Diabetes Technology Update: Use of Insulin Pumps and Continuous Glucose Monitoring in the Hospital

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The use of continuous subcutaneous insulin infusion (CSII) and continuous glucose monitoring (CGM) systems has gained wide acceptance in diabetes care. These devices have been demonstrated to be clinically valuable, improving glycemic control and reducing risks of hypoglycemia in ambulatory patients with type 1 diabetes and type 2 diabetes. Approximately 30–40% of patients with type 1 diabetes and an increasing number of insulin-requiring patients with type 2 diabetes are using pump and sensor technology. As the popularity of these devices increases, it becomes very likely that hospital health care providers will face the need to manage the inpatient care of patients under insulin pump therapy and CGM. The American Diabetes Association advocates allowing patients who are physically and mentally able to continue to use their pumps when hospitalized. Health care institutions must have clear policies and procedures to allow the patient to continue to receive CSII treatment to maximize safety and to comply with existing regulations related to self-management of medication. Randomized controlled trials are needed to determine whether CSII therapy and CGM systems in the hospital are associated with improved clinical outcomes compared with intermittent monitoring and conventional insulin treatment or with a favorable cost-benefit ratio.

The prevalence of diabetes is steadily on the rise, such that more than 1 in every 10 adult individuals or 12.2% of the U.S. population aged 18 years or older is affected (1). Patients with diabetes have a threefold greater chance of hospitalization compared with those without diabetes (2). The annual incidence of diabetes as any listed diagnosis has more than doubled during the past two decades to a total of 7.2 million hospital discharges, accounting for a total of 43.1 million hospital days among U.S. adults affected (1,3). Current guidelines for the management of hyperglycemia recommend the use of intravenous insulin in the intensive care unit (ICU) and subcutaneous basal or basal-bolus insulin regimens in general medicine and surgery settings (4,5). Although effective in improving glycemic control and in reducing the risk of hospital complications (6,7), intensive insulin therapy results in frequent hypoglycemia, reported in 12–30% of patients (8–10). Thus, improving glycemic control while minimizing the rate of hypoglycemia is of major importance in the hospital because both hyperglycemia and hypoglycemia have been shown to be independent risk factors of poor clinical outcome and mortality (11–13).

During the past decade, diabetes technology has rapidly evolved, with new technologies being developed and improved every year. While most of the new technology development has aimed to improve diabetes care in the ambulatory setting, technology advances have also impacted the management of hospitalized patients with diabetes. Major areas of technology advances in diabetes are the use of continuous subcutaneous insulin infusion (CSII, or insulin pump) and the increasing

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availability of continuous glucose monitoring (CGM) systems for the management of patients with type 1 diabetes (T1D) and type 2 diabetes (T2D). These two critically important technologies have been studied in multiple randomized controlled trials in ambulatory patients, but there are few such trials in inpatients. This is in part because of the short duration of hospitalization, changes in clinical and nutritional status, and the time needed for device calibration and the warm-up period before accurate readings are obtained. In addition, among hospitalist physicians, there is lack of provider awareness and lack of health care professionals trained in the use of these devices, lack of uniform policies and guidelines for implementation in the hospital setting, and, in many hospitals, lack of expertise available for consultation on the use of insulin pumps and CGM technology.

We conducted a MEDLINE search for articles published between January 2005 and February 2018 using a combination of search terms including hospital hyperglycemia and diabetes, diabetes technology, insulin pump therapy/CSII, continuous glucose monitoring/CGM, and new therapies in inpatient diabetes care. In this article, we aim to review published evidence and discuss the application of these technological advances for the management of hospitalized patients with diabetes.

INSULIN PUMP USE IN THE HOSPITAL

Approximately 3 million children and adults are estimated to have T1D in the U.S. (14), with incidence rates that have gradually increased during the last two decades (15,16). Similarly, the incidence of T1D in European countries has increased by 3–4% per year (17), leading to growing demands on inpatient services (17,18). Hospitalization rates in patients with T1D are about threefold higher compared with the general population (19,20). Although few studies have reported differences in hospital outcomes between patients with T1D and T2D, patients with T1D have longer hospital stays and higher rates of complications and hospital mortality compared with patients with T2D (21). Management of hospitalized patients with T1D usually differs from that of patients with T2D. Patients with T1D are often admitted for procedures that would normally be carried out by outpatient services (18,22). T1D patients must be treated with insulin therapy to prevent ketoacidosis, and they frequently have worse glycemic control and higher rates of hyperglycemia and hypoglycemia compared with patients with T2D (18,23). Frequent challenges in patients with T1D include difficulties in adjusting insulin doses during short- and long-term fasting or during nutritional support and in maintaining a consistent source of carbohydrate while modifying scheduled daily insulin therapy (18,23).

It is estimated that 400,000 patients with T1D in the U.S. are using insulin pumps (24,25). A recent report from the T1D Exchange Clinic Registry indicated that 60% of the 16,061 adult and pediatric patients with T1D in that cohort used an insulin pump (26,27). The number of pump users is expected to increase, as this technology has demonstrated significant improvements in diabetes management for adults and children with T1D by improving glycemic control, decreasing severe hypoglycemic episodes, and improving quality of life (28). As the popularity of CSII increases, hospital health care providers will face the need to manage the inpatient care of patients under insulin pump therapy.

