



Perioperative management of diabetes

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Abstract: Diabetes is a highly prevalent, with serious peri-operative implications. Those with uncontrolled diabetes either preoperatively or postoperatively experience worse outcomes including increased morbidity and mortality. In this review, we aim to explore the appropriate glycemic targets both pre- and postoperatively based on available data. Management recommendations are provided for patients who were on insulin (including those on an insulin pump), on oral agents, and/or non-insulin injectables prior to surgery. Insulin remains the mainstay for management of hyperglycemia in the inpatient setting and recommendations are provided on dosing both for those previously on insulin and those newly initiated on it. Continued research into the best strategies for perioperative diabetes management is needed as many of our current recommendations are still based on empiric practices. However, in general, the data support optimizing glycemic management in the preoperative period to an HbA1c of <8.5% and in the postoperative period to between 140–180 mg/dL for optimal outcomes. Immediately preoperatively, patients should be advised to hold oral hypoglycemic and non-insulin injectables while both basal insulin should be reduced and bolus insulin held the day of surgery while patients are not permitted enteric intake.

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Introduction

Diabetes is a highly prevalent problem affecting 425 million individuals over the age of 18 years globally with incidence projected to increase by 48% by the year 2045 by the International Diabetes Federation (1). Therefore a large proportion of individuals undergoing surgery will have diabetes as a comorbidity, creating challenges for management in the perioperative period. Furthermore, with surgery, there is the added layer of stress-related hyperglycemia which leads to increased glucose production and transient worsening of insulin resistance (2). There are robust data supporting that perioperative hyperglycemia, both pre- and post-surgery, are associated with increased morbidity and mortality. In addition, the management of hyperglycemia in the surgical population has been

associated with improved outcomes.

Glycemic targets for perioperative risk reduction

Preoperative targets

Much of the data on preoperative targets are observational and drawn from the cardiothoracic field. These studies have demonstrated that at hemoglobin A1c (HbA1c) >6.5% and >7% preoperatively, there is a great incidence of morbidity (i.e., complications of surgery, infections, ICU and hospital stay) in addition to increased 5-year mortality (3,4). In a study on patients undergoing coronary artery bypass grafting (CABG), HbA1c >8.6% prior to surgery had a four-fold greater risk of death and morbidity (i.e., myocardial infarction, cerebrovascular events, sternal wound infection) (5). These

data show that, in the post-cardiac surgery cohort, there is a linear relationship between preoperative HbA1c and increased morbidity, starting at relatively lower HbA1c levels of >7%.

In the non-cardiac surgery population, Underwood *et al.* matched 449 patients with diabetes undergoing general and vascular procedures to nondiabetic control subjects and showed that an HbA1c >8% was associated with a longer hospital stay (6). In studies of patients with diabetes undergoing joint replacement and spinal arthrodesis, an HbA1c \geq 7% or hyperglycemia \geq 126 mg/dL were associated with higher risk of surgical site infection (7-9).

Based on the data from patients undergoing cardiac and non-cardiac surgeries, a number of guidelines have suggested that an HbA1c >8.5–9% preoperatively may necessitate delay of non-urgent elective surgeries due to concern for increased risk of mortality (10,11) and that any HbA1c >7% should be targeted for improved glycemic control to optimize preoperative risk. The Chinese Medical Association Anesthesiology Branch recommendations similarly suggest that clinicians should consider delaying surgery if the HbA1c >8.5% (12). These guidelines further emphasize the need to have a current (within 3 month) HbA1c for more appropriate risk stratification of the preoperative patient. However, we must emphasize at this point that there have been no prospective randomized studies looking at whether reducing HbA1c to “optimal” levels truly results in reduced postoperative morbidity and mortality. This remains an area for further research.

Postoperative targets

In contrast to the studies supporting preoperative targets, there are randomized clinical trials (RCTs) demonstrating that improved glycemic control postoperatively leads to improved outcomes, particularly in the intensive care setting.

Over the last two decades, many RCTs have examined outcomes of patients in intensive care unit (ICU) who have received intensive versus conventional insulin therapy. van den Berghe *et al.* demonstrated in a largely post-cardiac surgical ICU population that intensive glycemic control targeting between 80–110 mg/dL compared with a conventional target of 180–200 mg/dL resulted in less morbidity and a 34% reduction in hospital mortality, greatest in those with multi-organ failure related to sepsis (13). These results were brought into question by the GLUCO-CABG and NICE-SUGAR trials. The NICE-SUGAR trial of both medical and surgical patients not only failed to demonstrate a

benefit of intensive blood glucose control (81–108 mg/dL) but actually showed increased 90-day mortality associated with increased hypoglycemia incidence in the intensive control cohort (14). However, these data are not to suggest that conventional therapy is without problems as a post-hoc analysis did reveal a significant number of hypoglycemic events and death in both arms (15). In the GLUCO-CABG trial of post-CABG patients, intensive control targeting blood glucose 100–140 mg/dL (versus a target of 141–180 mg/dL) showed no difference in the rate of mortality or morbidity (16).

