**Name of Journal:** *Artificial Intelligence in Gastroenterology*

**Manuscript NO:** 75829

**Manuscript Type:** MINIREVIEWS

**Artificial intelligence in critically ill diabetic patients: current status and future prospects**

Juneja D *et al*. AI in critically ill diabetic patients

Deven Juneja, Anish Gupta, Omender Singh

**Deven Juneja, Anish Gupta, Omender Singh,** Institute of Critical Care Medicine, Max Super Speciality Hospital, Saket, New Delhi 110092, India

**Author contributions:** Juneja D and Gupta A performed the majority of the writing, prepared the tables and performed data accusation; Singh O provided the input in writing the paper and reviewed the manuscript.

**Corresponding author: Deven Juneja, FCCP, MBBS, Director,** Institute of Critical Care Medicine, Max Super Speciality Hospital, Saket, 1, Press Enclave Road, Saket, New Delhi 110092, India. devenjuneja@gmail.com

**Received:** February 16, 2022

**Revised:** April 21, 2022

**Accepted: April 28, 2022**

**Published online:**

**Abstract**

Recent years have witnessed increasing numbers of artificial intelligence (AI) based applications and devices being tested and approved for medical care. Diabetes is arguably the most common chronic disorder worldwide and AI is now being used for making an early diagnosis, to predict and diagnose early complications, increase adherence to therapy, and even motivate patients to manage diabetes and maintain glycemic control. However, these AI applications have largely been tested in non-critically ill patients and aid in managing chronic problems. Intensive care units (ICUs) have a dynamic environment generating huge data, which AI can extract and organize simultaneously, thus analysing many variables for diagnostic and/or therapeutic purposes in order to predict outcomes of interest. Even non-diabetic ICU patients are at risk of developing hypo or hyperglycemia, complicating their ICU course and affecting outcomes. In addition, to maintain glycemic control frequent blood sampling and insulin dose adjustments are required, increasing nursing workload and chances of error. AI has the potential to improve glycemic control while reducing the nursing workload and errors. Continuous glucose monitoring (CGM) devices, which are Food and Drug Administration (FDA) approved for use in non-critically ill patients, are now being recommended for use in specific ICU populations with increased accuracy. AI based devices including artificial pancreas and CGM regulated insulin infusion system have shown promise as comprehensive glycemic control solutions in critically ill patients. Even though many of these AI applications have shown potential, these devices need to be tested in larger number of ICU patients, have wider availability, show favorable cost-benefit ratio and be amenable for easy integration into the existing healthcare systems, before they become acceptable to ICU physicians for routine use.

**Key Words:** Artificial intelligence; Blood glucose; Critical care; Diabetes mellitus; Intensive care unit; Machine learning

Juneja D, Gupta A, Singh O. Artificial intelligence in critically ill diabetic patients: current status and future prospects. *Artif Intell Gastroenterol* 2022; In press

**Core Tip:** Increasing number of applications and devices based on artificial intelligence are being tested and approved for medical care. These devices have the potential to change the way we presently manage chronic diseases like diabetes. Moreover, their application in data rich and dynamic intensive care unit environment may have great implications in detecting hypo or hyperglycemia and reducing glycemic variability, while improving safety and accuracy and reducing nursing workload. Devices like artificial pancreas and continuous glucose monitoring regulated insulin infusion systems have shown promise as comprehensive glucose control solutions and may change the future of care for critically ill diabetic patients.

**INTRODUCTION**

As per the International Diabetes Federation 2021 estimates, about 537 million people are living with diabetes signifying a 10% prevalence rate worldwide with an estimated 6.7 million deaths in 2021. This number will rise exponentially in the coming years which will place a heavy burden on the already stressed healthcare system[1]. These patients are at increased risk of developing complications like sepsis, diabetes keto-acidosis and other complications necessitating intensive care unit (ICU) admission. In addition, critically ill diabetic patients are at an increased risk of developing nosocomial infections, having a longer ICU stay and increased ICU mortality[2-4].

All components of diabetes care including prevention and management of hyperglycemia and hypoglycemia, are essential to improve outcomes. In critically ill patients, these complications may be multifactorial and may also occur in non-diabetic patients, complicating their disease course. In addition to hyper- and hypoglycemia, glycemic variability (GV) and time in target range (TITR) are recently recognized components of dysglycemia which may affect patient outcomes[5-7]. However, the exact target for blood glucose (BG) control in ICU is not well established. Moreover, targeting tight glucose control necessitates frequent blood sampling and adjustment of insulin dose, increasing the work-load on ICU staff. In addition, targeting tight glucose control has not shown to have any mortality benefit but is associated with five-fold increased risk of hypoglycemia[8].

It has been difficult to establish a safe blood sugar level but as per American Diabetes Association (ADA) a BG level below 180 mg/dL is acceptable[9]. The surviving sepsis guidelines further recommend a target BG levels between 140-180 mg/dL in patients with sepsis[10].

Artificial intelligence (AI) is a rapidly evolving science which is gradually changing the landscape of many industries including healthcare. As ICUs have a dynamic environment which generates a huge amount of data, AI has a tremendous scope and now is increasingly being used in advanced mechanical ventilation, weaning from ventilation, predicting development of sepsis, antibiotic dosing and radiological assessment and monitoring[11-15]. In this review, we will be discussing the current applications and potential role AI may have in managing critically ill diabetic patients.

**ARTIFICIAL INTELLIGENCE**

There is no standard definition of AI but as per the Encyclopaedia Britannica, AI refers to “a system endowed with the intellectual processes characteristic of humans, such as the ability to reason, discover meaning, generalize, or learn from past experience”[16]. Basically, AI based systems should be able to perform tasks comparable to human intelligence.

AI has great potential and has been used in the field of medicine for discovery of new drug molecules, diagnostics, radiology and imaging, molecular biology, bioinformatics and therapeutics. AI has the ability to analyze and scrutinize massive amounts of data and help understand disease patterns. The human brain can store a limited amount of information at any one time and may be unable to analyze and visualize patterns embedded in vast quantities of data[17]. In contrast computers have a large storage capacity and can discern even small associations within the data. However, computer programming has limitations as they are able to follow only certain specific patterns, as per the programming instructions. AI in contrast differs from traditional computer programming as it learns from exposure to various experiences and inputs, assimilates the data and can improve on its own intelligence and modify the output behavior.

AI consists of a wide spectrum of complex algorithms and is broadly divided into machine learning (ML), deep learning, and cognitive computing. In ML, AI systems are trained with large repository of data and algorithms to enable them to follow a format to examine relationships and learn from them. Deep learning based systems develop insights by conducting complex interventions on the available data while cognitive AI systems are the most complex and try and match the human intelligence by understanding, reasoning, interacting, and learning from the data. Such systems are able to process and interpret exponential amounts of data (both structured and unstructured) and thus help in proposing any valid connections or hypothesis[18].

The AI functioning can be broken down in a systematic way and the processes involved can be divided into 3 main functions which occur in succession, which are knowledge discovery followed by learning and finally reasoning.

***Knowledge discovery/ retrieval***

The discovery of knowledge is the essence of AI. It works by creating algorithms for acquiring relevant and potential information from databases and is referred to as knowledge discovery in databases (KDD). For KDD to be effective it should have an in-depth knowledge of the area of interest as it will evaluate and interpret patterns and models to decide what data constitutes knowledge and what does not. KDD, hence plays a pivotal role in identifying information which is useful and valid.

***Learning***

Once the KDD process is complete the next step is learning from the knowledge or information acquired. Systems are allowed to automatically learn without human intervention or assistance. It usually consists of an inductive component which could be a simple process or could consist of a convolutional neural network (CNN). The various techniques used are artificial neural networks (ANNs), support vector machines (SVMs), random forest (RF), evolutionary algorithms, deep learning, Naive Bayes (NB), decision trees, and regression algorithms.

Certain types of AI algorithms are more commonly employed in healthcare settings than others. SVMs are used to predict clearly defined outcomes and adherence to medications. ANNs are algorithms which have been inspired by neuronal organization of animal brains, and have been employed to analyze data from computed tomography images, mammograms *etc*., to predict complications and outcomes. Logistic regression, is a ML algorithm which has been used to predict and classify probability of an event using predictor variables. Using data from electronic records or patient’s medical history, RF algorithms have been used to predict risk of disease, and NB are the most advanced ML algorithms which have been used recently to predict development of disease in specific patient populations[19].

