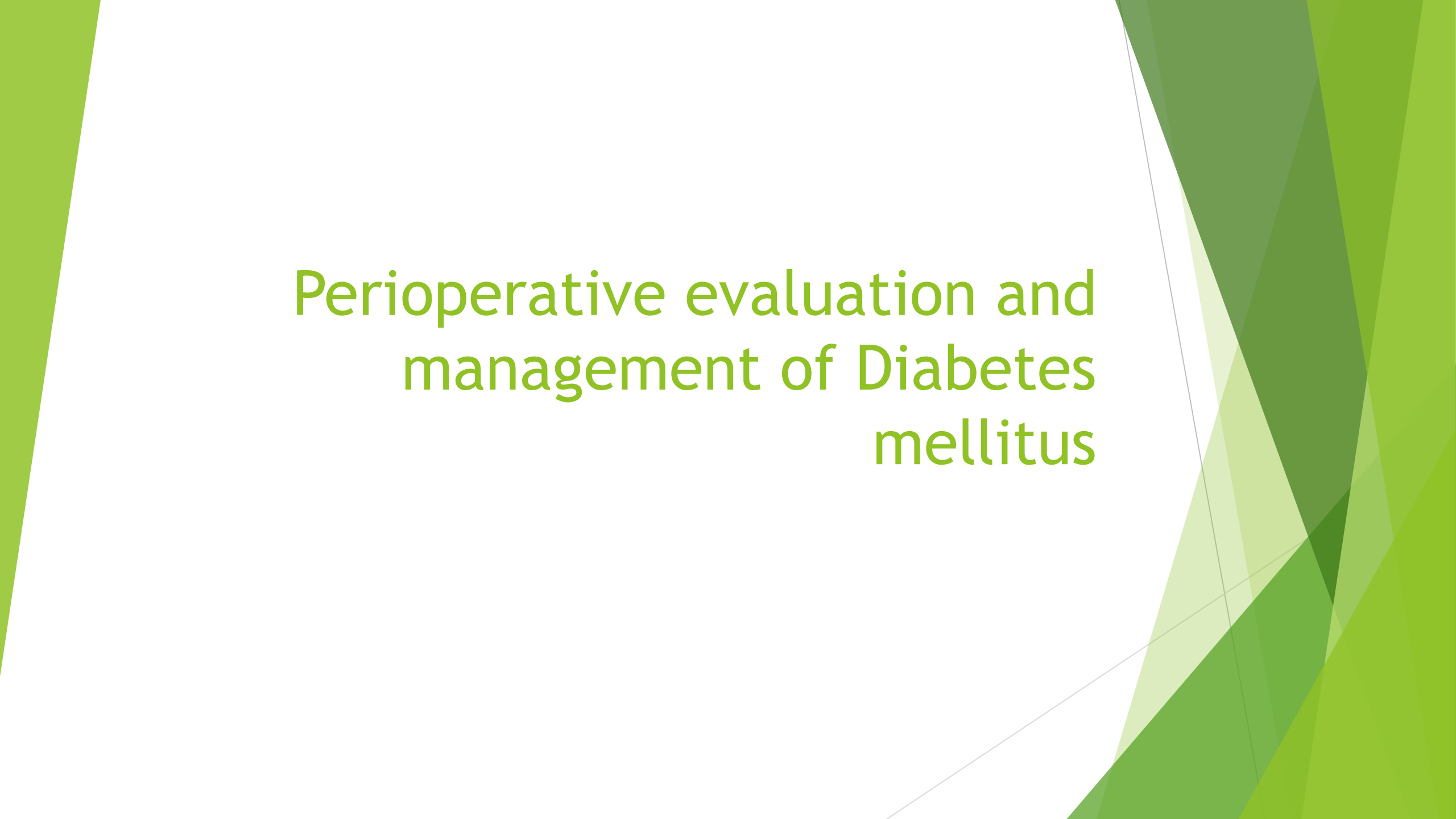


The background features abstract, overlapping green geometric shapes, primarily triangles and polygons, in various shades of green, creating a modern and dynamic visual effect.