Though there were differences in target glucose range, nutrition, and study population demographics amongst the different trials noted, there has been enough concern raised for hypoglycemia that endocrine and anesthesia society recommendations have aimed for more moderate glycemic control. The newest guidelines from the American Diabetes Association (ADA) have recommended that in the ICU setting, the target glucose level for patients should be between 140–180 mg/dL (17). The Chinese Medical Association Anesthesiology Branch, French-Speaking Society of Diabetes and the Joint British Diabetes Societies have all recommended similar targets of <180 mg/dL in the postoperative, hospitalized setting (11,12,18).

Outside of the ICU setting, most of the data on postoperative glycemic control and post-surgical outcomes is from retrospective studies. The Portland Diabetic Project demonstrated that after CABG, blood glucose levels >200 mg/dL were associated with increased infection and mortality and that targeting a glucose <150 mg/dL with a continuous intravenous insulin infusion improved, both mortality and infection rates (19). Data from the Surgical Care and Outcomes Assessment Program in Washington State similarly after non-cardiac procedures that glucose >180 mg/dL is associated with morbidity (i.e., infection, reoperation) and death (odds ratio 2.71) (20). Similarly, other retrospective studies have shown that after cardiac and non-cardiac surgeries, mortality and morbidity (infection, renal failure, myocardial infarction, etc.) is increased when there is hyperglycemia >200 mg/dL (5,21,22). These data support that glucose above 180–200 mg/dL tends to be associated with worse outcomes in the non-ICU post-surgical cohort. Hence, the ADA has recommended a glucose target between 140–180 mg/dL for the non-critically ill. For those in whom the risk of hypoglycemia is relatively low, lower targets of 110–140 mg/dL can be applied (17). The Chinese guidelines have gone further in suggesting that those with long-standing uncontrolled

Table 1 Preoperative and postoperative glyceimic targets

	Glyceimic targets
Pre-operative	HbA1c >7%: target for improved glyceimic control HbA1c >8.5%: consider delay of non-urgent elective surgery
Post-operative	ICU: 140–180 mg/dL Non-ICU: 140–180 mg/dL Non-ICU & low hypoglycemia risk: 110–140 mg/dL Non-ICU & uncontrolled pre-operative diabetes (HbA1c >8.5%): Fasting \leq 180 mg/dL Random \leq 216 mg/dL

ICU, intensive care unit.

hyperglycemia prior to admission should have a fasting glucose target of \leq 180 mg/dL and a random glucose target of \leq 216 mg/dL (12). The aim would be to avoid reducing perioperative blood glucose too quickly and causing harm.

Overall considerations

When patients in the preoperative period have HbA1c >8.5–9% or in the postoperative period have glucose >180–200 mg/dL, special attention should be paid to improving glyceimic control in an effort to reduce mortality and morbidity postoperatively. Our recommendations for glyceimic targets are summarized in *Table 1*. However, the robust data from the ICU also provide a warning about the significant harm that can come with hypoglycemic events seen with intensive glucose control so a balance must be maintained in the postoperative period.

Pharmacologic therapy

Non-insulin diabetes medications

Many diabetes medications can be continued until the day before or the day of the surgery. However, there is lack of agreement concerning how best to manage these medications in the preoperative and postoperative period with different guidelines presented by various groups and countries. For an overview of the recommendations which are noted below, please reference *Table 2*.

- ❖ Metformin: there is in theory concern for lactic acidosis associated with the medication in those with renal, hepatic or cardiac dysfunction or in those who are receiving iodinated contrast (23,24). However,

this is rarely seen and the data do not support system-wide increases in morbidity or mortality associated with use of the agent (25). In general, for elective outpatient surgeries in individuals with intact renal function the medication can be continued even the day of surgery. In those with risk factors for lactic acidosis perioperatively or undergoing major surgeries, metformin should be held at the minimum the day before and day of the surgery (11,18,26,27). If there is any renal impairment postoperatively, it should be held until the patient returns to a baseline renal function.

- ❖ Sulfonylurea (SFU): these should be held the morning of the surgery due to the risk of hypoglycemia in the fasted state. The metabolites from certain sulfonylureas are known to be active and able to cause hypoglycemia and their clearance can be unpredictable, further exacerbating the risk of prolonged hypoglycemia (28,29). This is in contrast to insulin which can similarly cause hypoglycemia but has a predictable course of action. There is additional risk beyond hypoglycemia with this particular class of medications. These work on not only the ATP dependent potassium channels of the beta cells of the pancreas leading to insulin release, but also have been shown to be able to impact potassium channels on cardiac myocytes. The ultimate consequence of this is that there is a blockage of ischemic preconditioning (30,31). This some guidelines recommend holding the medication for up to 24 hours prior to surgery (i.e., holding the day before as well). There is no clear role for the use of these medications as primary therapy