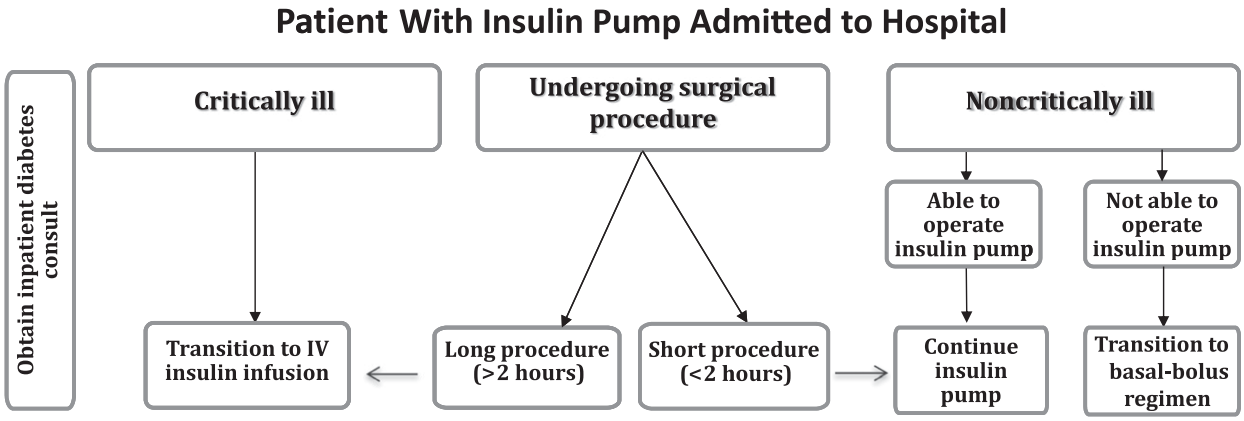
When patients using CSII are hospitalized, a decision must be made as to whether the patient can continue on the insulin pump or not (Fig. 1). The conclusion depends on the ability of the patient to safely operate the pump and the health care provider's familiarity with CSII (29). Inpatient health care professionals may not be familiar with insulin pump use, which may lead to medication errors, confusion among hospital staff, and potentially harmful outcomes for patients. Most insulin pump users are more knowledgeable than their hospital health care providers about diabetes management; therefore, experienced pump users may be encouraged to self-manage their diabetes during their hospitalization (30,31). Better patient satisfaction has been reported if patients can use their pump while in the hospital (31).

Studies on insulin pumps in the hospital are sparse, uncontrolled, and mostly retrospective analyses. In a retrospective study of 136 patients involved in 253 hospitalizations over a 6-year period, CSII was continued for the entire duration of the hospital stay in 65% of the hospitalizations, used intermittently in 20%, and discontinued in 15%, with alternative insulin regimens given. There were no differences in the mean daily glucose levels; however, there were significantly fewer episodes of severe hyperglycemia (glucose >350 mg/dL [19.4 mmol/L]) and hypoglycemia (glucose <40 mg/dL [2.2 mmol/L]) in those who continued CSII compared with those taken off the pump (32). Similarly, a more recent study on 50 patients with 51 hospital admissions, 86% of whom had T1D, also reported no differences in mean blood glucose (BG), frequency of hyperglycemia, or hypoglycemic events among patients treated with CSII compared with those who were transitioned to a multiple daily injection (MDI) regimen (33). The authors concluded that with appropriate patient selection and usage guidelines, most patients using insulin pumps could safely have their therapy transitioned to the inpatient setting.

Bailon et al. (34) conducted a retrospective chart review in 35 admitted patients who had been receiving outpatient insulin pump therapy. The authors found that 91% had T1D. Of them, 62% were deemed candidates for continued insulin pump therapy during hospitalization. Reasons for discontinuing pump therapy at the time of admission were lack of additional pump supplies, threats of suicide or actual suicide attempts, malfunction of the pump, and altered level of consciousness. In a different study, the reasons for CSII discontinuation included patient preference, inability to safely demonstrate pump settings, and inexperience owing to recent initiation of CSII, while inability to correctly demonstrate appropriate pump settings, lack of family support, and postoperative mental status precluded restarting use of the insulin pump upon discharge (33).

The American Diabetes Association (ADA) and the American Association of Clinical Endocrinologists advocate allowing patients who are physically and mentally able to continue to use their pumps when hospitalized, having a hospital policy for CSII use, and engaging hospital personnel with expertise on pump management (35–37). They recommend that shortly after admission the inpatient diabetes team and/or the endocrinology service become promptly involved in helping with insulin adjustment and pump settings as well as in coordinating care after hospital discharge.

