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SURVEY

Photoplethysmography and Artificial Intelligence for Blood Glucose Level Estimation in Diabetic Patients: A Scoping Review

SARA LOMBARDI, (Member, IEEE), LEONARDO BOCCHI, (Member, IEEE), AND PIERGIORGIO FRANCIA

Department of Information Engineering, University of Florence, 50139 Florence, Italy

Corresponding author: Sara Lombardi (sara.lombardi2@unifi.it)

ABSTRACT New technologies, including artificial intelligence (AI), offer significant opportunities to improve blood glucose level (BGL) estimation systems, potentially enhancing care and quality of life for diabetic patients. This study aimed to assess the accuracy of BGL estimation using photoplethysmographic signal (PPG) analysis and AI methods by comparing various studies in terms of population, PPG signal acquisition and analysis, AI approaches, and BGL estimation performance. A systematic search was conducted in Scopus, Web of Science, Embase, PubMed and CINAHL databases. Conference proceedings and book chapters were included, excluding other gray literature, focusing on English-language studies published from 2010 to February 2024. Only publications concerning PPG signal analysis using AI algorithms for noninvasive estimation of BGL in patients with diabetes were considered. Of 48 identified articles, 24 were reviewed in full text, and 5 were deemed eligible. These studies varied in methodology (populations, devices, AI solutions) and evaluation metrics. However, all studies used Clarke error grid or Parkes error grid, with over 98% of estimates falling into clinically acceptable zones A or B. Current research confirm that PPG-based BGL estimation is feasible and accurate. Further studies are needed to overcome existing limitations and make this procedure available, accurate, and easy to perform.

INDEX TERMS Artificial intelligence, blood glucose level, diabetes, glycemia, photoplethysmography.

LIST OF ABBREVIATIONS

AI	Artificial Intelligence.
BGL	Blood Glucose Level.
CEG	Clarke's Error Grid.
CGM	Continuous Glucose Monitoring.
FBG	Fasting Blood Glucose.
MAE	Mean Absolute Error.
MAPE	Mean Absolute Percentage Error.
MARD	Mean Absolute Relative Difference.
PEG	Parkes' Error Grid.
PPG	Photoplethysmography.
RBG	Random Blood Glucose.
RMSE	Root Mean Square Error.
SMBG	Self-Monitoring of Blood Sugar.

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I. INTRODUCTION

A. RATIONALE

Diabetes is a dreaded disease and a main cause of morbidity and mortality in many countries around the world [1], [2]. In addition to having a large negative impact on the health and quality of life of patients, with an increasing incidence worldwide, diabetes also represents a huge cost for healthcare systems. It is known that today, more than ten percent of adults worldwide are affected by diabetes and the number of young patients is also constantly growing. In particular, it has been reported that diabetes is a global epidemic affecting over 530 million patients worldwide and that this number may rise over 780 million in 2045 [1], [2], [3]. All this makes diabetes one of the most challenging health problems for many healthcare systems and indicates the need to prevent the disease or treat patients in a timely and appropriate manner [4], [5].

Diabetes is caused by the loss, even partial, of the body's ability to produce or use insulin. This condition can lead to too high levels of glucose in the blood (hyperglycaemia). The presence of hyperglycemia is particularly feared and should be avoided since it can cause dangerous acute and chronic consequences. In the short term, hyperglycemia can lead to dangerous conditions such as diabetic ketoacidosis and hyperosmolar hyperglycemic state. In the long term, chronic hyperglycemia contributes significantly to the development of microvascular complications, such as diabetic retinopathy, diabetic nephropathy, and diabetic neuropathy, as well as macrovascular complications, including cardiovascular disease, stroke, and atherosclerosis [6], [7]. The appropriate management of blood sugar levels (Blood Glucose Level (BGL)) is the main objective of the treatment of patients with diabetes [8], [9].

To obtain this results it is necessary to know the exact blood glucose level (BGL) of the patients. Over time, increasingly reliable, easy-to-perform and less invasive methods have emerged for the evaluation of BGL in patients with diabetes [10], [11], [12]. In this sense, almost 2 centuries have passed since the first attempts to evaluate the quantity of glucose in urine. Only at the beginning of the last century, tests were made available to perform this evaluation in the clinical setting. More recently, in 1957, a methodology for the semi-quantitative clinical assessment of blood sugar levels through the use of a blood test strip was developed [12], [13], [14]. A few years later, glucose meters increasingly precise and usable even at home by patients began to be available. Over the years, these devices have become less invasive, painful and expensive, resulting in better precision and ease of use. All this has favoured their increasing use by patients, promoting the monitoring and treatment of diabetes. In this regard, self-monitoring of blood glucose has become the standard of care for an ever-increasing number of patients. Initially, in fact, self-monitoring of blood sugar (Self-Monitoring of Blood Sugar (SMBG)) was indicated for patients with greater needs, such as those with type 1 diabetes or, more generally, on insulin therapy [12], [13], [15]. It was only at the end of the last century that continuous glucose monitoring (Continuous Glucose Monitoring (CGM)) was introduced under the supervision and management of specialized healthcare personnel. A first real-time, non-invasive BGL monitoring system (Glucowatch Biographer) was introduced about 25 years ago [12], [14], [15]. Subsequently, some CGM system were marketed within a few years. Devices capable to alert patients in case of hyperglycemia or hypoglycemia and real-time CGM devices represented a great opportunity for the management of patients with diabetes. Another important technology was developed and made available during this period. In particular, a real-time CGM system was integrated with an insulin delivery device. Over time, diabetes centers have increasingly used systems to remotely monitor patients' blood glucose levels, using data obtained and stored by CGM devices [12], [13], [15].

The use of these technologies for the treatment of patients with diabetes has become increasingly systematic [11], [16]. Indeed, the achievements obtained in the BGL evaluation and, in particular, those associated with the CGM and the new technologies typical of the last 20 years, have revolutionized the way diabetes, particularly type 1 diabetes, is managed [12], [14], [15]. Over the last few years, the increasingly strong technological development has offered other potentially useful techniques for the assessment of blood sugar levels [12], [15], [17]. In particular, technologies based on optical techniques, e.g., laser doppler and videomicroscopy, have found increasing use in the assessment of microcirculatory district function [18], [19]. Among these techniques, photoplethysmography (Photoplethysmography (PPG)) emerges as one of the most promising for application in health care. Photoplethysmography is a noninvasive technique that uses the optical properties of light to assess changes in blood flow in the microvascular bed of the skin [20], [21].