Table 2 Recommendations for the management of oral anti-diabetic agents pre- and postoperatively

Medication (Category)	Before surgery	After surgery
Metformin	Outpatient, Elective: Continue	Hold while NPO
	Inpatient, Major Surgery, Risk for Lactic Acidosis: Hold day before & day of surgery	Hold until return to baseline renal function
Sulfonylurea	Hold day before and day of surgery	Hold while NPO
Meglitinides	Hold day before and day of surgery	Hold while NPO
Amylin analogues	Hold day of surgery	Hold while NPO
Thiazolidinediones	Outpatient, Elective: Continue	Hold until patient stable
	Inpatient, Major: Hold day of surgery	
Alpha-glucosidase inhibitors	Hold day of surgery	Hold while NPO
DPP IV Inhibitors	Hold day of surgery	Hold while NPO
		[Data exists supporting use in the hospital setting]
GLP-1 analogues	Hold if normally taken day of surgery	Hold while NPO vs. Hold while inpatient
SGLT-2 inhibitors	Hold day before and day of surgery vs. Hold 3 days prior to surgery	Hold while NPO vs. Hold while inpatient
	[Consider if prolonged NPO status postoperatively (>24 hours)]	
Bromocriptine	Hold day before and day of surgery	Hold while NPO
Colesevelam	Hold day before and day of surgery	Hold while NPO

NPO, nothing by mouth.

in the hospital. Providers could consider resumption when there is a return to oral intake.

- ❖ Meglitinides: similar to the SFU class, these should be held at a minimum while the patient is in the fasted state due to the risk for hypoglycemia. Importantly, they have a similar effect at the level of the potassium channels to SFU. Hence, some guidelines have also recommended holding this the day prior to the surgery as well (26). Providers can consider resuming postoperatively when there is a return to oral intake.
- ❖ Amylin analogues: the only available agent in this class is pramlintide, an injectable agent utilized prior to meals. It should be held while the patient is fasted as its mechanism of action affects postprandial hyperglycemia. Like other agents, it can have significant gastrointestinal side effects and also carries the risk for significant hypoglycemia when used with insulin in the T1DM population (32). It can be resumed when the patient is consistently

tolerating oral intake.

- ❖ Thiazolidinediones: these are typically stopped the morning of surgery as they can lead to the undesirable side effect of fluid retention but can be continued in those undergoing elective outpatient surgical procedures. Postoperatively can be resumed when the patient is stable (11,18).
- ❖ Alpha-glucosidase inhibitors: this class of medications has no role for a patient in the fasted state as they function by blocking the enteric absorption of carbohydrates. They also have undesirable gastrointestinal side effects that can be exacerbated in the postsurgical state (11,18). Can consider resumption when patient stable.
- ❖ DPP IV inhibitors: this class of medications target postprandial hyperglycemia and have little role in the fasted state. However, here there is good data supporting their efficacy and safety in reducing hyperglycemia, particularly when combined with basal insulin, in the hospital setting (11,18). When a

patient is tolerating oral intake postoperatively, this can be resumed.

- ❖ GLP-1 analogues: similar to DPP-IV inhibitors, this class of medications is targeted toward reducing postprandial hyperglycemia, with some effect on overnight/fasting glucose levels. They should be held the day of surgery if dosed daily as they may result in significant nausea, affecting nutrition in the postoperative period. For the weekly versions, the medication can be taken as normal unless typically taken the day of the surgery. In that situation, the dose should be delayed until the postoperative period when oral intake is resumed or held altogether. These medications have the potential for significant gastrointestinal side effects which can be exacerbated in the postsurgical state (11,18).
- ❖ SGLT-2 inhibitors: the Food and Drug Administration first released a safety statement noting the risk for euglycemic DKA with this class in 2015 (33). The complication of euglycemic DKA has led to a majority of societies recommend that this medication should be held at minimum the morning of the surgery. However, holding SGLT-2 inhibitors even up to 48 hours prior to surgery has still been seen to result in euglycemic DKA and hence some providers are moving towards holding the medication for up to 3 days prior to surgery (34). Other have recommended a more nuanced approach based on the patient characteristics and type of surgery with special consideration to how long the patient will be without caloric intake postoperatively, as dramatic reductions in dietary intake appear to be an important trigger for euglycemic DKA (35). Overall, this class of medications is not recommended for use in the hospital at this time, although there may be certain circumstances where use is acceptable (17,36).
- ❖ Bromocriptine: given the relative infrequency of its use, fewer society recommendations exist concerning the management of this medication in the perioperative period. The medication works via insulin sensitization and is typically taken with food given the potential for gastrointestinal side effects. It has a half-life of around 6 hours and should be held 24 hours prior to surgery and while the patient is fasted (37).
- ❖ Colesevelam: similar to bromocriptine, this medication is infrequently utilized and few society recommendations exist for its perioperative

management. This is a bile acid sequestrant which has been demonstrated to improve glycemic control. It is known to have the potential for significant gastrointestinal side effects and should be held 24 hours prior to surgery and while the patient is fasted (38).