Current recommendations advocate the establishment of clear policies and procedures to guide patients and hospital staff in the management of diabetes with



Changes to Pump Therapy With Imaging Studies	
X-ray/CT	Pump should be covered by lead apron
MRI	Pump and metal infusion set should be removed
Ultrasound	No need to remove pump but transducer should not be pointed directly at the pump
Cardiac catheterization	Pump should be covered by lead apron
Pacemaker/automatic implantable cardioverter defibrillator (AICD)	Pump should be covered by lead apron
Colonoscopy/EGD	Pump can remain in place
Laser surgery	Pump can remain in place

Figure 1—Recommendations on the course of action for hospitalized patient with T1D wearing an insulin pump (18). IV, intravenous; EGD, esophagogastroduodenoscopy.

the use of insulin pumps (18) (Table 1). The hospital provider should obtain a detailed record of the type of insulin formulation and the pump settings on admission, including basal rate/rates, the carbohydrate ratio (grams of carbohydrate for 1 unit of insulin), and the correction or sensitivity factor. Clear physician's orders with specifics on the type of diet, frequency of point-of-care glucose testing, basal rate, bolus, and correction-dose insulin settings should also be in place. In addition, the patient's cognitive, emotional, and physical ability to manage his/her insulin pump during the hospitalization should also be considered when deciding whether to continue use of the pump while the patient is hospitalized. A signed patient agreement that specifies all the necessary tasks to be performed by the patient, consent to share information regarding pump settings with the health care staff, and the need to report any issues is also recommended.

The pump settings also include a target glucose level. In the outpatient setting, many patients with T1D aim for tight glucose control with a target set at 80–100 mg/dL (4.4–5.5 mmol/L), which may be too low for the hospital setting (18,38). No large randomized controlled trials have examined best glucose target levels for hospitalized patients with T1D; however, a systematic review of 19 studies (9 randomized and 10 observational) reported that in surgical noncritically ill hospitalized patients, the overall rate of infections can be significantly reduced by keeping glucose concentrations between 100 and 180 mg/dL (5.5–10 mmol/L) (6). The ADA (39) and the Endocrine Society (5) guidelines for the management of hyperglycemia in noncritically ill hospitalized patients recommended that patients with either T1D or T2D maintain goal fasting and premeal BG $<$140 mg/dL (7.8 mmol/L) and random glucose $<$180 mg/dL (10 mmol/L). Since 2017, the ADA's *Standards of Medical Care in Diabetes* modified inpatients' target glucose, recommending levels between 140 and 180 mg/dL (7.8–10 mmol/L) for most ICU as well as non-ICU medical surgery patients with diabetes (35). More stringent goals lower than 140 mg/dL (7.8 mmol/L) may be appropriate for selected patients, such as cardiac surgery patients and those with acute ischemic cardiac or neurological events, provided the targets can be achieved without significant hypoglycemia (31).

CONTRAINDICATIONS TO INSULIN PUMP USE IN THE HOSPITAL

Contraindications to the use of insulin pumps in the hospital are shown in Table 1. If the decision is reached to discontinue insulin pump use, then the patient should be switched to a subcutaneous multidose insulin regimen (pump holiday protocol) (Table 2). The 24-h basal dose of insulin delivered by the pump should be replaced by long-acting basal insulin (glargine, detemir, or degludec). The insulin pump should be discontinued at least 2 h after the first injection of basal insulin. Mealtime

Table 1—Contraindications to insulin pump therapy in the hospital

Impaired level of consciousness (except during short-term anesthesia)
Patient's inability to correctly demonstrate appropriate pump settings
Critical illness requiring intensive care
Psychiatric illness that interferes with a patient's ability to self-manage diabetes
Diabetic ketoacidosis and hyperosmolar hyperglycemic state
Refusal or unwillingness to participate in self-care
Lack of pump supplies
Lack of trained health care providers, diabetes educators, or diabetes specialist
Patient at risk for suicide
Health care decision

insulin should be provided with subcutaneous rapid-acting insulin (aspart, lispro, or glulisine). The dose can be calculated as half of a patient's usual total daily dose of insulin divided by three and given before each meal. Alternatively, the prandial dose can be calculated by allowing the patient to select the dose of insulin using the usual insulin-to-carbohydrate ratio. A correction dose of rapid-acting insulin should be ordered for high glucose levels based on the patient's usual insulin sensitivity factor. For example, if the usual insulin sensitivity factor is 1 unit per 40 mg/dL (2.2 mmol/L), then for each 40 mg/dL (2.2 mmol/L) above the target range, the patient should receive 1 extra unit of rapid-acting insulin (40).

INSULIN PUMP USE IN SPECIAL SITUATIONS

Diabetic Ketoacidosis

Insulin pump failure can lead to diabetic ketoacidosis. Pump malfunction may result from blockage or leakage in the infusion set or connectors, causing an interruption of infusion flow (41). Because the subcutaneous depot of insulin is small with pump therapy (smaller than with an MDI regimen) and because it uses rapid-acting insulin with a short duration of action, any short-term interruption in the continuous flow of insulin could result in hyperglycemia and possibly diabetic ketoacidosis. In patients with diabetic ketoacidosis, the pump must be discontinued and the patient should be treated with continuous intravenous insulin administration as per hospital protocol. The patient may be transitioned back to the pump after resolution of the diabetic ketoacidosis when clinically stable and when the acid-base disorder is corrected. The intravenous insulin is continued for the first 2 h of the pump restart to allow the formation of a subcutaneous depot of insulin. Frequent BG monitoring is needed for several hours after the pump is restarted to ensure glycemic control.

