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Noninvasive Self-monitoring of Blood Glucose at Your Fingertips, Literally!: Smartphone-Based Photoplethysmography

Auto monitoramento não invasivo da glicemia na ponta dos seus dedos, literalmente!: Fotopletismografia baseada em smartphone

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Abstract

Diabetes is a chronic disease and one of the major public health problems worldwide. It is a multifactorial disease, caused by genetic factors and lifestyle habits. Brazil had ~ 16.8 million individuals living with diabetes in 2019 and is expected to reach 26 million people by 2045. There are global increasing needs for the development of noninvasive diagnostic methods and use of mobile health, mainly in face of the pandemic caused by the coronavirus disease 2019 (COVID-19). For daily glycemic control, diabetic patients use a portable glucometer for glycemic self-monitoring and need to prick their fingertips three or more times a day, generating a huge discomfort throughout their lives. Our goal here is to present a review with very recent emerging studies in the field of noninvasive diagnosis and to emphasize that smartphone-based photoplethysmography (spPPG), powered by artificial intelligence, might be a trend to self-monitor blood glucose levels. In photoplethysmography, a light source travels through the tissue, interacts with the interstitium and with cells and molecules present in the blood. Reflection of light occurs as it passes through the biological tissues and a photodetector can capture these interactions. When using a smartphone, the built-in flashlight is a white light-emitting LED and the camera works as a photodetector. The higher the concentration of circulating glucose, the greater the absorbance and, consequently, the lesser the reflected light intensity will be. Due to these optical phenomena, the signal intensity captured will be inversely proportional to the blood glucose level. Furthermore, we highlight the microvascular changes in the progression of diabetes that can interfere in the signals captured by the photodetector using spPPG, due to the decrease of peripheral blood perfusion, which can be confused with high blood glucose levels. It is necessary to create

Keywords

- ► diabetes mellitus
- ► blood glucose self-monitoring
- ► smartphone
- ► photople-thysmography
- ► coronavirus infections

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strategies to filter or reduce the impact of these vascular changes in the blood glucose level analysis. Deep learning strategies can help the machine to solve these challenges, allowing an accurate blood glucose level and interstitial glucose prediction.

Resumo

O diabetes é uma doença crônica e um dos principais problemas de saúde pública em todo o mundo. É uma doença multifatorial, causada por fatores genéticos e hábitos de vida. O Brasil tinha 16,8 milhões indivíduos com diabetes em 2019 e espera-se que atinja 26 milhões de pessoas até 2045. São crescentes as necessidades globais para o desenvolvimento de métodos para diagnóstico não invasivo e uso de saúde móvel, principalmente diante da pandemia causada pela COVID-19. Para o controle glicêmico diário, os pacientes diabéticos usam um glicosímetro portátil para automonitoramento do nível de glicose sanguínea, havendo a necessidade de furar a ponta dos dedos três ou mais vezes ao dia, o que causa um grande desconforto ao longo de suas vidas. Nosso objetivo aqui é apresentar uma revisão com estudos muito recentes no campo do diagnóstico não invasivo e enfatizar que fotopletismografia baseada em smartphone (spPPG) combinada com a inteligência artificial pode ser uma tendência no automonitoramento do nível de glicose no sangue. Na fotopletismografia, uma fonte de luz atravessa o tecido, interage com o interstício, com células e com moléculas presente no sangue. A reflexão da luz ocorre conforme ela passa pelos tecidos biológicos e um fotodetector é capaz de capturar essas interações. Quando se utiliza um smartphone, a lanterna é um LED branco que emite luz e a câmera funciona como um fotodetector. Quanto maior for a concentração de glicose circulante, maior será a absorbância e, consequentemente, menor será a intensidade da luz refletida. Devido a esses fenômenos ópticos, a intensidade do sinal captado será inversamente proporcional ao nível de glicose no sangue. Além disso, nós destacamos as alterações microvasculares na progressão do diabetes que podem interferir nos sinais captados pelo fotodetector usando spPPG, devido à diminuição na perfusão sanguínea periférica, a qual pode ser confundida com níveis elevados de glicose no sangue. É necessário criar estratégias para filtrar ou reduzir o impacto dessas alterações vasculares na análise do nível glicêmico. Estratégias de aprendizagem profunda podem ajudar a máquina a resolver esses desafios, permitindo uma predição acurada do nível de glicose sanguínea e intersticial.