When patients are nearing time of discharge from hospital postoperatively (about 1–2 days out), reintroduction of previously used oral agents should be attempted unless the patient had developed a contraindication to use of one or more of the agents, bearing in mind whether the particular hospital has a policy of whether oral agents can be given or not, or if the agents are available in the hospital formulary (11,18,23,26). This is to provide additional information to providers concerning the likelihood of reasonable glycemic control in the outpatient setting. If there is evidence on admission that there was poor preoperative control (i.e., HbA1c within 3 months >7%) then there should be further adjustments of medications prior to discharge (39).

Insulin management

In the hospital setting, insulin therapy remains the mainstay of management. Concerning the perioperative period, there will be two different populations of patients with diabetes, those who were previously on insulin and those who were not. For clarity, *Table 3* contains an overview of the various insulin types and their onset and duration of action divided into categories of basal and bolus for reference for the following discussions (40,41). For the purposes of our discussion, basal insulin is insulin the patient requires in the fasted state. Bolus insulin references short-acting prandial (i.e., mealtime coverage) and/or correctional insulin (i.e., insulin designed to lower blood glucose to target).

Previously on insulin

In the preoperative period, insulin should not be withheld for patients already on insulin. However, dose adjustments may need to be made (*Table 4*).

During the preoperative visit, some important pieces of information should be elucidated. Firstly, the specific insulin types, their doses and the typical times of administration. Attention should be given to whether the regimen represents roughly a 50%/50% division between basal and prandial. Secondly, the provider should have a sense of how well the diabetes regimen controls hyperglycemia while preventing hypoglycemia, particularly with an attention towards hypoglycemic events and when they occur. Overnight hypoglycemic events are suggestive

Table 3 Onset and duration of action of commonly used basal, bolus and premixed insulin

Insulin type	Specific agent	Time of onset	Duration of action, hours
Basal			
Long-acting	Glargine (Lantus)	2 hours	22–24
	Detemir (Levemir)	2 hours	22–24
Intermediate-acting	Neutral Protamine Hagedorn (NPH)	1–2 hours	12–16
Bolus			
Fast-acting	Lispro (Humalog)	15 minutes	3–4
	Aspart (Novolog)	15 minutes	3–4
	Glulisine (Apidra)	10–15 minutes	2–4
Short-acting	Regular (Novolin R, Humulin R)	30–60 minutes	6–8
Pre-Mixed	70/30 NPH/Regular	30–60 minutes	12–16
	75/25 NPH/Lispro	30–60 minutes	12–16

Table 4 Recommendation for the management of insulin preoperatively and postoperatively for patients already on insulin preoperatively

Medication	Before surgery	After surgery
Basal Insulin	Long-Acting: 20–25% reduction in dose night before or morning of surgery	Continue reduced dose while NPO
	Intermediate-Acting	
	NPH: half normal dose Premixed: all daily doses and provide half as long-acting basal insulin vs. Provide all as premixed insulin	
Prandial Insulin	Reduce coverage for the last meal day before surgery if evidence of over-coverage	Hold until there is reliable prandial intake
	Hold day of surgery	

NPO, nothing by mouth.

of supraphysiologic basal coverage, which would then necessitate a reduction in the basal prior to surgery. If there is confidence that the basal truly represents an accurate coverage of hepatic glucose output in the fasted state, the full dose can be provided. However, in reality, a 20–25% reduction of the basal dose is typically appropriate for long-acting basal insulins for the evening or morning dose, depending on normal dosing patterns for the patient. For intermediate-acting neutral protamine Hagedorn (NPH), a half normal dose can be given the morning of surgery. For premixed insulins, there are 2 options. The first is to add the doses of the premixed insulin in a day and provide half as long-acting basal insulin the morning of surgery. Alternatively, half of the total daily dose can be provided as the premixed insulin morning of surgery especially if

there are financial or logistical concerns about switching to a different insulin for just one dose. However, special attention should be paid to the fact that the premixed insulins have a faster-acting component that might predispose to hypoglycemia more than the intermediate-acting component.

Regarding prandial insulin, provision should be as normal until the fasted state. Reductions of prandial insulin the day prior to surgery, particularly for the last meal prior to the fasted state, can be considered if there is evidence of over-coverage for prandial intake (11,18,40,42).

After surgery, basal insulin at the reduced doses noted should be continued until there is a resumption of oral intake. Similarly, prandial insulin should be held until there is consistent intake. Until there is reliable prandial intake,

Table 5 Recommendation for the management of insulin postoperatively for patients not on insulin preoperatively

Medication	After surgery
Basal insulin	Long-acting
	If blood glucose 140–200 mg/dL: 0.25 units/kg/day
	If blood glucose >200 mg/dL: 0.20 units/kg/day
	If renal dysfunction or age >70 years: consider 0.1 units/kg/day
Prandial insulin	Hold until there is reliable prandial intake
	Correctional sliding scale insulin using the Rule of 1800 (See text)

correctional insulin sliding scale coverage alone can be considered (40,42,43).

