An Update on Perioperative Management of Diabetes

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Surgery in the patient with diabetes mellitus is relatively common, as the numbers of persons with diabetes is increasing and diabetes predisposes to medical conditions that require surgical intervention. An estimated 25% of diabetic patients will require surgery, and advances in perioperative care of these patients allow them to safely undergo the most complicated surgical procedures. We will review issues of preoperative, intraoperative, and postoperative care of diabetic patients.

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Today, advances in perioperative management have enabled diabetic patients to undergo complex surgery with increasing safety[1-4] such that more surgery is performed in an outpatient setting, and for those performed on an inpatient basis, the length of hospital stay is being shortened dramatically. This creates a logistical challenge to the perioperative treatment of the patient with diabetes mellitus. Many factors are involved in determining the glycemic response to a surgical procedure; although some may be adequately anticipated, others are very difficult to predict. Insulin secretory capability, insulin sensitivity, overall metabolism, and nutritional intake may change radically from the preoperative period through to the postoperative recuperation and may also differ greatly from one procedure to another. For this reason many physicians tend to be reactive as opposed to proactive in their management of hyperglycemia in surgical patients with diabetes. Nevertheless, marked hyperglycemia in the patient with diabetes should be prevented, as it may lead to dehydration and electrolyte abnormalities, impair wound healing, and predispose to infection or diabetic ketoacidosis in the patient with type 1 diabetes mellitus.[5,6]

PREOPERATIVE EVALUATION AND PREPARATION

The operative risk assessment of the patient with diabetes mellitus (**Table 1**) is generally similar to that of any other patient in whom it is important to diagnose, evaluate, and treat underlying cardiac, pulmonary, and renal disease; electrolyte abnormalities; and/or anemia before surgery. Additionally, this assessment should focus on the long-term complications of diabetes (microvascular, macrovascular, and neuropathic), which may potentiate risk. Particular attention should be given to assessment of cardiovascular and renal function, abnormalities of which may be undiagnosed. Since cardiovascular disease is inordinately common in patients with diabetes mellitus,[7,8] assessment of cardiac risk assumes a high priority in the preoperative examination of the patient with diabetes. In persons with diabetes and a history of myocardial infarction or unstable angina, the risk of postoperative cardiac complications may be decreased if coronary angiography and, if warranted, angioplasty or coronary bypass surgery are performed before other elective surgery.[9] Diabetic autonomic neuropathy may further complicate and prolong the postoperative recovery phase and has been associated with nonsurgical excess mortality.

The effects of antecedent metabolic control independent of the extent of the chronic complications of diabetes are not well established, and few recommendations can be made regarding the outcome of surgical patients with chronically poor diabetes control and/or those whose glucose levels have been rapidly normalized preoperatively. Although, in the past, near-optimal blood glucose control has been advocated in preparation for elective surgical procedures,[5] little evidence exists to

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Table 1. Preoperative Assessment of the Surgical Candidate With Diabetes Mellitus

Operative risk assessment
Routine risk factors
Cardiac
Pulmonary
Renal
Hematologic
Diabetes-related risk factors
Macrovascular complications
Microvascular complications
Neuropathic complications
Diabetes therapeutic regimen
Reestablish correct diagnostic classification of diabetes
Pharmacological regimen
Medication type
Dosage
Timing
Meal plan
Carbohydrate content
Timing of meals
Activity level
Hypoglycemia
Frequency
Awareness
Severity
Anticipated surgery
Type of surgical procedure
Inpatient or outpatient
Type of anesthesia
Start time
Duration of procedure

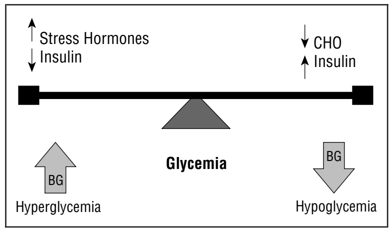

Figure 1. *The balancing of perioperative glycemia. Hypoglycemia results from a predominance of the glycemic effects of a decrease (downward arrow) of carbohydrate (CHO) intake and an increase (upward arrow) of circulating insulin, and hyperglycemia results from a predominance of the glycemic effects of an increase in stress hormones and a decrease of circulating insulin levels. BG indicates blood glucose.*

substantiate this approach. However, it does appear important to optimize the patient's nutritional status if time permits.[5,6] Hypertension, a common comorbid condition associated with diabetes mellitus,[7] should be well controlled before elective surgery. These recommendations are idealized, and the relative contraindications to the operative procedure must be balanced against the urgency and benefit of the procedure itself. It has been recommended that insulin-treated patients, particularly those with type 1 diabetes, should be hospitalized at least 1 day before an elective operation to establish reasonably good metabolic control and to correct any fluid and electrolyte abnormalities.[5,6,10-12] Today, in countries where the health care system has become intensively regulated with goals of increasing cost-effectiveness, this is not practical, and such patients are generally admitted to the hospital on the day of surgery.