Palavras-chaves
- diabetes mellitus
- automonitorização da glicemia
- smartphone fotopletismografia
- infecções por coronavirus

Introduction

Diabetes is a chronic disease and one of the major public health problems worldwide. It is a multifactorial disease, caused by genetic factors and lifestyle habits.[1,2] The top five countries with the highest number of people with diabetes in 2014 were China (102.9 million), India (64.5 million), United States (22.4 million), Brazil (11.7 million), and Indonesia (11.0 million).[3] In 2019, Brazil had $\sim$ 16.8 million individuals living with diabetes, and the number of Brazilians with diabetes is expected to reach 26 million by 2045.[4]

One of the goals of the treatment is the careful monitoring of glycemia, in face of diet and/or pharmacological interventions. Considering the pandemic caused by the coronavirus disease 2019 (COVID-19) and the global increasing needs of development of noninvasive diagnostic methods and use of mobile health, this is an important moment to bring recent emerging studies in the field of noninvasive diagnosis and to emphasize that the smartphone-based photoplethysmography (spPPG), powered by artificial intelligence, might be a trend to self-monitor blood glucose levels.

Recent studies point to possible associations between diabetes and the progression of COVID-19, being type 2 diabetes as a major risk factor for COVID-19 severity.[5,6] Chinese studies analyzing patients admitted with COVID-19 showed that between 12 and 16% had diabetes mellitus (DM); among critical ill patients, 40% had previous chronic disease and, among those who died, 7.3% had DM. The more accepted explanation for these results considers the fact that DM increases the inflammatory process and contributes to the progression of the COVID-19 disease.[4]

Glycated hemoglobin is the preferred method for long-term glycemic control; the percentage of hemoglobin glycation is directly associated with the concentration of blood glucose; however, to perform this exam, it is necessary to use a needle and a syringe to collect the blood sample. For daily glycemic control, diabetic patients monitor their capillary glucose using portable glucometers. The portable glucometer for self-monitoring glycemic levels is indubitably simple to use.[7] However, imagine patients who prick their fingertips three or more times a day, and the discomfort that this practice generates throughout their lives.

Therefore, it is necessary to develop noninvasive strategies for blood glucose self-monitoring and put an end to the fingertip prick.

Smartphone-based Photoplethysmography

Photoplethysmography (PPG) is a promising new technique, which has presented promising results for the prediction of diabetes. Photoplethysmography is an optical technique in which a light source travels through the tissue, interacts with cells and molecules present in the blood and the interstitium. Reflection of light is possible as it passes through the biological tissues, and a photodetector will capture these interactions. When using a smartphone, the built-in flashlight is a white light-emitting LED, and the camera acts as a photodetector.[8]

The smartphone camera records a video of the patient's fingertips, so the spPPG method is similar to the operation of the pulse oximeter. The flash must be on and in direct contact with the finger, and the smartphone camera records a video of the patient's fingertips. The video is then processed by a computer program or a smartphone application to process the footage. Then the software extracts the frames and analyzes the signal pattern from each frame. The differences of optical densities captured by the camera allow the formation of a time wave series, the PPG waves. The characteristics of the waves are used, combined with clinical assessments and laboratory tests, to train machine learning algorithms and allow the machine to make classifications and predictions of blood glucose levels.[9–11]

The concentration of circulating glucose interferes with the refractive index, obeying the Beer-Lambert law, which explains that the absorption of light from a solution is proportional to the concentration of this solution. Thus, the higher the concentration of circulating glucose, the greater the absorbance and, consequently, the lesser the reflected light intensity will be.[9] Due to these optical phenomena, the signal intensity captured will be inversely proportional to the blood glucose level (►**Figs. 1A** and **1B**).

Microvascular changes and other vascular modifications can occur during diabetes progression and may lead to decrease in peripheral blood perfusion. As PPG analyzes the signal intensity per time, if blood flow remains lower, a weaker light signal will be detected, which may be confused with high blood glucose levels. Vascular changes occur due to decreased secretion of prostacyclin (PGI_2) and nitric oxide (NO), which reduces the capacity of vasodilation. Additionally, there may be membrane remodeling and thickening, the formation of microaneurysms, increased coagulation factors, and formation of clots and atheroma along the blood vessel wall.[12] Because of this artifact, it is crucial to consider these vascular factors to obtain better accuracy results of blood glucose levels (►**Fig. 1C**).

