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PRACA POGLĄDOWA
REVIEW

Photoplethysmography as a non-invasive technique to measure the level of LDL cholesterol in the population

Fotopletyzmografia jako nieinwazyjna technika pomiaru poziomu cholesterolu LDL w populacji

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ABSTRACT

Photoplethysmography (PPG) is a low-cost, non-invasive optical technique widely used in clinical settings and wearable devices, particularly in cardiovascular diseases. The method shows promise for testing the levels of lipids. This review aims to synthesise current evidence on the application of PPG in assessing atherosclerosis and its correlation with lipid profiles, and it discusses the technological foundations and future of wearable cardiovascular monitoring. A narrative review was conducted following a literature search of the PubMed, IEEE Xplore, Google Scholar and Scopus databases. The analysis included studies focussing on PPG morphology, the physics of light-tissue interaction and emerging technologies such as graphene-based sensors. The literature indicates that PPG signal morphology, particularly features related to pulse wave velocity and arterial stiffness, correlates with subclinical atherosclerosis. Recent proof-of-concept studies suggest that machine learning models can predict cholesterol levels from PPG features with increasing accuracy. The combination of PPG and smartwatches (or electronic rings) has potential in medical diagnosis: arteriosclerosis, ageing of blood vessels in real-time or low-density lipoprotein cholesterol (LDL-C) measurement. The light technique is a versatile technology that bridges the gap between engineering and clinical diagnostics. While it cannot yet replace laboratory blood tests, it serves as a powerful screening tool for early cardiovascular risk stratification. Future research should focus on refining multi-wavelength sensors and artificial intelligence-driven data analysis.

KEYWORDS

photoplethysmography, LDL-C level, smartwatch, optical technique, diagnostics of arteriosclerosis

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STRESZCZENIE

Fotopletyzmografia (*photoplethysmography* – PPG) jest niskokosztową, nieinwazyjną techniką optyczną, powszechnie stosowaną w warunkach klinicznych oraz w urządzeniach typu *wearable*, zwłaszcza w diagnostyce chorób układu sercowo-naczyniowego. Metoda ta wykazuje potencjał w zakresie oceny profilu lipidowego. Celem niniejszego przeglądu jest podsumowanie aktualnych dowodów naukowych dotyczących zastosowania PPG w ocenie miażdżycy oraz jej związku z profilami lipidowymi, przy jednoczesnym omówieniu podstaw technologicznych oraz perspektyw monitorowania sercowo-naczyniowego za pomocą urządzeń noszonych na nadgarstku. Przeprowadzono przegląd narracyjny na podstawie analizy literatury dostępnej w bazach danych PubMed, IEEE Xplore, Google Scholar oraz Scopus. Analiza objęła badania koncentrujące się na morfologii sygnału PPG, fizyce oddziaływania światła z tkanką oraz nowoczesnych rozwiązaniach technologicznych, takich jak sensory oparte na grafenie. Badania wskazują, że morfologia sygnału PPG – szczególnie cechy związane z prędkością fali tętna i sztywnością tętnic – koreluje z subkliniczną postacią miażdżycy. Wyniki najnowszych badań typu *proof-of-concept* sugerują, że modele uczenia maszynowego z coraz większą dokładnością pozwalają przewidywać poziom cholesterolu na podstawie cech sygnału PPG. Integracja technologii PPG z inteligentnymi zegarkami (smartwatchami) lub pierścieniami elektronicznymi otwiera nowe możliwości w diagnostyce medycznej, m.in. w ocenie miażdżycy, starzenia się naczyń w czasie rzeczywistym czy poziomu cholesterolu frakcji lipoprotein o niskiej gęstości (*low-density lipoprotein cholesterol* – LDL-C). Technika optyczna oferuje wszechstronne możliwości, łącząc inżynierię z diagnostyką kliniczną. Choć nie może jeszcze zastąpić laboratoryjnych badań krwi, jest skutecznym narzędziem przesiewowym we wczesnej stratyfikacji ryzyka sercowo-naczyniowego. Przyszłe badania powinny koncentrować się na udoskonalaniu czujników wielofalowych oraz na analizie danych wspomaganej przez sztuczną inteligencję.

