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AIMS AND SCOPE

The primary aim of *Artificial Intelligence in Gastroenterology* (*AIG*, *Artif Intell Gastroenterol*) is to provide scholars and readers from various fields of artificial intelligence in gastroenterology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

AIG mainly publishes articles reporting research results obtained in the field of artificial intelligence in gastroenterology and covering a wide range of topics, including artificial intelligence in gastrointestinal cancer, liver cancer, pancreatic cancer, hepatitis B, hepatitis C, nonalcoholic fatty liver disease, inflammatory bowel disease, irritable bowel syndrome, and *Helicobacter pylori* infection.

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MINIREVIEWS

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

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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

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.

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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 to 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.

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

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].

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.

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.

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.

FOOTNOTES

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