The growing interest in the study of photoplethysmographic signal in health care is due to several factors. Recent studies showed that PPG is a technique that can provide important information about the health status of the cardiovascular system and its aging, as well as several other important conditions (e.g., sepsis, sleep quality) [22], [23], [24]. Moreover, PPG acquisition requires a noninvasive, easy-to-perform, and low-cost procedure [24], [25], [26]. In this sense, further interest in the study of the PPG signal is due to the fact that the acquisition of the signal has become increasingly possible and easy to use also thanks to different devices such as smartphones [24], [25]. Furthermore, the spread of the use of photoplethysmography in the management of patients has been favoured by the use of Artificial Intelligence (AI) in the analysis of the signal and the results obtained.

An increasing number of AI solutions were used to study PPG for the BGL assessment in patients with diabetes or at risk of developing diabetes. Although these studies seem to have yielded interesting results, the complexity of this recent field of AI application requires a thorough overview and mapping of the available scientific literature.

In particular, it is important to highlight, review and summarize emerging evidence, as well as to analyze the characteristics of the proposed procedures.

Our scoping review could represent an important opportunity to reduce or eliminate any knowledge or procedural gaps.

The purpose of this work was to explore and critically evaluate studies on the effectiveness of AI algorithms applied to PPG signal analysis for the estimation of blood glucose level in patients with diabetes or at risk of developing diabetes.

Furthermore, the examination of the selected studies with respect to the procedures for acquisition and analysis of the PPG signal, creation of the datasets and quantification of the BGL represented a further objective of the study.

B. OBJECTIVES

The main objective of this scoping review was to provide an overview of available studies and to examine emerging evidence related to glycemia assessment based on PPG signal

analysis and AI algorithms in patients with diabetes or at risk of diabetes. Summarizing the results obtained from the bibliographic search and describing the characteristics of the selected studies represented a further objective [27], [28].

Finally, this study was conducted to identify and analyze the knowledge gaps and limitations of the considered studies, particularly with respect to the role of PPG analysis in blood glucose assessment. The research question of the study was: ''How many and what are the characteristics of the published studies related to the use of artificial intelligence algorithms for the analysis of the PPG signal and the estimation of blood glucose levels in diabetic patients?''

II. METHODS

This study was conducted according to the framework proposed by Arksey and O'Malley [29], and complies with the recommendations of the Joanna Briggs Institute for elaborating scoping reviews [30]. We used the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews) as the guideline for this scoping review [31].

A. ELIGIBITY CRITERIA

We conducted this review in five key phases: (1) identifying the research question, (2) identifying relevant studies, (3) selecting the studies, (4) charting the data and (5) collating, summarising and reporting the results [32]. To answer our research question we defined specific eligibility criteria to ensure the relevance and quality of the examined research.

Eligibility criteria of this scoping review were the selection of research articles from peer-reviewed journals and conference proceedings that deal with PPG signal analysis using artificial intelligence algorithms for noninvasive blood glucose estimation in diabetic patients. Our approach includes all research designs, from randomized controlled trials to cross-sectional studies, to capture the broadest spectrum of advances in this field. We considered studies applied specifically to human diabetic populations, without imposing limitations on age, gender, ethnicity, or comorbidities. Studies with an incomplete description of the AI procedure performed were not considered. Particular attention was given to the type of the procedure adopted for dataset construction, data analysis and application of AI solutions. Indeed, understanding whether and in what way the analysis of PPG signals through AI can allow the correct estimation of the BG level of patients with diabetes is the main objective of this scoping review. In terms of temporal scope, the review focused on studies published between January 1, 2010, and February 2024, to incorporate the most current contributions to this field of research. In addition, to facilitate universal accessibility and understanding, only studies published in English were considered. Conversely, the review deliberately excluded abstracts, literature reviews, commentaries, editorials, and opinion articles to maintain an exclusive focus on original research. Studies involving animals were also excluded, reinforcing the review's commitment to directly applicable human research findings. In addition, studies published in languages other than English and published before 2010 were not considered.

B. INFORMATION SOURCES AND SEARCH STRATEGY

To identify relevant studies, we performed a systematic search of the following electronic databases: Scopus, Web Of Science, Embase, PubMed, and Cumulative Index to Nursing and Allied Health Literature (CINAHL). Conference proceedings and book chapters were included to ensure a complete coverage, excluding other forms of grey literature. The search strategies used the following keywords to capture concepts related to diabetes (*diabetes, diabetes mellitus, diabetic patients*), photoplethysmography (*photoplethysmography, photoplethysmogram, PPG signal*), artificial intelligence (*AI, artificial intelligence, machine learning, deep learning, predictive models*), and blood glucose level in diabetic patients (*metabolic control, blood glucose level, glycaemia, glycemia, glycemic index, glycated hemoglobin, hemoglobin A1c, HbA1c, glycosylated hemoglobin*). The query string was adapted to the specific characteristics and requirements of each database. The complete search strings can be found in the Appendix.

C. DATA EXTRACTION

In accordance with inclusion criteria, two of the authors (SL and PF) independently selected the articles considering the title and abstract. Articles were collected in an EndNote X9 library (Clarivate) by both authors and, once duplicates were removed, were compared. The final list of considered articles was imported into an Excel spreadsheet by one of the authors and checked by another. The information considered was: date of publication, population investigated including type of diabetes, sex, BMI, ethnicity, skin characteristics, duration of the disease, blood glucose and glycosylated hemoglobin values, therapy, presence of complications and comorbidities. In addition, the following elements were taken into account: blood glucose measurement device and PPG signal acquisition device, type of PPG signal evaluation (duration, acquisition protocol), data set characteristics, data set processing, artificial intelligence method and main results. The studies were sorted by year of publication. For each of the studies considered, the information analyzed was presented in summary tables.

III. RESULTS

A. SEARCH RESULTS

The bibliographic search carried out in the various libraries identified a total of 48 articles after the removal of duplicates. The distribution by publishing year of these articles is shown in Figure 1.

After the analysis of the title and the abstract 17 works were removed. An additional 8 articles were retrieved and assessed for eligibility by comparison between the two reviewers.