To calculate the insulin sensitivity (i.e., expected glycemic improvement with 1 unit of insulin) for correctional sliding scale coverage, a couple of methods may be applied. The “1800 Rule” states that for those already on insulin, 1,800/(total daily dose of insulin) should provide the insulin sensitivity. For those not already on insulin or in whom the total daily dose is not known, a sensitivity of around 40 is typically reasonable (23). These sensitivities should be further adjusted to account for the potential for hypoglycemia and also evidence for significant insulin resistance (44).

Insulin-Naïve

Even if a patient has not previously been on insulin therapy, insulin is the therapy of choice in the hospital in patients who have tenuous food intake. There have been a number of RCTs assessing insulin regimens for patients with diabetes in the hospital. The RABBIT 2 Surgery trial demonstrated that the use of a regimen containing basal and bolus insulin in the post-surgical population with diabetes results in superior glycemic control and reduced postoperative complications compared with a regimen of only correctional insulin. In the trial, the dose of the basal was weight-based at 0.2 units/kg/day if blood glucoses ranged between 140–200 mg/dL and 0.25 units/kg/day if the blood glucoses were consistently >200 mg/d (45). For those who are older (>70 years) and/or with renal dysfunction, a lower weight-based dose can be utilized with some recommendations calling for the halving of the dose that would be otherwise used (26). Please see *Table 5* for additional details.

Postoperatively in intensive care unit

There is a large amount of data which supports the use of IV insulin infusions using computerized nomograms in the

ICU setting (19,23). When transitioning to subcutaneous insulin postoperatively, it is important to perform a proper transition. For those on basal insulin at home, this is not relevant as they will have already received long-acting insulin prior to the surgery. However, for those not on insulin previously, insulin infusions should be continued 2 hours after the provision of the long-acting basal insulin. Dosing recommendations for the basal insulin are as previously noted (46).

Intra-operative glycemic management

The “bridge” between preoperative and postoperative periods, though brief in comparison to the other two periods, is riddled with variability. This probably results from the uncertainty as to which patients will benefit from intraoperative glucose control and the lack of resources to implement intravenous insulin infusion and frequent glucose monitoring.

Studies on intraoperative glucose control show reduction in adverse outcomes such as infections or prolonged ventilation when intraoperative blood glucose is targeted with insulin therapy (47,48). To mitigate hypoglycemia and to provide metabolic substrate, the infusion of glucose together with IVII has been studied in myocardial infarction, and is also being investigated for surgical procedures. In cardiothoracic surgery patients, infusion of insulin and glucose intravenously with targets of 80–110 mg/dL resulted in a 0.62 relative risk (95% CI: 0.39–0.97) of at least one of the following outcomes: 30-day mortality, mechanical circulatory support, infection, renal or neurologic morbidity compared to IVII targeting blood glucose 70–150 mg/dL (49).

With these benefits in mind, guidelines by different societies recommend checking blood glucose hourly and targeting blood glucose as follows: French Society of Anaesthesia

and Intensive Care Medicine—80 to 180 mg/dL (50), Association of Anesthetists in Great Britain and Ireland—108 to 180 mg/dL (51), Chinese Medical Association Anesthesia Branch—140–180 mg/dL (11). However, guideline adherence and clinical practices vary. National adherence on intraoperative blood glucose monitoring was found to be suboptimal in one study, with only 56% of patients receiving hourly checks in one study (52). Hypoglycemia may be a reason for anesthesiologists to demur from implementing glucose lowering measures in the operating room although actual rates of severe hypoglycemia are typically <1% (49,53).

With the above data in mind, intraoperative glucose control should be afforded the same importance as the periods before and after and additional attention is needed to this critical time period.

Special consideration: insulin pumps perioperatively

Insulin pumps [continuous subcutaneous insulin infusions (CSII)] represent an area with special considerations in the perioperative period. As a general rule, when insulin pumps are used, the patient must be able to appropriately self-manage the pump, although there are select situations in which a pump may be allowed while a patient is sedated intraoperatively which will be covered in this section. There are few data which look specifically at the use of insulin pumps in the perioperative period. Preoperatively when the patient is being assessed, there should be a careful history obtained of the details of the pump: type of insulin utilized, its duration of action, basal and bolus settings (i.e., carbohydrate ratio, insulin sensitivity factor), and glucose targets. A sense of the patient's ability with the pump should also be assessed, particularly their ability to change settings and also perform maneuvers such as temporary basal rates. In order to assess the accuracy of the basal rates, providers could consider the use of a "basal test" several days prior to the surgery by requesting that the patient remain in a fasted state and check blood glucose every 3 hours starting at midnight until the expected time of the surgery. The key is to look for excursions towards hypo- or hyperglycemia and also variation in the basal rate between measurements >30 mg/dL. Basal settings can be adjusted and retested then prior to the operation. Alternatively, since many patients have supra-physiologic basal rates which are partially covering their prandial intake through the day, an empiric 20% reduction in the basal rate has been suggested during the fasted time period.

