REVIEW

Managing diabetes mellitus in the surgical patient

Diabetes Management



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Practice points

- Patients with diabetes mellitus have increased surgical morbidity and mortality.
- Both sustained hyperglycemia and glycemic variability are associated with higher morbidity and mortality in the surgical patient.
- Basal-bolus insulin therapy is the most effective means of controlling hyperglycemia in the postoperative inpatient.
- In the absence of consensus guidelines, local standards can be developed and successfully implemented that can ultimately enhance care and ensure patient safety of the diabetes patient undergoing surgery.
- Appropriate treatment and monitoring protocols throughout the continuum of surgical care should be established.
- Institutions should assess their management of these patients as part of their overall diabetes mellitus quality improvement efforts.

SUMMARY Patients with diabetes mellitus (DM) who undergo surgery experience higher morbidity and mortality than patients without DM. Hyperglycemia is a determinant of risk for surgical complications. Data are limited about whether controlling glucose improves outcomes, but current information supports treating high glucose levels throughout the continuum of surgical care. Despite its high-profile nature, little is known about the quality of care provided to patients with DM undergoing surgery, and no consensus standards exist on how to manage these patients throughout the surgical continuum. Here we provide an overview of DM and surgery, discuss what is known about glycemic control and its relationship to surgical outcomes in noncritically ill patients, review results of efforts to standardize their care, and highlight areas requiring further study and discussion.

Scope of the problem

Diabetes mellitus (DM) is becoming increasingly prevalent in the USA, with approximately 8.3% of the population (25.8 million people) now estimated to have the diagnosis [1]. The prevalence of DM continues to increase worldwide, and the number of affected persons is predicted to increase to 300 million by 2025 [2]. The estimated total economic cost of diagnosed DM in 2012 was US\$245 billion, a 41% increase from the previous estimate in 2007 of \$174 billion [3]. Hospital admissions of patients with a DM diagnosis are also rising in the USA [4].

Compared with patients without DM, those with DM have an increased risk of requiring surgery. Moreover, patients with DM who undergo surgery represent a higher risk population, with higher morbidity (e.g., increased surgical site infections) and increased mortality. The higher morbidity

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KEYWORDS

- diabetes mellitus
- hyperglycemia insulin
- pump perioperative
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and mortality in patients with DM are further increased in those with poor perioperative and postoperative glycemic control [5–7].

A substantial amount of research has examined what the optimal glycemic targets should be in critically ill patients, including those in the surgical intensive care unit. Data have shown variable results in regard to the level of glucose control that should be achieved, and controversy remains about glucose targets in the critically ill population [8-10]. While a number of organizations have published recommendations on management of DM in patients undergoing surgery [11-13], surgical and nonsurgical specialties with interest in the topic have not coordinated the mutual development of guidelines for these patients. Consequently, hospitals need to develop, implement and track their own institutionally established standards. In this paper, we provide an overview of the management of the surgical patient with DM, discuss what is known about glycemic control in this population and its relationship to outcomes, review results of efforts to standardize the care of these patients, and highlight areas in need of further study. This review focuses on the noncritically ill patient with DM who is undergoing elective surgery under general anesthesia.

Pathophysiology

The relationship between hyperglycemia and surgical outcomes is highly complex. During and after surgery, even patients without DM may experience hyperglycemia that is modulated by multiple factors, including preoperative metabolic state, intraoperative management, neuroendocrine stress response, use of certain medications (e.g., glucocorticoids), and acute insulin resistance [14]. Hyperglycemia is associated with abnormalities in granulocyte adherence, impaired phagocytosis, delayed chemotaxis and depressed bactericidal capacity. Hyperglycemia also increases the generation of reactive oxygen species and the concentration of inflammatory cytokines [14]. These alterations in cellular function and homeostasis subsequently result in delayed wound healing, increased susceptibility to infections, delayed recovery and the potential for end-organ dysfunction [14].