Machine learning is within the artificial intelligence (AI) approach, inspired by one of the human's learning procedures, through examples and errors. A machine can recognize patterns and, at the end of the process, give a predictive answer to a complex question. One set of data is used to train the algorithms and another set to perform the tests aiming to check the accuracy of the model.[13,14]

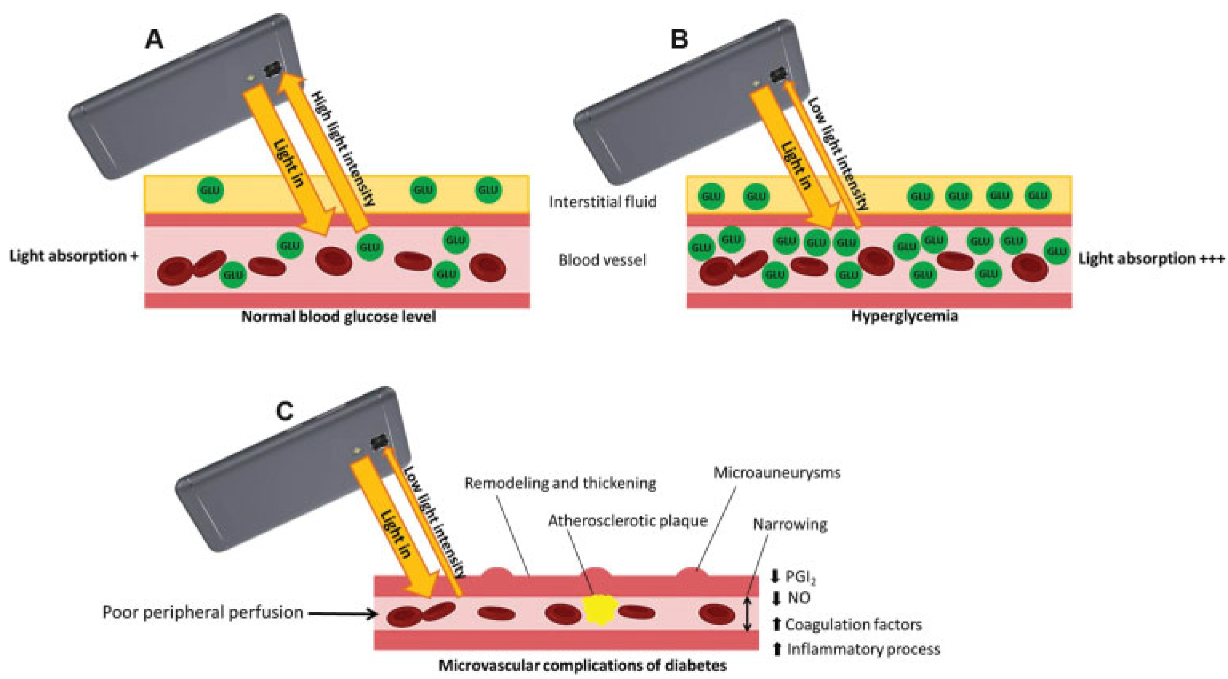

Fig. 1 Smartphone-based photoplethysmography (spPPG) method for analyzing blood glucose levels. (**A**) Average blood glucose level. (**B**) High blood glucose level with decreased signal intensity captured by the camera. (**C**) A highlight of the main microvascular changes in the progression of diabetes that can interfere in the signals obtained by the photodetector using spPPG.

In March 2019, Avram et al[15] presented a very innovative proposal that applies only the smartphone and deep learning techniques to predict diabetes, involving 22,298 patients. The Azumio (Azumio, Inc, Redwood City, CA, USA) smartphone app was used to capture video from the fingers of patients. The datasets were separated as follows: 70% for training algorithm, 10% for development and 20% for testing. The method also showed good accuracy, measured by using the area under the receiver operating characteristic curve (ROC), area under the curve (AUC) = 0.772.

In February 2020, Zhang et al,[10] also demonstrated a smartphone-based approach to measure blood glucose by incorporating PPG and machine learning. This approach highlights the hypothesis that the signal intensity derived is inversely proportional to blood glucose. A 60-second video was obtained from the index finger of 80 individuals using the smartphone's camera. A computer with the MATLAB (MathWorks, Inc., Natick, Massachusetts, USA) program processed the videos. The algorithm extracted the data, adjusted the baseline and classified the information. Counting the frames and measuring the pixel intensity of each frame provided the information to plot a graph correlating the color intensity variation in time. The conventional glucometer was used as a reference point to measure the glucose levels of individuals. The method showed an accuracy of 81.49% in estimating the blood glucose levels.

Final Considerations

These approaches are very recent, dating from 2019 and 2020, and they are in a preliminary phase. Hopefully, it is possible to note the potential of using spPPG and machine learning techniques to become a noninvasive, portable, and low-cost alternative for self-monitoring of blood glucose levels. It is possible that, soon, smartphone applications will measure the signal intensity captured by the smartphone camera and, furthermore, microvascular and other vascular changes caused by the progression of diabetes should be considered and added to the algorithm. It is necessary to create strategies to filter or reduce the impact of these vascular changes in the blood glucose level analysis. Deep learning strategies can help the machine to solve these challenges, allowing accurate blood glucose levels and interstitial glucose prediction.

Conflict of Interests

The authors have no conflict of interests to declare.

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