SŁOWA KLUCZOWE

fotopletyzmografia, poziom LDL-C, smartwatch, technika optyczna, diagnostyka miażdżycy

Introduction

Worldwide, the human population has a growing problem with obesity (body mass index [BMI] $\geq$30 kg/m^2). This situation has occurred due to changes in lifestyle. People are not as active as their ancestors. Their diet has changed as well, including higher consumption of trans fat. These factors might contribute to the growth of low-density lipoprotein cholesterol (LDL-C) [1].

Cholesterol is a common fat-like substance that changes the flow of the cell membranes and, as a precursor of bile acids and steroid hormones, flows with other blood cells in blood vessels. There are a few types of cholesterol, but the most common is LDL-C [2]. The primary element of LDL-C is apolipoprotein B-100 (apoB). All of the apoB-containing lipids are markers of major adverse cardiovascular events. Among patients with a high degree of cardiovascular risk factors, rising levels of apoB may indicate the prospect of a cardiovascular incident better than LDL alone [3]. If the LDL-C level in serum is higher than 160 mg/dl or 4.14 mmol/l, it is a conservative indication for therapy [4]. Moreover, the currently normal level of LDL-C has a strong unfavourable correlation with arteriosclerosis [5], so a common and widely available method to measure this type of cholesterol could minimise the chance of vascular blockage or prevent arteriosclerosis.

The most affordable measurement of LDL-C is to take a blood sample via a finger prick, which may be cause for complaints during frequent measurements. In future, it may be possible to monitor human health more often, but the method for examining our cholesterol level is the method discovered by Alrick Hertzman in 1937. Photoplethysmography (PPG), the main topic of this research, currently uses the pulse oximeter [6].

This technique is widely known as a low-cost and simple gadget in wearable technology. The smartwatch market in 2016 was valued at over $13.2 billion, and by the end of 2020 it was forecast to be over $34 billion. This shows that modern wearable devices are no longer limited to pulse oximeters and simple calorie measurement (including the number of the steps taken during a whole day) [7]. The prospects for using PPG in modern and open-access health care is very promising, especially for measuring the level of LDL-C.

High LDL-C level – Resonance and diagnostics

Elevated levels of cholesterol in the blood are connected with steady weight gain and rising BMI in the population. This tendency was shown clearly in the research conducted at the Cardiology Department of Lady Reading Hospital in Peshawar, Pakistan in 2008–2009, involving 2,270 individuals [8]. That study concentrated on the global problem, which is correlated with changing lifestyles. As a result of the observation, a positive correlation between BMI and a general concentration of cholesterol was found (r = 0.205; $p < 0.001$). The correlation between higher body weight and higher lipid levels converge with trends noted in other studies [9].

Excessive LDL-C levels may cause arteriosclerosis, an illness which does not have strong, specific symptoms. This dangerous pathophysiological process is due to an aggregation of LDL-C in the walls of blood vessels. This causes the aortic walls to stiffen and thicken [10]. The results of these changes are visible on B-mode +

USG Doppler (duplex). This technique is a developed way to diagnose arteriosclerosis. Despite this, few people can do this test immediately from one day to the next. It seems that the population is not as aware of the consequences of detaching arteriosclerotic plaque, a situation which is life--threatening. Focussing on the diagnosis itself, a scanner visualises the stenosis of the main arteries produced by atheroma. In addition, B-mode shows the structure of the blood vessel walls and the presence of any atheromas. The Doppler method shows that the velocity of blood flow increases in concert with atheroma. This diagnostic method is based on ultrasound and its reflection from flowing blood cells. The frequency of the reflected waves is changed compared to the output wave [11].

Photoplethysmography and biological optic window

One of the most rapidly developing non-invasive methods to measure human vital signs (e.g. pulse rate or oxygen saturation) is PPG, which uses the different wavelengths reflecting from tissues. This technique also uses biochemical parameter assays. Moreover, the PPG signal's morphology of high LDL-C concentration, especially at the beginning of systolic phase, has come to the attention of researchers [12].

The phenomenon of transmitting and indenting the light is described by physics. The initial law describing the mechanism behind PPG is the Beer–Lambert law, which is expressed by the following formula:

$$I = I_0 \cdot e^{-\alpha \cdot d}$$

where I is the transmitted light intensity, I_0 is the incident light intensity, α is the molar absorptivity (wavelength-dependent) and d is the optical path length.

Unfortunately, the Beer–Lambert law is used only for specific media, which must be homogenic, without scattering or local field scattering. This is the main reason why this law has been modified so as to enable the measurement of other substances dissolved in serum [13].