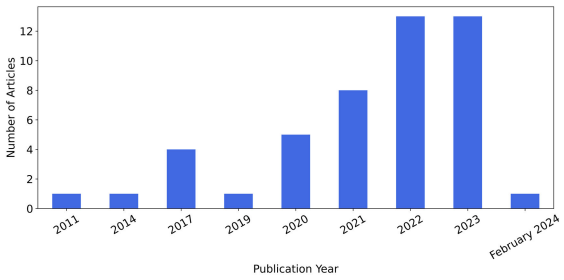

FIGURE 1. Year of publication of revised articles (N=48).

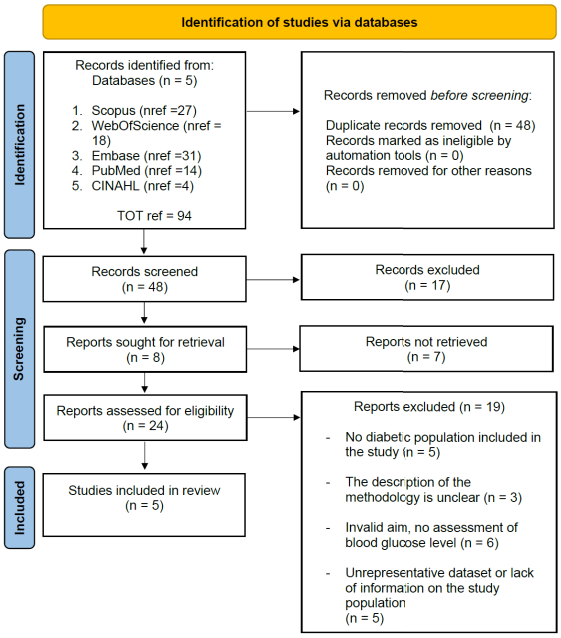

FIGURE 2. Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Scoping Reviews (PRISMA) flow diagram of the search and study selection process.

Among them, one article was retrieved and thus a total of 24 articles were examined as full text. Of the reviewed articles, 20 were journal publications and 4 conference proceedings. At the end of the full-text examination procedure, a further 19 articles were excluded for the following reasons: the group of subjects investigated by PPG analysis was not diabetic (n=5), unclear description of the methodology (n=3), PPG analysis to evaluate the presence of diabetes and not the blood sugar level (n=6), lack of data or lack of characteristics on the study population (n=5). The PRISMA flowchart illustrating the study selection process is outlined in Figure 2.

B. CHARACTERISTICS OF THE INCLUDED STUDIES

After the selection process, 5 studies were considered eligible for this scoping review [33], [34], [35], [36], [37]. All studies were published in peer-reviewed journals and are reported in Table 1.

Among the included studies, two are from China, one from Taiwan, one from India, and one from Spain. One study was published in 2011, while all other studies have been published recently, starting from 2022 (Table 1). The studies were analyzed in terms of study population, study protocol and design, AI methodologies used, and results obtained in blood glucose level estimation. With regard to the characterisation of the population included in the 5 studies considered, Table 2, the description of the participants was partial or incomplete apart from the study by Lu et al. [36]. In this sense, even the main characteristics of clinical interest, such as gender, age, BMI, metabolic control, type of diabetes, years of disease and therapy, were not described in detail. Moreover, in some studies there was an under-representation of the population with diabetes (Table 2). In the Monte-Moreno study [33], only 79 out 410 subjects investigated were patients with diabetes, while in the study by Li et al. [35], investigated 21 subjects included only 4 patients with diabetes. In these studies, the characteristics of the two populations investigated, with and without diabetes, were not specified. In contrast, in the article by Lu et al. [36], PPG and BGL measurements were acquired in 30 diabetic subjects. However, this study did not include a control group. In this study, important parameters for the evaluation of the PPG signal were considered, namely gender, type of treatment, smoking, age and BMI. In the study by Padmavilochanan et al. [34], the 283 participants included in the dataset had glucose levels in the normal, pre-diabetic range and diabetic range. However, the study does not report a description of the specific population characteristics for the three groups. The same condition is present in the article published by Chen et al. [37]. In this study, 3 subgroups of patients are considered without specifying the characteristics of the three populations. In addition, Table 2 reports recruitment strategies, including inclusion and exclusion criteria, and provides guidance on study design and potential bias in results. As reported, some studies lack a clear description of inclusion and exclusion criteria for the recruitment of participants. Indeed, only 2 studies (Padmavilochanan et al. and Li et al. [34], [35]) report exclusion criteria (see Table 2).

C. DEVICES AND PROCEDURES

The examined research studies used a variety of PPG devices, ranging from commercially available devices [33], [35] to customised sensors designed specifically for the research [34], [36], [37] (see Table 3). The glucometers used for measuring the blood glucose level (BGL) also differed between the studies. Chen et al. [37] used BGL measurement by blood test, while Li et al. [35] adopted a continuous blood glucose monitoring patch without fingertip sampling. The other studies adopted commercial glucometers requiring acquisition by finger prick. Two different commercial glucometers were used in the study by Padmavilochanan et al. [34] however, their type was not specified. Most studies opted for fasting blood glucose (Fasting Blood Glucose (FBG)) measurement [34], [35], [36], [37], in line with standard practice for reliably assessing glucose levels. One study [33]

TABLE 1. Selected articles.

Study	Research Aim	Country
Monte-Moreno E., 2011 [33]	Develop a system for simultaneous non-invasive estimate of BGL and blood pressure using PPG signal and machine learning techniques	Spain
Padmavilochanan D. et al., 2023 [34]	Develop an Internet of Medical Things (IoMT) based wearable device for non-invasive and real-time measurement of BGL	India
Lu WR. et al., 2022 [36]	Develop a noninvasive method for measuring BGL from PPG signal with a limited number of data collection sessions using a Deduction Learning approach	Taiwan
Li J. et al., 2023 [35]	Construct a novel multi-modal framework based on ECG and PPG signal fusion to establish a universal BGL monitoring model	China
Chen S. et al., 2024 [37]	Development of a noninvasive method for measuring BGL using PPG signal	China

employed random blood glucose (Random Blood Glucose (RBG)) measurement.