Perioperative Period

Many patients undergoing ambulatory and short-term surgical procedures for up to 2–3 h could continue using their CSII device during the procedure (18,25,33,38,42). Table 3 includes a recommended insulin pump protocol for minor surgical procedures with anticipated length of surgery $<$2 h. This decision is to be based on the length of the procedure, postoperative recovery time, and whether exposure to an electromagnetic field (MRI, computed tomography, therapeutic radiation, or electric shock for defibrillation) is expected during or after surgery (Fig. 1). Prior to surgery, the patient's pump settings should be reviewed and adjusted as needed by a trained professional. The patient should bring all necessary pump supplies to the hospital or outpatient surgical facility and insert a new subcutaneous infusion set outside the planned surgical area the day before surgery. Hospital policy for managing insulin pumps should be reviewed with the patient, and the patient should give written consent to abide by the policy. The presence of the insulin pump should be documented on admission and the pump inspected regularly throughout the hospital stay by nursing staff to ensure proper functioning. The infusion site should be inspected for signs of inflammation or leakage and to ensure that it is in a location away from the area where the surgery will occur. The anesthesiologist must have access to the insulin pump during surgery to allow it to be suspended or disconnected if necessary. If use of the insulin pump is to be discontinued during surgery in a patient with T1D, the patient should be managed with intravenous insulin infusion or with frequent subcutaneous insulin injections.

Although no prospective randomized studies are available to prove the efficacy of CSII during the perioperative period, several retrospective studies and case reports have shown that CSII can be maintained safely. A retrospective study of 92 surgical cases found similar intraoperative

Table 2—Transition from CSII to subcutaneous (SC) insulin regimen "pump holiday protocol"

Stop CSII ~2 h after SC basal insulin is given.	
Calculate 24-h basal dose of insulin delivered from pump setting. Total basal daily insulin can be given as once-daily or twice-daily injections.	
Prandial insulin can be calculated as half of a patient's usual total daily dose of insulin divided by 3.	
Capillary BG should be measured before meals and bedtime.	
A correction-dose algorithm of rapid-acting insulin to be added to the prandial dose should be ordered for high BG levels based on the patient's usual insulin sensitivity factor or by a sliding-scale protocol:	
BG before meals	Dose
$<$180 mg/dL ($<$10 mmol/L)	No correction
181–220 mg/dL (10.1–12 mmol/L)	1 unit
221–260 mg/dL (12.1–14 mmol/L)	2 units
261–300 mg/dL (14.1–16 mmol/L)	3 units
301–340 mg/dL (16.1–18 mmol/L)	4 units
341–380 mg/dL (18.1–20 mmol/L)	5 units
$>$380 mg/dL ($>$20.1 mmol/L)	6 units, notify physician
Adjust basal and prandial insulin dose daily based on glucose values and nutritional intake.	
The pump can be restarted when the patient is able to resume responsibility or at hospital discharge.	

Table 3—Recommended insulin pump protocol for minor surgical procedure with anticipated length of surgery <2 h

Document insulin pump settings and current basal rate.

Check BG every hour:	
BG <100 mg/dL (5.5 mmol/L)	Hold basal infusion rate, check BG every 30 min.
BG 101–140 mg/dL (5.6–7.7 mmol/L)	Decrease basal rate by 25%.
BG 141–180 mg/dL (7.8–10 mmol/L)	Maintain basal rate.
BG 181–220 mg/dL (10.1–12.2 mmol/L)	Increase basal rate by 25%.
BG >220 mg/dL (>12.2 mmol/L)	Increase basal rate by 25–50% and give 2–4 units as bolus insulin.

glycemic control between patients on CSII continuation of basal rate with or without correctional insulin bolus and those converted to intravenous insulin (43). There was no significant difference in mean BG between continuation or conversion, with one or more intraoperative BG levels >180 mg/dL (10 mmol/L) in about 40% of patients in both groups. In a different retrospective study from a tertiary care hospital, Sobel et al. (42) reported their experience with 49 patients using insulin pump therapy who presented for 57 elective same-day surgeries. Patients treated with CSII had no episodes of intra- or postoperative hypoglycemia, and the mean postoperative glucose concentration was lower in patients with anticipated or actual surgical length ≤120 min compared with those with longer procedures (42).

Pregnancy and Delivery

Poorly controlled T1D has been associated with an increased risk of congenital birth defects, miscarriage, fetal death, and preeclampsia. Improved glycemic control and rigorous medication adjustments during gestation are associated with reduced complications. Insulin requirements follow a characteristic pattern in pregnancy, with a decrease in the first trimester and a rise in the second and third trimesters. Increases in insulin requirements of 36% to 114% from preconceptional baseline to the second and third trimesters have been reported (44,45). Recent studies have demonstrated that patients can be treated effectively with insulin pumps when compared with multiple subcutaneous insulin injections. Glycemic control and maternal or neonatal outcomes were comparable between women on insulin pump therapy and women on MDI (46–48). During labor and delivery, the maternal glucose level should be kept between 70 and 140 mg/dL (4–8 mmol/L). Intrapartum glucose levels, more than antepartum glucose levels, affect the risk of neonatal hypoglycemia, with hypoglycemia risk increasing for glucose levels <100 mg/dL (5.5 mmol/L) (49). Glucose should be measured every 1–2 h and dextrose 5% solution should be administered to prevent maternal hypoglycemia. After delivery, insulin requirement falls sharply and it is prudent to decrease the insulin dose to 25–40% of the predelivery dose to prevent hypoglycemia. This is particularly more important after cesarean section in women who may not be allowed to eat for several hours. Breastfeeding lowers insulin requirements, and the insulin dose should be decreased if necessary to prevent hypoglycemia.