During the cycle of heart nonaction, when the blood volume increases, the fraction of received light is lower than during diastole. Pulsatile changes in blood volume cause corresponding changes in light attenuation, described by the modified Beer–Lambert law, enabling heart rate to be measured with PPG [14].

The most significant aspect of PPG is the integration of light with tissues, based on optical attenuation deeper into tissues. The signal is produced by the absorption and scattering of the photon flux. Scattering in tissues is highly anisotropic. It is caused by erythrocytes, whose aggregation and orientation changes during the blood cycle. Furthermore, it is essential to isolate the detector and reflector, i.e. to delete optical crosstalk. Effective signal capture requires motion artefacts and the influence of ambient light to be minimised, which is achieved by modulating the emitter signal and using bandpass filters in the receiving system [15].

The crucial fact in this method is the correct choice of wavelength. When selecting the correct wavelength, the researcher should focus on the penetration depth of light in human tissues. The shorter the wavelength, the weaker the penetration. However, the maximum penetration is observed at 800–900 nm or 1000–1100 nm [14,16]. In the near-infrared (NIR) spectral range, the maximum spectral range of lipids (including LDL-C) is at 1710–1780 nm, while the maximum spectral range of water is 970 nm, 1410 nm and 1925 nm [15]. This interaction between electromagnetic radiation and human biology is governed by the competing forces of absorption and scattering, which typically render the body opaque to most wavelengths. However, a specific spectral gap known as the biological optical window provides a unique opportunity for light to penetrate deep into living tissue. This phenomenon occurs primarily in the NIR spectrum, where the primary absorbers of the human body – haemoglobin in the blood and melanin in the skin – reach their minimum extinction levels, while the absorption of water remains relatively low. There are a few types of biological optical windows [17]. The primary one, often referred to as NIR-I, spans approximately from 650 nm to 950 nm. Within this range, the molar extinction coefficient of haemoglobin drops significantly, allowing photons to travel several centimetres through highly vascularised zones without being proximately captured by red blood cells. This clearness is further enhanced in the second and third optical windows (NIR-II and NIR-III) at longer wavelengths, where reduced Rayleigh scattering allows for even higher image contrast and deeper penetration. The realistic implications of this window are foundational to modern non-invasive diagnostics. Because blood is relatively 'transparent' in this region, clinicians can utilise technologies like pulse oximetry and NIR spectroscopy to monitor arterial oxygen saturation and cerebral activity through intact skin and bone [18,19]. Furthermore, this spectral gap is the basis of photobiomodulation and fluorescence-guided surgery, as it provides a clear pathway for therapeutic lasers and analytic signals to reach targets that would otherwise be obscured by the intense absorption of the visible light spectrum. These different values make an optic window, which could improve the non-invasive method to measure the level of different substances, e.g. LDL-C.

The commonplace devices that have a built-in PPG ability consist of a light source and a photodetector. The system emits a wave whose wavelength is particularly

defined, and its changed reflection is picked up by the photodetector. There are two options for arranging the system: transmissional (e.g. in a ring, which is just entering the technology market) and reflectional (e.g. in a smartwatch) (Figure 1) [14,20].

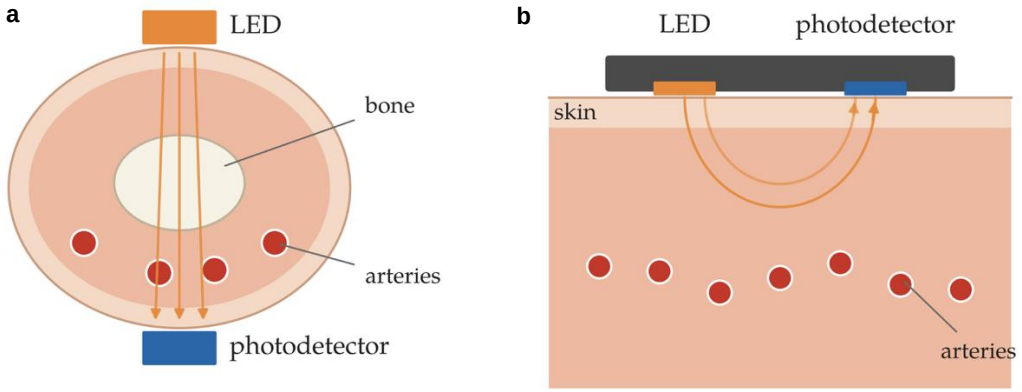

Fig. 1. Configurations of photoplethysmographic sensors: a – transmission mode (e.g. finger clip, ring); b – reflection mode (e.g. smartwatch). Based on [14,20].