***Reasoning***

Reasoning is the final step in the AI process and involves the use of logical techniques to come to a conclusion from the available data. The primary objective of reasoning is to perform tasks at the level of a human intelligence and in a specialized manner with the final objective to generate inferences in the most precise manner.

***AI algorithms***

AI is a rapidly evolving technology with increasing number of subsets being introduced regularly, each having their own advantages and limitations. For prediction and management of diabetes, commonly used AI algorithms include linear regression (LR), classification/decision trees (DTs), RF, SVMs, ANNs, and NB.

LR is a regression model which analyses the data and predicts a continuous output, finding solution following a linear curve. DTs are predictive models which predict outcome from the given data, but can find solution using both linear and non-linear curves. DTs also fare better than LR models for categorical independent variables. RF is a variation of DT, supporting both linear and non-linear solutions, but is better at handling of missing values and outliers. It is more favorable than DTs as it is more robust, accurate and provides a more generalized solution.

SVMs are supervised learning algorithms which are recently gaining popularity for their applications in healthcare settings. Even though they are mostly used for classification problems in ML, they can also be applied for regression problems. They also support linear and non-linear solutions and are better than LR in handling outliers and analyzing data with large number of features.

ANN is an advanced technology based on the brain and the nerves and programmed to mimic the biological neural system. ANNs can also find non-linear solutions and are sub-classified as convolutional (feedforward networks) and recurrent (feedback loop) neural networks. ANNs have better accuracy but require larger training data as compared to LR.

As compared to LR, DT and RF, which are discriminative models, NB is a generative model which works well even with small data sets. This supervised learning algorithm is based on Bayes theorem and can provide solutions to classification problems. It is easy, fast and performs well in case of categorial data. However, it is a bad estimator and its probability outputs are not reliable.

**ROLE OF AI IN MANAGEMENT OF DIABETES MELLITUS**

Medical management forms only a small part of the entire spectrum of diabetes care, as diabetes mellitus (DM) is mainly a life-style disorder. Apart from medications, education on self-management (meal schedules, calorie counting, exercising, routine BG monitoring) and continuous medical care is paramount not only to prevent acute complications but also to minimize the risk of long-term complications like nephropathy, retinopathy, diabetic foot, cardiovascular disease, or stroke. As a result, diabetes care is complex and various medical and life-style related factors need to be taken into account to optimize management.

The use of AI in DM is not new and a number of studies have shown the role of AI applications in the care of diabetic patients[20-24]. A number of complex AI systems, and their clinical applications have been described (Table 1). Deep-learning based AI algorithms may help in early diagnosis of diabetic retinopathy using retinal photographs with a reported sensitivity and specificity of more than 90%[25]. IDx-DR is the first such AI-based device approved by US-FDA for screening of diabetic patients for retinopathy[26]. As it does not require a clinician to interpret the results, this automated system can help the non-eye specialists to recognize early signs of retinopathy and send the patients to eye-specialists only if indicated, thereby simplifying the process and achieving higher patient satisfaction[27].

Dreamed Advisor pro assimilates data regarding the glucose levels, insulin dose and carbohydrate intake and using AI-based MD-Logic algorithms it then makes recommendations for insulin dose adjustments. These recommendations have been shown to be similar to those given by experienced physicians in the real-world settings validating the use of such devices in day-to-day clinical practice[23,28]. Several real-time Continuous Glucose Monitoring (CGM) devices like Medtronic Guardian Connect and Dexcom G6 CGM systems, are commercially available which can act as self-monitoring tools for diabetic patients (Table 1). These devices can provide real-time glucose values which can be displayed on the patient’s mobile phones and can raise an alarm if the BG levels go beyond the predefined range. These devices can further be connected to insulin pumps and hence aid in insulin dose adjustments. However, these devices require repeated calibrations with the capillary blood glucose levels, to be measured by finger pricks. Use of these glucose sensors for more than 70% of the time, has shown to improve the HbA1c by 0.4 to 0.6% and reduce the incidence of hypoglycemic episodes[29]. Presently, these devices and applications have not been validated in ICU patients but can be further modified and tested to be applied in the management of critically ill patients.

**AI IN DIABETES MANAGEMENT IN ICU**

Hyperglycemia is a common phenomenon in the ICU irrespective of the reason for admission and may occur even in the absence of pre-existing DM. The pathophysiology of hyperglycemia in ICU is multifactorial and can occur secondary to release of stress hormones (corticosteroids and catecholamines), proinflammatory mediators, administration of exogenous drugs (corticosteroids, vasopressors, ascorbic acid), parenteral solutions containing dextrose, stress hyperglycemia and use of commercial dietary feeds or supplements[30]. Irrespective of cause, hyperglycemia is associated with an increase in ICU stay, hospitalization costs, morbidity, and mortality[4,31].

Apart from hyperglycemia, hypoglycemia and GV have also been shown to be associated with increase in mortality in critically ill patients[5,6]. Use of variable insulin protocols which are not clinically validated and inaccurate blood sugar measurements are responsible for this GV seen in the ICUs. In addition, insulin sensitivity in critically ill patients follows a very erratic course and is plagued with frequent changes which could be secondary to the underlying illness, dietary changes or medications.

TITR has been recognized as another domain of dysglycemia in critically ill patients[7]. It may be defined as the total time spent in the target range and is expressed as the percentage of time. Data suggests that critically ill patients having more than 70% TITR, have significantly higher survival rates[32]. However, the exact cut-offs for TITR remain unclear with different studies suggesting TITR ranging from 50-80% for improving outcomes[33,34].

In spite of several widely accepted applications for out-patient and long-term management of DM, AI applications in management of critically ill patients are limited. The possible applications of AI in critically ill diabetes patients are given in Table 2[35].

***Blood glucose monitoring and prediction***

Blood glucose management requires frequent sampling and insulin dose adjustments. Capillary BG monitoring still remains the most commonly employed method, even in critically ill patients. However, its accuracy may be affected in patients with subcutaneous oedema, shock, and hypoxemia, which commonly affect ICU patients. Hence, using arterial blood is preferred but it requires repeated arterial punctures or presence of an invasive arterial line. The characteristics of an ideal method to monitor BG is given in the Table 3.

***Continuous glucose monitoring***

Continuous Glucose Monitoring has been employed in the management of DM for more than a decade. Several CGM devices have been developed and are presently commercially available and approved for in-hospital use (Table 4). They can be broadly classified as transdermal (non-invasive), subcutaneous (minimally invasive) and intra-vascular (invasive) devices. Subcutaneous and transdermal devices are not considered ideal in critically ill patients because the presence of subcutaneous oedema, hypoxemia, and shock may affect their accuracy. Hence, intravascular devices may be preferable in these patients. However, the continuous subcutaneous flash glucose monitoring (FGM) system (FreeStyle Libre) has been recently tried in critically ill patients and has shown to have high test-retest reliability and acceptable accuracy[36-38].

A recently published meta-analysis reported that the use of CGM was associated with significantly reduced HbA1c values and reduced risk of severe hypoglycaemia[39]. In addition, use of FGM was associated with significant reduction in episodes of mild hypoglycemia and was associated with increased treatment satisfaction in patients with type-I diabetes. Hence, it is suggested that real time monitoring with CGM or FGM has the potential to achieve better control in short-time fluctuations in BG levels, improve glycemic control and may also reduce healthcare costs[40]. Although several studies have been conducted testing these devices in critically ill patients, their impact on reducing length of stay in ICU or overall patient outcomes remains unknown[41].

While these devices may not benefit all ICU patients, they may be particularly useful in specific patient populations like those on intravenous insulin or corticosteroids, patients with end stage renal or liver disease, neurosurgery or traumatic brain injury patients and post-transplant patients[42-44]. However, these devices need to be further tested in larger patient cohorts before they find mainstream application.

***Detection of adverse glycemic events***

Detection of adverse events in the form of both hypoglycemia and hyperglycemia using AI technologies have been studied by various research groups mainly in type 1 and type 2 diabetes patients[35]. The studies used either CGM devices or self-monitoring of blood glucose monitors to detect the individual events. The results were based on the sensitivity and specificity of the modalities used. For example the DCBPN algorithm used by Zhang *et al*[45] provided an accuracy of 88.5% in predicting the BG levels. In the study by Otto *et al*[46]*,* identification of episodes of hypoglycemia, hyperglycemia, severe hypoglycemia, and severe hyperglycemia were 120%, 46%, 123%, and 76% more likely after pattern identification as compared to periods when no pattern was identified. Another study by Nguyen *et al*[47] used electrocardiographic (ECG) parameters to detect episodes of hyperglycemia with a reported sensitivity and specificity of 70.59% and 65.38%, respectively. The results suggested that ECG signal and ANN patterns could be used to detect adverse hyperglycemic events in diabetic patients. Overall, AI has a potential role to predict adverse events and thus help modify treatment protocols so as to rectify them.