Although exposure to chronic hyperglycemia is associated with more complications in the surgical patient, glycemic variability is another glycemic marker that has recently emerged as a concern. Animal and in vitro studies have demonstrated that variability in glucose concentrations can lead to endothelial cell damage [15,16]. Markers of oxidative stress are elevated in patients with Type 2 DM who experience swings in glucose levels [17]. Glucose variability is associated with increased mortality in critically ill patients (including those in the surgical intensive care unit) [18-20], in patients who experience sepsis [21], in patients with burns [22], and in patients on total parenteral nutrition [23]. Glucose variability has also been linked to poorer outcomes in noncritically ill patients [24]. Therefore, strategies to control hyperglycemia in the surgical patient may have to take into consideration not only mean glucose levels but also methods to reduce glucose variability.

Modeling the care of the surgical patient with DM

Care of the surgical patient with DM occurs along a continuum, but for purposes of quality improvement and analysis it can be separated into discrete preperioperative, perioperative and postperioperative phases (Figure 1). The preperioperative phase includes the patient's history of DM and its management (i.e., mode of therapy, presence of DM complications, metabolic control) that could impact glycemic control and patient outcomes throughout the remaining phases. The perioperative phase is separated into preoperative, intraoperative and postanesthesia recovery segments, which are defined by discrete start and end times. The postperioperative phase represents the management that would occur following discharge from the postanesthesia care unit (PACU). The postperioperative phase is management occuring either in the hospital (if the patient is admitted) or what might take place on an outpatient basis (if the patient is discharged directly home after the procedure). Each phase and each segment within each phase represent discrete transitions in care occurring throughout the continuum of surgical DM management that place the patient at risk for adverse consequences (e.g., life-threatening hypoglycemia, wound infections) if appropriate glucose monitoring and treatment are not performed. This model has been used to construct studies designed to assess current state of care and to develop and test interventions targeted at improving the different phases of surgical DM management [25].



Figure 1. Model for the analysis of diabetes management during the continuum of surgical care, divided into preperioperative, perioperative and postperioperative phases. The nomenclature for the different phases and segments is used throughout the text. The preperioperative phase reflects the patient's history of diabetes and its management that could have an impact on perioperative and/or postperioperative glycemic control and patient outcomes. The perioperative phase is divided into preoperative, intraoperative phase represents a recovery segments defined by discrete start and end times identified in the medical record. The postperioperative phase represents glycemic control and management after discharge from the PACU, which would take place during a hospital stay or when the patient is discharged home.

PACU: Postanesthesia care unit.

Adapted with permission from [25].

Preperioperative glycemic control & outcomes

Chronic outpatient exposure to hyperglycemia, which can be estimated with hemoglobin A_{1c} (HbA,) levels, is associated with poorer surgical outcomes, including increased surgical site infection, longer inpatient length of stay, other morbidities and higher mortality [26-30]. Additionally, preperioperative hyperglycemia has been correlated with perioperative mortality [31]. Although no randomized controlled trials exist, limited retrospective data suggest that lower HbA₁ levels result in a decreased risk for infections in noncardiac surgery patients [30,32]. Although it has not yet been established that optimizing outpatient glucose levels will improve surgical outcomes, at the very least, better glucose control prior to surgery could increase the chances of successfully transitioning a patient within a desired glucose range across the continuum of care. Studies are needed to evaluate whether intensive glucose control during the preperioperative phase of care improves surgical outcomes.

Perioperative glycemic control & outcomes

No consistent definition of the perioperative period has been used in the medical literature, and it is often defined as even including the first 48 h after a surgical procedure. For purposes of this review and per previous reports [33,34], the perioperative period is defined as the time from patient admission to the preoperative area, through the intraoperative period, to the time of discharge from the PACU (Figure 1). There are no consensus standards on managing hyperglycemia during the perioperative phase surgical care.

As with preperioperative glucose control, intraoperative hyperglycemia is correlated with adverse outcomes in surgical patients, with increased mortality [6], infections [7,35] and overall morbidity [36]. Despite these observations, the benefits of intraoperative glucose control is has not been established. One study demonstrated that patients with hyperglycemia who received perioperative insulin to treat hyperglycemia were at no greater risk for adverse outcomes than were patients with normal glucose levels [7]. However, another study did not show any benefit of intensive intraoperative insulin therapy [10]. Additional studies are required to better determine whether treatment of hyperglycemia intraoperatively will reduce morbidity during the postperioperative phase of care.