The perioperative management of diabetes should be approached logistically. The variety of diabetes treatment regimens for both type 1 and type 2 diabetes; the myriad surgical procedures compounded by varying start times, durations, and anesthetic approaches; and the unpredictability of recuperation present considerable challenges to the maintenance of stable glycemic control and the resumption of the patient's usual diabetes regimen. To anticipate the multiplicity of potential perioperative diabetes problems, a detailed history of diabetes therapy is important. First, it is necessary to correctly ascertain the type of diabetes, since this may ultimately impact on future pharmacological requirements and risk of metabolic complications, vis-a-vis insulin sensitivity and insulinopenia. This history should include not only the details of the pharmacological regimen but also the prescription for energy intake and carbohydrate content of the meal plan. It is important to elicit such daily routines as mealtimes, usual level of activity, and timing of medication (eg, especially taking care to properly define a "PM" insulin dose as before bedtime, 10 PM, as opposed to before supper, 6 PM). It is also important to understand this regimen's ability to achieve glycemic goals and the patient's degree of adherence. Finally, the history should define the patient's experience of hypoglycemia, such as the frequency, the glucose level at which the patient is aware of hypoglycemia, and whether the patient has recently experienced neuroglycopenia.

The physician responsible for management of the diabetes (if other than the surgeon) should ascertain the details of the surgical procedure. Is it inpatient or outpatient, what is the anticipated start time and duration of the procedure, and what type of anesthesia is to be used? The purpose of these inquiries is to determine to what degree the diabetes regimen will be perturbed and for what duration. If the procedure is short and can be performed early in the day and the patient can be expected to eat shortly after the surgery, then the patient's diabetes regimen can be shifted a few hours later in the day. Minimal disruption of the regimen tends to be the easiest course of management. These details are very helpful in formulating a rational approach to intraoperative and postoperative management recommendations.

GLYCEMIC GOALS DURING SURGERY

The metabolic effects of surgery on the control of glucose homeostasis (**Figure 1**) are not the purview of this article and have been reviewed elsewhere.[6] Surgical stress and some general anesthetic agents themselves are associated with increases in the counterregulatory hormones epinephrine, norepinephrine, glucagon, growth hormone, and cortisol. The metabolic effects of these hormones will result in increased insulin resistance, thereby increasing hepatic glucose production and decreasing peripheral glucose utilization.[5,6] This will promote hyperglycemia in the diabetic patient and, additionally, ketogenesis (and potentially ketoacidosis) in the patient with type 1 diabetes. Patients receiving pharmacological therapy, however, may also be at risk for developing hypoglycemia, especially when they fast preoperatively to minimize the risks of emesis and aspiration of gastric contents during induction of anesthesia. Unfortunately, to avoid being caught up in this glycemic balancing act, many physicians may elect to permit short-term hyperglycemia. In general, the goal for glucose control during surgery is to maintain the glucose level between 8 and 11 mmol/L (approximately 150 and 200 mg/dL) during surgery to protect against hypoglycemia.[5,6,10-18] The above metabolic effects on glucose control are hard to anticipate, and it is best to rely on assessment of ambient glycemia. Glucose level may be monitored adequately by means of any of the systems designed for inpatient bedside use and approved for capillary, arterial, and/or venous blood glucose measurements.[13-15] Obviously, the more unstable the diabetes, the more frequent the need for glucose monitoring.

DIABETES THERAPY IN ANTICIPATION OF SURGERY

Different regimens have been recommended for treating diabetic patients undergoing surgical procedures.[5,6,10-18] Recommendations are generally categorized on the basis of antecedent pharmacological therapy. For patients receiving diet therapy alone and those treated with diet and oral agents, no intraoperative therapy is usually recommended if preoperative glucose levels approximate the above-stated intraoperative glycemic goals. In addition to those already receiving insulin, patients with poorly controlled type 2 diabetes who are taking oral agents will often require insulin during the perioperative period.