***Blood glucose control strategies***

There are various AI methodologies, fuzzy logic (FL), ANN, RF, which have been used for sugar control. Out of these FL is the most commonly used methodology as it mimics the management strategies by actual diabetes caregivers. Various studies have been performed using the FL methodology for BG control, mainly in type 1 diabetic patients[48,49]. The results have shown better control of nocturnal glucose levels with a low risk of hypoglycaemia as compared to standard insulin pump treatment.

Now, more complex methodologies are being proposed for BG control such as complimentary AI algorithms to support traditional AI controllers. The latest technology is the development of neural networks for regulation of BG[50,51].

From the above data it is evident that AI may potentially help to control BG but similar research in critically ill patients is limited. The LOGIC-1 trial was a single centre randomized control trial (RCT) which compared LOGIC-Insulin computerized algorithm to expert nurses in BG control for critically ill patients[52]. LOGIC-Insulin improved the efficacy of tight glucose control without increasing the risk of hypoglycemia. Encouraged by the results, a larger multi-center RCT, the LOGIC-2 trial, was conducted comparing software guided glucose control to nurse directed orders. This trial also showed better control of BG without an increase in hypoglycemia[53].

Hence, research shows that algorithmic based approach may be beneficial to control BG levels. Even the ability to anticipate excursions in sugar levels could provide early warnings regarding ineffective treatments. Newer CGM could lead to prediction of future glucose levels but reliability may be affected due various physiological and technical factors. Pappada *et al*[54] studied a neural network model for predicting glucose levels in a surgical critical care setting and found CGM to be useful in this patient population. However, further research and studies may be required in real time to test their validity in other critically ill patients.

***Artificial pancreas***

For BG control one of the most extensively researched modality is the artificial pancreas (AP) which consists of a glucose sensor, a closed-loop control algorithm, and an insulin infusion device. The glucose sensor estimates the BG level which in turn is fed to the control unit with the closed loop algorithm. This is turn directs the infusion device to inject the programmed amount of insulin. Thus, it has been developed to mimic the Islet cells of the pancreas which secrete insulin based on the BG levels.  The majority of algorithms used by AP have been derived from control engineering theory and include proportional-integral-derivative (PID), model-predictive control, adaptive control, and FL control[55,56]. However, the major limiting factor is a reliable glucose sensor and hence, now AI is being used to develop better models of AP.

At present, AP are of two types viz a viz single hormone (insulin only) and dual hormone (insulin and glucagon) systems. Overall, AP has been shown to be safe and effective in controlling BG, reducing episodes of hypoglycemia and hyperglycemia, and increase the proportion of TITR. Weisman *et al*[57] conducted a meta-analysis which showed that AP improves the TITR by 12.59% (equivalent to 172 minutes per day) compared to conventional treatment. Furthermore, this analysis showed that dual-hormone AP systems were associated with greater improvements, especially with respect to hypoglycemic events as compared to single hormone systems. The average time spent in hypoglycemia was reduced by 35 minutes/day. These benefits were more pronounced at night time.

In critically ill patients, use of AP to control BG has shown to reduce the frequency for sampling, reduce the nursing workload, achieve stable glycemic control with reduced episodes of hypo or hyperglycemia, and cause less GV[58-62]. In addition, its use has been associated with significant reduction in postoperative infectious complications in patients undergoing major surgeries[62]. However, use of AP was unable to achieve any significant improvement in mean glucose concentration, improve clinical outcome or show a favorable cost-benefit ratio.

***Insulin bolus calculators and advisory systems***

Insulin dependent patients routinely require calculation of insulin dosages based on their consumption of carbohydrates. The bolus doses are based on multiple factors like previous insulin dose, BG measurements, approximate calorie count *etc.* This may be a challenging task and could lead to errors in judgement and calculation, eventually leading to adverse glycemic events. Various applications are being developed to simplify this daunting task. Various research groups have used the case-based reasoning methodology for these calculations which has proved to be a safe decision tool. Some studies have also shown that complimenting this system to an AP leads to an improvement in glycemic control[62,63]. Since the cause of hyperglycemia in ICU is multifactorial, probably a combination of an AP with case-based methodology may be of help as glucose excursions could be treated in a more standardized way with better control.

MD-Logic controller, developed on the FL systems, have shown to provide superior glycemic control with fewer nocturnal hypoglycemic episodes as compared to insulin pump treatment[49]. However, it still needs to be validated in ICU patients.

***Software based algorithms for insulin dosing***

Software based algorithms have been developed to determine insulin dosage depending on the BG levels. These programs, although more complicated than the paper-based protocols, can reduce errors and improve adherence. The simplest of these are based on PID models. Devices based on this model titrate insulin administration based on the previous BG values and predicting the changes in glucose value for a given insulin dose using a dynamic multiplier response to insulin sensitivity. The advantages of this model include the need for minimal patient related information for initiation and its ability to provide real-time dose adjustments. However, this model necessitates multiple blood sampling, which may be up to 18 times per day for BG measurements[64,65].

A more complex modification of software is Glucose Regulation for Intensive Care Patients which not only takes into account the BG values and insulin infusion rates but also includes the change in these values over time. This may increase its effectiveness and may potentially reduce overtreatment and hence, hypoglycemic episodes[66,67].

The most recent algorithms are classified as model predictive controls, which not only include insulin sensitivity and dextrose administration but also include several patient-specific parameters like their age and diabetes status. Based on these factors, these algorithms try to predict the patient’s response to hyperglycemia and insulin therapy and adjust the insulin dose accordingly. As the number of parameters required to be entered at the time of initiation are more, the devices based on these algorithms are more complicated and time consuming but they have advantages of increased accuracy, significantly reduced need for repeated blood sampling and may offer a more individualized insulin therapy[68-70].

***CGM regulated insulin infusion system***

Newer technologies like CGM which have been validated in non-critically ill patients are now increasingly been used with increased accuracy in ICU patients. Integration of these CGM devices with automated insulin suspension with AI algorithms (Basal-IQ™ technology) have been approved by US-FDA. Use of these predictive low-glucose suspend (PLGS) algorithms offer clinical advantage over the more conventional threshold suspend systems which stop insulin only when the predefined threshold of glucose is breached. Glucose values are obtained by the integrated CGM device (Dexcom G6™) and the Basal-IQ™ has the ability to predict when the glucose value is going to drop below the predefined level and it stops the insulin infusion[71]. Control-IQ is a more advanced hybrid closed-loop system which also uses activity and sleep settings to adjust the insulin requirements. Basal-IQ™ and Control-IQ™ algorithms can predict hypoglycemic events up to 30 minutes in advance and hence, can titrate the insulin dose accordingly.

Integration of CGM with an automated insulin suspension has shown to reduce the frequency and duration of hypoglycaemia with a reported relative risk reduction of 45%[72]. This effect has been shown to exist across different age groups, and is persistent over multiple weeks with real-world use. A large randomized crossover trial comparing the PLGS with sensor-augmented insulin pump showed 31% reduction in time spent in hypoglycemia (< 70 mg/dL) with no increase in incidence of rebound hyperglycemia[73]. It may be suggested that, use of this technology may be feasible and effective for patients with difficult to control DM and those at higher risk for developing hypoglycemia[72].

***Risk and patient stratification***

Diabetes is a chronic disease associated with many complications. Even though most of the complications develop over a period of time, diabetic patients are also prone to develop acute life-threatening complications like nosocomial infections, acute kidney injury and even cardiovascular complications. AI using deep-learning techniques have been able to produce algorithms which are able to predict long-term micro-angiopathic complications like diabetic retinopathy, diabetic foot, diabetic neuropathy and diabetic nephropathy, with reasonable accuracy[74-77]. Role of AI in predicting the development of macro-angiopathic complications like acute myocardial infarction has also been assessed but there is a dearth of data regarding its role in predicting other acute complications, especially in critically ill patients[78].