There is no consensus on the best method to treat intraoperative hyperglycemia. Establishing such standards may be difficult, given the lack of randomized controlled studies in this population, and the variety of surgical procedures with their diverse complexity and duration. Intravenous insulin infusion may be the best approach for longer procedures, especially in patients with Type 1 DM. In other cases, intermittent subcutaneous rapid-acting insulin could suffice. Intravenous boluses of rapid-acting or short-acting insulin would not have a sustained impact on glucose levels due to their short duration of action and probably should be avoided. In some circumstances, continued use of a patient's outpatient insulin pump therapy can be allowed (see section below titled 'Insulin pump therapy in the patient with DM undergoing surgery').

Postperioperative care

Little is known about the outcomes of patients with DM who have been discharged home the day of surgery, and this topic requires further study. In general, the strongest data supporting management of hyperglycemia in surgical patients come from studies of postoperative inpatients [37-39]. Postoperative hyperglycemia is associated with increased morbidity and mortality in hospitalized patients [5,37,38,40-43]. Studies of patients undergoing cardiac surgery were some of the first to demonstrate the benefits of optimizing glucose - in this instance a reduction in deep sternal wound infections [37]. Other studies have correlated a decrease in the number of infectious complications with better glycemic control [38,39]. Current guidelines suggest a fasting glucose of <140 mg/dl and a random glucose of <180 mg/dl, with a target range of 140 mg/ dl to 180 mg/dl in noncritically ill inpatients; and these values have been applied to surgical patients [13,44,45].

In the hospital, the use of correction insulin only - also called sliding-scale insulin - without concurrent use of basal insulin - results in ineffective inpatient glycemic control and a high degree of variability in glucose levels [46-49]. In noncritically ill hospitalized patients with DM, including those who are postoperative, the most effective approach to treating hyperglycemia is the combination of a basal insulin, which is typically a long-acting or intermediate-acting insulin, and a short-acting or rapid-acting insulin given with meals when the patient is eating, supplemented by correction doses for high glucose values [13,45,48-50]. This regimen is often termed 'basal-bolus' insulin therapy, and it has become the cornerstone of hyperglycemia therapy in the hospital outside of the intensive care unit [44,45].

However, substantial numbers of patients are incorrectly and inadequately treated with only correction insulin. A failure to intensify therapy when needed and appropriate has been termed 'clinical inertia', and one of the earliest descriptions of clinical inertia in the hospital noted a failure to intensify use of basal-bolus insulin therapy despite ongoing hyperglycemia [51,52]. Others have also identified clinical inertia in the management of inpatient hyperglycemia [53-56]. A recent analysis identified clinical inertia in the treatment of a subset of postoperative inpatients with DM, with a failure to intensify therapy to a basal-bolus insulin regimen despite their ongoing hyperglycemia [57]. Strategies are needed to assist hospital-based healthcare providers to optimize insulin therapy in their postoperative patients.

Strategies to standardize care of the surgical patient with DM

Randomized clinical trials designed to address the benefits of controlling hyperglycemia during all phases of the continuum of surgical care are lacking, except for those on the care of the postoperative hospitalized patient. Until such data become available, medical facilities can at least turn their attention to standardizing care processes to ensure patient safety and potentially improve patient satisfaction. However, consensus recommendations do not exist on how best to approach the patient with DM during the preperioperative and perioperative phases of care. For instance, there are no standards addressing how often to measure glucose, no agreement on the method of glucose measurement, and no guidelines on how best to treat hyperglycemia during the perioperative phase of care. The following discussion examines standards that have been developed and implemented for use at one institution, with a summary of how those care processes have altered care positively.

• Improving preperioperative & perioperative DM standards of care

Whenever possible, the preparation of the DM patient for surgery should begin prior to the procedure. For many elective cases, there should be no reason why a period of time could not be allowed to introduce glycemic control measures in preparation for surgery. This approach begins with an adequate history and physical examination, which includes assessing the type of DM, the duration of the condition, its current medical management, and the effectiveness of the current management. The goal should be to optimize blood glucose control preoperatively through lifestyle modifications, medications and education. It is also necessary to evaluate the patient for associated comorbidities and chronic complications. These include hypertension, chronic renal disease, autonomic neuropathy and coronary artery disease. Patients with DM have an increased chance of surgical morbidity; they may have cardiovascular complications of the disease; and they tend to have elevated physical status scores per the guidelines of the American Society of Anesthesiologists [33,58,59]. Thus, a preoperative evaluation should be undertaken by someone with knowledge of the patient or expertise in anesthesia risk.