Perioperative evaluation and management of Diabetes mellitus

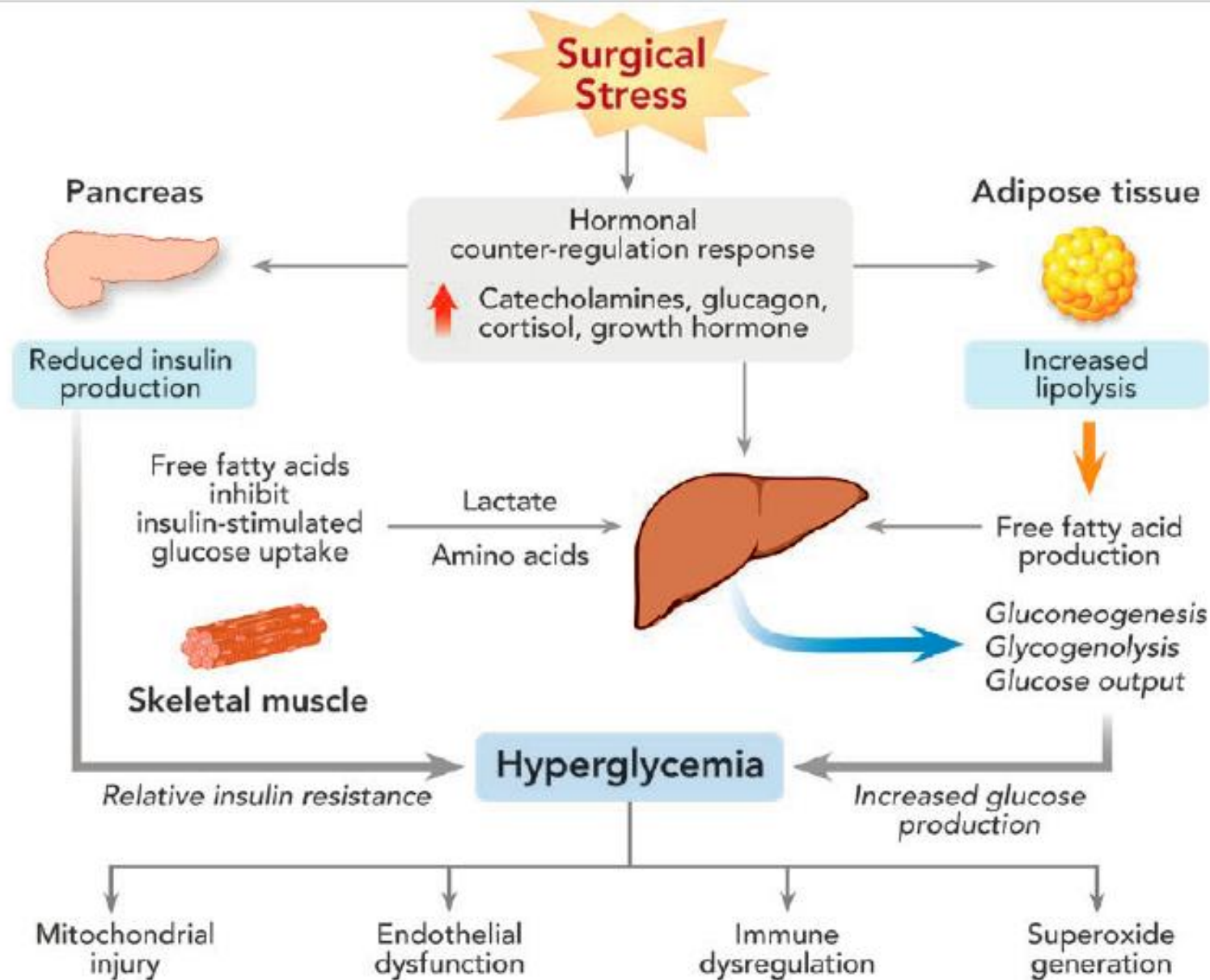
Introduction

- ▶ In surgical patients, the presence of diabetes mellitus (DM) or hyperglycemia is associated with increased morbidity.
- ▶ Suboptimal diabetes control is associated with adverse perioperative outcomes such as metabolic derangements, infection, poor wound healing.