AI has been used effectively to determine patients at risk for developing sepsis and life-threatening nosocomial infections like catheter related blood stream infections and *Clostridium difficile* infections and also to predict which ward patients may deteriorate and require ICU admission. However, such models currently do not exist specifically for diabetes patients[13,79-81].

A few studies have also used AI in predicting mortality in critically ill diabetes patients. In their study, Ye *et al*[82] using the MIMIC-III database, reported that AI using CNN was highly accurate in predicting mortality in critically ill diabetes patients with an area under the curve (AUC) of 0.97. Using the same MIMIC-III database, Anand *et al*[83] developed simple predictive tools with AI, to predict mortality in critically ill diabetics. Their models could achieve AUCs of 0.787 and 0.785 to predict mortality. However, these models need to be compared to more widely used and validated models for mortality prediction in ICU patients like acute physiology and chronic health evaluation and sequential organ failure and assessment scores.

***Coronavirus disease critical care***

The recent pandemic of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has put an unprecedented strain on the healthcare with enhanced need for infection control and patient isolation. Separate coronavirus disease 2019 (COVID-19) ICUs had to be developed with negative pressure chambers with treating staff wearing personal protection equipment at all times. Diabetes is one of the most common comorbidities among COVID-19 patients. Diabetic patients developing COVID-19 are at higher risk for requiring ICU admission and have poorer outcomes. The need for personal protection and risk of transmission of infection has put immense pressure on already limited clinical workforce. In such a scenario, labour intensive work like frequent BG monitoring and insulin dose adjustments may get seriously hampered. AI may be especially helpful by reducing the burden on the healthcare workers (HCWs) and reducing their risk of exposure.

Computerized algorithms, automated closed loop systems and remote monitoring may all be used effectively to manage critically ill COVID-19 patients. CGM devices are capable of continuous BG tracking enabling real-time monitoring of BG levels while reducing the need for bedside monitoring, thereby reducing the risk of exposure for the HCWs. The efficacy and safety of CGM in managing critically ill COVID-19 patients has been tested and verified and it has been reported to reduce the need for bedside BG testing by up to 71%. In addition, the efficacy of CGM devices was not significantly affected by presence of fever, hypoxemia, need for vasopressors, acidosis or with use of corticosteroid or parenteral nutrition[84-86]. Based on this, US-FDA has allowed the use of CGM in COVID-19 ICUs to reduce the exposure of HCWs[87].

AI based devices have the potential to improve patient care and outcomes by providing a better glucose control without increasing the nursing workload and avoiding risk of transmission of infection. Hence, it is recommended to prefer CGM to reduce the need for frequent nurse contact for patients with active COVID-19 infection[88]. Moreover, AI has also been instrumental in achieving glycemic control in COVID-19 patient on extracorporeal membrane oxygenation support by using AP[89].

**STRENGTHS OF AI**

AI-based devices have the potential to improve glycemic control, reduce GV, increase the TITR, and reduce episodes of hyper and hypoglycemia, thus providing comprehensive diabetes care. AI may allow us to achieve a better and more individualized glycemic control taking into account specific patient requirements as per their calorie intake, exercise and underlying comorbidities. In addition, AI may be better suited to care for patients at risk for adverse effects and those with changing needs, like those in critical care areas. It may enable HCWs to monitor their patients remotely with reduced need for close contact thereby, reducing their workload and exposure to infective patients. By reducing the need for frequent blood sampling and providing close glucose monitoring and insulin dose titration, AI-based algorithms may increase patient safety and satisfaction.

**LIMITATIONS OF AI**

Healthcare applications of AI are rapidly increasing. However, it still has several limitations affecting its widespread applicability (Table 5). Even though many AI applications have found acceptability in out-patients and ward patients with diabetes, data regarding its safety and accuracy in critically ill patients remains limited. As AI application is largely data-driven, involving collection of sensitive personal data, it may have privacy issues leading to medico-legal problems. Lack of regulations, recommendations and guidelines pertaining to use of AI further limit its applicability. These safety, liability and reliability issues prevent widespread use of AI in critical care practice. In addition, challenges of integrating AI into existing healthcare infrastructure and user acceptance also persist.

**FUTURE DIRECTIONS**

The future of healthcare development is in AI. Its large-scale applicability requires widespread availability, low cost and ease of use. In addition, AI needs to be adapted gradually in the existing healthcare system and HCWs need to be trained not only to better utilize AI but also to be aware of how to avoid any medico-legal issues arising from its application. Changes in the laws and regulations are also required to safeguard patient’s interest and avoid any violation of patient’s privacy. With technological improvements in AI, the dosing algorithms for insulin delivery may become individualized for closed-loop control of glycemia. Larger studies, evaluating their efficacy and safety, especially in critically ill patients, along with standardization of AI algorithms and techniques need to be done to improve the acceptability of AI.

**CONCLUSION**

Many currently available devices and techniques which have proven their role in management of non-critically ill patients, may soon be available for ICU patients, with improved accuracy. CGM is already being recommended for use in critically ill COVID-19 patients and soon may be available for use in all critically ill patients. Its integration with automated insulin suspension holds greater promise. Use of AP may also provide a comprehensive glycemic control option. AI has the potential of reducing the workload of HCWs, provide better glycemic control and prevent related complications, however, larger RCTs may be required before we implement these techniques in our day-to-day critical care. Even though presently AI might not be in its prime for managing critically ill diabetic patients, it is the future of healthcare.

**REFERENCES**

1 IDF Diabetes Atlas 10th edition Internet. 2217. Cited 26 January 2022. Available from: https://idf.org/aboutdiabetes/what-is-diabetes/facts-figures.html

2 **Kompoti M**, Michalia M, Salma V, Diogou E, Lakoumenta A, Clouva-Molyvdas PM. Glycated hemoglobin at admission in the intensive care unit: clinical implications and prognostic relevance. *J Crit Care* 2015; **30**: 150-155 [PMID: 25239822 DOI: 10.1016/j.jcrc.2014.08.014]

3 **Abu-Ashour W**, Twells L, Valcour J, Randell A, Donnan J, Howse P, Gamble JM. The association between diabetes mellitus and incident infections: a systematic review and meta-analysis of observational studies. *BMJ Open Diabetes Res Care* 2017; **5**: e000336 [PMID: 28761647 DOI: 10.1136/bmjdrc-2016-000336]

4 **Egi M**, Bellomo R, Stachowski E, French CJ, Hart GK, Hegarty C, Bailey M. Blood glucose concentration and outcome of critical illness: the impact of diabetes. *Crit Care Med* 2008; **36**: 2249-2255 [PMID: 18664780 DOI: 10.1097/CCM.0b013e318181039a]

5 **NICE-SUGAR Study Investigators.**, Finfer S, Liu B, Chittock DR, Norton R, Myburgh JA, McArthur C, Mitchell I, Foster D, Dhingra V, Henderson WR, Ronco JJ, Bellomo R, Cook D, McDonald E, Dodek P, Hébert PC, Heyland DK, Robinson BG. Hypoglycemia and risk of death in critically ill patients. *N Engl J Med* 2012; **367**: 1108-1118 [PMID: 22992074 DOI: 10.1056/NEJMoa1204942]

6 **Krinsley JS**. Understanding glycemic control in the critically ill: three domains are better than one. *Intensive Care Med* 2011; **37**: 382-384 [PMID: 21210079 DOI: 10.1007/s00134-010-2110-3]

7 **Krinsley JS**. Glycemic control in the critically ill: What have we learned since NICE-SUGAR? *Hosp Pract (1995)* 2015; **43**: 191-197 [PMID: 26224425 DOI: 10.1080/21548331.2015.1066227]

8 **Yamada T**, Shojima N, Noma H, Yamauchi T, Kadowaki T. Glycemic control, mortality, and hypoglycemia in critically ill patients: a systematic review and network meta-analysis of randomized controlled trials. *Intensive Care Med* 2017; **43**: 1-15 [PMID: 27637719 DOI: 10.1007/s00134-016-4523-0]

9 **American Diabetes Association.**. 15. Diabetes Care in the Hospital: *Standards of Medical Care in Diabetes-2021*. *Diabetes Care* 2021; **44**: S211-S220 [PMID: 33298426 DOI: 10.2337/dc21-S015]