Regarding the acquisition protocol, the adoption of standardized procedures is critical to ensure that measurements are robust and can be reliably compared while minimizing the influence of external factors. In the selected articles, the PPG measurement site was the fingertip for all studies involved, with possible differences from the finger considered. Notably, only in the studies of Lu et al. and Li et al. [35], [36], it was specified that the measurement were conducted on the left middle finger for all subjects involved in the study. In Monte-Moreno's study [33], experiments to assess BGL were conducted in different environments and by different operators. In particular, some measurements were acquired within the university research laboratory by the author, while others were acquired in out-patient clinics by a physician.

Four out of five studies [34], [35], [36], [37] specified that data acquisition took place after a resting phase. In addition, in Li's study [35], restrictions were adopted on the use of drugs and physical activity two hours before the experiment, while in Chen's study [37], the use of glucose-lowering drugs was avoided from the day before the experiment.

In 3 studies [33], [35], [37] PPG and BGL measurements were performed only once per subject investigated. In the study by Lu et al. [36], the acquisition was repeated several times on different days, while in the study by Li et al. [35] the duration of the period of signal acquisition and test performance was longer than in the other works considered. In fact, the experiments started at 9:00 a.m. and lasted 150 minutes for each participant. In addition, signals were also acquired after the participants ate 100 g of bread and 250 ml of water.

D. ARTIFICIAL INTELLIGENCE METHODS

Table 4 provides an overview of the artificial intelligence methods applied to blood glucose level estimation using the PPG signal. It can be seen that 3 out of 5 studies adopted deep learning techniques, indicating a prevalent trend toward complex models that can capture and analyze fine patterns in PPG data. Conversely, in his work, Monte-Moreno [33] used the random forest model, an ensemble approach that often offers robustness and ease of interpretation. The random forest regressor was also used in Li's study [35], in which its integration with other ensemble models, namely gradient boosting and bagging, via the choquet integral was explored. All 5 studies used supervised learning approaches using the BGL value measured by commercial devices or blood test as ground truth. Regarding the input used for artificial intelligence algorithms, it is possible to distinguish between two main approaches: the use of pre-processed portions of the signal and the use of features extracted from signals through a feature engineering process. Regarding the construction of data sets for model training and evaluation, 3 studies [33], [34] adopted a data set split into training set and test set, assigning part of the subjects to the training test and part to the evaluation set. In Lu and Li's studies, however, the division was made according to the time of acquisition. Li et al. [35] divided the training and evaluation sets according to days of acquisition, assuming that physiological signals collected between different individuals and on different days may reflect physiological changes for a partial population. Lu et al. [36] used the first 12 round of PPG acquisition to train the model and the last 3 rounds (13-15) for model evaluation. Only one study, Padmavilochan et al. [34], included the construction of an additional test set (deployment dataset) to evaluate their model. The different input data and dataset construction adopted for the artificial intelligence methods are described in detail in Table 4.

To train and validate the models, 4 out of 5 studies [33], [35], [36], [37] used a cross-validation approach. In the study by Padmavilochanan et al. [34] the GlucoNet model was trained and evaluated on a dataset of 283 participants of which 10% used as validation set and 30% used as test set. Finally, the generalization ability of the GlucoNet was evaluated on an additional dataset of 600 subjects (deployment dataset).

E. BLOOD GLUCOSE LEVEL ESTIMATION

The reviewed studies used several metrics to evaluate the performance of artificial intelligence approaches. Only one study used the coefficient of determination R^2 [33], while

TABLE 2. Population of selected studies.

Study	Partecipants [#]	Diabetic subjects [#]	Gender* [M/F]	Age* (yrs) [range; mean ± std]	Ethnicity*	Recruitment of subjects
Monte-Moreno, E. [33]	410	79	213 / 197	(9-80); (37.97 ± 13.32)	N/A	Universitat Politecnica de Catalunya staff (#71) and an ambulatory primary care center (#339)
Padmavilochanan D et al. [34]	357 (283 included in dataset)	88 pre-diabetic (BGL: 5,6-6,9 mmol/L) 124 diabetic (BGL > 6.9 mmol/L)	205 / 152	(26-82); (60 ± 14)	Indian	Development Study: Custom Glucose monitoring IoT platform **Exclusion Criteria:** $BGL > 11.1 mmol/L$
Lu WR et al. [36]	30	30	18 / 12	(38-76); (60.36 ± 8.86)	N/A	Laboratory of Academia Sinica, Taiwan
Li J et al. [35]	21	4	12 / 9	(20-63); N/A	N/A	Shenzhen Institute of Advanced Technology Chinese Academy of Sciences (SIAT-CAS) **Exclusion Criteria:** Heart-related or blood diseases
Chen S et al. [37]	260	40 pre-diabetic (BGL: 6,1-6,9 mmol/L) 49 diabetic (BGL: 7,0-12,0 mmol/L)	126 / 134	(16-82); (43 ± 13, 8)	N/A	Ninth People's Hospital of Chongqing

*Data related to the total number of participants, not available for the group of patients with diabetes

TABLE 3. Measurement protocol of selected studies.

Study	PPG Device	BGL Device	BGL Measure	Measurement Protocol
Monte-Moreno, E. [33]	iPod Digital Oximeter	Accu-Chek Aviva glucometer, Roche	RBG	PPG sensor placed on the finger. One measurement of BGL and PPG was taken for each subject.
Padmavilochanan D et al. [34]	Custom IoMT- based PPG wearable device	2 different commercial glucometers	FBG	Partecipants fasted before the experiment. Participants rested for two minutes before measurements. PPG sensor placed on the finger. Ground truth BGL measurements obtained using commercial glucometers followed by 90 s acquisition of PPG signals.
Lu WR et al. [36]	Custom TI AFE4490 Integrated Analog Front End PPG sensor	Accu-check mobile, Roche	FBG	Partecipants fasted before the experiment. Subjects were asked to rest in a sitting position at least 5 minutes. PPG sensor placed on the left middle finger. 6 to 15 recurring rounds of PPG signal measurements and FBG were taken for each subject.
Li J et al. [35]	Biopac acquisition system	CGM system-Dexcom G6	FBG	Partecipants fasted 8h before the experiment and avoided to exercise or use drugs 2 h prior measurement. Partecipants were in a relaxed sitting position before and during measurements. PPG sensor placed on the left middle finger. The BGL values were measured every 5 min automatically by CGM system, the acquisition of PPG lasted 30 minutes.
Chen S et al. [37]	Custom HKG-07C PPG sensor	Blood Test	FBG	Partecipants fasted 8 hours before data collection and avoided glucose-lowering drugs the day before experiment. Subjects were asked to rest in a sitting position for 5 minutes before measurements. PPG sensor placed on the fingertip. A sample of venous blood was collected and then the PPG signal was acquired for about 3 minutes.