Photoplethysmography method in the diagnosis of blood cholesterol levels

To address the limitation of standard invasive cholesterol measurement, Argüello-Prada et al. [21] investigated a non-invasive approach utilising PPG. They explored the relationship between extracted PPG waveform features and total cholesterol levels using various supervised learning regression models. The researchers conducted an experiment which included 46 participants. They reported that cholesterol has better absorbance than other substances dissolved in blood at a wavelength of 1200 nm. For that study, they embedded an L13072-0120L (with peak emission wavelength at 1200 nm), a compatible built-in KP-3216P3C photodiode and a NellcorTM adult finger clip in order to convert the transmitted light levels into an electrical signal. This signal was digitised at 100 Hz by the analogue-to-digital converter (10-bit resolution) of an Arduino Nano microcontroller. The whole experiment was enriched by machine learning algorithms. Their research demonstrates that a Rational Quadratic Gaussian Process Regression model, integrated with the ReliefF feature selection method, significantly outperformed linear regression, regression trees and support vector machines. In the results, the coefficient of determination was 0.832 and the computed correlation coefficient r was 0.912 ($p < 0.001$, 95% confidence interval: 0.874–0.951).

Moreover, elevated LDL-C accelerates vascular ageing, leading to measurable changes in PPG pulse wave morphology [22]. These two things are connected with hardening of blood vessels. If the tissue is less elastic than it was, the PPG signal is less diverse. That tendency is shown in Figure 2, which presents pulse waveform templates for successive age group based on Charlton et al. [23]. Figure 2a compares all four temples, while Figures 2b–2e present them separately. In healthy, young individuals (Figure 2b) we pay attention to the presence of two different peaks, which represent the systolic and diastolic phases. The systolic phase has higher amplitude because of the power of the left part of heart during systole. The second peak shows the diastole of the heart. In healthy subjects with low LDL-C, these two peaks are differentiated by the dicrotic notch (Figure 2b and 2c). Unfortunately, that tendency dwindles over time. In early vascular ageing, the diastolic peak is reduced to a late systolic shoulder (Figure 2d), and in older age the dicrotic notch is no longer visible (Figure 2e) [24]. On the other hand, standardising reference waveforms according to sex, age or BMI, for example, could help identify deviations from normal values. Such standardisation could accelerate the development of health-monitoring features in smartwatches.