10 **Evans L**, Rhodes A, Alhazzani W, Antonelli M, Coopersmith CM, French C, Machado FR, Mcintyre L, Ostermann M, Prescott HC, Schorr C, Simpson S, Joost Wiersinga W, Alshamsi F, Angus DC, Arabi Y, Azevedo L, Beale R, Beilman G, Belley-Cote E, Burry L, Cecconi M, Centofanti J, Yataco AC, De Waele J, Dellinger RP, Doi K, Du B, Estenssoro E, Ferrer R, Gomersall C, Hodgson C, Møller MH, Iwashyna T, Jacob S, Kleinpell R, Klompas M, Koh Y, Kumar A, Kwizera A, Lobo S, Masur H, McGloughlin S, Mehta S, Mehta Y, Mer M, Nunnally M, Oczkowski S, Osborn T, Papathanassoglou E, Perner A, Puskarich M, Roberts J, Schweickert W, Seckel M, Sevransky J, Sprung CL, Welte T, Zimmerman J, Levy M. Executive Summary: Surviving Sepsis Campaign: International Guidelines for the Management of Sepsis and Septic Shock 2021. *Crit Care Med* 2021; **49**: 1974-1982 [PMID: 34643578 DOI: 10.1097/CCM.0000000000005357]

11 **Sottile PD**, Albers D, Higgins C, Mckeehan J, Moss MM. The Association Between Ventilator Dyssynchrony, Delivered Tidal Volume, and Sedation Using a Novel Automated Ventilator Dyssynchrony Detection Algorithm. *Crit Care Med* 2018; **46**: e151-e157 [PMID: 29337804 DOI: 10.1097/CCM.0000000000002849]

12 **Kuo HJ**, Chiu HW, Lee CN, Chen TT, Chang CC, Bien MY. Improvement in the Prediction of Ventilator Weaning Outcomes by an Artificial Neural Network in a Medical ICU. *Respir Care* 2015; **60**: 1560-1569 [PMID: 26329358 DOI: 10.4187/respcare.03648]

13 **Nemati S**, Holder A, Razmi F, Stanley MD, Clifford GD, Buchman TG. An Interpretable Machine Learning Model for Accurate Prediction of Sepsis in the ICU. *Crit Care Med* 2018; **46**: 547-553 [PMID: 29286945 DOI: 10.1097/CCM.0000000000002936]

14 **Turnidge J**. Pharmacodynamics and dosing of aminoglycosides. *Infect Dis Clin North Am* 2003; **17**: 503-528, v [PMID: 14711074 DOI: 10.1016/s0891-5520(03)00057-6]

15 **Rachh P**, Levey AO, Lemmon A, Marinescu A, Auffermann WF, Haycook D, Berkowitz EA. Reducing STAT Portable Chest Radiograph Turnaround Times: A Pilot Study. *Curr Probl Diagn Radiol* 2018; **47**: 156-160 [PMID: 28705527 DOI: 10.1067/j.cpradiol.2017.05.012]

16 **Copeland BJ.** "Artificial Intelligence". Encyclopedia Britannica. Cited 22 January 2022. Available from: https://www.britannica.com/technology/artificial-intelligence

17 **Gobet F**, Clarkson G. Chunks in expert memory: evidence for the magical number four ... or is it two? *Memory* 2004; **12**: 732-747 [PMID: 15724362 DOI: 10.1080/09658210344000530]

18 **Raghupathi V**, Raghupathi W. Healthcare Expenditure and Economic Performance: Insights From the United States Data. *Front Public Health* 2020; **8**: 156 [PMID: 32478027 DOI: 10.3389/fpubh.2020.00156]

19 **Shillan D**, Sterne JAC, Champneys A, Gibbison B. Use of machine learning to analyse routinely collected intensive care unit data: a systematic review. *Crit Care* 2019; **23**: 284 [PMID: 31439010 DOI: 10.1186/s13054-019-2564-9]

20 **Nomura A**, Noguchi M, Kometani M, Furukawa K, Yoneda T. Artificial Intelligence in Current Diabetes Management and Prediction. *Curr Diab Rep* 2021; **21**: 61 [PMID: 34902070 DOI: 10.1007/s11892-021-01423-2]

21 **Ellahham S**. Artificial Intelligence: The Future for Diabetes Care. *Am J Med* 2020; **133**: 895-900 [PMID: 32325045 DOI: 10.1016/j.amjmed.2020.03.033]

22 **Abràmoff MD**, Lavin PT, Birch M, Shah N, Folk JC. Pivotal trial of an autonomous AI-based diagnostic system for detection of diabetic retinopathy in primary care offices. *NPJ Digit Med* 2018; **1**: 39 [PMID: 31304320 DOI: 10.1038/s41746-018-0040-6]

23 **Nimri R**, Battelino T, Laffel LM, Slover RH, Schatz D, Weinzimer SA, Dovc K, Danne T, Phillip M; NextDREAM Consortium. Insulin dose optimization using an automated artificial intelligence-based decision support system in youths with type 1 diabetes. *Nat Med* 2020; **26**: 1380-1384 [PMID: 32908282 DOI: 10.1038/s41591-020-1045-7]

24 **Dankwa-Mullan I**, Rivo M, Sepulveda M, Park Y, Snowdon J, Rhee K. Transforming Diabetes Care Through Artificial Intelligence: The Future Is Here. *Popul Health Manag* 2019; **22**: 229-242 [PMID: 30256722 DOI: 10.1089/pop.2018.0129]

25 **Lam C**, Yu C, Huang L, Rubin D. Retinal Lesion Detection With Deep Learning Using Image Patches. *Invest Ophthalmol Vis Sci* 2018; **59**: 590-596 [PMID: 29372258 DOI: 10.1167/iovs.17-22721]

26 **US Food and Drug Administration.** FDA permits marketing of artificial intelligence-based device to detect certain diabetes-related eye problems. Accessed April 18, 2022. Available from: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm604357.htm

27 **Keel S**, Lee PY, Scheetz J, Li Z, Kotowicz MA, MacIsaac RJ, He M. Feasibility and patient acceptability of a novel artificial intelligence-based screening model for diabetic retinopathy at endocrinology outpatient services: a pilot study. *Sci Rep* 2018; **8**: 4330 [PMID: 29531299 DOI: 10.1038/s41598-018-22612-2]

28 **Nimri R**, Dassau E, Segall T, Muller I, Bratina N, Kordonouri O, Bello R, Biester T, Dovc K, Tenenbaum A, Brener A, Šimunović M, Sakka SD, Nevo Shenker M, Passone CG, Rutigliano I, Tinti D, Bonura C, Caiulo S, Ruszala A, Piccini B, Giri D, Stein R, Rabbone I, Bruzzi P, Omladič JŠ, Steele C, Beccuti G, Yackobovitch-Gavan M, Battelino T, Danne T, Atlas E, Phillip M. Adjusting insulin doses in patients with type 1 diabetes who use insulin pump and continuous glucose monitoring: Variations among countries and physicians. *Diabetes Obes Metab* 2018; **20**: 2458-2466 [PMID: 29885025 DOI: 10.1111/dom.13408]

29 **Gómez AM**, Henao Carrillo DC, Muñoz Velandia OM. Devices for continuous monitoring of glucose: update in technology. *Med Devices (Auckl)* 2017; **10**: 215-224 [PMID: 28979168 DOI: 10.2147/MDER.S110121]

30 **Dungan KM**, Braithwaite SS, Preiser JC. Stress hyperglycaemia. *Lancet* 2009; **373**: 1798-1807 [PMID: 19465235 DOI: 10.1016/S0140-6736(09)60553-5]

31 **Siegelaar SE**, Hermanides J, Oudemans-van Straaten HM, van der Voort PH, Bosman RJ, Zandstra DF, DeVries JH. Mean glucose during ICU admission is related to mortality by a U-shaped curve in surgical and medical patients: a retrospective cohort study. *Crit Care* 2010; **14**: R224 [PMID: 21143980 DOI: 10.1186/cc9369]

32 **Signal M**, Le Compte A, Shaw GM, Chase JG. Glycemic levels in critically ill patients: are normoglycemia and low variability associated with improved outcomes? *J Diabetes Sci Technol* 2012; **6**: 1030-1037 [PMID: 23063028 DOI: 10.1177/193229681200600506]

33 **Penning S**, Chase JG, Preiser JC, Pretty CG, Signal M, Mélot C, Desaive T. Does the achievement of an intermediate glycemic target reduce organ failure and mortality? A post hoc analysis of the Glucontrol trial. *J Crit Care* 2014; **29**: 374-379 [PMID: 24679489 DOI: 10.1016/j.jcrc.2014.01.013]