RBG: Random Blood Glucose; FBG: Fasting Blood Glucose

the other 4 studies [34], [35], [36], [37] quantified mean prediction error using mean absolute error (Mean Absolute Error (MAE)) or root mean square error (Root Mean Square Error (RMSE)). Two studies [35], [36] used the accuracy score metric. Two studies [35], [36] expressed the percentage estimation error by resorting to the metrics Mean Absolute Percentage Error (Mean Absolute Percentage Error (MAPE)) and Mean Absolute Relative Difference (Mean Absolute Relative Difference (MARD)). All studies introduced Clarke's error grid (Clarke's Error Grid (CEG)) or Parkes'error grid (Parkes' Error Grid (PEG)) analyses as evaluation metrics. Both evaluation grids divide the results into five zones (A-E) according to the accuracy of clinical decisions resulting from the estimated blood glucose values with respect to reference values. Zone A includes estimates that lead to clinically correct decisions, while zone B includes clinically non-critical estimates, where the error does not expose the patient to risk. Zone C denotes potentially harmful over-corrections, while zone D indicates missing necessary corrections. Finally, zone E represents dangerous errors, where the estimate leads to making the opposite of the necessary decision (e.g. administration of insulin when the patient is hypoglycaemic). The later developed Parkes' Error Grid has a similar structure, but introduces smoother transitions between zones and specific differences for patients with type 1 and type 2 diabetes, making the assessment more adaptable to clinical practice [38]. The description of the models' performance is shown in Table 5. The study by Monte-Moreno [33] showed a high coefficient of determination ($R^2 = 0.88$), suggesting that the model is effective in explaining the variability in the observed data. In addition, the majority of predictions (87.71%) fell within the Clarke's Error Grid Zone A, indicating high clinical reliability of the measurements.

GlucoNet model by Padmavilochanan et al. [34] achieved a MAE of 1.4 mmol/L and a mean absolute percent error (MAPE) of 17.8 % (±12.8 %) on the test set. The Clarke's Error Grid (CGE) analysis shows a significant percentage of predictions (45%) in zone B, even though all predictions fall within the clinically acceptable A and B zones. Regarding the additional deployment set, the metrics values of MAE (1.3 ± 1.0), MAPE (21.8%), CGE-Zone A (57%) and CGE-Zone B (43%) obtained in this test scenario further confirm the robustness of the model.

The results of Li et al. [35] demonstrated a solid performance of their AI model in predicting glucose levels, with most predictions falling within clinically acceptable ranges (CGE Zone A (80.09%)).

The model proposed by Chen et al. [37] obtained a lower MAE value of 0.656 mmol/L, but an higher RMSE value of 1.129 mmol/L. Regarding the clinical acceptability of the predictions, most of the predictions falling in Zone A (87.89%) and a small percentage in Zone B (12.11%).

IV. DISCUSSION

The results of this scoping review show that in recent years there has been a growing interest in the study of the relationship among PPG signal analysis and AI solutions for monitoring blood glucose level (Figure 1). However, evidence regarding the possibility of using PPG signal analysis to estimate the BGL of patients with diabetes is still limited. In fact, only a limited number of studies applied this method of analysis to a diabetic patients' population. Among these, only 5 papers [33], [34], [35], [36], [37] provided sufficient methodological description and met the inclusion criteria to be considered in our study. In accordance with the main purpose of this scoping review, particular attention was paid to the adopted PPG signal acquisition and analysis procedures as well as to the implemented AI solutions.

A direct comparison of results across studies is hindered by the variation in methods and evaluation metrics used to analyze datasets. Indeed, each article presented differences in the methods adopted as well as in the characteristics of the investigated population. Likewise, each study applied distinct evaluation metrics. The selection of different accuracy metrics across studies can be justified by the fact that each method has specific purposes and characteristics. Furthermore, the combined use of multiple metrics within individual studies offers a more comprehensive assessment of model robustness [39]. Regarding the evaluation of AI performance in the 5 studies considered, only one of them [33] used the coefficient of determination R^2. The other four studies [34], [35], [36], [37] quantified mean prediction error using Mean Absolute Error (MAE) or Root Mean Square Error (RMSE). Moreover, Accuracy score metric, Mean Absolute Percentage Error (MAPE) and Mean Absolute Relative Difference (MARD) were used. Finally, all studies introduced Clarke or Parkes error grid analyses.

Given these differences, we focused on analysing each study individually, highlighting the specific strengths and limitations of each approach. This analysis allows us to present an insight into the contributions and challenges of each study, thus highlighting the diversity of methodologies while recognising the advancements made in this emerging field.

For the BGL estimation performed, the high coefficient of determination obtained by Monte-Moreno [33] suggested that their model was effective in explaining the variability of the observed data. Moreover, the result of the performed Clarke Error Grid test indicated high clinical reliability of the BGL estimates. Notably, this study used Random Blood Glucose measurements rather than Fasting Blood Glucose measurements, which were employed in all the other studies. A key strength of using RBG is that it allows for glucose monitoring at any time of the day without the need for fasting. This approach aligns well to real-time BGL monitoring, through the use of wearable devices, where photoplethysmography can be easily integrated.

However, it is important to consider that less then 20% of the study subjects had a diagnosis of diabetes. This small percentage of diabetic individuals could imply that the majority of the dataset consists in normal glucose level readings. This scenario could significantly affect the variability and range of blood glucose levels considered by

TABLE 4. Comparative overview of AI methods.