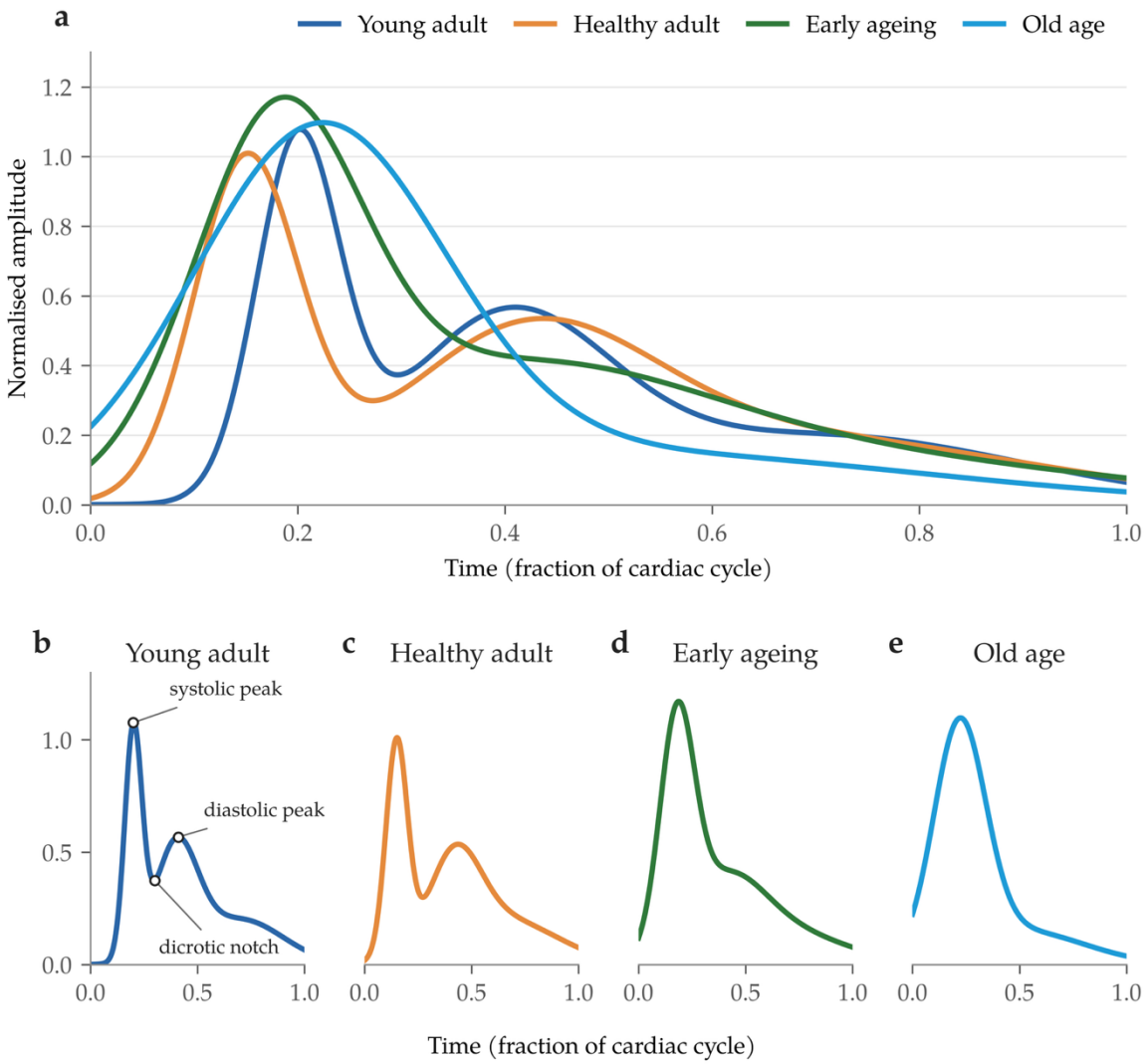

Fig. 2. Pulse waveform templates in different age groups: a – comparison of all four templates; b – young adult with the systolic peak, dicrotic notch and diastolic peak indicated; c – healthy adult; d – early vascular ageing; e – old age. Based on Charlton et al. [23] and used under license (CC BY 4.0) as well as on digitised experimental data.

Future prospects

Like every technological device, the technique of PPG also has prospects for development. Firstly, engineers could concentrate on the photodiode. There are many options to rebuild the photon detector. With the currently used silicone diodes, one of the most innovative ideas is the diode itself, which is based on a graphene–metal junction. This type of detector is suitable for wavelengths which respond to NIR or visible light [20]. The basic information about such photodetectors, which are based on graphene and silicon, is that they could reach an external quantum efficiency of 98% at a wavelength of 850 nm [25]. That information might encourage engineers to develop such photodiodes or to find the specific structure of LDL-C that reflects wavelengths of 850 nm.

Secondly, a subtle change of the wavelength may cause an extremal divide in the technique; then, the most important assumption is the change of the wavelength. Optical experimentation may reveal the most suitable wavelength to reflect photons from LDL-C in blood. That step of developing PPG is also corelated with the results being broken down into lipoprotein fractions. While the current proof-of-concept model focusses on total cholesterol, clinical cardiology requires precise differentiation between LDL and HDL (high--density lipoprotein) fractions. Consequently, these observations and findings prompt the following questions regarding the meaning of a pulse wave in relation to two different types of cholesterol in the blood.

To build on these findings, the datasets should be expanded to include diverse clinical patient profiles. This will enable better calibration of the model regarding physiological variables such as age, body mass and comorbid cardiovascular conditions which may alter PPG waveform morphology. A more

extensive cohort of volunteers will enable a robust validation of the ideal wavelength and the specific reflectance properties associated with cholesterol deposits that contribute to atherosclerosis.

Conflict of interest

The author declares that she has no conflicts of interest.

Ethical approval

This article does not contain any studies with human participants or animals performed by the author.

Use of AI tools statement

Google Gemini was used to check the correctness of language of the article.

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