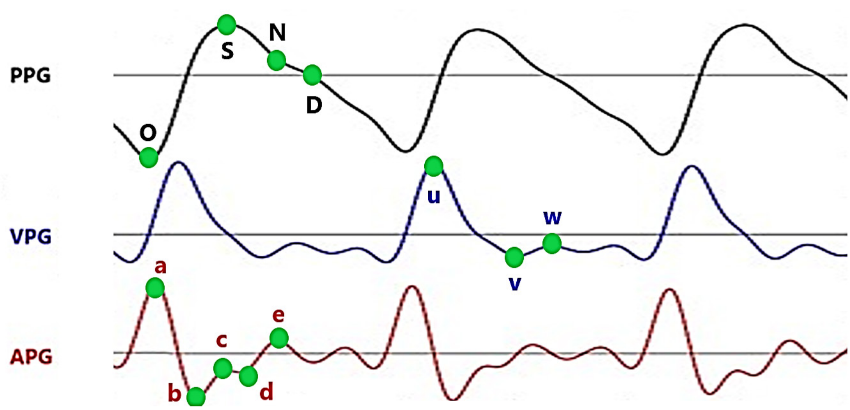

FIGURE 1 PPG and its Derivative Waveforms

METHODOLOGY

The detection of CAD from PPG is commonly involving data collection, signal processing, feature extraction and classification methods (Banerjee et al. 2016; Banerjee, Bhattacharya & Alam 2018; Ihsan, Mandala & Pramudyo 2022; Paradkar & Roy Chowdhury 2017). The description on each process is discussed in the following section.

1. Data

   A total of 88 elective CAD patients aged 21 to 65 years (54.23 ± 9.56), who were scheduled for ICA or CTA procedure at Hospital Canselor Tuanku Muhriz (HCTM), Cheras, Malaysia, are investigated in this study. They are newly diagnosed IHD patients, not pregnant and have no history of heart attack, cancer, or any other chronic disease. Fifty-four of them (61.4%) were in the case group while the other 34 of them (38.6%) were in the control group. PPG data was recorded for 10 minutes from each patient using the wireless battery powered MAX86150EVS module, produced by Maxim Integrated. A proper casing for the module was designed beforehand to ensure clean recording to reduce noise from motion artifacts and ambient light, as shown in Figure 2.

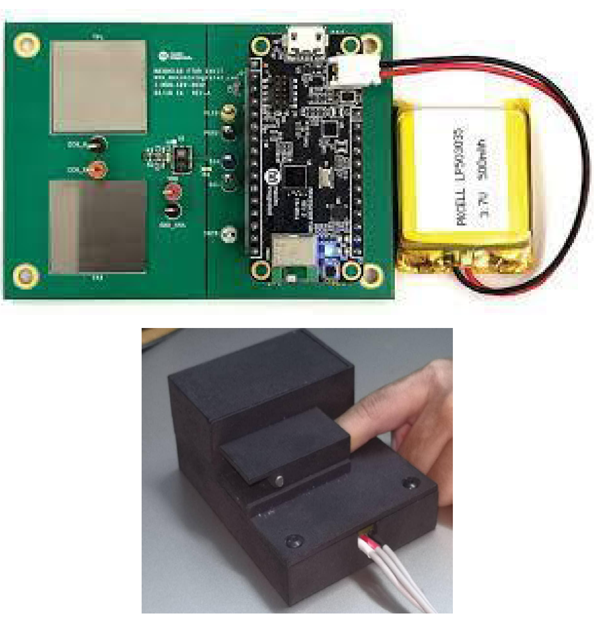

FIGURE 2 (a) MAX86150EVS Module for PPG Data Collection, (b) Designed Casing for MAX86150EVS Module

2. Signal Processing

The PPG data was recorded at 400 Hz sampling rate. Denoising was done using a Chebyshev Type II filter at the frequency band of 0.5 to 8 Hz, as suggested by (Liang et al. 2018). The quality of the recording is investigated for each 10-second window using the properties described in (Nayan & Hamid 2019). Figure 3 shows an example of the signal quality indexing (SQI) method, where the blue waveform indicates good quality PPG, while the red waveform indicates poor quality PPG. Each square bracket signifies a window of a 10-second segment. The longest continuous good-quality PPG was selected for analysis.

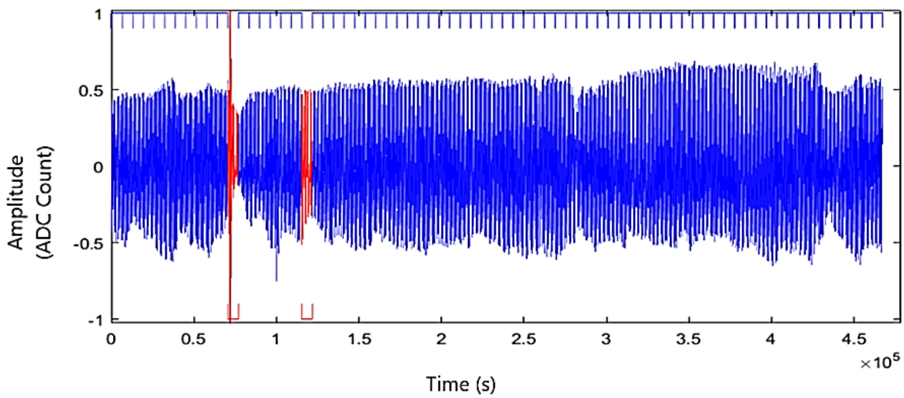

FIGURE 3 Signal Quality Indexing with 2 Poor Quality Segments (Shown in Red)