Most patients undergoing surgery will have their pump

removed as there are a number of conditions in which wearing a pump intraoperatively is not appropriate. These include procedures involving external imaging beyond ultrasound (i.e., X-ray, CT, MRI), major or emergency/urgent surgery, longer surgeries (>2 to 4-hour duration) and an expectation postoperatively of multiple missed meals leading to a prolonged fasted state. In this situation, they should receive glargine or detemir given at 80% of the total daily basal dose the morning of the surgery and pump discontinued 2 hours later. An alternative method and the likely one in an emergent or urgent setting is that IV insulin should be initiated at the predetermined basal rate from the pump then shut off a half hour later. During the operation itself and postoperatively, each institution should have a nomogram in place for titration of the insulin rate. For shorter operations lasting less than 3–4 hours in a T1DM, subcutaneous bolus insulin (e.g., lispro or aspart) can be provided to cover approximately 1–2 hours of the missing basal rate and the pump immediately reapplied postoperatively. This is not preferred due to the risk of hypoglycemia in the fasted state with bolus insulin. For T2DM patients in shorter procedures, the pump can simply be suspended (54-56).

If a patient is wearing a pump into the operating suite (more reasonable consideration for short outpatient elective surgery), then the site could be changed the afternoon before or the morning of to ensure proper functionality with a couple of glucose checks prior to the surgery. The site of the pump insertion should be removed from the site of the surgery and accessible to the anesthesia team throughout the operation. The reduction in basal rate should apply and frequent glucose monitoring (i.e., hourly) intraoperatively and postoperatively until a diet is re-established should take place, at which point a return to prior settings can take place (54-56).

When the patient's pump is removed or if it is subsequently determined by the medical team or patient preference that it should be removed postoperatively (generally due to patient alteration in mentation), a plan should be in place to instate multiple subcutaneous doses of insulin or basal-bolus regimen. If the patient is on IV insulin, there should be a half hour overlap with subcutaneous fast-acting insulin and a two-hour overlap with subcutaneous basal insulin. When the pump is reinstated (typically when the patient is alert and tolerating oral intake) and if basal insulin was given for coverage, the basal rate should be suspended until 1–2 hours prior to the when the next basal subcutaneous dose is due (54-56).

Conclusions

The goal of perioperative management of diabetes is to reduce morbidity and mortality. In order to achieve this, focus is placed on reducing both hyperglycemia and hypoglycemia through various pharmacologic therapies. Despite the lack of consensus and robust studies, a number of recommendations for perioperative diabetic management can be made and have been reviewed here. Further research is required to confirm a number of our empiric practices.

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References

1. International Diabetes Federation. IDF Diabetes Atlas, 8th ed. Brussels, Belgium: International Diabetes Federation; 2017. Available online: <http://www.diabetesatlas.org>.

2. Palermo NE, Gianchandani RY, McDonnell ME, et al. Stress Hyperglycemia During Surgery and Anesthesia: Pathogenesis and Clinical Implications. *Curr Diab Rep* 2016;16:33.
3. Sato H, Carvalho G, Sato T, et al. The Association of Preoperative Glycemic Control, Intraoperative Insulin Sensitivity, and Outcomes after Cardiac Surgery. *J Clin Endocrinol Metab* 2010;95:4338-44.
4. Halkos ME, Lattouf OM, Puskas JD, et al. Elevated Preoperative Hemoglobin A1c Level is Associated With Reduced Long-Term Survival After Coronary Artery Bypass Surgery. *Ann Thorac Surg* 2008;86:1431-7.
5. Halkos ME, Puskas JD, Lattouf OM, et al. Elevated preoperative hemoglobin A1c level is predictive of adverse events after coronary artery bypass surgery. *J Thorac Cardiovasc Surg* 2008;136:631-40.
6. Underwood P, Askari R, Hurwitz S, et al. Preoperative A1C and Clinical Outcomes in Patients With Diabetes Undergoing Major Noncardiac Surgical Procedures. *Diabetes Care* 2014;37:611-6.
7. Hikata T, Iwanami A, Hosogane N, et al. High preoperative hemoglobin A1c is a risk factor for surgical site infection after posterior thoracic and lumbar spinal instrumentation surgery. *J Orthop Sci* 2014;19:223-8.
8. Jämsen E, Nevalainen P, Kalliovalkama J, et al. Preoperative hyperglycemia predicts infected total knee replacement. *Eur J Intern Med* 2010;21:196-201.
9. Cook KD, Borzok J, Sumrein F, et al. Evaluation and Perioperative Management of the Diabetic Patient. *Clin Podiatr Med Surg* 2019;36:83-102.
10. Cheisson G, Jacqueminet S, Cosson E, et al. Perioperative management of adult diabetic patient. Review of hyperglycaemia: definitions and pathophysiology. *Anaesth Crit Care Pain Med* 2018;37:55-8.
11. Joint British Diabetes Societies for inpatient care. Management of adults with diabetes undergoing surgery and elective procedures: Improving standards. 2016. Retrieved online: https://abcd.care/sites/abcd.care/files/resources/Surgical_guidelines_2015_full_FINAL_amended_Mar_2016.pdf.
12. Chinese Medical Association Anesthesia Branch. [Perioperative blood glucose management expert consensus (Abbreviated version)]. *J Clin Anesthesiol* 2016;32:93-5.
13. van den Berghe D, Wouters P, Weekers F, et al. Intensive Insulin Therapy in Critically Ill Patients. *N Engl J Med* 2001;345:1359-67.

