

Epidemiological Relationship of Photoplethysmography Signal Derived from Arterial Stiffness and Blood Pressure to Coronary Artery Disease: A Systematic Review

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ABSTRACT

Current photoplethysmography (PPG) signals and electronic devices had a lot of attention including analysis of coronary heart disease, ageing of blood vessels, metabolic syndrome, endothelial cell damage, predicting the risk of coronary artery disease, and community-acquired pneumonia. This systematic review aims to analyze current technologies used to measure PPG signals. Analysis of PPG signals with patients involved in coronary artery disease and arterial stiffness and other important interests toward the future trends of computational medicine. The hypothesis is that arterial stiffness is epidemiologically related to the risk of coronary heart disease. A systematic search was conducted in different databases to acquire literature examining the use of PPG with coronary artery disease in terms of epidemiological correlations. Search terms included arterial stiffness, epidemiology, PPG, blood pressure, and coronary artery disease. Articles that do not measure PPG signals on real patients/subjects were excluded from the analysis. A total of 17 studies met the inclusion criteria for this systematic review. Nearly half of the studies used PPG with artificial intelligence/machine learning for analytical study patients, while 18% were PPG studies related to endothelial damage and blood pressure profiles, and another 18% were new development of PPG measurement devices. The rest was PPG analyzing coronary artery disease and atherosclerosis. Systematic review findings reveal PPG applications range from the epidemiology of damaged endothelial cell proliferation to advanced digital PPG analysis. Managing cardiovascular risk and exploring new areas including chronic kidney disease and ovarian cancer must be of interest and considered in future studies.

KEYWORDS:

biomedical signal, coronary artery disease, photoplethysmography, vascular ageing

INTRODUCTION

Vascular geometry plays an important role in determining endothelial cell function. Changes in the geometry of blood vessels cause dynamic changes in vascular biology that lead to the development of atherosclerotic lesions and

subsequently to coronary artery disease¹⁻⁷. These changes can cause infection, causing arterial stiffness, which spreads arterial lesions in the cardiovascular system^{1,3}. Numerous epidemiological studies have repeatedly reported that arterial stiffness is associated with the risk of coronary heart disease⁸.

The arterial stiffness index usually estimates the distance traveled by blood flow divided by the time it takes to travel that distance in meters per second. It is a highly standardized, noninvasive technique for the diagnosis and assessment of arterial stiffness⁹⁻¹⁰.

Arterial stiffness is a marker of vascular ageing, a predictor of hypertension, and can be characterized by a photoplethysmography (PPG) signal⁹⁻¹⁰. Subsequently, PPG signals are hugely receiving attention and are increasingly being used as noninvasive tools to monitor blood oxygen, heart rate, and blood pressure parameters related to coronary heart disease. It is challenging to exploit the potential of PPG signals as a personal health management device for risk management of coronary artery disease and provide more information than typical coronary artery disease clinical trials. The objective of this systematic review is to analyze and discuss current technologies used to measure PPG signals with patients dealing with arterial stiffness associated with coronary artery disease and other related significant interests. Then, an examination of the epidemiological relationship between PPG signals and coronary heart disease recommended the role of PPG in the development of atherosclerotic lesions. In addition, technical considerations such as software and electronics used for PPG signal processing and machine learning (ML) are also considered. Artificial intelligence (AI) and the possibility of developing computer-aided medical diagnosis systems for noninvasive tools and personalized medicine are included, and future directions are also highlighted.

LITERATURE SEARCH STRATEGY

The structured search was performed on PubMed, ScienceDirect, Scopus, and Google Scholar to identify studies reporting about PPG signals associated with arterial stiffness involving coronary artery disease according to the preferred reporting guideline for systematic reviews and meta-analysis^{3,11-12}. The last structured search was completed on 16 April 2024. A variety of

key search terms include: [(“photoplethysmography” OR “PPG” OR “arterial stiffness”) AND (“epidemiology” OR “blood pressure” OR “coronary artery disease”)]. We used these key search terms because we intended to cover the analysis of all studies on the epidemiological relationship of PPG signals derived from arterial stiffness linked to coronary artery disease in this review.