The second derivative of PPG was then obtained using Equation (1). This derivative is known as acceleration plethysmogram (APG). The fiducial points of PPG (onset(O), systolic peak (S), dicrotic notch (N) and diastolic peak (D)) and APG (a, b, c, d and e peaks) were first determined using derivative marker method before further processing of feature extraction (Suboh et al. 2022). Figure 4 shows the example of PPG, APG and the detected fiducial points.

$$APG = \frac{d}{dt}(VPG) = \frac{d}{dt}[x(t) - 2x(t-1) + x(t-2)] \quad (1)$$

3. Feature Extraction and Analysis

Four types of features were extracted from the time-series information of PPG and APG. These include time intervals between peaks, amplitude, slope and area. Figure 4 shows an example of a few time interval features extracted based on the fiducial points of PPG and APG. Time interval features are denoted as (T_), peak amplitude as (PA_), area as (A_), real crest time as (RCT_) and jerk as (J_). The ratio between the same feature types is also analyzed, which is denoted with 'R' before the underscore symbol. The letters after the underscore symbol are for the fiducial points. Table 1 lists all features analyzed in this study. Independent t-test and correlation analysis were done afterward to select the best features for classification.

4. Classification using Machine Learning

The best machine learning (ML) models to distinguish the case group from the control group were investigated from the algorithms of discriminant analysis (DA), decision tree (DT), k-nearest neighbors (KNN), support vector machine (SVM) and artificial neural network (ANN). Each ML model is trained with 70% of the total data and validated using a 5-fold cross-validation technique.

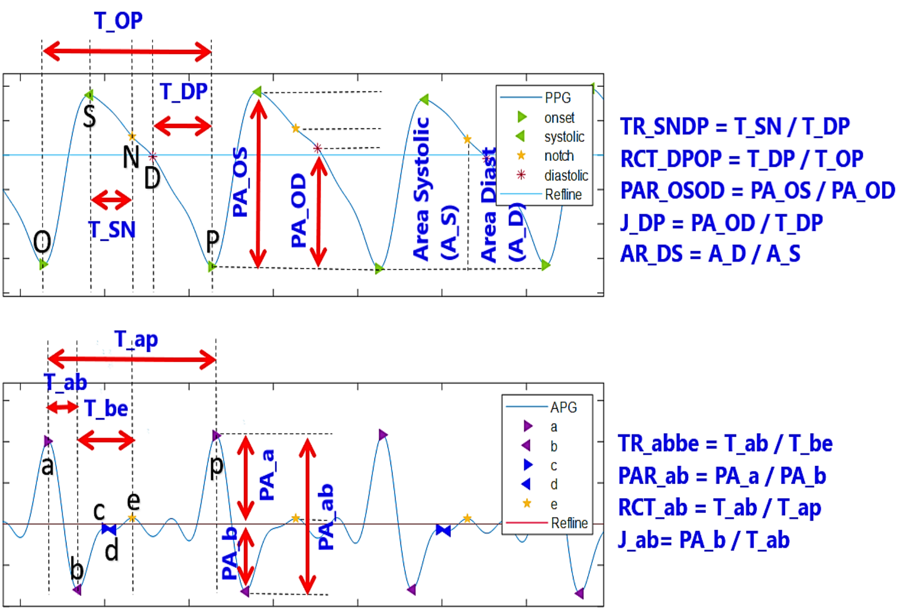

FIGURE 4 A few Examples of Extracted Features in the Time Domain from PPG and APG

TABLE 1 Seventy-three Features from PPG and APG

Feature Domain	Feature Type	PPG (onset, systolic, dicrotic notch and diastolic peaks)	APG (a, b, c, d and e peaks)
Time	Interval (T)	T_OS, T_ON, T_OD, T_OP, T_SN, T_SD, T_SP, T_ND, T_NP, T_DP	T_ab, T_ae, T_be, T_pa, T_pb, T_pe
	Interval ratio (TR)	TR_OSSP, TR_ODDP, TR_ONNP, TR_OSND, TR_SNDP	TR_abae, TR_abbe, TR_abpa, TR_abpb, TR_abpe, TR_aepa, TR_aepb, TR_aepe, TR_bepa, TR_bepb, TR_bepe, TR_papb, TR_pape
	Real crest time (RCT)	RCT_OSOP, RCT_ONOP, RCT_ODOP, RCT_SNOP, RCT_SDOP, RCT_SPOP, RCT_NDOP, RCT_NPOP, RCT_DPOP	RCT_ab, RCT_be, RCT_ae
Amplitude	Peak (PA)	PA_OS, PA_ON, PA_OD, PA_NS, PA_ND	PA_a, PA_b, PA_e, PA_ab, PA_ae, PA_eb
	Peak ratio (PAR)	PAR_OSON, PAR_OSOD, PAR_NSND	PAR_ab, PAR_ae, PAR_be
Slope	Jerk (J)	J_OS, J_ND, J_NS, J_DP	J_ab, J_be
Area	Area (A)	A_OP, A_S, A_D	
	Area ratio (AR)	AR_DS	

Legend: O=onset PPG, S=systolic PPG, N=dicrotic notch PPG, D=diastolic PPG, P=next cycle of onset PPG, while a, b, c, d and e is the fiducial points of APG waveform.