34 **Omar AS**, Salama A, Allam M, Elgohary Y, Mohammed S, Tuli AK, Singh R. Association of time in blood glucose range with outcomes following cardiac surgery. *BMC Anesthesiol* 2015; **15**: 14 [PMID: 25670921 DOI: 10.1186/1471-2253-15-14]

35 **Contreras I**, Vehi J. Artificial Intelligence for Diabetes Management and Decision Support: Literature Review. *J Med Internet Res* 2018; **20**: e10775 [PMID: 29848472 DOI: 10.2196/10775]

36 **Zhang Y**, Liu X, Zhang J, Fu J, Li S, Chen S, Chen Y, Lu B. Evaluation for the feasibility and accuracy of Freestyle Libre Flash Glucose Monitoring System used by COVID-19 patients in intensive care unit. *J Diabetes* 2021; **13**: 603-605 [PMID: 33787006 DOI: 10.1111/1753-0407.13181]

37 **Kotzapanagiotou E**, Tsotridou E, Volakli E, Dimitriadou M, Chochliourou E, Kalamitsou S, Kotzapanagiotou F, Sdougka M, Christoforidis A. Evaluation of continuous flash glucose monitoring in a pediatric ICU setting. *J Clin Monit Comput* 2020; **34**: 843-852 [PMID: 31482363 DOI: 10.1007/s10877-019-00384-y]

38 **Ancona P**, Eastwood GM, Lucchetta L, Ekinci EI, Bellomo R, Mårtensson J. The performance of flash glucose monitoring in critically ill patients with diabetes. *Crit Care Resusc* 2017; **19**: 167-174 [PMID: 28651513]

39 **Dicembrini I**, Cosentino C, Monami M, Mannucci E, Pala L. Effects of real-time continuous glucose monitoring in type 1 diabetes: a meta-analysis of randomized controlled trials. *Acta Diabetol* 2021; **58**: 401-410 [PMID: 32789691 DOI: 10.1007/s00592-020-01589-3]

40 **Wood A**, O'Neal D, Furler J, Ekinci EI. Continuous glucose monitoring: a review of the evidence, opportunities for future use and ongoing challenges. *Intern Med J* 2018; **48**: 499-508 [PMID: 29464891 DOI: 10.1111/imj.13770]

41 **Umpierrez GE**, Klonoff DC. Diabetes Technology Update: Use of Insulin Pumps and Continuous Glucose Monitoring in the Hospital. *Diabetes Care* 2018; **41**: 1579-1589 [PMID: 29936424 DOI: 10.2337/dci18-0002]

42 **Wallia A**, Umpierrez GE, Nasraway SA, Klonoff DC; PRIDE Investigators. Round Table Discussion on Inpatient Use of Continuous Glucose Monitoring at the International Hospital Diabetes Meeting. *J Diabetes Sci Technol* 2016; **10**: 1174-1181 [PMID: 27286715 DOI: 10.1177/1932296816656380]

43 **Wallia A**, Umpierrez GE, Rushakoff RJ, Klonoff DC, Rubin DJ, Hill Golden S, Cook CB, Thompson B; DTS Continuous Glucose Monitoring in the Hospital Panel. Consensus Statement on Inpatient Use of Continuous Glucose Monitoring. *J Diabetes Sci Technol* 2017; **11**: 1036-1044 [PMID: 28429611 DOI: 10.1177/1932296817706151]

44 **Krinsley JS**, Chase JG, Gunst J, Martensson J, Schultz MJ, Taccone FS, Wernerman J, Bohe J, De Block C, Desaive T, Kalfon P, Preiser JC. Continuous glucose monitoring in the ICU: clinical considerations and consensus. *Crit Care* 2017; **21**: 197 [PMID: 28756769 DOI: 10.1186/s13054-017-1784-0]

45 **Zhang Y**, Zhu JM, Liang YB, Chen HB, Yin SM, Chen ZC. Non-invasive blood glucose detection system based on conservation of energy method. *Physiol Meas* 2017; **38**: 325-342 [PMID: 28107204 DOI: 10.1088/1361-6579/aa50cf]

46 **Otto EA**, Tannan V. Evaluation of the utility of a glycemic pattern identification system. *J Diabetes Sci Technol* 2014; **8**: 830-838 [PMID: 24876425 DOI: 10.1177/1932296814532210]

47 **Nguyen LL**, Su S, Nguyen HT. Neural network approach for non-invasive detection of hyperglycemia using electrocardiographic signals. *Annu Int Conf IEEE Eng Med Biol Soc* 2014; **2014**: 4475-4478 [PMID: 25570985 DOI: 10.1109/EMBC.2014.6944617]

48 **Nimri R**, Atlas E, Ajzensztejn M, Miller S, Oron T, Phillip M. Feasibility study of automated overnight closed-loop glucose control under MD-logic artificial pancreas in patients with type 1 diabetes: the DREAM Project. *Diabetes Technol Ther* 2012; **14**: 728-735 [PMID: 22853723 DOI: 10.1089/dia.2012.0004]

49 **Phillip M**, Battelino T, Atlas E, Kordonouri O, Bratina N, Miller S, Biester T, Stefanija MA, Muller I, Nimri R, Danne T. Nocturnal glucose control with an artificial pancreas at a diabetes camp. *N Engl J Med* 2013; **368**: 824-833 [PMID: 23445093 DOI: 10.1056/NEJMoa1206881]

50 **Fernandez de Canete J**, Gonzalez-Perez S, Ramos-Diaz JC. Artificial neural networks for closed loop control of in silico and ad hoc type 1 diabetes. *Comput Methods Programs Biomed* 2012; **106**: 55-66 [PMID: 22178070 DOI: 10.1016/j.cmpb.2011.11.006]

51 **Catalogna M**, Cohen E, Fishman S, Halpern Z, Nevo U, Ben-Jacob E. Artificial neural networks based controller for glucose monitoring during clamp test. *PLoS One* 2012; **7**: e44587 [PMID: 22952998 DOI: 10.1371/journal.pone.0044587]

52 **Van Herpe T**, Mesotten D, Wouters PJ, Herbots J, Voets E, Buyens J, De Moor B, Van den Berghe G. LOGIC-insulin algorithm-guided versus nurse-directed blood glucose control during critical illness: the LOGIC-1 single-center, randomized, controlled clinical trial. *Diabetes Care* 2013; **36**: 188-194 [PMID: 22961576 DOI: 10.2337/dc12-0584]

53 **Dubois J**, Van Herpe T, van Hooijdonk RT, Wouters R, Coart D, Wouters P, Van Assche A, Veraghtert G, De Moor B, Wauters J, Wilmer A, Schultz MJ, Van den Berghe G, Mesotten D. Software-guided versus nurse-directed blood glucose control in critically ill patients: the LOGIC-2 multicenter randomized controlled clinical trial. *Crit Care* 2017; **21**: 212 [PMID: 28806982 DOI: 10.1186/s13054-017-1799-6]

54 **Pappada SM**, Cameron BD, Rosman PM, Bourey RE, Papadimos TJ, Olorunto W, Borst MJ. Neural network-based real-time prediction of glucose in patients with insulin-dependent diabetes. *Diabetes Technol Ther* 2011; **13**: 135-141 [PMID: 21284480 DOI: 10.1089/dia.2010.0104]

55 **Bothe MK**, Dickens L, Reichel K, Tellmann A, Ellger B, Westphal M, Faisal AA. The use of reinforcement learning algorithms to meet the challenges of an artificial pancreas. *Expert Rev Med Devices* 2013; **10**: 661-673 [PMID: 23972072 DOI: 10.1586/17434440.2013.827515]

56 **Bertachi A**, Ramkissoon CM, Bondia J, Vehí J. Automated blood glucose control in type 1 diabetes: A review of progress and challenges. *Endocrinol Diabetes Nutr (Engl Ed)* 2018; **65**: 172-181 [PMID: 29279252 DOI: 10.1016/j.endinu.2017.10.011]

57 **Weisman A**, Bai JW, Cardinez M, Kramer CK, Perkins BA. Effect of artificial pancreas systems on glycaemic control in patients with type 1 diabetes: a systematic review and meta-analysis of outpatient randomised controlled trials. *Lancet Diabetes Endocrinol* 2017; **5**: 501-512 [PMID: 28533136 DOI: 10.1016/S2213-8587(17)30167-5]