Study	AI Model	AI Input	Ground Truth	Dataset Construction	Train Strategy	Evaluation Metrics
Monte-Moreno E. [33]	Random Forest Regressor	33 PPG waveform features and BMI, Age, weight features	BGL measured with commercial device	80% train set (328 subjects) 20% test set (82 subjects)	k-fold crossvalidation (k=10) for model selection on training data and evaluation on test set Evaluation of model generalization with an additional k-fold crossvalidation (k=10) on training data	R^2 CGE
Padmavilochanan D et al. [34]	GlucoNet: custom light-weight 1-dimensional input-reinforced ANN architecture	1° input: concatenated InfraRed PPG and II derivative PPG 2° input: concatenated Red PPG and II derivative PPG	Average BGL obtained from 2 commercial glucometers	Development Dataset: 283 samples divided as 70% train set, 30% test set, and 10% validation set from train data Deployment Dataset: 600 additional samples	Trial and error approach for ANN hyperparameter tuning, early stopping by monitoring validation loss. Evaluation on test set and on the deployment dataset	MAE MAPE CGE
Lu WR et al. [36]	Custom Deductive Learning CNN model	Paired adjacent rounds of PPG signal recordings	BGL measured with commercial device	Train set: first 12 round of PPG acquisitions Test set: rounds 13-15 for model evaluation	Model was trained with first round data and tested on subsequent rounds.	Accuracy Score RMSE MAE CGE
Li J et al. [35]	Weight-based Choquet integral multi-model (Random Forest, Gradient Boosting, Bagging) fusion	Spatio-temporal features fusion extracted with numerical analysis and ResNets. Features were selected using and intersection of methods: Univariate Feature Selection (UFS), Recursive Feature Elimination (RFE), L1-based feature selection (L1-FS)	BGL measured with continuous glucose monitoring	Training and testing dataset were split based on days, and the ten-fold cross validation method was adopted. 10 days were used as the testing dataset, and the remaining 93 days were adopted as training dataset.	k-fold crossvalidation (k=10)	RMSE MARD PGE
Chen S et al. [37]	Multi-view cross-fusion transformer	kinetic features and derivatives obtained from 6second-PPG samples	FPG measurement obtained from blood test	All subjects were tested by using a crossvalidation approach	Subject-wise k-fold crossvalidation (k=5)	Accuracy Score MAE RMSE CGE

R^2 Coefficient of Determination, MAE: Mean Absolute Error, RMSE: Root Mean Squared Error, MAPE: Mean Absolute Percentage Error, MARD: Mean Absolute Relative Difference, CGE: Clarke Error Grid, PGE: Parkes Error Grid

TABLE 5. Performances of AI models.

Study	R^2	MAE $[mmol/L]$	RMSE$[mmol/L]$	MAPE	MARD	Accuracy Score	Clarke's or Parkes' Error Grid		
							Zone A	Zone B	Other
Monte-Moreno, E. [33]	0.88	-	-	-	-	-	87.71%	10.32%	1.96%
Padmavilochanan D et al. [34]	-	1.4	-	17.8% (±12.8%)	-	-	55%	45%	-
Lu WR et al. [36]	-	0.671	0.774	-	-	93.50%	100%	-	-
Li J et al. [35]	-	1.49	-	-	13.42%	83.75%	80.09%	19.40%	-
Chen S et al. [37]	-	0.659	1.129	-	-	-	87.89%	12.11%	-

the model, tilting the results toward a lower variability typical of non-diabetic ranges. The absence of targeted validation on diabetic subjects may limit the generalizability of the model's results to the broader diabetic population. Therefore, although the model demonstrates robust performance, the results should be interpreted with caution, particularly with regard to their application to the management of glucose levels in diabetes.

GlucoNet model used by Padmavilochanan et al. [34] achieved good MAE and MAPE results. Regarding the performed Clarke's Error Grid analysis, even though all predictions fall within the clinically acceptable A and B zones, a significant percentage of predictions were in zone B. This indicated a lower accuracy in the estimation of BGL compared with the estimates in zone A.

Compared to the other considered studies, the strength of the research by Padmavilochanan et al. [34] is the inclusion of a large population with a significant representation of diabetic patients. Additionally, the authors validated their model using an additional dataset (deployment set) collected from various sources, including a university hospital clinic, intensive care units, and rural check-up health clinics. This diverse testing framework ensure the versatility and adaptability of the model across different clinical settings. Moreover, the model proposed by the authors showed to generalize well across different patient demographics, as indicated by the variations in age and sex distribution across the test set and deployment datasets reported by the authors.

Despite its strengths, the study does not describe in detail the characteristics and the performance metrics of the three considered subgroup populations. This lack may limit a properly understanding of the model's effectiveness across different blood glucose levels and its potential clinical utility in the diabetic population.

The results of Li et al. [35] demonstrated a solid performance of their AI model in estimating glucose levels. In fact, most of the BGL predictions fell within clinically acceptable ranges (CGE zone A and B). However, regarding the estimation of BGL in patients with diabetes this is a preliminary study. Specifically, the study involved a small sample size compared to other larger studies included in this scoping review and included only 4 participants diagnosed with diabetes. Consequently, the results of the study should be interpreted with caution regarding their applicability to larger populations. The lack of a detailed demographic and clinical profile limits the possibility of assessing whether the performance of the AI model may vary among different subgroups. Therefore, the promising results achieved require the extension of the study to more diverse and larger populations, as well as providing more detailed subgroup analyses.

In contrast, Lu et al. [36] focused exclusively on a diabetic population but targeted short-term glucose level estimation. The authors trained their model on sequential acquisition rounds and used subsequent rounds for validation. This method ensures that the model is trained on a comprehensive temporal dataset, capturing potential day-to-day variations in glucose levels and physiological response. At the same time, it is important to consider that this methodology may result in models that are finely tuned to predict short-term fluctuations in glucose levels with high accuracy but, it might not perform as well when compared to long-term physiological changes or significantly different conditions. This aspect is crucial for clinical applications where conditions can vary widely over time. Therefore, while Lu et al. [36] achieved high performance in blood glucose estimation, on the other hand these results could be due to blood glucose values with lower variability than those tested in other studies [34], [37].

In comparison to the other studies considered, the model proposed by Chen et al. [37] obtained a lower MAE but a higher RMSE. These results indicate that the average prediction error is relatively low and that the model predictions are, on average, aligned with actual glucose measurements. However, the higher RMSE value, which gives greater weight to large errors, suggests that although most predictions are accurate, significant deviations occasionally occur. This is a particularly important aspect to investigate, indeed if this type of error involves patients with poorer glycemic control, the results obtained would be less promising. Similar to Padmavilochanan's study [34], Chen's study included three groups of subjects, with and without diabetes, but lacks a detailed descriptions of these subgroups.