ELIGIBILITY CRITERIA FOR ANALYSIS

The analysis criteria are the studies must be peer-reviewed studies that were published in English literature; studies were original research studies that reported findings, characteristics, and features of PPG associated with blood pressure and coronary artery disease epidemiologically; study included at least 10 patients with well-characterized PPG signals, this is because studies with fewer than 10 samples are considered low-level evidence on patients with PPG signals; studies must be published within the last 10 years. Each article was then assessed for title and abstract to determine its relevance to the objectives of the review^{2,12-13}. Once the article had passed the title and abstract evaluation, its full text was then extracted for further analysis. These criteria were used with our structured search to classify the search results for inclusion in the analysis in this review. Additionally, studies reported with disaggregated data/single-ended data analysis and a sample size of < 10 patients were excluded from this review due to the low level of evidence. Conferences, commentaries, editorials, opinions, and other types of publications were also excluded.

DATA EXTRACTION AND AGGREGATION

The search results were completed by physically screening the titles and abstracts of all identified literature by an independent evaluator (TC). Data verification was then performed to verify the findings by the data observer (TC and ZS). The following study characteristics of PPG epidemiologically related to blood pressure and coronary heart disease were classified:

first author's name, country, year of publication, sample size, and main study findings. The data aggregation was the main pattern of a summary of the literature on similar directions of investigation¹²⁻¹³. Data disaggregation was a separation of collected data into multiple patterns to account for underlying trends and patterns in the focal pattern of the data aggregation¹²⁻¹³. As a result, three subgroups of data segmentation were identified from data aggregation: I) arterial AND stiffness AND epidemiology AND PPG, II) arterial AND stiffness AND blood AND pressure AND PPG, and III) arterial AND stiffness AND coronary AND artery AND disease AND PPG.

RESULTS

The literature search identified a maximum of 29,523 titles in ScienceDirect and at least 512 titles in PubMed, while Google Scholar and

Scopus listed 20,400 and 2,692 titles, respectively. A total of 53,000 titles were retrieved in the form of [(photoplethysmography_or_PPG_or_arterial-stiffness)+(epidemiology_or_blood-pressure_or_coronary-artery-disease)] format. Therefore, only 214 titles and abstracts were screened. The remainder was separated from the data segmentation keywords because it is irrelevant to the topic. Figure 1 presents a flow diagram gaining the search strategy for selecting these studies. Figure 2 illustrates how blood flow relates to the PPG sensor¹⁴. Table 1 reveals how algorithms contribute to defining PPG signals¹⁴. Finally, a total of 17 articles were included in this systematic review. This paper presents a novel epidemiological relationship between PPG signal and arterial stiffness related to coronary artery disease contributed to the fields of urban health and medicine.