Type 2 Diabetes Treated With Diet Alone

For patients with type 2 diabetes who are treated with diet alone, a retroactive approach to management of glucose control is taken. Patients are to abstain from oral intake, usually overnight, and hydration may be maintained with or without a dextrose-containing intravenous solution. Blood glucose may be measured before and after the operative procedure and intraoperatively if the procedure is long. Hyperglycemia is treated with supplemental short-acting insulin (regular or lispro), usually administered subcutaneously. In these individuals, the stress of the surgery may lead to decompensation of glycemic control, requiring pharmacological intervention.[15] For those undergoing outpatient surgery, it is prudent to remind these patients before discharge from the ambulatory surgical center of the signs and symptoms of hyperglycemia and to reinforce guidelines for contacting their physician.

Type 2 Diabetes Treated With Oral Antidiabetes Agents

For patients treated with oral agents, these agents are generally administered on the day before surgery and withheld on the day of surgery. If patients manifest marked hyperglycemia, supplemental insulin can be administered to achieve better glycemic control, and the surgery may be performed if electrolyte levels are acceptable. Hyperglycemia during the perioperative period in patients previously treated with these agents should be corrected with insulin (**Figure 2**).

α-Glucosidase inhibitors (acarbose and miglitol) attenuate the postprandial glycemic excursion by inhibiting intestinal brush border oligosaccharidases and disaccharidases. This class of agent is not efficacious in the fasting state, and therefore there would be no utility in administering an α-glucosidase inhibitor until the patient resumes eating.[19]

Biguanides (metformin) sensitize target tissues to insulin action and therefore inhibit hepatic glucose production and augment peripheral glucose uptake in the muscle and fat. Practices in Europe, where biguanides have been used routinely for more than 20 years, differed from those in the United States, where extreme caution was exercised and it was recommended that metformin be discontinued 48 hours before surgery. Currently, in both Europe and the United States, metformin is discontinued on the day of surgery because complications or alterations in renal function arising intraoperatively may potentiate the risk of development of lactic acidosis.[20,21]

Thiazolidinediones (troglitazone, rosiglitazone, and pioglitazone) are a new class of insulin sensitizer that may be used to treat type 2 diabetes as monotherapy or in combination with sulfonylureas, metformin, or insulin. These drugs also improve peripheral glucose uptake in the muscle and fat and inhibit hepatic glucose production, but, unlike metformin, are not associated with lactic acidosis. Thiazolidinediones are not insulin secretagogues and may be discontinued on the day of surgery.[22]

Sulfonylureas stimulate insulin secretion and have the potential for producing hypoglycemia during the fasting of surgery. This risk is dependent on the duration of action of the particular sulfonylurea but can be minimized by glucose monitoring and the use of dextrose-containing intravenous solutions. Sulfonylureas are routinely continued on the day before surgery and withheld on the operative day. If patients have inadvertently taken these medications on the operative day, surgery need not be postponed, but more attentive glucose monitoring in addition to continuous intravenous dextrose is appropriate.[21,23]

Type 1 or Type 2 Diabetes Treated With Insulin

Many patients who use insulin can be treated with conventional subcutaneous insulin therapy.[5,6,10-18] For individuals who take long-acting insulin (ie, extended insulin zinc [Ultralente]) and short-acting insulin, a switch to an intermediate-acting type a day or two before planned surgery is appropriate. If this cannot be accomplished, then glucose should be monitored more intensively and the dextrose infusion rate adjusted appropriately to prevent hypoglycemia and substantial hyperglycemia. If patients experience well-controlled glycemia and/or morning hypoglycemia, the afternoon or evening intermediate-acting insulin may be decreased slightly to produce glycemic levels commensurate with the above-stated intraoperative goals. Preoperative insulin recommendations are much more complex and require more logistic contingencies (**Figure 3**).

Subcutaneous Insulin Regimens

For early-morning procedures of short duration where the patient may still be expected to eat according to his or her usual meal plan, it is easiest to give the morning insulin and food after the procedure. Shortening the intervals between later meals may compensate for this delay and gradually realign the patient's mealtimes back to the usual schedule. This operative schedule is the easiest for patients and physicians because it has the least disrupting effect on the diabetes regimen and should be advocated by both patient and the physician responsible for managing the diabetes. However, frequently these requests cannot be fulfilled.