RESULT AND DISCUSSION

Statistical analysis was used to rank the features using p-value and correlation strength (R2). The top 15 features are listed in Table 2. The area ratio between diastolic and systolic regions of PPG (AR_DS) was found statistically significant (p=0.022) in differentiating case and control groups. The significance is obtained due to the changes on the location of dicrotic notch that separates the systolic and diastolic region. It signified that the volume of blood especially on the diastolic part are different between narrowed and normal arteries. However, the correlation strength is weak. Thus, more input features were needed to help the ML model to learn better.

TABLE 2 Feature Ranking

Rank	Feature	Description	p-value	R^2
1	AR_DS	Area ratio between diastolic and systolic region.	0.022*	0.245
2	T_OD	Time interval between onset and diastolic peak of PPG.	0.075	0.191
3	T_ON	Time interval between onset and dicrotic notch of PPG.	0.102	0.176
4	T_ae	Time interval between a-peak and e-peak of APG.	0.164	0.150
5	PAR_NSND	Peak amplitude ratio between systolic and diastolic peak from the notch of PPG.	0.236	0.128
6	T_ab	Time interval between a-peak and b-peak of APG.	0.256	0.122
7	PAR_be	Peak amplitude ratio between b-peak and e-peak APG.	0.266	0.120
8	T_OS	Time interval between onset and systolic peak of PPG.	0.278	0.117
9	J_ND	Slope between notch and diastolic peak of PPG	0.302	0.111
10	PA_ND	Peak amplitude difference between notch and diastolic peak of PPG.	0.306	0.110
11	RCT_NDOP	Relative crest time between notch and diastolic peak of PPG to a complete PPG cycle.	0.359	0.099
12	PA_NS	Peak amplitude difference from notch to systolic peak of PPG.	0.379	0.095
13	T_SN	Time interval between systolic to dicrotic notch of PPG.	0.387	0.093
14	PAR_ae	Peak amplitude ratio between a-peak and e-peak of APG.	0.411	0.089
15	T_SD	Time interval between systolic to diastolic peak of PPG.	0.413	0.088

*Indicates significant difference

The ML training was conducted using a different number of input features, from one to the accumulated fifteen features. The best classification accuracy for each ML algorithm on each number of features is shown in Figure 5. It is found that accuracy is generally increased as more input features are given to the model, except for KNN and DT. DA and SVM classifiers have reached their maximum classification accuracy at 8 input features. DA algorithm with the 'diagQuadratic' type has performed the best using 8 top features with the classification performance of 88.46% accuracy, 70% specificity, 100% sensitivity and 0.1154 mean squared error. Specificity was quite low as the number of samples for control subjects is slightly lower than the case subjects. Furthermore, there are eight subjects from the control group had moderate disease (>50% stenosis), which complicates the differentiation of severe disease that had around 70% stenosis.

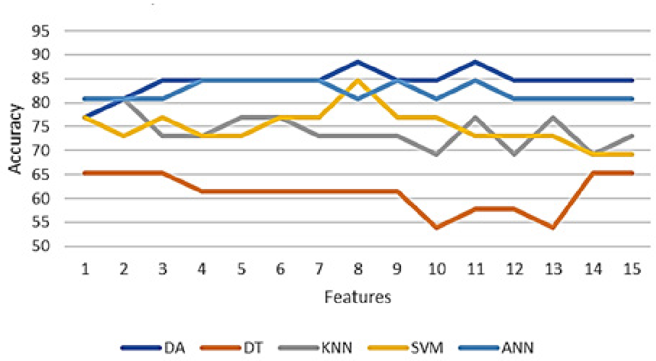

FIGURE 5 The Best Classification Accuracy for Each ML Algorithm with Different Input Features

In general, this preliminary study showed the capability of non-invasive techniques of PPG to detect the severity of stenosis in the coronary arteries. Future works should involve more sample data to improve ML performance. The combination of PPG with other non-invasive methods such as electrocardiogram (ECG) can also significantly improve the detection performance.

CONCLUSION

In conclusion, this study has successfully distinguished between severe and non-severe blocked arteries with an accuracy of 88.46% using the DA classifier, thus demonstrating the potential of non-invasive PPG techniques to pre-diagnose CAD. This alternative method is hopefully can be realized in the near future to enable self-monitoring or self-management of IHD, even in pandemic situations.

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