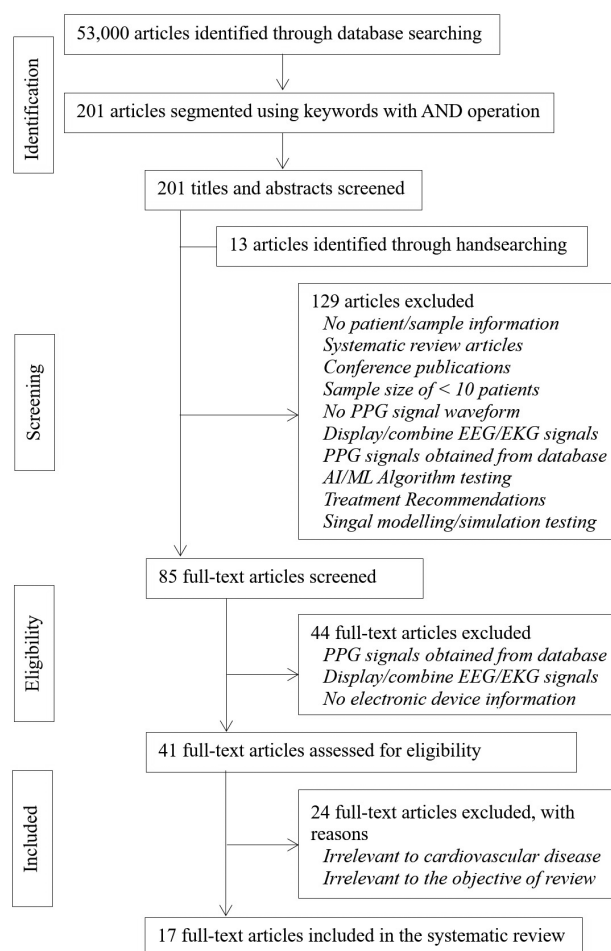


Figure 1 A flowchart shows the search strategy to identify the selected studies

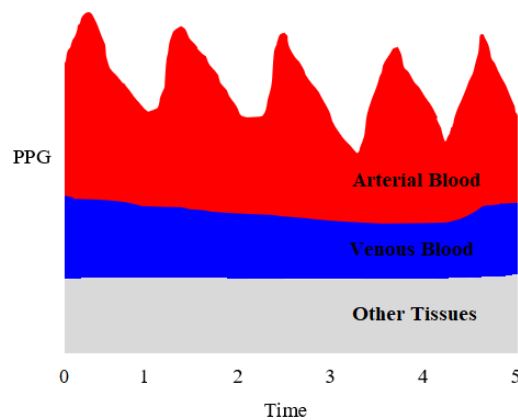


Figure 2 Illustrates how blood flow relates to the photoplethysmography sensor

Table 1 Reveals algorithms that contribute to defining photoplethysmography signals accompanied with Figure 2

PPG algorithm	
Input	Optical radiation
Process	Optical light illuminates through the index finger
	Lights are absorbed and scattered through different tissue layers
	Lights are transmitted through or reflected from the tissue surfaces
	The intensity of the attenuated light passed through Figure 2 (raw PPG signal) is detected by an optical sensor
An optical sensor records a voltage signal called a photoplethysmography	
Output	PPG waveform

Abbreviation: PPG, photoplethysmography

CHARACTERISTICS OF SELECTED LITERATURE

Of the 17 articles, six (35%) used PPG with AI/ML for analytical study patients¹⁵⁻²⁰, three of which (18%) were PPGs related to endothelial damage and one of them blood pressure profiles²¹⁻²³. One of them (5%) was a technical problem in acquisition of PPG signals²⁴. Two of them (12%) were overnight

PPG analysis to analyze long-term cardiovascular events and coronary artery disease risk²⁵⁻²⁶. Two of them (12%) were arterial stiffness associated with metabolic syndrome and sports science²⁷⁻²⁸. Finally, three of them (18%) were the development of new PPG measurement devices²⁹⁻³¹. Table 2 summarizes characteristics of included studies in this systematic review.

Table 2 The characteristics of studies that met the criteria in this review

Country	First author	Year of publication	Sample size	Main study findings
United Kingdom	Sadaf Iqbal ¹⁵	2023	37 patients	Deep learning PPG analysis was confirmed with blood samples of endothelial function, which showed good agreement with coronary artery disease angiography.
Italy	Caterina Franco ²¹	2022	23 patients	Hypertensive patients were assessed for endothelial damage and arterial stiffness. This suggests an overall antioxidant capacity related to recovery of arterial stiffness.
Taiwan	Chin-Jung Ku ²²	2022	48 patients	Blood pressure can be measured continuously from a PPG that shows systolic and diastolic blood flow profiles. This result was confirmed with the PPG signal database.

Table 2 The characteristics of studies that met the criteria in this review (continued)

Country	First author	Year of publication	Sample size	Main study findings
China	Chenbin Ma ²³	2024	24 patients	Noninvasive blood pressure using PPG signals to derive blood pressure values confirmed with clinical standards.
Finland	Jukka-Pekka Sirkiä ²⁴	2024	19 subjects	Identified errors arising from contraction of the sensor pressure while measuring the PPG signal on the index finger. This suggests that PPG device design should account for these errors in changes in diastolic blood pressure levels.
Pakistan	Kehkashan Kanwal ¹⁶	2024	31 subjects	ML-based PPG signal analysis for community-acquired pneumonia (CAP) diagnosis shows potential to improve clinical decision-making and patient outcomes in pediatric pneumonia health care. CAP causes cardiovascular complications (e.g., heart failure, arrhythmias, myocardial infarction and/or stroke).
Turkey	A. Reşit Kavsaoğlu ¹⁷	2015	33 people	Hemoglobin measurement using PPG signals with ML confirms that this noninvasive method may replace clinical laboratory hemoglobin testing with blood samples.
India	Abhishek Chakraborty ¹⁸	2020	52 normal subjects	Myocardial infarction identification using PPG signals with ML shows positive predictive results for the potential development of personalized healthcare systems.
Australia	Sobhan Salari Shahrabaki ²⁵	2023	1957 participants	Nocturnal pulse amplitude attenuation derived from overnight PPG signals has been found to be associated with long-term cardiovascular events. The PPG-derived nocturnal pulse wave amplitude attenuation index may be a marker of cardiovascular risk.
Taiwan	Hsin Hsiu ¹⁹	2022	280 subjects	Measurement of arterial pulse waves with ML analysis to discern how vascular aging contributes to the progression of vascular dysfunction. This suggests that the development of wearable devices can be used for noninvasive methods to reduce the threat of vascular dysfunction caused by vascular aging.
Australia	Lisa M. Walter ²⁶	2018	185 subjects	Overnight PPG analysis of people with sleep breathing problems reveals pulse wave velocity related to arterial stiffness and central systolic blood pressure as predictor of cardiovascular outcome. These results confirm the treatment of breathing disorders and obesity to reduce the risk of cardiovascular disease.
United Kingdom	Elisa Mejía-Mejía ²⁰	2022	18 healthy subjects	ML analysis of morphological features from PPG along with pulse rate variability features. It shows relatively good and feasible performance in estimating blood pressure. It is a measurement of high blood pressure that causes chronic and acute diseases such as diabetes and heart failure.
Poland	Tadeusz Sondej ²⁹	2021	108 subjects	A new PPG measurement device has been developed to produce verified pulse wave velocities with SphygmoCor XCEL as a reference device. The new device uses different sensor locations (e.g. on the forehead, left earlobe, right earlobe, fingers, and toes) to provide highly accurate signals. This suggests that PPG devices can be used to generate pulse wave velocity to predict cardiovascular risk, replacing the use of pulse wave velocity devices.