If the surgery can be performed in the morning, but it is likely that the breakfast meal will be omitted, preoperative insulin should be administered.[5,6,10-18] If the patient is treated with a single morning dose of intermediate-acting insulin, then two thirds of that dose should be administered in the morning as intermediate-acting insulin if the patient is likely to eat lunch. If the patient is treated with a twice-daily dose of insulin, then one half of the total morning dose (including short-acting insulin if prescribed) should be administered in the morning as intermediate-acting insulin. If the likelihood of consuming lunch is low, one half of the total morning dose (including short-acting) should be administered as intermediate-acting insulin for the patient treated with a single dose of insulin and one third for a twice-daily regimen. For those on a regimen of morning intermediate-acting and short-acting insulin, short-acting insulin at supper, and bedtime intermediate-acting insulin, recommendations are similar to those for the twice-daily insulin regimen. For the patient who is taking multiple doses of short-acting insulin (MDI regimen) one third of the premeal dose of short-acting insulin is administered at the appropriate time. Patients treated with continuous insulin infusion therapy (insulin pumps) may be treated with their usual basal infusion rate.

When surgery is scheduled later in the day, more complex modifications are frequently necessary, and an intravenous infusion of glucose is recommended at 5 g/h.[5,6,10-18] For individuals previously treated with a single dose of insulin, one half of the total dose of morning insulin should be given as intermediate-acting insulin in the morning. For those treated with 2 or 3 doses, one third of the morning total dose is given as intermediate-acting insulin. Patients taking multiple doses of short-acting insulin may receive one third of the morning dose of short-acting insulin and one third of the lunch dose of short-acting insulin at the appropriate time. Patients with pumps may maintain their basal rates without boluses. Marked hyperglycemia may be treated with supplemental short-acting insulin.

Intravenous Insulin Regimens. Intravenous regular insulin is indicated during the perioperative period for previously insulin-treated patients undergoing long, complex operative procedures; patients who require emergency surgery while in ketoacidosis; and patients with unstable type 1 diabetes.[5,6,10-18] It may also be indicated for pregnant women with type 1 diabetes. Many intravenous insulin protocols have been described and comparatively studied.[12,15,24-32] Intravenous insulin is typically administered as intermittent, small intravenous boluses of regular insulin (every 2 hours), variable "single-solution" glucose-potassium-insulin infusions, and variable separate infusions of glucose and regular insulin. Evaluations of such regimens are complicated by inclusion of patients with both type 1 and type 2 diabetes, a wide variety of surgical procedures, and lack of randomization. The superiority of any method remains controversial.[30-33] In states of peripheral vasoconstriction where the subcutaneous compartment is

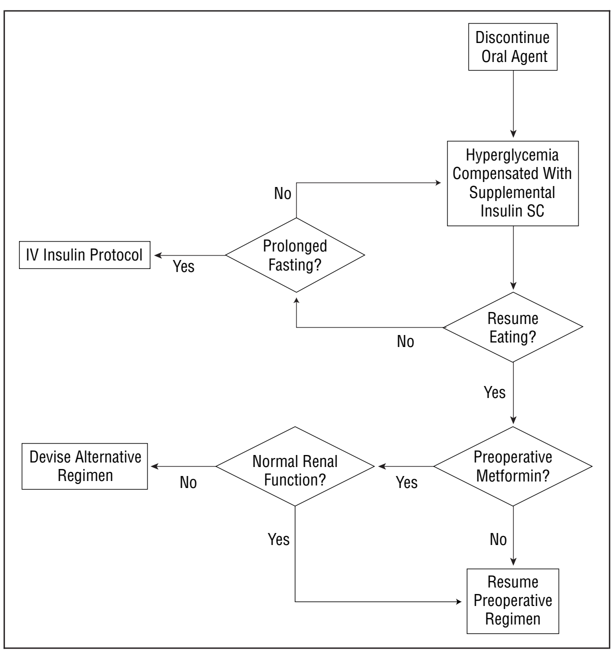

Figure 2. *Management algorithm for oral antidiabetes agents. SC indicates subcutaneously; IV, intravenous.*