Metabolic consequences of surgical stress and anesthesia

- ▶ The stress of surgery and anesthesia alters the balance between hepatic glucose production and glucose utilization in peripheral tissues.
- ▶ Increased secretion of counterregulatory hormones (catecholamines, cortisol, glucagon, and growth hormone) causes release of TNF- α , interleukin-6, and interleukin-1 β .
- ▶ Cortisol increases hepatic glucose production, stimulates protein catabolism, and promotes gluconeogenesis, resulting in elevated Blood Glucose levels.

Metabolic consequences of surgical stress and anesthesia



Metabolic consequences of surgical stress and anesthesia

- ▶ Surgeries involving the thorax and abdomen are associated with prolonged duration of hyperglycemia compared to peripheral procedures.
- ▶ Laparoscopic procedures demonstrate a decreased incidence of insulin resistance and hyperglycemia compared to open procedures.
- ▶ General anesthesia is more frequently associated with hyperglycemia and higher levels of catecholamines, cortisol, and glucagon than local or epidural anesthesia.
- ▶ Volatile anesthetic agents inhibit insulin secretion and increase hepatic glucose production

Risk of Hyperglycemic Crises

- ▶ Patients with type 1 diabetes are at risk for diabetic ketoacidosis (DKA) even in the absence of severe hyperglycemia if insulin is not titrated.
- ▶ In type II DM hyperosmolar non ketotic states can occur with profound elevation of blood glucose and significant dehydration.

Complications of Perioperative Hyperglycemia

- ▶ Hyperglycemia interrupts the stages of normal wound healing by impeding blood flow, endothelial dysfunction and prolonging an inflammatory state.
- ▶ Hyperglycemia also impairs neutrophil phagocytic function and increases the risk of infection.
- ▶ It is associated with increased risk of acute renal failure

Surgical planning

- ▶ The main goals are to reduce fasting period, ensure normoglycemia.
- ▶ If patient's fasting time is limited to one missed meal, the option is to change his/her normal medication for diabetes.
- ▶ If longer periods of fasting are predicted, a variable rate intravenous insulin infusion (VRII) should be used.
- ▶ On the day of surgery, the patient should receive written instructions on medication management, control of peri-operative hypo- or hyperglycemia, and effects of surgery on diabetes control

Preoperative assessment

Symptoms of Hyperglycemia	Planned Operation	Risk for Perioperative Glycemic Disturbance Hyperglycemia
• Polyphagia • Polydipsia • Polyuria • Blurred vision • Fatigue • Weight loss • Poor wound healing • Dry mouth	• Type of surgery ◦ Cardiac ◦ Noncardiac • Length of surgery • Planned anesthesia • Timing of surgery • Length of time NPO	• Diabetes • Stress from acute illness • Medications ◦ Glucocorticoids ◦ Octreotide ◦ Vasopressors ◦ Immunosuppressants • Enteral and parenteral nutrition
Past Medical History	Postoperative Plan	Hypoglycemia
• Type 1 or 2 diabetes • Glucose intolerance • Previous hospitalizations for diabetes • Outpatient glycemic control Medications • Outpatient oral glycemics or insulin • Glucocorticoids • Immunosuppressants	• Resume oral diet • NPO • Enteral nutrition • Parenteral nutrition	• Insulin use • Altered nutritional status • Heart failure • Liver or renal failure • Malignancy • Infection, sepsis • Iatrogenic ◦ Sudden reduction in steroid use while on long-acting insulin ◦ NPO or decreased oral intake ◦ Inappropriate timing of insulin administration ◦ Decreased dextrose administration • Interruptions in enteral or parenteral nutrition

Preoperative evaluation of diabetes

- ▶ **History:** symptoms of cardiac, retinal, renal, neurologic, and peripheral vascular disease.
- ▶ **Physical examination:** orthostatic hypotension, sign of autonomic neuropathy.