Use of CSII After Hospital Discharge

Many studies and meta-analyses have shown that CSII represents one of the best available methods of physiological delivery of basal/prandial insulin in ambulatory patients with diabetes. Thus, it makes sense to continue CSII therapy while patients are in hospital and after discharge, if they can manage their pumps. Compared with MDI, CSII has been associated with improved glycemic control with lower levels of HbA_{1c} and reduction of hypoglycemia in ambulatory patients with T1D and T2D. In addition, increasing evidence indicates that CSII is cost-effective compared with MDI for children and adults with T1D (37) and that it can improve quality of life. The American Association of Clinical Endocrinologists has published good-practice guidelines for the use of CSII. Prior to discharge, the physician or diabetes specialist should program the basal rate, which regulates the food-independent insulin requirements. This is usually done taking into consideration preadmission insulin requirements, activity levels, and overall glycemic control. Providers should reassess knowledge and the need for reeducation and adjustment of basal/prandial insulin recommendations as well as education on sick-day management and pump troubleshooting.

CGM

From the early 1970s, CGM prototypes were available for research projects aiming to develop a glucose sensor–controlled insulin infusion system. In 1977, Miles Laboratories produced the Biostator, a large bedside unit that incorporated an in-line venous cannula to measure glucose and calculated the correct insulin and dextrose infusion rate (50). This device had serious limitations in clinical practice, including its large size, the need for constant supervision, and the continuous withdrawing and discarding of venous blood to measure glucose levels ex vivo using a glucose oxidase–containing membrane. The first CGM device made available in the U.S. was the GlucoWatch Biographer (no longer in use). This device was worn like a wristwatch and provided glucose measurements every 10 min via transdermal extraction of tissue fluid by reverse iontophoresis, a process by which a device extracts glucose samples from fluids in the body by applying extremely low electric currents to intact skin (51). The first CGM system, a retrospective CGM device by MiniMed, was first approved by the U.S. Food and Drug Administration (FDA) in 1999 (50). During the past two decades, considerable technological progress has resulted in the regulatory approval of multiple continuous and semicontinuous glucose monitors, which have provided benefits to many people with diabetes.

CGM devices can be invasive (intravascular—venous and arterial), minimally invasive (subcutaneous), and noninvasive (transdermal). Glucose is measured in interstitial fluid using the glucose oxidase method through fluorescence or measured intravenously through electrochemistry, fluorescence, mid-infrared spectroscopy, or electrochemical impedance spectroscopy (52). Sampling and measurement frequencies typically range from 1 to 15 min and most commonly are every 5 min. More than 15 CGM or semi-CGM devices have been described (53). For the purpose of ambulatory monitoring, a sensor is considered continuous if it provides a value at least every 15 min or more frequently (54).

There is consensus among experts and medical societies that compared with intermittent point-of-care (POC) capillary BG testing, CGM technology offers benefits in the prevention of severe hyperglycemia and hypoglycemia, allowing insulin dosage to be adjusted in a more accurate way (53,55) as well as decreasing the nursing workload related to ICU patients (55). Technological limitations that reduce the accuracy of subcutaneous CGM sensors

include the need for regular calibration because of sensor drift, measurement lag, and substance interference (acetaminophen, maltose, ascorbic acid, dopamine, mannitol, heparin, uric acid, and salicylic acid) (25,56). There is lack of evidence on the accuracy of sensors during periods of arterial hypotension, hypothermia, or hypoxia, all common events in the ICU. In addition, intravascular CGMs carry risks of thrombus formation, catheter occlusion, and catheter-related infections (56). Despite these concerns, studies performed have shown acceptable device accuracy and no safety signals in either adult or pediatric populations (Tables 4 and 5) (57–89).

Despite close to a billion dollars spent by more than 15 different companies in developing CGM, this technology remains largely experimental in the inpatient setting, with few FDA-approved devices. In Europe, there are currently four CGM systems approved for intravenous use in hospitals: *1*) GlucoClear by Edwards Lifesciences (Irvine, CA), *2*) Glysure System by Glysure (Abingdon, U.K.), *3*) Eirus by Maquet Getinge Group (Rastatt, Germany), and *4*) OptiScanner 5000 by OptiScan (Hayward, CA); in addition, there is one CGM system approved for subcutaneous use in hospitals: Sentrino by Medtronic (Northridge, CA). Two CGM systems are FDA-approved for use in U.S. hospitals: GlucoScout (International Biomedical, Austin, TX) and recently the OptiScanner 5000 (83,90).