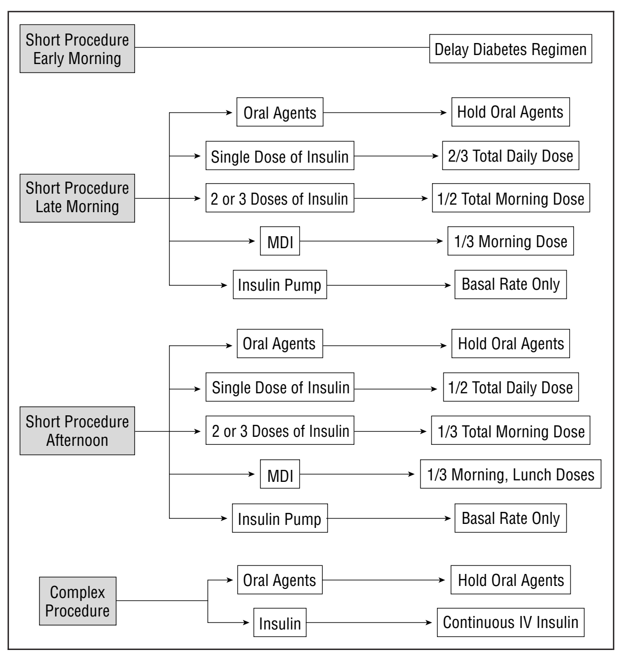

Figure 3. *Summary of perioperative management recommendation based on therapeutic regimen and the complexity and scheduling of the operative procedure. MDI indicates multiple doses of short-acting insulin; IV, intravenous.*

suboptimally perfused, intravenous insulin administration ensures a more controlled and effective tissue delivery than subcutaneous administration. Furthermore, because the half-life of intravenous insulin is short (<10 minutes), insulin dosing may be more rapidly titrated. This pharmacokinetic principle may justify the preference for continuous intravenous infusions over intermittent intravenous bolus therapy for patients with type 1 diabetes, although this remains controversial when evaluated in insulin-treated patients with type 2 diabetes.[31] In the intermittent bolus technique, 10 U of regular insulin is administered every 2 hours and supplemented by 5 U every 60 minutes for blood glucose levels greater than 11 mmol/L (approximately 200 mg/dL).[25,31] Continuous intravenous insulin infusion rates are generally 0.5 to 5.0 U/h, commensurate with the amount of glucose infused.[6,12,15] This generally translates to infusion of 0.3 U of insulin per gram of glucose, with upward adjustments made for increasing insulin resistance. The glucose-potassium-insulin infusion is widely used in Europe and offers some advantages in its simplicity and single-solution technique, which ensures simultaneous infusion of both insulin and glucose. This eliminates concerns about metabolic complications resulting from obstruction of the infusion of either glucose or insulin.[15,24,26,27]

The glucose-potassium-insulin infusion (**Figure 4**) is initiated at a rate of 100 mL/h of a solution of 500 mL of 10% dextrose, 10 mmol of potassium, and 15 U of insulin. Adjustments in the insulin dose are made in 5-U increments according to blood glucose measurements performed at least every 2 hours. Potassium is added to prevent hypokalemia and is monitored at 6-hour intervals if the use of the glucose-potassium-insulin infusion is prolonged. Closer scrutiny of the addition of potassium is warranted when the patient has underlying renal disease or is treated with an angiotensin-converting enzyme inhibitor. Separate continuous glucose and insulin infusions[6,12,32] are used more frequently in the United States than the glucose-potassium-insulin in-