A fundoscopic examination provide insight into the patient's risk of developing postoperative blindness .

Cardiac examination, Abdominal examination (hepatomegaly), Evaluation of pulses by palpation and with auscultation, Skin examination (insulin-injection sites),

Effects of hyperglycemia on various systems

- ▶ **Musculo skeletal system**
- ▶ Chronic hyperglycemia leads to non-enzymatic glycosylation of proteins and abnormal collagen cross-links in joints, limiting mobility and leads to stiff joint syndrome .
- ▶ Temporomandibular, atlanto-occipital, and cervical spine joints may be affected
- ▶ Diabetes scleredema is characterized by firm, wood-like, non-compressible nuchal edema and upper dorsum regions with reduced joint mobility, limit the neck range of motion and hinder orotracheal intubation.

Effects of hyperglycemia on various systems

- ▶ Renal system -Diabetic nephropathy - this is seen in poor diabetes control causes albuminuria and progressive reduction of renal function.
- ▶ Neurological system -presence of hyperglycemia is a strong predictor of worse outcomes in various forms of acute brain injury.
- ▶ Autonomic neuropathy : reduced esophageal motility and gastroparesis may lead to vomiting and aspiration of gastric content.
- ▶ Cardiovascular **system**: Diabetic patients are at increased risk of myocardial ischemia, systolic and diastolic heart failure, and congestive heart failure.