A recent retrospective review demonstrated gaps in both preperioperative and perioperative DM care. For instance, despite a preexisting diagnosis of DM, patients underwent HbA_{1c} testing infrequently and less than one-half had intraoperative glucose monitoring [33]. The lack of standards in the medical literature led to a recognition of the need to ensure a smooth transition across the continuum of surgical care, and institutional guidelines (**Box 1**) were developed and introduced to the surgical and the anesthesiology staff at our institution.

A multidisciplinary team comprising an endocrinologist, a surgeon, an anesthesiologist, a surgical nurse practitioner and members of the nursing staff met regularly to discuss the elements of preperioperative and perioperative DM care that needed to be addressed. The primary aim was to establish processes to measure and maintain blood glucose of <180 mg/dl without increasing the frequency of hypoglycemia. The guidelines were targeted for patients with known DM who were undergoing elective surgery under general anesthesia. The threshold to treat hyperglycemia was set at 140 mg/dl in order to achieve the goal of maintaining perioperative glucose at <180 mg/dl. Intravenous boluses of insulin were discouraged as a means to correct hyperglycemia because of the limited duration of action. Rather, subcutaneous insulin utilizing the institutional correction scale was recommended. Another goal was to increase the frequency of HbA₁, monitoring in preparation for surgery [25]. A referral to the endocrinology staff for any patient with an HbA_{1c} value >8.0% was suggested, with elective surgery being delayed until glycemic control improved (Box 1).

After consensus was reached on the guidelines, they were disseminated to the surgical and the anesthesia staff via educational sessions [25]. A preliminary evaluation of the guidelines was conducted (n = 326 cases) and compared with a historical cohort (n = 254 cases) [25]. Preperioperative HbA_{1c} measurement improved from 47% of cases in the historical cohort to 80% (p < 0.01) after implementation of the guidelines. Additionally, preoperative glucose monitoring increased, and intraoperative glucose monitoring improved, while PACU data were unchanged (Figure 2). Insulin use increased throughout the perioperative phase ($p \le 0.04$) (Figure 3). Mean preoperative glucose was 141 mg/dl in the historical period vs 130 mg/dl after implementation of the guidelines (p < 0.01), and for postanesthesia care, the mean glucose value decreased from

Box 1. Guidelines for preperioperative and perioperative assessment and management of the adult patient with diabetes undergoing elective surgery under general anesthesia.

Preperioperative period

- Conduct preoperative medical examination
- Obtain HbA₁, level (if not performed within past 3 months)
- Perioperative period:
- Preoperative
 - Measure glucose level on arrival, then hourly
- Treat glucose ≥140 mg/dl with insulin
- Intraoperative
- Measure glucose hourly
- Treat glucose to ≥140 mg/dl with insulin
- PACU
 - Measure glucose level on arrival, then hourly
- Treat glucose to ≥140 mg/dl with insulin

HbA_{1c}: Hemoglobin A_{1c}; PACU: Postanesthesia care unit.

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Figure 2. Number of cases with glucose monitoring during the perioperative phase of surgery. Data represent changes occurring after development and implementation of care guidelines. Perioperative segments defined as outlined in **Figure 1**. PACU: Postanesthesia care unit; POC-BG: Point-of-care blood glucose.

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162 to 152 mg/dl (p = 0.01). There was no significant increase in hypoglycemic events. Thus, our preliminary analysis indicated that these institutional guidelines specifically developed for DM patients undergoing elective surgery could improve the frequency of their perioperative glucose monitoring, insulin administration and, potentially, glucose control [25]. Longer-term follow-up is underway, and the generalizability of this approach needs to be evaluated

• Improving postperioperative DM standards of care

An initiative was developed to reduce the frequency of clinical inertia previously identified with regard to the use of basal-bolus insulin therapy in postoperative inpatients [57]. Representatives from the endocrinology staff and the surgery staff met to review available published guidelines regarding recommended inpatient glucose target ranges and insulin therapy, and a care process model was developed (**Figure 4**). The care process model targeted those patients with known DM, emphasizing the need to obtain and monitor point-of-care blood glucose (POC-BG) levels. Use of basal-bolus insulin therapy was recommended for patients who were already on insulin as outpatients, and otherwise for patients who had at least 2 POC-BG levels >180 mg/dl within the first 24 h after their surgical procedure. The new care process model was introduced to surgery staff via grand rounds and reinforced through small group sessions. The initiative included a surgical nurse practitioner, who monitored all glucose levels and interventions using the electronic health record on a daily basis, contacted the surgical service to encourage the use of basal-bolus insulin therapy, and provided advice on how to calculate, order and adjust insulin doses [60].