CGM Use in the ICU

CGM systems have been evaluated for the management of hyperglycemia in ICU patients with and without diabetes over the past 10 years (Table 4). Most of these studies included a small sample size; outcomes were mostly accuracy of glucose control, and there were few with other clinical end points. To determine whether CGM could be an effective tool to titrate intravenous insulin infusion, Holzinger et al. (64) randomized 124 patients in a medical ICU (24 with diabetes, 100 without diabetes) to undergo intravenous insulin titration based on nonblinded Guardian CGM versus arterial BG with blinded CGM (CGM System Gold) (both manufactured by Medtronic MiniMed, Northridge, CA). Arterial glucose values were checked every 1–2 h in the control group. The primary end point was percentage of time within a target glucose level of 80–110 mg/dL (4.4–6.1 mmol/L). No difference was found in percentage of time within target glucose or mean interstitial glucose levels between treatment arms. The frequency of severe hypoglycemia (<40 mg/dL [2.2 mmol/L]) was lower in the nonblinded Guardian CGM group compared with the blinded CGM group (64).

Logtenberg et al. (62) randomized 31 cardiac surgery subjects to blinded versus nonblinded Paradigm CGM (Medtronic MiniMed) starting 1 day prior to surgery. No significant difference in preoperative mean interstitial glucose was found, but postoperative mean glucose improved with nonblinded CGM compared with blinded CGM; however, there was no significant difference in frequency of or time spent in hypoglycemia. Similarly, several additional studies comparing different blinded versus nonblinded CGM in patients after cardiac surgery or with acute coronary syndrome (68,69,71,74) confirmed the accuracy and reliability of CGM technology in titrating intravenous insulin therapy; however, none of them demonstrated significant improvement in mean glucose or in the frequency of hypoglycemia in the ICU. A recent systematic review of 37 studies, both randomized controlled trials and observational studies, concluded that in terms of efficacy, the use of subcutaneous CGM systems does not seem to improve the glycemic control of critically ill patients in a clinically significant manner.

Overall, the results of ICU studies indicate that the use of CGM combined with an appropriate insulin dosing protocol has the potential to improve glucose control in the ICU; however, the results have been conflicting. Some studies, but not others, have reported improvement in mean glucose values and reduction in hypoglycemia frequency with blinded CGM (55). Larger and well-designed multicenter studies are needed to convincingly demonstrate the safety and efficacy of CGM devices in reducing length of stay and improving clinical outcome before recommending their use in the ICU. A recent panel of experts concluded that use of CGM now might not be feasible for every ICU patient (91), but there are populations of high interest who may benefit from further study of CGM owing to their high risk for glucose variability and hypoglycemia. These populations include patients receiving intravenous insulin or high-dose glucocorticoids; those undergoing cardiac surgery, transplant, or traumatic or vascular brain surgery; those with end-stage renal or liver disease or hypoglycemia unawareness; and those in neonatal ICU (53,55).

CGM Use in Non-ICU Settings

Several studies have reported on the use of CGM in non-ICU settings in patients with T2D (Table 5). Burt et al. (86) reported on 26 adult patients with diabetes (23 with T2D and 3 with T1D) who were treated with basal-bolus insulin during hospitalization using blinded CGM System Gold in medical and surgical general wards. The mean daily glucose was similar between interstitial and capillary monitoring. Ten hypoglycemic episodes (<4 mmol/L) were detected during CGM; only one was detected by finger-prick BG level monitoring. Schaupp et al. (87) recruited 84 medicine patients with T2D and applied a blinded iPro2 CGM device (Medtronic MiniMed) for up to 21 days of hospital stay or until discharge. A remarkable consistency between CGM and BG measurements was reported without differences between groups, with 99% of data points in the clinically accurate or acceptable Clarke error grid zones, and the relative numbers of correctly identified episodes of glucose <3.9 and >13.9 mmol/L detected by CGM (sensitivity) were 47.3% and 81.5%, respectively. The number of hypoglycemic episodes (3.3 to <3.9 mmol/L) during nighttime detected by CGM (compared with values from the BG measurements) was 15-fold higher, and the number of episodes >13.9 mmol/L detected by CGM during nighttime was 12.5-fold higher (94) compared with capillary POC glucose testing in general medicine patients with T2D treated with a basal-bolus insulin regimen for ≥3 days. In addition, the use of CGM, compared with POC testing, uncovered a greater number of hypoglycemic events, and 60% of the episodes were during the night. Gu et al. (89) compared the accuracy and time required to reach predefined glycemic targets with sensor-augmented pump technology (Medtronic MiniMed Paradigm 722 system), which combines CSII and real-time CGM, versus MDI with blinded CGM (Medtronic MiniMed CGM System Gold) in 81 adult patients with T2D. Glycemic targets were defined as three preprandial measurements between 80 and 130 mg/dL (4.4–7.2 mmol/L) and three 2-h postprandial measurements between 80 and 180 mg/dL (4.4–10.0 mmol/L) within the same day. The authors reported that sensor-augmented pump technology resulted