Table 2 The characteristics of studies that met the criteria in this review (continued)

Country	First author	Year of publication	Sample size	Main study findings
Taiwan	Yaw-Wen Chang ²⁷	2016	65 volunteers	PPG analysis distinguishes different arterial pulse transmission conditions between metabolic syndrome and healthy volunteers. The results confirmed PPG waveforms can provide information about metabolic syndrome-induced changes in arterial pulse transmission and cardiovascular disease.
United States	Nathan Zavanelli ³⁰	2023	19 variety of ethnicities	A new wireless PPG device has been developed to measure blood pressure for vasoconstriction or atherosclerosis. The device was validated with a commercial device in an overnight PPG analysis with patients with sleep apnea, with a high level of agreement in detecting vasoconstriction.
United Kingdom	Denis J. Wakeham ²⁸	2023	46 healthy males	The central artery stiffness can adjust the pressor responses during stimuli associated with increases in cardiac output and sympathoexcitation in healthy men. The results suggest differences in systolic pressure between young and healthy middle-aged men. Central arterial stiffness was found to play a greater role than the increase in sympathetic transmission in middle-aged men. Sympathetic transmission involves blood pressure and coronary blood flow.
China	M.A. Xiaotian ³¹	2024	133 participants	A multi-sensor pulses diagnostic device that assesses coronary artery lesions using PPG shows practical value in detecting the degree of coronary artery occlusion in patients with coronary artery disease. The results provide valuable insights into the development of new diagnostic devices imbued with time domain analysis principles and their potential in the management of cardiovascular disease.

Abbreviations: CAP, community-acquired pneumonia; ML, machine learning; PPG, photoplethysmography

CURRENT PPG TECHNOLOGY

Pulse oximeter is an instrument used to estimate and display arterial saturation of oxygen. It was originally based on the Beer-Lambert law. Pulse oximetry estimates arterial saturation of oxygen with an accuracy in the range of 90%–100%. Later, Takuo Aoyagi realized that only pulsatile variations in light transmission

were required to estimate hemoglobin concentration³². [Figure 3](#) shows a simple diagram of a classic pulse oximeter configuration³³. Nowadays, pulse oximeters have become an important tool in patient monitoring, intensive care units, and operating rooms in hospitals, as well as caring for patients with sleep problems at home.

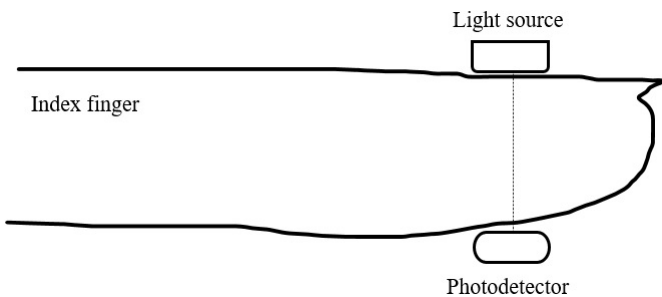


Figure 3 Generalization of optical configuration for PPG transmission mode

Currently, many studies are focused on the research and development of both non-contact and skin contraction pulse oximeters. Zavanelli et al. (2023) developed a soft wireless sternum patch device to be placed on the chest to detect vasoconstriction³⁰. His device presents a new concept of modern mobile devices to defeat traditional PPG devices that place sensors on fingers, toes, and ears. His device implants an electronic chip combined with a nanobattery that detects PPG signals at the location of the sternum. The analyzed PPG results of vasoconstriction were verified with a commercial device with an accuracy of 78%. He stated this new paradigm of electronic devices offers continuous monitoring of blood vessel contraction with potentially important medical applications and is broadly applicable to monitoring biological signals from novel anatomical regions such as the sternum.