An analysis was conducted shortly after implementation of the care process model that showed its positive impact on management of the hospitalized postoperative patient with DM [60]. Compared with the use of basal-bolus insulin during the historical period, the use of basalbolus insulin post-guidelines implementation rose with the increasing frequency of hyperglycemia (**Figure 5**). Mean glucose levels improved after implementation of the care process model compared with mean glucose levels during the historical period, while the frequency of hypoglycemia did not significantly change (**Figure 6**). These preliminary results demonstrated that it is





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possible to overcome clinical inertia in the management of postoperative patients with DM, with greater utilization of basal-bolus insulin therapy and improved glucose control. Institutional efforts continue to ensure delivery of effective inpatient DM care by all surgical services.

Insulin pump therapy in the patient with DM undergoing surgery

Professional societies promulgating guidelines for management of inpatient DM (see [13,44,45] for instance) make no distinction about management of hyperglycemia based on etiology of diabetes. For instance, patients with Type 1 or Type 2 DM are not held to different standards of care in terms of glucose targets. The only population that deserves special attention and a different approach to care relates to those patients receiving insulin pump therapy. In the USA, approximately 400,000 patients with DM are utilizing insulin pump therapy to optimize their glucose control [61]. Although these devices are intended for outpatient management of DM, healthcare practitioners may encounter this technology in clinical settings where they were not intended to be used, such as the inpatient setting and in patients about to undergo surgery. It is not known how many patients on insulin pump treatment are hospitalized or how many undergo a surgical procedure under general anesthesia.

No guidelines exist on the use of insulin pumps in these different scenarios, and specialty organizations are mostly silent or lack specifics on the topic of insulin pump therapy in the hospital or during the perioperative phase of care when discussing DM management [11–13,44,45].

A previous analysis demonstrated that, for patients on insulin pump therapy who underwent elective surgery, there was inconsistent perioperative documentation regarding the status of the device, coupled with a low frequency of intraoperative glucose monitoring [34]. As with perioperative DM care in the surgical patient, a process has been developed to allow the patient on an insulin pump to continue treatment throughout all perioperative segments of care [62]. General requirements for glucose monitoring and glucose targets were identical to that developed for perioperative DM management (Box 1), except that documentation of the insulin pump was required during each segment of care. As the paitent is under general anesthesia, higher glucose levels could be corrected with boluses of subcutaneous short or rapid acting insulin. The standards were implemented, and the impact on care was evaluated [63]. Documentation and glucose monitoring subsequently improved. No adverse events were noted among patients allowed to stay on their insulin pumps during the perioperative period and safety was assured.

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Figure 4. Care process model for management of diabetes in the postoperative inpatient. The model was introduced to encourage use of basal-bolus insulin therapy. [†]Before each meal and at bedtime or every 6 h, if fasting. [‡]Fasting glucose of <140 mg/dl or random glucose of <180 mg/dl. POC-BG: Point-of-care blood glucose.

Preliminary data indicated that DM patients on insulin pump therapy did not necessarily have to disconnect from their devices during the surgical procedure.

Previous data also have indicated that patients using insulin pump devices who were hospitalized, including postoperative patients, did not have to discontinue that treatment. Published data demonstrate that enacting specific guidelines allows a safe and successful transition of insulin pump treatment from the outpatient setting to the inpatient setting [64]. Institutions should have guidelines in place to establish whether a patient on an insulin pump can continue that treatment as an inpatient.