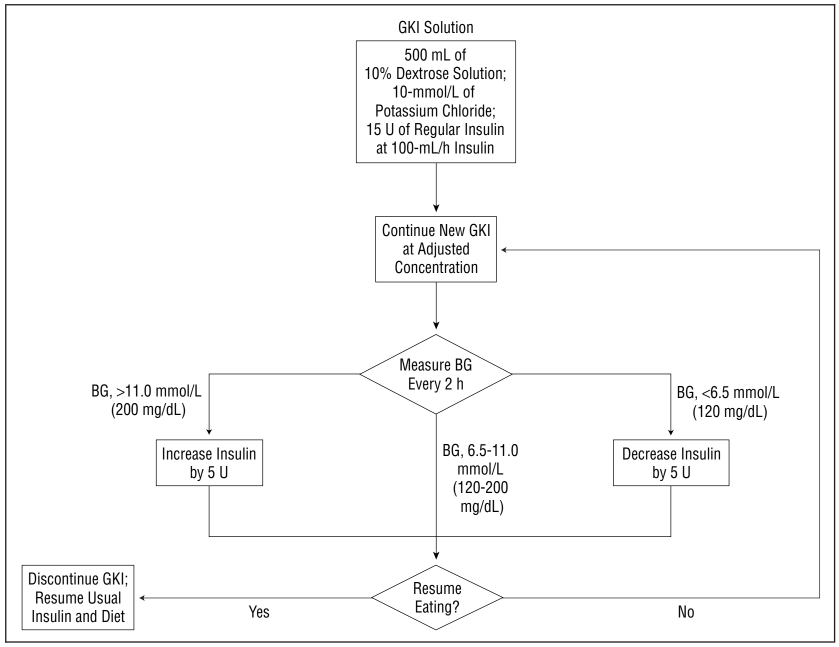

Figure 4. *Management algorithm for glucose-potassium-insulin (GKI) intravenous infusion. BG indicates blood glucose. (For convenience, conversion of BG values from millimoles per liter to milligrams per deciliter are approximate.)*

fusion. These infusions (**Figure 5**) may be quickly adjusted and offer greater flexibility in responding to changes in blood glucose levels and ketosis. Infusions are modulated to accommodate alterations in blood glucose level, insulin sensitivity as reflected by the patient's preoperative total daily insulin dose, and surgical stress as anticipated by the type of procedure. Dextrose, 5%, is administered at 100 mL/h and insulin is initiated at 1.0 U/h. This initial rate is modulated for the type of procedure (2- to 5-fold increase) and an "insulin sensitivity" factor (the preoperative total daily insulin [TDI] dose divided by 30).[12,34] The latter can easily be calculated mentally as follows:

$$TDI/30 = (TDI/100) \times 3.$$

At our institution, however, we substitute a more aggressive factor of 25:

$$TDI/25 = (TDI/100) \times 4.$$

The insulin infusion rate may be adjusted downward to compensate for hypoglycemia or hyperglycemia. This incremental rate of 0.5 U/h is also factored according to the patient's TDI and operative procedure. For blood glucose level above 11 mmol/L (approximately 200 mg/dL), the increment is increased again at 3-mmol/L (approximately 50 mg/dL) levels (eg, for a blood glucose level of 18 mmol/L [325 mg/dL], the insulin infusion is increased by 1.5 U/h with a starting rate of 1.0 U/h). Blood glucose is measured hourly and potassium is administered on an as-needed basis. Cardiopulmonary bypass surgery presents considerable challenges to diabetes management because of the stress of the procedure and because dextrose solutions are used to prime the perfusion pump. Organ transplantation is similarly challenging because of the use of immunosuppressive agents and glucocorticosteroids. Such procedures, as well as prolonged neurosurgical procedures, are probably best managed with this form of therapy.[15]

DIABETES THERAPY AFTER SURGERY

For patients undergoing outpatient surgery, their preoperative regimen may be reinstituted when the patient resumes eating. An exception to this approach exists when the procedure is performed in conjunction with iodinated radiocontrast dye and the patient is treated with a biguanide. The biguanide should not be resumed for 72 hours postoperatively, when serum creatinine is measured to document the absence of dye-induced renal toxic effects and normal renal function.[20,21]