14. NICE-SUGAR Study Investigators, Finfer S, Chittock DR, et al. Intensive versus Conventional Glucose Control in Critically Ill Patients. *N Engl J Med* 2009;360:1283-97.
15. NICE-SUGAR Study Investigators, Finfer S, Liu B, et al. Hypoglycemia and Risk of Death in Critically Ill Patients. *N Engl J Med* 2012;367:1108-18.
16. Umpierrez G, Cardona S, Pasquel F, et al. Randomized Controlled Trial of Intensive Versus Conservative Glucose Control in Patients Undergoing Coronary Artery Bypass Graft Surgery: GLUCO-CABG Trial. *Diabetes Care* 2015;38:1665-72.
17. American Diabetes Association. Diabetes Care in the Hospital: Standards of Medical Care in Diabetes—2019. *Diabetes Care* 2019;42:S173-81.
18. Cosson E, Catargi B, Cheisson G, et al. Practical management of diabetes patients before, during and after surgery: A joint French diabetology and anaesthesiology position statement. *Diabetes Metab* 2018;44:200-16.
19. Furnary AP, Wu Y, Bookin SO. Effect of hyperglycemia and continuous intravenous insulin infusions on outcomes of cardiac surgical procedures: the Portland Diabetic Project. *Endocr Pract* 2004;10:21-33.
20. Kwon S, Thompson R, Dellinger P, et al. Importance of Perioperative Glycemic Control in General Surgery. *Ann Surg* 2013;257:8-14.
21. Frisch A, Chandra P, Smiley D, et al. Prevalence and clinical outcome of hyperglycemia in the perioperative period in noncardiac surgery. *Diabetes Care* 2010;33:1783-8.
22. van den Boom W, Schroeder RA, Manning MW, et al. Effect of A1C and Glucose on Postoperative Mortality in Noncardiac and Cardiac Surgeries. *Diabetes Care* 2018;41:782-8.
23. Duggan EW, Carlson K, Umpierrez GE. Perioperative Hyperglycemia Management: An Update. *Anesthesiology* 2017;126:547-60.
24. Mercker SK, Maier C, Neumann G, et al. Lactic acidosis as a serious perioperative complication of antidiabetic biguanide medication with metformin. *Anesthesiology* 1997;87:1003-5.
25. Duncan AI, Koch CG, Xu M, et al. Recent metformin ingestion does not increase in-hospital morbidity or mortality after cardiac surgery. *Anesth Analg* 2007;104:42-50.
26. Duncan AE. Hyperglycemia and Perioperative Glucose Management. *Curr Pharm Des* 2012;18:6195-203.
27. Meneghini LF. Perioperative management of diabetes: Translating evidence into practice. *Cleve Clin J Med* 2009;76:S53-9.
28. Douros A, Yin H, Yu OHY, et al. Pharmacologic differences of sulfonylureas and the risk of adverse cardiovascular and hypoglycemic events. *Diabetes Care* 2017;40:1506-13.
29. Krentz AJ, Bailey CJ. Oral antidiabetic agents: current role in type 2 diabetes mellitus. *Drugs* 2005;65:385-411.
30. Garratt KN, Brady PA, Hassinger NL, et al. Sulfonylurea drugs increase early mortality in patients with diabetes mellitus after direct angioplasty for acute myocardial infarction. *J Am Coll Cardiol*. 1999;33(1):119-24.
31. Tomai F, Crea F, Gaspardone A, et al. Ischemic preconditioning during coronary angioplasty is prevented by glibenclamide, a selective ATP-sensitive K⁺ channel blocker. *Circulation* 1994;90:700-5.
32. Symlin (pramlintide) [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2014.
33. U.S. Food and Drug Administration. Drug Safety Communication: FDA warns that SGLT2 inhibitors for diabetes may result in a serious condition of too much acid in the blood. 15 May 2015. Available online: <http://www.fda.gov/downloads/Drugs/DrugSafety/UCM446954.pdf>.
34. Lau A, Bruce S, Wang E, et al. Perioperative implications of sodium-glucose cotransporter-2 inhibitors: a case series of euglycemic diabetic ketoacidosis in three patients after cardiac surgery. *Can J Anaesth* 2018;65:188-93.
35. Thiruvankatarajan V, Meyer EJ, Nanjappa N, et al. Perioperative diabetic ketoacidosis associated with sodium-glucose co-transporter-2 inhibitors: a systematic review. *Br J Anaesth* 2019;123:27-36.
36. Levine JA, Karam SL, Aleppo G. SGLT2-I in the Hospital Setting: Diabetic Ketoacidosis and Other Benefits and Concerns. *Curr Diab Rep* 2017;17:54.
37. Shivaprasad C, Kalra S. Bromocriptine in type 2 diabetes mellitus. *Indian J Endocrinol Metab* 2011;15:S17-24.
38. Handelsman Y. Role of Bile Acid Sequestrants in the Treatment of Type 2 Diabetes. *Diabetes Care* 2011;34:S244-50.
39. Umpierrez GE, Reyes D, Smiley D, et al. Hospital discharge algorithm based on admission HbA1c for the management of patients with type 2 diabetes. *Diabetes Care* 2014;37:2934-9.
40. Dobri GA, Lansang MC. How should we manage insulin therapy before surgery? *Cleve Clin J Med* 2013;80:702-4.
41. Sebranek JJ, Lugli AK, Coursin DB. Glycaemic control in the perioperative period. *Br J Anaesth* 2013;111:i18-34.
42. Joshi GP, Shung F, Rann MA, et al. Society for Ambulatory Anesthesia consensus statement on perioperative blood