Perioperative & inpatient glucosemonitoring controversies

Regarding the method of intraoperative monitoring, there are various modalities available to measure glucose, including venous sampling, arterial sampling and POC-BG. It is well established that commercial glucose meters currently used in hospitals are less accurate than laboratory-based analyses [65,66]. Sampling source (arterial, venous or capillary) can also lead to variability in results [67,68]. Studies have demonstrated variability in glucose levels measured by POC-BG vs other modalities secondary to differing levels of oxygenation [69-72]. However, the majority of patients undergoing elective surgery do not sustain clinically significant hemodynamic compromise. Those at risk of such events will likely have arterial blood pressure monitoring established at the time of surgery, giving the anesthesiologist adequate access to arterial blood glucose monitoring. Despite its limitations, POC-BG technology remains the most convenient method for obtaining rapid data on glucose levels.

Hypoglycemia considerations

Studies in the critical care setting have suggested that intensive management of hyperglycemia can lead to a greater frequency of hypoglycemia and higher mortality [9,73]. Similar types of randomized control trials have not been undertaken in the non-critically ill patient, so



Figure 5. Changes in insulin regimen. Insulin therapies are according to tertiles of the percentage of point-of-care glucose measurements >180 mg/dl for hospitalized postoperative patients during a control period (left panel) and following implementation of a care process model (intervention period, right panel) that was designed to improve management of hospitalized postoperative patients with diabetes mellitus. The number on top of each bar indicates the number of cases in that tertile. Adapted from [60], with permission from the American Association of Clinical Endocrinologists.

the risk of glycemic control measures on hypoglycemia risk and its associated mortality have not been established in the non-critical care setting. Nonetheless, concerns over hypoglycemia remain in the non-critically ill surgical patient population with DM, and the appropriate balance must be struck in efforts to achieve desired glucose target ranges and the risk of hypoglycemia. As illustrated by the studies above, and has been shown by others, it is possible to



Figure 6. Glucose control. Differences in mean POC-BG, frequency of hyperglycemia (POC-BG >180 mg/dl) and frequency of hypoglycemia (POC-BG <70 mg/dl) during a control period and following implementation of a care process model (intervention period) that was designed to improve management of hospitalized postoperative patients with diabetes mellitus. BedGluc_{avg}: Mean POC-BG for the patient stay; POC-BG: Point-of-care blood glucose. Adapted from [60], with permission from the American Association of Clinical Endocrinologists. intensify hyperglycemia management in the surgical patient with DM without increasing the frequency of hypoglycemia [25,60,74].

Conclusion

Hyperglycemia in the surgical patient can exist outside of the context of diabetes (e.g., due to stress or use of certain medications such as glucocorticoids). Additionally, there are other factors that might need to be considered when evaluating the patient with diabetes for surgery, such as assessing cardiovascular risk. However, most hyperglycemia that surgical practitioners will encounter will be in the context of the patient with known DM, and this review has centered primarily on discussion of hyperglycemia management within the framework of these patients.

Overall, DM continues to increase in prevalence and will likely be encountered more frequently in both inpatient and outpatient surgical populations. The pathophysiology behind perioperative hyperglycemia is complex but appears to result in deleterious outcomes when hyperglycemia is not well controlled. Thus, it is imperative to establish appropriate treatment of these patients throughout the continuum of surgical care, especially in the setting of elective surgery, which allows for adequate time for planning and glucose control. Patients should be counseled about the unique risks DM imposes on surgical outcomes. It is essential for surgical staff and anesthesia staff to be aware of any special circumstances surrounding these patients (e.g., insulin use, use of an insulin pump). Institutions should assess their management of these patients as part of overall DM quality improvement efforts. Local standards can be developed and successfully implemented that can ultimately enhance care and ensure patient safety.

Future perspective

There are multiple areas about the care of the surgical patient with DM that require additional work or formal study. For instance, representatives from various surgical, anesthesiology and endocrinology professional organizations should convene to discuss and develop consensus standards on the care of the patient with DM who is to undergo surgery. These standards should include such elements as desired glucose targets, frequency of perioperative glucose monitoring, acceptable methods for glucose monitoring, insulin treatment algorithms, and use of insulin pumps. Further work needs to be done to establish whether controlling hyperglycemia during the preperioperative period translates to better perioperative and postperioperative glucose control, and to determine whether such optimization reduces postsurgical complications and reduces length of hospital stay. Additionally, the optimal degree of preperioperative glucose control must still be defined. Different educational models should be tested to determine which is most effective to encourage and train surgical and anesthesiology specialists to take on management of a nonsurgical problem such as DM - a diagnosis which is outside their usual scope of care. Continued work in this field should be encouraged and supported.

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