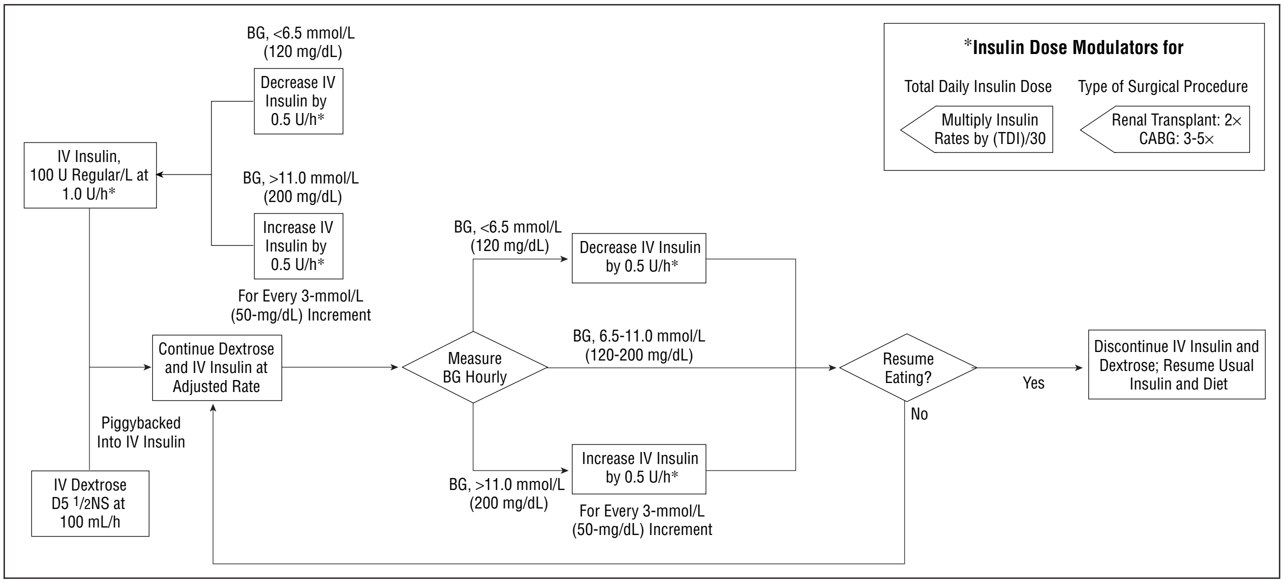

Figure 5. *Management algorithm for separate glucose and insulin intravenous infusions. IV indicates intravenous; D5 ½NS, 5% dextrose, 0.45 sodium chloride; BG, blood glucose; TDI, total daily insulin dose; and CABG, coronary artery bypass grafting. (For convenience, conversion of BG values from millimoles per liter to milligrams per deciliter are approximate.)*

Table 2. Calculation of a Compensatory Subcutaneous Short-Acting Insulin Algorithm*

Blood Glucose, mmol/L (mg/dL)†	Increment Formula	Calculation	Short-Acting Insulin, U
0-11.0 (0-200)	0	0	0
11.1-14.0 (201-250)	1 × (TDI/30)	1 × (120/30)	4
14.1-17.0 (251-300)	2 × (TDI/30)	2 × (120/30)	8
17.1-20.0 (301-350)	3 × (TDI/30)	3 × (120/30)	12
20.1-23.0 (351-400)	4 × (TDI/30)	4 × (120/30)	16
23.1-26.0 (401-450)	5 × (TDI/30)	5 × (120/30)	20
>26.0 (>450)	Call physician	Call physician	Call physician

*Example uses a preoperative total daily insulin dose (TDI) of 120 U.
†For convenience, conversions of millimoles per liter to milligrams per deciliter are approximate.

During the postoperative period, diabetes control may be markedly unstable. Operative procedures may necessitate that a patient abstain from oral intake for prolonged periods. Many patients may have difficulty eating because of side effects of anesthesia and other postoperative complications, such as ileus. During intervals of uncertain alimentation, patients may require continued infusion of dextrose or, for more prolonged periods, parenteral nutrition. Dextrose infusion rates should be sufficient to prevent hypoglycemia and ketosis (5-10 g of glucose per hour).[6] Total daily insulin requirements under these circumstances are dependent on the rate of dextrose solution and the patient's level of metabolic stress. Divided doses of intermediate-acting insulin (twice daily) or short-acting insulin (4-6 times per day) can be supplemented by a subcutaneous insulin algorithm to compensate for hyperglycemia. The increment for the insulin algorithm is determined empirically from the patient's TDI as previously described. The increment to compensate for hyperglycemia above the target glucose level is calculated as the TDI divided by 30 for every 3 mmol/L (approximately 50 mg/dL) above goal (**Table 2**). For patients treated intraoperatively with intravenous insulin infusions, it is easiest to continue the intravenous insulin along with the dextrose infusion until the patient resumes eating (Figures 4 and 5). When feeding is reliably resumed, the infusions may be discontinued and the patient's usual diabetes regimen (oral agents or insulin) may be reinstated.

CONCLUSIONS

Perioperative management of diabetes is generally more art than clinical science. There are myriad protocols for managing this problem, but there is none with any clear superiority. Circumstances governing glucose homeostasis during this period are highly variable and often unpredictable. Optimal methods, such as intravenous insulin infusions, may be expensive and labor intensive and may not be necessary in many cases. Although various strategies have been reviewed, clinical judgment remains a key component in good perioperative treatment of the patient with diabetes mellitus.

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