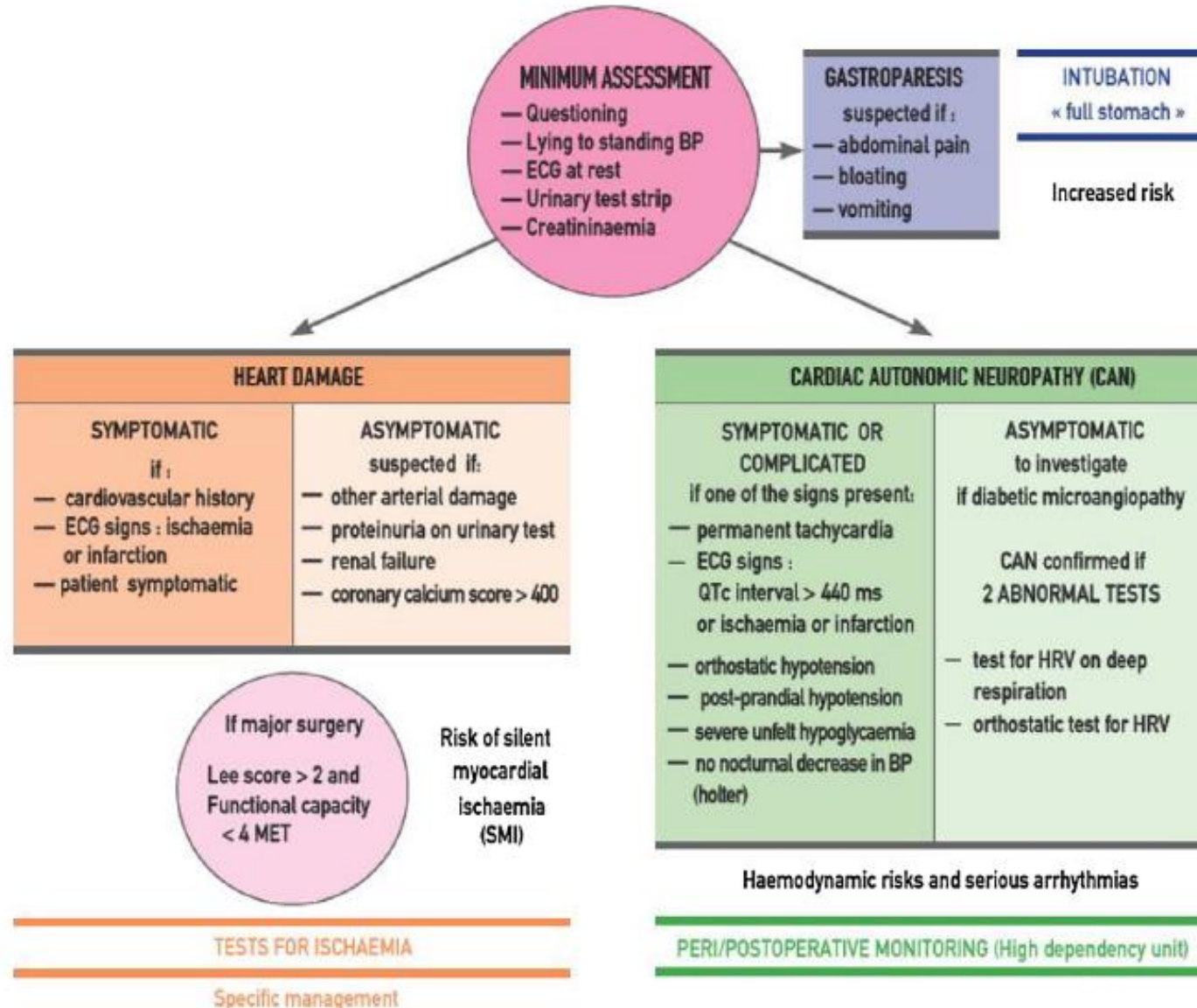
Key elements of the initial assessment

- ▶ Determination of the type of diabetes, since type 1 diabetes patients are at much higher risk of diabetic ketoacidosis and must have basal insulin supplied at all times
- ▶ Long-term complications of diabetes mellitus, including retinopathy, nephropathy, neuropathy, autonomic neuropathy, coronary heart disease, peripheral vascular disease, and hypertension
- ▶ Assessment of baseline glycemic control, including frequency of monitoring, average blood glucose levels, range of blood glucose levels, and glycated hemoglobin (A1C) level.
- ▶ Assessment of hypoglycemia, including frequency, timing, awareness, and severity

Key elements of the initial assessment

- ▶ Detailed history of diabetes therapy, including insulin type, dose, and timing
- ▶ Other pharmacologic therapy, including type of medication, dosing, and specific timing
- ▶ Characteristics of surgery including : when the patient must stop eating prior to surgery, type of surgery, timing of the operative procedure, and duration of the procedure.
- ▶ Type of anesthetic, including epidural or regional versus general anesthesia (epidural or regional anesthesia has minimal effects on glucose metabolism and insulin resistance).

Assessment of patients with Diabetes mellitus



Cardiac evaluation

- ▶ **ECG** -presence of Q waves or significant ST-segment elevation or depression, the possibility of myocardial ischemia or infarction, left ventricular hypertrophy, QTc prolongation, bundle-branch block, or arrhythmia.
- ▶ **ECHO** -
 1. is not indicated in the perioperative patient unless to evaluate valve function in patients with a murmur or left ventricular systolic function in patients with heart failure or dyspnea of unknown cause.
 2. The presence of significant left ventricular systolic dysfunction or severe valvular heart disease is associated with a worse outcome- postoperative heart failure

Cardiac evaluation

► Computed tomography —

1. Electron beam CT scan can noninvasively detect the presence of coronary artery calcification (CAC) and coronary artery atherosclerosis.
2. Asymptomatic men and women with diabetes have higher median CAC scores on electron beam CT scanning than individuals without diabetes.