Overall, the articles considered in this scoping review showed good performances with respect to the ability to estimate the BGL of the subjects investigated. However, the limited number of patients enrolled and the lack of the description of the patients themselves limit the possibility of using and comparing the results obtained. In fact, detailed

and targeted knowledge of the population characteristics is important because many factors (e.g., obesity, age, gender, skin tone, skin thickness, body site of measurement, local body temperature, health condition and sweat) can influence the PPG signal and should be taken into account [25], [40], [41].

As regards the study protocol the quality of data acquisition procedures is critical to ensure that the data collected are not only accurate but also reproducible in different contexts. At the same time, the adoption of restrictions such as those adopted in some of the studies considered [35], [37] (i.e. diet, lifestyle, pharmacological therapy) should be managed carefully. In fact, it is important to consider that the main objective was to obtain an accurate estimate of BGL through PPG analysis in all conditions of daily life in patients with diabetes [42], [43], [44]. Differences between the studies considered also concerned the preparation of patients for the test. Four of the five used the fasting blood glucose measure, which requires subjects to fast for at least 8 hours before measurement. In contrast, the study conducted by Monte-Moreno [33] did not specify any particular acquisition conditions, which makes us assume that the measurement is random blood glucose.

Regarding other parameters, four out of five studies [34], [35], [36], [37] specified that data were collected after a resting phase. In addition, in Li's study [35], restrictions were adopted on the use of drugs and physical activity two hours before the experiment, while in Chen's study [37], the use of glucose-lowering drugs was avoided from the day before the experiment.

The studies conducted by Li et al. and Chen et al. [35], [37] standardized acquisition conditions with the goal of minimizing the influence of external factors. In fact, their protocols included considerations such as pre-measurement conditions, drug control, and body site measurement. In Monte-Moreno's study [33], experiments to assess BGL were conducted in different environments and by different operators. While some measurements were carried out by the author within the university research laboratory, other measurements were conducted in out-patient clinics by a physician. This procedure may be a limitation with respect to intra-observer and inter-observer reliability [45] as well as to the conditions under which the test was administered. In fact, both blood glucose and the PPG signal may be affected by the environmental conditions (e.g. motion artefact, sensor positioning, environmental light, applied pressure to the skin) [40], [41], [46].

All this demonstrates how complex it is to develop a reliable, real-time, non-invasive glucose estimation system based on PPG.

At the same time, the complexity of this estimation procedure does not mean that further important objectives cannot be achieved. In particular, in addition to estimate the current BGL, the use of artificial intelligence may be used for the prediction of BGL in patients with diabetes [47]. Predicting patients' BGL with acceptable accuracy would represent a great step forward in the treatment of patients with diabetes and could allow us to reduce the negative impact on glycemic control of many important factors, such as the effect of nutrition, physical activity, sleep characteristics, seasonal changes, working activity [42], [43]. In this sense, it is known that diabetes is chronic disease that highlights the importance of a constant and personalized management of patients. In addition, the ease with which the PPG signal can be acquired through a wide range of user-friendly wearable products (e.g., pulse oximeter, smartwatch, smartphones, smart bracelets, and smart rings) may further encourage the spread of this technology [24], [25]. If, on one hand, the results of this scoping review provide the first evidence regarding the possibility of defining a potentially useful technical solution to evaluate glycemia and improve diabetes monitoring, on the other hand, there are only a limited number of studies in this field to date. Furthermore, the shortcomings of the considered studies with regard to the population investigated hindered the drafting of this scoping review, limiting the ability to generalize the results and make meaningful comparisons between the different works. Similarly, the various approaches used to acquire and analyze photoplethysmographic signals, including different artificial intelligence methods, prevented an easy and clear definition of the strengths and weaknesses of the different reviewed studies. This methodological heterogeneity made it difficult to synthesize results and identify common trends, representing a significant limitation of the scoping review process. In this sense, the definition of an accessible database, of appropriate size and characteristics, relating to patients at risk or with diabetes, as well as to a control group, could represent a significant progress in the study of the role of PPG analysis in the assessment of glycaemia. Such a database would allow standardisation of data collection and analysis methods, facilitating comparison between studies and improving the robustness of the developed methodologies.

As a result, there is currently no definitive evidence regarding the presence of immediately usable devices and adequately validated procedures for the assessment of BGL in patients with diabetes. At the same time, the technologies available today appear to be suitable to achieve this objective.

The results presented in this scoping review highlight limitations and strengths of the studies in the literature and represent a starting point for future research in this area aimed at translating this promising technology into practical tools for diabetes management in clinical practice.

V. CONCLUSION

Some studies have verified the possibility of using PPG analysis and AI solutions to estimate BGL in patients with diabetes. Although only 5 articles were considered in this scoping review, overall these studies provided the first important evidence regarding the possibility of estimating BGL with good accuracy using PPG analysis. The availability of a non-invasive, affordable, and user-friendly method for

estimating BGL could represent an important step forward for the quality of monitoring and life of patients with diabetes. Unfortunately, the limited number of studies conducted in this field and some limitations found such as those relating to the differences in the devices, datasets and AI solutions confirm the need for further studies. New studies should consider larger populations of patients with diabetes and take into account numerous factors that may influence the PPG signal, overcoming the limitations present in the reviewed publications. Overall, the results published to date confirm how the estimation of the BGL starting from the PPG signal is possible and accurate. Further studies are needed to overcome the limitations found in the considered articles and to make this procedure accurate, safe and easy to perform.

APPENDIX
SEARCH STRATEGIES FOR ELECTRONIC DATABASE

See Table 6.

TABLE 6. Search strategies for electronic database.