58 **Mibu K**, Yatabe T, Hanazaki K. Blood glucose control using an artificial pancreas reduces the workload of ICU nurses. *J Artif Organs* 2012; **15**: 71-76 [PMID: 21947674 DOI: 10.1007/s10047-011-0611-7]

59 **DeJournett L**, DeJournett J. In Silico Testing of an Artificial-Intelligence-Based Artificial Pancreas Designed for Use in the Intensive Care Unit Setting. *J Diabetes Sci Technol* 2016; **10**: 1360-1371 [PMID: 27301982 DOI: 10.1177/1932296816653967]

60 **Hanazaki K**, Tanioka N, Munekage M, Uemura S, Maeda H. Closed-loop artificial endocrine pancreas from Japan. *Artif Organs* 2021; **45**: 958-967 [PMID: 34105784 DOI: 10.1111/aor.14008]

61 **Yang Z**, Tao G, Guo M, Sun B, Gong L, Ding Y, Ye S, Liu W, Yang X. [Efficacy and safety of simulated artificial pancreas in modulating stress hyperglycemia in critically ill patients: a prospective randomized controlled study]. *Zhonghua Wei Zhong Bing Ji Jiu Yi Xue* 2018; **30**: 165-169 [PMID: 29402368 DOI: 10.3760/cma.j.issn.2095-4352.2018.02.014]

62 **Herrero P**, Pesl P, Reddy M, Oliver N, Georgiou P, Toumazou C. Advanced Insulin Bolus Advisor Based on Run-To-Run Control and Case-Based Reasoning. *IEEE J Biomed Health Inform* 2015; **19**: 1087-1096 [PMID: 24956470 DOI: 10.1109/JBHI.2014.2331896]

63 **Herrero P**, Bondia J, Adewuyi O, Pesl P, El-Sharkawy M, Reddy M, Toumazou C, Oliver N, Georgiou P. Enhancing automatic closed-loop glucose control in type 1 diabetes with an adaptive meal bolus calculator - in silico evaluation under intra-day variability. *Comput Methods Programs Biomed* 2017; **146**: 125-131 [PMID: 28688482 DOI: 10.1016/j.cmpb.2017.05.010]

64 **Juneja R**, Roudebush C, Kumar N, Macy A, Golas A, Wall D, Wolverton C, Nelson D, Carroll J, Flanders SJ. Utilization of a computerized intravenous insulin infusion program to control blood glucose in the intensive care unit. *Diabetes Technol Ther* 2007; **9**: 232-240 [PMID: 17561793 DOI: 10.1089/dia.2006.0015]

65 **Newton CA**, Smiley D, Bode BW, Kitabchi AE, Davidson PC, Jacobs S, Steed RD, Stentz F, Peng L, Mulligan P, Freire AX, Temponi A, Umpierrez GE. A comparison study of continuous insulin infusion protocols in the medical intensive care unit: computer-guided vs. standard column-based algorithms. *J Hosp Med* 2010; **5**: 432-437 [PMID: 20945468 DOI: 10.1002/jhm.816]

66 **Vogelzang M**, Loef BG, Regtien JG, van der Horst IC, van Assen H, Zijlstra F, Nijsten MW. Computer-assisted glucose control in critically ill patients. *Intensive Care Med* 2008; **34**: 1421-1427 [PMID: 18389221 DOI: 10.1007/s00134-008-1091-y]

67 **Hoekstra M**, Schoorl MA, van der Horst IC, Vogelzang M, Wietasch JK, Zijlstra F, Nijsten MW. Computer-assisted glucose regulation during rapid step-wise increases of parenteral nutrition in critically ill patients: a proof of concept study. *JPEN J Parenter Enteral Nutr* 2010; **34**: 549-553 [PMID: 20852185 DOI: 10.1177/0148607110372390]

68 **Pachler C**, Plank J, Weinhandl H, Chassin LJ, Wilinska ME, Kulnik R, Kaufmann P, Smolle KH, Pilger E, Pieber TR, Ellmerer M, Hovorka R. Tight glycaemic control by an automated algorithm with time-variant sampling in medical ICU patients. *Intensive Care Med* 2008; **34**: 1224-1230 [PMID: 18297268 DOI: 10.1007/s00134-008-1033-8]

69 **Hoekstra M**, Vogelzang M, Verbitskiy E, Nijsten MW. Health technology assessment review: Computerized glucose regulation in the intensive care unit--how to create artificial control. *Crit Care* 2009; **13**: 223 [PMID: 19849827 DOI: 10.1186/cc8023]

70 **Amrein K**, Ellmerer M, Hovorka R, Kachel N, Fries H, von Lewinski D, Smolle K, Pieber TR, Plank J. Efficacy and safety of glucose control with Space GlucoseControl in the medical intensive care unit--an open clinical investigation. *Diabetes Technol Ther* 2012; **14**: 690-695 [PMID: 22694176 DOI: 10.1089/dia.2012.0021]

71 Tandem Diabetes Care Announces Health Canada Approval of t:slim X2 Insulin Pump with Basal-IQ Predictive Low-Glucose Suspend Technology. Cited 6 January 2022. Available from: http://investor.tandemdiabetes.com/news-releases/news-release-details/tandem-diabetes-care-announces-health-canadaapproval-tslim-x2/

72 **Müller L**, Habif S, Leas S, Aronoff-Spencer E. Reducing Hypoglycemia in the Real World: A Retrospective Analysis of Predictive Low-Glucose Suspend Technology in an Ambulatory Insulin-Dependent Cohort. *Diabetes Technol Ther* 2019; **21**: 478-484 [PMID: 31329468 DOI: 10.1089/dia.2019.0190]

73 **Forlenza GP**, Li Z, Buckingham BA, Pinsker JE, Cengiz E, Wadwa RP, Ekhlaspour L, Church MM, Weinzimer SA, Jost E, Marcal T, Andre C, Carria L, Swanson V, Lum JW, Kollman C, Woodall W, Beck RW. Predictive Low-Glucose Suspend Reduces Hypoglycemia in Adults, Adolescents, and Children With Type 1 Diabetes in an At-Home Randomized Crossover Study: Results of the PROLOG Trial. *Diabetes Care* 2018; **41**: 2155-2161 [PMID: 30089663 DOI: 10.2337/dc18-0771]

74 **Ting DSW**, Cheung CY, Nguyen Q, Sabanayagam C, Lim G, Lim ZW, Tan GSW, Soh YQ, Schmetterer L, Wang YX, Jonas JB, Varma R, Lee ML, Hsu W, Lamoureux E, Cheng CY, Wong TY. Deep learning in estimating prevalence and systemic risk factors for diabetic retinopathy: a multi-ethnic study. *NPJ Digit Med* 2019; **2**: 24 [PMID: 31304371 DOI: 10.1038/s41746-019-0097-x]

75 **Cruz-Vega I**, Hernandez-Contreras D, Peregrina-Barreto H, Rangel-Magdaleno JJ, Ramirez-Cortes JM. Deep Learning Classification for Diabetic Foot Thermograms. *Sensors (Basel)* 2020; **20** [PMID: 32235780 DOI: 10.3390/s20061762]

76 **Williams BM**, Borroni D, Liu R, Zhao Y, Zhang J, Lim J, Ma B, Romano V, Qi H, Ferdousi M, Petropoulos IN, Ponirakis G, Kaye S, Malik RA, Alam U, Zheng Y. An artificial intelligence-based deep learning algorithm for the diagnosis of diabetic neuropathy using corneal confocal microscopy: a development and validation study. *Diabetologia* 2020; **63**: 419-430 [PMID: 31720728 DOI: 10.1007/s00125-019-05023-4]

77 **Norouzi J**, Yadollahpour A, Mirbagheri SA, Mazdeh MM, Hosseini SA. Predicting Renal Failure Progression in Chronic Kidney Disease Using Integrated Intelligent Fuzzy Expert System. *Comput Math Methods Med* 2016; **2016**: 6080814 [PMID: 27022406 DOI: 10.1155/2016/6080814]

78 **Yamada T**, Iwasaki K, Maedera S, Ito K, Takeshima T, Noma H, Shojima N. Myocardial infarction in type 2 diabetes using sodium-glucose co-transporter-2 inhibitors, dipeptidyl peptidase-4 inhibitors or glucagon-like peptide-1 receptor agonists: proportional hazards analysis by deep neural network based machine learning. *Curr Med Res Opin* 2020; **36**: 403-409 [PMID: 31855074 DOI: 10.1080/03007995.2019.1706043]