- glucose management in diabetic patients undergoing ambulatory surgery. *Anesth Analg* 2010;111:1378-87.
43. Demma LJ, Carlson KT, Duggan EW, et al. Effect of basal insulin dosage on blood glucose concentration in ambulatory surgery patients with type 2 diabetes. *J Clin Anesth* 2017;36:184-8.
 44. Duggan EW, Klopman MA, Berry AJ, et al. The Emory University perioperative algorithm for the management of hyperglycemia and diabetes in non-cardiac surgery. *Curr Diab Rep* 2016;16:34.
 45. Umpierrez GE, Smiley D, Zisman A, et al. Randomized study of basal-bolus insulin therapy in the inpatient management of patients with type 2 diabetes (RABBIT 2 trial). *Diabetes Care* 2007;30:2181-6.
 46. Jacobi J, Bircher N, Krinsley J, Agus M, et al. Guidelines for the use of an insulin infusion for the management of hyperglycemia in critically ill patients. *Crit Care Med* 2012;40:3251-76.
 47. Ehrenfeld JM, Wanderer JP, Terekhov M, et al. A Perioperative Systems Design to Improve Intraoperative Glucose Monitoring Is Associated with a Reduction in Surgical Site Infections in a Diabetic Patient Population. *Anesthesiology* 2017;126:431-40.
 48. Kang R, Han S, Kee JW, et al. Portland Intensive Insulin Therapy During Living Donor Liver Transplantation: Association with Postreperfusion Hyperglycemia and Clinical Outcomes. *Sci Rep* 2018;8:16306.
 49. Duncan AE, Sessler DI, Sato H, et al. Hyperinsulinemic Normoglycemia during Cardiac Surgery Reduces a Composite of 30-day Mortality and Serious In-hospital Complications: A Randomized Clinical Trial. *Anesthesiology* 2018;128:1125-39.
 50. Cheisson G, Jacqueminet S, Cosson E. et al. Perioperative management of adult diabetic patients. Intraoperative period. *Anaesth Crit Care Pain Med* 2018;37:S21-5.
 51. Membership of the Working Party, Barker P, Creasey PE, et al. Peri-operative management of the surgical patient with diabetes 2015: Association of Anaesthetists of Great Britain and Ireland. *Anaesthesia* 2015;70:1427-40.
 52. Jackson MJ, Patvardhan C, Wallace F, et al. Perioperative management of diabetes in elective patients: a region-wide audit. *Br J Anaesth* 2016;116:501-6.
 53. Grunzweig K, Nair BG, Peterson GN, et al. Decisional practices and patterns of intraoperative glucose management in an academic medical center. *J Clin Anesth* 2016;32:214-23.
 54. Boyle ME, Seifert KM, Beer KA, et al. Guidelines for application of continuous subcutaneous insulin infusion (insulin pump) therapy in the perioperative period. *J Diabetes Sci Technol* 2012;6:184-90.
 55. Partridge H, Perkins B, Mathieu S, et al. Clinical recommendations in the management of the patient with type 1 diabetes on insulin pump therapy in the perioperative period: a primer for the anaesthetist. *Br J Anaesth*. 2016;116:18-26.
 56. Simha V, Shah P. Perioperative Glucose Control in Patients With Diabetes Undergoing Elective Surgery. *JAMA* 2019;324:399-400.

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