Table 4—Clinical trials of adult CGM use in the ICU

First author, year (ref.)	Population	Sample size	No. of sites	Type of CGM	Performance measurement	Comparator
Goldberg, 2004 (57)	ICU	22	1	CGMS Gold	Accuracy	Capillary BG monitor
Corstjens, 2006 (58)	ICU	45	1	CGMS Gold	Accuracy	Arterial by blood gas analyzer
De Block, 2006 (59)	MICU	50	1	GlucoDay	Reliability	Arterial
Yamashita, 2009 (60)	ICU	50	1	STG-22	Accuracy	Arterial by blood gas analyzer
Holzinger, 2009 (61)	MICU	50	1	CGMS Gold	Accuracy and reliability	Arterial by blood gas analyzer
Logtenberg, 2009 (62)	Cardiac surgery	30	1	Paradigm REAL-Time	Accuracy and effect on glycemia with an alarm activation	Capillary, arterial, venous blood on a BG monitor
Rabiee, 2009 (63)	SICU/BICU	19	1	Dexcom	Accuracy and reliability	Capillary POC and lab
Holzinger, 2010 (64)	ICU	24	1	Guardian	Glycemic control, mortality	CGMS Gold (blinded)
Jacobs, 2010 (65)	ICU	29	1	Guardian RT	Accuracy	Capillary BG monitor
Brunner, 2011 (66)	ICU	174	1	CGMS Gold or Guardian	Accuracy	Arterial by blood gas analyzer
Lorencio, 2012 (67)	ICU	41	1	Guardian	Accuracy	Arterial by blood gas analyzer
Kopecký, 2013 (68)	ICU, cardiac surgery	12	1	Guardian REAL-Time	Accuracy and time in various ranges	Arterial by blood gas analyzer
Kopecký, 2013 (68)	ICU, cardiac surgery	12	1	Guardian	Glycemic control	Computer (eMPC) algorithm alone
Rodríguez-Quintanilla, 2013 (69)	CCU	16	1	Guardian RT	Time to normoglycemia	Capillary and venous blood
Ballesteros, 2015 (70)	ICU	18	1	Soft-Sensor	Accuracy	Capillary BG monitor
Boom, 2014 (71)	MICU/SICU	78	1	Navigator	Accuracy	Arterial by blood gas analyzer
Kosiborod, 2014 (72)	Cardiac ICU	21	1	Sentrino	Accuracy and reliability	Central venous POC or lab
Leelarantha, 2014 (73)	Neurosurgical ICU	24	1	Navigator	Accuracy	Standard IV insulin protocol
De Block, 2015 (74)	ICU	35	2	GlucoDay S	Time in various ranges, accuracy	Arterial by blood gas analyzer
Punke, 2015 (75)	SICU	14	1	Sentrino	Accuracy	Arterial by blood gas analyzer
van Hooijdonk, 2015 (76)	ICU	50	1	Sentrino	Accuracy and reliability	Arterial by blood gas analyzer
Gottschalk, 2016 (77)	Extracorporeal cardiac life support	25	1	Sentrino	Accuracy	Arterial by blood gas analyzer
Umbrello, 2014 (78)	MICU	6	1	OptiScanner 5000	Glucose control	None
Sechterberger, 2015 (79)	Cardiac ICU	8	1	Navigator	Accuracy	Arterial by blood gas analyzer
Nohra, 2016 (80)	SICU	23	1	OptiScanner 5000	Accuracy	Yellow Springs Instrument
Righy Shinotsuka, 2016 (81)	ICU	88	1	OptiScanner 5000	Accuracy	Arterial by Yellow Springs Instrument
Wollersheim, 2016 (82)	MICU	20	1	Sentrino	Accuracy	Arterial or venous
Bochicchio, 2017 (83)	ICU	243	4	OptiScanner 5000	Venous	Yellow Springs Instrument
Rijkenberg, 2017 (84)	ICU	155	1	FreeStyle Navigator	Accuracy	Arterial by blood gas analyzer
Schierenbeck, 2017 (85)	Cardiac ICU	26	1	FreeStyle Libre	Accuracy	Arterial by blood gas analyzer

BICU, burn intensive care unit; CGMS, continuous glucose monitoring system; eMPC, enhanced model predictive control; IV, intravenous; MICU, medical intensive care unit; SICU, surgical intensive care unit.

in a shorter time to reach the glucose targets (3.7 ± 1.1 days vs. 6.3 ± 3.1 days for MDI) and less hypoglycemia (sensor glucose <50 mg/dL [2.8 mmol/L]: 0.04% vs. 0.32%, respectively). In another study of 38 hospitalized patients with T2D treated with a basal-bolus insulin regimen, CGM use was compared with bedside POC glucose testing (88). There were no differences in mean daily glucose or premeal, fasting, or 2-h postprandial glucose levels between the two groups. However, CGM detected a higher

Table 5—Clinical trials of CGM in non-ICU settings

First author, year (ref.)	Population	Sample size	No. of sites	Type of CGM	Performance measurement	Comparator
Burt, 2013 (86)	General ward	26	1	iPro	Accuracy	Capillary BG monitoring
Schaupp, 2015 (87)	General ward	84	1	iPro	Accuracy	Capillary BG monitoring
Gómez, 2015 (88)	General ward	38	1	iPro2	Accuracy	Capillary BG monitoring
Gu, 2017 (89)	General ward	81	8	Sensor-augmented pump	Accuracy	MDI with blinded CGM

number of hypoglycemic events compared with capillary glucose testing. About a third of the hypoglycemic episodes were asymptomatic and more than 50% of the events occurred between dinner and breakfast, suggesting that these episodes would be missed by standard glucose testing.