Xiaotian et al. (2024) researched and developed a new electronic device to detect blockage and narrowing of coronary arteries with an accuracy of 78.79%³¹. Xiaotian's device introduces a new concept of fingertip-PPG signal created by placing sensors on the index finger and wrist. This provides valuable insights into the development of new diagnostic devices embedded in the principles of time domain analysis in the potential management of cardiovascular disease. Owens et al. (2022) developed a 1064 nm pulsed laser source and a short-wave infrared camera with a digital holography system in the off-axis image plane recording geometry³⁴. Owen's device produced the pulse diagnostic measurement that can be referenced for pulse rate oximetry. In 2023, Bautista of the UK proposed contactless photoacoustic spectroscopy (cPPG) to measure physiological signals in 654 adults³⁵. Bautista's study shows that cPPG is the use of a camera to detect changes in the volume of pulsating blood in the blood vessels in a person's face. Sondej et al. (2021) developed a new device

to measure coronary pulse wave velocity from a PPG device to overcome expensive pulse wave velocity measurement devices and complications in the diagnosis of coronary artery disease²⁹. Sondej's device was validated with a commercial device, the SphygmoCor XCE (CardieX, New South Wales, Australia). The results of the static analysis signal verification showed that Sondej's device was acceptable for measuring pulse wave velocity. Therefore, the current development trend of PPG technology is based on computer-aided medical diagnosis systems for non-invasive tools and personalized medicine.

PPG FORECASTS CARDIOVASCULAR DISEASE AND EPIDEMIOLOGY

High blood pressure or hypertension is one of the major risks of heart attack, stroke, and kidney failure caused by vascular stiffness or vascular ageing. The PPG signal is a measurement of red blood cells in blood vessels using the transmission of light through tissue⁸⁻¹⁰. It decreases during systole and increases during diastole. The general interpretation of these oscillations is that they are associated with an increase in arterial blood volume during systole. It allows the detection of arterial stiffness from changes in blood flow that occur through the PPG sensor⁸⁻¹⁰.

In addition, PPG can also be used to determine pulse wave velocity. Wakeham et al. (2023) examined whether exercise blood pressure is influenced by arterial stiffness²⁸. This is an increase in blood pressure in the aortic flow which causes aortic pulse wave velocity. This leads to an assessment of the cardiovascular response to exercise. Previous researchers in 2016, Chang's study characterized the peak-to-peak PPG signal index in patients with metabolic syndrome²⁷. Changes in the systolic and diastolic phases in the PPG signal reveal cardiac dysfunction. His investigation demonstrates the clinical application of

finger PPG signal measurement to improve early detection of cardiovascular disease.

Many current studies, Franco et al. (2022), Ku et al. (2022), and Ma et al. (2024) confirm endothelial damage, arterial stiffness, and abnormal blood pressure can be continuously measured using PPG signals that display systolic and diastolic blood flow profiles²¹⁻²³. These non-invasive blood pressure-based PPG signals are obtained a verification by clinical standards to gain accurate blood pressure values. Consistent with these review findings, much previous research suggests that endothelial cell damage in the main bifurcation of the coronary artery may be an epidemiological consequence of endothelial cell damage in the coronary side-branches infected stenosis plaques. Therefore, this systematic review suggests that PPG signals derived from arterial stiffness and blood pressure have a strong epidemiological relationship with coronary heart disease.