Medline (PubMed, 2010 to February 29, 2024)

No.	Query
14	(diabetes[mh] OR diabetes OR "Diabetes Mellitus"[Mesh] OR "diabetic patients") AND (photoplethysmography[mh] OR photoplethysmography OR photoplethysmogram OR "ppg signal") AND ("Metabolic Control"OR "Blood Glucose"[mh] OR "blood glucose level" OR glycaemia OR "Glycemic Index"[mh] OR "glycemic index" OR "glycated hemoglobin" OR "hemoglobin A1c" OR HbA1c OR "glycosylated hemoglobin" OR glycemia) AND (ai OR "Artificial Intelligence"[mh] OR "artificial intelligence" OR "Machine Learning"[mh] OR machine learning OR predictive models) AND English[lang] AND ("2010/01/01"[PDAT] : "2024/12/31"[PDAT])

Embase (Elsevier/Embase.com, 2010 to February 29, 2024)

No.	Query
31	('diabetes' OR 'diabetes'/exp OR diabetes OR 'diabetes mellitus'/exp OR 'diabetes mellitus' OR 'diabetic patients'/exp OR 'diabetic patients') AND ('photoplethysmography'/exp OR photoplethysmography OR 'photoplethysmogram'/exp OR photoplethysmogram OR 'ppg signal') AND ('metabolic control'/exp OR 'metabolic control' OR 'blood glucose'/exp OR 'blood glucose' OR 'blood glucose level'/exp OR 'blood glucose level' OR 'glycaemia'/exp OR glycaemia OR 'glycemic index'/exp OR 'glycemic index' OR 'glycated hemoglobin'/exp OR 'glycated hemoglobin' OR 'hemoglobin a1c'/exp OR 'hemoglobin a1c' OR 'hba1c'/exp OR hba1c OR 'glycosylated hemoglobin'/exp OR 'glycosylated hemoglobin' OR 'glycemia'/exp OR glycemia) AND ((ai OR 'artificial intelligence'/exp OR 'artificial intelligence' OR 'machine learning'/exp OR 'machine learning' OR 'machine'/exp OR machine) AND ('learning'/exp OR learning) OR 'predictive models') AND [english]/lim AND [2010-2024]/py

Scopus (Elsevier, 2010 to February 29, 2024)

No.	Query
27	(TITLE-ABS-KEY (diabetes OR "diabetes mellitus" OR "diabetic patients") AND TITLE-ABS-KEY (photoplethysmography OR photoplethysmogram OR "ppg signal") AND TITLE-ABS-KEY ("metabolic control" OR "blood glucose" OR "blood glucose level" OR glycaemia OR glycemia OR "glycemic index" OR "glycated hemoglobin" OR "hemoglobin A1c" OR hba1c OR "glycosylated hemoglobin") AND TITLE-ABS-KEY (ai OR "artificial intelligence" OR "machine learning" OR "predictive models")) AND (LIMIT-TO (LANGUAGE , "English") OR LIMIT-TO (LANGUAGE , "2010-2024"))

TABLE 6. *(Continued.)* **Search strategies for electronic database.**

Web of Science (Clarivate, 2010 to February 29, 2024)

No.	Query
18	(((TS=((diabetes OR "diabetes mellitus" OR "diabetic patients"))) AND TS=(photoplethysmography OR photolplehysmogram OR "PPG signal")) AND TS=("metabolic control" OR "blood glucose" OR"blood glucose level" OR glycaemia OR glycemia OR "glycemic index" OR "glycated hemoglobin" OR "hemoglobin A1c" OR HbA1c OR "glycosylated hemoglobin")) AND TS=(AI OR "artificial intelligence" OR "machine learning" OR "predictive models")

CINAHL (EbscoHost, 2010 to February 29, 2024)

No.	Query
4	(MH "Diabetes Mellitus" OR diabetes OR "diabetic patients") AND (MH "Photoplethysmography" OR photoplethysmography OR photoplethysmogram OR "ppg signal") AND (MH "Metabolic Control" OR MH "Blood Glucose" OR "blood glucose level" OR glycaemia OR glycemia OR "glycemic index" OR "hemoglobin A1c" OR HbA1c OR "glycosylated hemoglobin") AND (MH "Artificial Intelligence" OR ai OR "artificial intelligence" OR MH "Machine Learning" OR machine learning OR "predictive models")

DECLARATIONS

Ethical Approval: This article does not contain any studies with human or animal subjects performed by any of the authors.

Availability of Data and Materials: Not applicable.

Conflict of Interest: The authors declare no competing interests.

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SARA LOMBARDI (Member, IEEE) received the bachelor's degree in electronic and telecommunications engineering and the master's degree in biomedical engineering. She is currently pursuing the Ph.D. degree with the Department of Information Engineering, University of Florence. In 2022, she was a Research Fellow in physiological signal modeling for microcirculation analysis with the Department of Information Engineering, University of Florence. She is a Biomedical Engineer. Her research interests include biosignal analysis, bioimage processing, and artificial intelligence. She is a member of the Engineering in Medicine and Biology Society.

LEONARDO BOCCHI (Member, IEEE) is currently an Associate Professor of biomedical engineering with the University of Florence, Italy. He is the author of about 120 indexed publications in the field of biomedical engineering. His research interests include medical image analysis and interpretation, modeling of physiological systems, and noninvasive early diagnosis with artificial intelligence techniques (in particular on COVID and sepsis). He is a member of the IEEE Technical Committee on Cardiovascular Systems, a Project Evaluator, and a reviewer of EU and national projects; he acts as a referee for several international journals (among others, IEEE TRANSACTIONS ON MEDICAL IMAGING, IEEE TRANSACTIONS ON BIOMEDICAL ENGINEERING, *Pattern Recognition*, *Signal Processing*, and *Biomedical Signal Processing and Control*) and an Associate Editor of *Frontiers in Network Physiology*. Under different roles, he participated in organizing various conferences (EuroGP & EvoWorkshops, ACIVS, MAVEBA, and Interspeech).

PIERGIORGIO FRANCIA is currently carrying out his research activity together with the Bioimaging Group, University of Florence, Italy. In particular, he is studying the applications of non-invasive analysis in patients with diabetes and of microcirculation for the early identification of patients with COVID-19 and the stratification of the risk of developing organ failure. Studying the alterations of microcirculation, his research activity is also aimed at the early recognition of sepsis in hospitalized patients. Previously, he was with the Laboratory of Human Movement Applied to Medicine, Department of Clinical and Experimental Medicine, Faculty of Human Health Sciences, University of Florence. During this period, he studied the relationship between metabolic control, tissue, and functional alterations in patients with diabetes of different ages. In particular, he focused on the systematic use of new technologies for the continuous monitoring of blood sugar and physical activity as well as on the prevention of diabetic foot. The development of appropriate strategies and preventive protocols for adapted physical activity were the goals of his work. Moreover, he studied the alterations of joint mobility in subjects practicing sports.

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