79 **Churpek MM**, Yuen TC, Winslow C, Hall J, Edelson DP. Differences in vital signs between elderly and nonelderly patients prior to ward cardiac arrest. *Crit Care Med* 2015; **43**: 816-822 [PMID: 25559439 DOI: 10.1097/CCM.0000000000000818]

80 **Beeler C**, Dbeibo L, Kelley K, Thatcher L, Webb D, Bah A, Monahan P, Fowler NR, Nicol S, Judy-Malcolm A, Azar J. Assessing patient risk of central line-associated bacteremia via machine learning. *Am J Infect Control* 2018; **46**: 986-991 [PMID: 29661634 DOI: 10.1016/j.ajic.2018.02.021]

81 **Li BY**, Oh J, Young VB, Rao K, Wiens J. Using Machine Learning and the Electronic Health Record to Predict Complicated *Clostridium difficile* Infection. *Open Forum Infect Dis* 2019; **6**: ofz186 [PMID: 31139672 DOI: 10.1093/ofid/ofz186]

82 **Ye J**, Yao L, Shen J, Janarthanam R, Luo Y. Predicting mortality in critically ill patients with diabetes using machine learning and clinical notes. *BMC Med Inform Decis Mak* 2020; **20**: 295 [PMID: 33380338 DOI: 10.1186/s12911-020-01318-4]

83 **Anand RS**, Stey P, Jain S, Biron DR, Bhatt H, Monteiro K, Feller E, Ranney ML, Sarkar IN, Chen ES. Predicting Mortality in Diabetic ICU Patients Using Machine Learning and Severity Indices. *AMIA Jt Summits Transl Sci Proc* 2018; **2017**: 310-319 [PMID: 29888089]

84 **Sadhu AR**, Serrano IA, Xu J, Nisar T, Lucier J, Pandya AR, Patham B. Continuous Glucose Monitoring in Critically Ill Patients With COVID-19: Results of an Emergent Pilot Study. *J Diabetes Sci Technol* 2020; **14**: 1065-1073 [PMID: 33063556 DOI: 10.1177/1932296820964264]

85 **Faulds ER**, Boutsicaris A, Sumner L, Jones L, McNett M, Smetana KS, May CC, Buschur E, Exline MC, Ringel MD, Dungan K. Use of Continuous Glucose Monitor in Critically Ill COVID-19 Patients Requiring Insulin Infusion: An Observational Study. *J Clin Endocrinol Metab* 2021; **106**: e4007-e4016 [PMID: 34100545 DOI: 10.1210/clinem/dgab409]

86 **Agarwal S**, Mathew J, Davis GM, Shephardson A, Levine A, Louard R, Urrutia A, Perez-Guzman C, Umpierrez GE, Peng L, Pasquel FJ. Continuous Glucose Monitoring in the Intensive Care Unit During the COVID-19 Pandemic. *Diabetes Care* 2021; **44**: 847-849 [PMID: 33361145 DOI: 10.2337/dc20-2219]

87 **Dexcom**. Fact sheet for healthcare providers: use of Dexcom continuous glucose monitoring systems during the COVID-19 pandemic. Cited 1 February 2022. Available from: https://www.dexcom.com/hospitalfacts

88 **Galindo RJ**, Umpierrez GE, Rushakoff RJ, Basu A, Lohnes S, Nichols JH, Spanakis EK, Espinoza J, Palermo NE, Awadjie DG, Bak L, Buckingham B, Cook CB, Freckmann G, Heinemann L, Hovorka R, Mathioudakis N, Newman T, O'Neal DN, Rickert M, Sacks DB, Seley JJ, Wallia A, Shang T, Zhang JY, Han J, Klonoff DC. Continuous Glucose Monitors and Automated Insulin Dosing Systems in the Hospital Consensus Guideline. *J Diabetes Sci Technol* 2020; **14**: 1035-1064 [PMID: 32985262 DOI: 10.1177/1932296820954163]

89 **Hinoue T**, Yatabe T, Fujiwara H, Nishida O. Glucose control using an artificial pancreas in a severe COVID-19 patient on extracorporeal membrane oxygenation: a case report. *J Anesth* 2021; **35**: 586-590 [PMID: 34169361 DOI: 10.1007/s00540-021-02965-1]

**Footnotes**

**Conflict-of-interest statement:** The authors declare that they have no conflict of interest.

**Open-Access:** This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: https://creativecommons.org/Licenses/by-nc/4.0/

**Provenance and peer review:** Invited article; Externally peer reviewed.

**Peer-review model:** Single blind

**Peer-review started:** February 16, 2022

**First decision:** April 17, 2022

**Article in press:**

**Specialty type:** Critical care medicine

**Country/Territory of origin:** India

**Peer-review report’s scientific quality classification**

Grade A (Excellent): 0

Grade B (Very good): B

Grade C (Good): C, C

Grade D (Fair): 0

Grade E (Poor): 0

**P-Reviewer:** Li C, China; Villela-Nogueira CA, Brazil **S-Editor:** Liu JH **L-Editor:** A **P-Editor:** Liu JH

**Table 1 Clinical uses of artificial intelligence in management of diabetes**

|  |  |  |
| --- | --- | --- |
| **AI applications** | **Examples of AI devices** | **Clinical uses** |
| Retinal screening | IDx-DR device | Screening and diagnosis of diabetic retinopathy |
| Clinical diagnosis | Advisor Pro | Detection and monitoring of diabetes and its associated complications. Fine-tuning insulin dose |
| Patient self-management tools | Medtronic Guardian Connect System, Dexcom G6 CGM systems; Mobile applications | Improve blood glucose control, activity and dietary tracking |
| Risk stratification | AI using random forest and; gradient boosting techniques | Prediction of new-onset diabetes; Prediction of subpopulations at risk for complications, non-compliance to therapy and hospitalization |

AI: Artificial intelligence.

**Table 2 Possible critical care applications of artificial intelligence in diabetes management**

|  |
| --- |
| Blood glucose monitoring and prediction |
| Detection of adverse glycemic events |
| Blood glucose control strategies |
| Insulin bolus calculators and advisory systems |
| Risk and patient stratification |

**Table 3 Characteristics of an ideal tool to monitor blood glucose in intensive care unit**

|  |
| --- |
| Ease to use |
| Minimal burden on staff |
| Automated data entry |
| High rate of adherence  |
| Allow for minimal sampling |
| Comfortable to use for the patient |
| Use of a proven algorithm to calculate insulin dosage |
| Quickly correct hyperglycemia |
| Consistently maintain glucose within the predetermined optimal range  |
| Ensure minimal glycemic variability |
| Prevent episodes of hypoglycemia |
| Provide easy interface with other patient measurements and data |
| Easy to integrate into existing hospital systems  |
| Avoid the need for repeated data entry |
| Maintain results in a comprehensive, standardized database to facilitate multi-center comparison |

**Table 4 Continuous glucose monitoring devices**

|  |  |  |
| --- | --- | --- |
| **Type of device** | **Name of device** | **Comments** |
| Intravenous | GlucoClear by Edwards Lifesciences; (Irvine, CA) | Approved in Europe |
| Intravenous | Glysure System by Glysure (Abingdon, UK) | Approved in Europe |
| Intravenous | Eirus by Maquet Getinge Group (Rastatt, Germany) | Approved in Europe |
| Intravenous | OptiScanner 5000 by OptiScan; (Hayward, CA) | Approved in EuropeFDA-approved for use in US hospitals |
| Intravenous | GlucoScout (International Biomedical, Austin, TX) | FDA-approved for use in US hospitals |
| Intravenous | Dexcom G | FDA-approved and CEA approved |
| Intravenous | Guardian™ Connect system by Medtronic (San Diego, CA) | FDA-approved for use in US hospitals |
| Subcutaneous | Freestyle Libre by Abbott Diabetes Care | US FDA approved |

FDA: Food and Drug Administration; CEA: Carcinoembryonic antigen.

**Table 5 Limitations of artificial intelligence**

|  |  |
| --- | --- |
| **Factors** |  |
| Human factors | Inhibition, lack of experience  |
| Technical factors | Cost, availability and implementation |
| Data limitation | Lack of data in ICU patients, lack of large scale randomized trials |
| Design limitation | Devices tried in certain patient populations may not be applicable in ICU patients |
| Ethical | Lack of guidelines |

ICU: Intensive care unit.