PPG WITH AI/ML APPLICATIONS AND FUTURE DIRECTIONS

Analysis of PPG signals characterizing abnormal blood flow and blood pressure profiles is a branch of biomedical computation and mathematical signal processing. AI/ML is the mathematical processing of data to train and predict future data flows, and/or automatic decision-making^{12,36-37}. In this review, we have seen that the use of AI/ML with PPG signal processing has increased significantly over the past several decades. Iqbal et al (2023) proposed a deep learning (DL) analysis of bilateral PPG signals on participants with normal and coronary artery disease¹⁵. Scalogram/spectral images were obtained by measuring PPG with right and left index fingers for image classification using convolutional neural network and k-nearest neighbor (K-NN) for comparison with biochemical markers of endothelial function. Iqbal's algorithm shows a significant agreement found between DL classification of PPG signals

and coronary artery disease angiography, with the performance of DL clearly better than the K-NN method. Kanwal et al. (2024) used five different ML classification models with PPG signals: fine decision tree, linear discriminant analysis, weighted KNN, wide neural network, and ensemble of bagged trees¹⁶. Kanwal's research suggests that using weighted KNN can correctly predict PPG signals for 90 percent of the subjects studied.

Kavsaoğlu et al. (2015) employed ML with PPG signals to create a non-invasive hemoglobin prediction¹⁷. The most algorithm designs rely on classification and regression trees. Kavsaoğlu's study suggests that promising results can be obtained by using features selected by relief feature selection and support vector regression. With mean square error of 0.0027, his ML platform can predict clinical human hemoglobin levels from PPG signals without collecting and analyzing blood samples. Chakraborty et al. (2020) developed his own algorithm to automatically identify inter-arrhythmic variability in PPG signals for myocardial infarction (MI) analysis¹⁸. Chakraborty's algorithm is based on classification, mainly characterizing both normal signal properties and MI PPG signals, his algorithm achieved an accuracy of 95.40%, demonstrating that single-lead PPG signals are easy to use, inexpensive, and work independently at home.

Hsiu et al. (2022) used both multilayer perceptron (MLP) and random forest (RF) networks to help differentiate the frequency-domain pulse indices¹⁹. Hsiu's research reveals that the ML knowledge presented may be useful for the development of non-invasive and easy-to-use measurement techniques to detect changes caused by vascular aging in arterial pulse transmission conditions. Mejía-Mejía et al. (2022) used ML for feature extraction from PPG signals to recognize the time interval between beats to ultimately predict predicted blood pressure values²⁰. Mejía-Mejía's study pointed out that the best performance in estimating blood pressure

was obtained from a combined set of features. Therefore, this review proves that almost all ML algorithms with PPG signals based on classification models develop computer-aided medical diagnosis systems with the use of AI/ML for personalized medicine. This is because noninvasive tools are pivotal to the digital economy and future leading technologies in computational research. Future directions are suggested to digitize clinical and hospital data into digital databases. This includes a focus on noninvasive tools for personalized medicine.

The keys contribute to the field of urban health and medicine.

- PPG signals characterize abnormal blood flow and blood pressure profiles to enhance noninvasive cardiovascular monitoring in healthcare.

- AI/ML algorithms with PPG signals based on classification models develop computer-aided medical diagnosis systems for personalized medicine.

- cPPG to measure physiological signals in patients may be considered a new era of the urban healthcare system.

Future directions may include PPG with blood flow in the aorta near the kidneys, causing damage to ovarian endothelial cells and renal arteries. The study of PPG signals and the prediction of chronic kidney disease and ovarian cancer is a new area of investigation that needs much attention.

STUDY LIMITATIONS

The main concerns relate to bias and the strength of the selected articles in terms of their inability to critically evaluate them. Thus, the search strategy for this review followed PRISMA guidelines^{3,11-12}, which allows researchers to identify and validate findings from a comprehensive literature search by carefully describing keywords that accurately describe the review objectives. In addition, a comprehensive search was conducted across four databases to retrieve full

text of original articles to categorize the review objectives. The ScienceDirect site is primarily focused on digital literature. Most researchers do not measure PPG signals from real patients. They use PPG from public databases published on internet. Therefore, their results do not reflect the results of the original study using current technology used to measure PPG signals on patients.

CONCLUSION

The systematic review and meta-analysis provide a detailed analysis of the current literature on current technologies that measure PPG signals in patients with arterial stiffness related to coronary artery disease and other important interests. Despite widespread use of PPG measurement in the past ten years, there is not yet the systematic review studied on the epidemiological relationship between PPG signals and coronary heart disease, as well as the determination of significant AI/ML applications with PPG signals appear to no current direction. Diagnosis of vital signs using PPG such as blood flow and pressure is traditional. Computational analysis of PPG signals relevant to cardiovascular disease prediction still has room for improvement. This systematic review suggests that the development of noninvasive tools for PPG signal analysis is of interest and will benefit knowledge leaders in the digital economy and computational medicine.

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