Previous studies in non-ICU settings have shown that the inpatient use of CGM is more effective in identifying trends toward hypoglycemia and hyperglycemia compared with standard POC glucose testing (86,92). However, these trials used blinded CGM, and therefore interventions to prevent impending hypoglycemia were not performed (86–88,93). Another limitation is that although glucose values are captured in the CGM device, results are not transmitted to the nursing station to allow providers to detect and treat impending hypoglycemia. In addition, hypoglycemia alarms are only visible and audible at the bedside; as a result, nurses need to frequently enter the patient's room to monitor glucose values on the CGM receiver. To overcome these limitations, a recent promising pilot study reported on the feasibility of a continuous glucose telemetry system in high hypoglycemia–risk patients in non-ICU settings (94). Elderly patients receiving high-dose insulin treatment and with multiple comorbidities were included in this study. Data collected on a Dexcom G4 CGM sensor were transmitted via Bluetooth technology from the patient's room wirelessly to an iPad located centrally at the nursing station on the same floor. By setting the lower glucose alarms at 85 mg/dL, the glucose telemetry system allowed the nursing staff to initiate preventive actions for impending hypoglycemia (94).

ARTIFICIAL PANCREAS: CLOSED-LOOP INSULIN DELIVERY SYSTEM

Recent technological advances in CSII devices, CGM systems, and insulin delivery algorithms have resulted in the development of artificial pancreas for inpatient care (95,96). An artificial pancreas, or a closed-loop system, combines a real-time glucose-sensing component, an insulin delivery device (pump), and a computer that calculates the amount of insulin needed in response to the BG concentration (95). During the past decade, a variety of closed-loop systems have been explored in various groups of critically ill patients (97,98), during the perioperative period (99), and in insulin-treated patients with T2D (100). These studies reported that the closed-loop technology is safe and effective in improving glycemic control and proportion of time spent in the target glucose concentration range, but they found no significant improvement in mean glucose concentration or in the frequency of hypoglycemic events compared with multidose insulin regimens. Despite this evidence supporting the efficacy and feasibility of closed-loop use, there are several limitations that need to be addressed to support wider adoption in the hospital setting. The need for intravascular access for intravenous closed-loop insulin systems limits their use in noncritical-care general ward settings. More importantly, no previous studies have shown that use of closed-loop systems is associated with improved clinical outcomes compared with intermittent monitoring and conventional insulin treatment and/or with favorable cost-benefit ratio.

WHAT LIES AHEAD IN DIABETES TECHNOLOGY?

Diabetes management devices including insulin pumps and CGM have gained wide acceptance among physicians and ambulatory patients with T1D, and their use has been associated with improved glycemic control and reductions in hypoglycemia. The Endocrine Society (101), the American Association of Clinical Endocrinologists (102), and the Diabetes Technology Society (53) support the inpatient use of CSII in selected patients, such as those with appropriate insulin pump and diabetes self-management skills, with noncritical illness, without mental status changes, and with the prompt involvement of inpatient diabetes specialists. The consensus among diabetologists is to allow the patient to continue to self-manage their diabetes using the pump. If a patient is unable to manage their pump for whatever reason or a hospital lacks specialist consultation, then the pump should be removed and conventional insulin management should be initiated. CSII can be restarted once the patient has recovered.

Despite broad-based evidence supporting the use of CGM devices as a mean of facilitating glucose control in hospitalized patients and decreasing nursing workload, the technology remains largely investigational. Clinical guidelines have advised against the hospital use of CGM because of the lack of safety and efficacy outcome studies (53,101,102); however, they support continuation of outpatient CGM in the hospital under specific circumstances if proper institutional procedures and guidelines are developed (5,53). In recent years, improvement in the accuracy of CGM sensors has resulted in a reduced need for frequent calibration, or any calibration (103), which is an attractive feature in the hospital. A pragmatic evaluation of CGM proving accuracy and clinical effectiveness is needed and may facilitate more widespread adoption of this technology in the hospital setting.

Because an increasing number of people with diabetes are using insulin pumps and CGM, it is inevitable that health care professionals working in hospitals will have to care for patients using pumps and CGM devices. Technology for management of diabetes in the hospital is improving and is expected to significantly reduce the added burden and risk of diabetes for hospitalized patients. In the near term, the availability of accurate CGM systems combined with automatic insulin dosing systems using software algorithms will facilitate glycemic control and reduction of hypoglycemia

and hyperglycemia in critically and non-critically ill patients with T1D and T2D (100). As artificial intelligence becomes more established, the dosing algorithms for insulin delivery in hospitalized patients will become individualized for closed-loop control of glycemia (104).

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