► Stress testing-

1. Patients with type 2 diabetes have silent ST segment depression and coronary perfusion abnormalities during stress testing.
2. Stress testing with radionuclide myocardial perfusion imaging (rMPI) is more sensitive than exercise stress testing alone for the diagnosis of CHD

Goals of glycemic control

- ▶ Avoidance of hypoglycemia -
 1. Hypoglycemia is a potentially life-threatening complication of poor perioperative metabolic control.
 2. Severe hypoglycemia (ie, serum glucose concentration <40 mg/dL [2.2 mmol/L]), even for short periods of time, can induce arrhythmias, other cardiac events, or transient cognitive deficits.
 3. Hypoglycemia and subsequent neuroglucopenia can be difficult to detect in sedated or anesthetized patients
- ▶ Prevention of ketoacidosis/hyperosmolar states
- ▶ Maintenance of fluid and electrolyte balance
- ▶ Avoidance of marked hyperglycemia

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Perioperative management in Diabetes Mellitus

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Perioperative Management strategies

Table 1. Indications, advantages and disadvantages of four perioperative diabetes management strategies

Management	Indications	Advantages	Disadvantages
Modification of usual therapy	HbA1c <8.5% Short starvation period (<1 meal missed)	Lowest risk for hypoglycaemia Decreased burden on ward staff Suitable for patient self-management	Often not possible, as patients have poor baseline control or there is prolonged starvation
Basal-bolus SC insulin with correction doses	Those already on basal-bolus insulin Type 1 diabetes Patients with poor baseline control Newly diagnosed DM requiring perioperative insulin therapy Short surgical duration Where IV insulin therapy is not feasible	Improved glycaemic control Flexible dosing Decreased risk of hypoglycaemia	Intensive Regular monitoring required Not to be used if the patient is not eating meals Unpredictable absorption when there is impaired tissue perfusion
Alberti's glucose-insulin-potassium infusion	Poor control on SC insulin (CBG >12.0 mmol/L) Prolonged starvation period (>1 meal missed) Long surgical duration Periods of inadequate tissue perfusion High-care or ICU setting VRIII is not an option	Improved glycaemic control Flexible	Labour intensive Need trained staff Risk of hypo-Na ⁺ /K ⁺ Risk of hypoglycaemia
VRII	Poor control with SC insulin (CBG >12.0 mmol/L) Prolonged starvation period (>1 meal missed) Long surgical duration Periods of inadequate tissue perfusion High-care or ICU setting	Improved glycaemic control Flexible	Requires specialised equipment Labour intensive Need trained staff Risk of hypo-Na ⁺ /K ⁺ Risk of hypoglycaemia

Perioperative adjustment of oral hypoglycemics

Agent	Day before admission	Day of surgery		Whilst a VRlll is being used
		Surgery in the morning	Surgery in the afternoon	
<i>Drugs that require omission when fasting owing to risk of hypoglycaemia</i>				
Meglitinides (e.g. repaglinide, nateglinide)	Take as normal	Omit morning dose if nil by mouth	Give morning dose if eating	Stop until eating and drinking normally
Sulphonylurea (e.g. glibenclamide, gliclazide, glipizide)	Take as normal	Omit morning dose (whether taking once or twice daily)	Omit (whether taking once or twice daily)	Stop until eating and drinking normally
<i>Drugs that require omission when fasting owing to risk of ketoacidosis</i>				
SGLT-2 inhibitors* (e.g. dapagliflozin, canagliflozin)	No dose change	Halve the usual morning dose; check blood glucose on admission; leave evening meal dose unchanged	Halve the usual morning dose; check blood glucose on admission; leave the evening meal dose unchanged	Stop until eating and drinking normally
<i>Drugs that may be continued when fasting</i>				
Acarbose	Take as normal	Omit morning dose if nil by mouth	Give morning dose if eating	Stop until eating and drinking normally
DPP-IV inhibitors (e.g. sitagliptin, vildagliptin, saxagliptin, alogliptin, linagliptin)	Take as normal	Take as normal	Take as normal	Stop until eating and drinking normally
GLP-1 analogues (e.g. exenatide, liraglutide, lixisenatide)	Take as normal	Take as normal	Take as normal	Take as normal
Metformin (procedure not requiring use of contrast media†)	Take as normal	Take as normal	Take as normal	Stop until eating and drinking normally
Pioglitazone	Take as normal	Take as normal	Take as normal	Stop until eating and drinking normally

Barker et al. | Guidelines on peri-operative management of diabetes

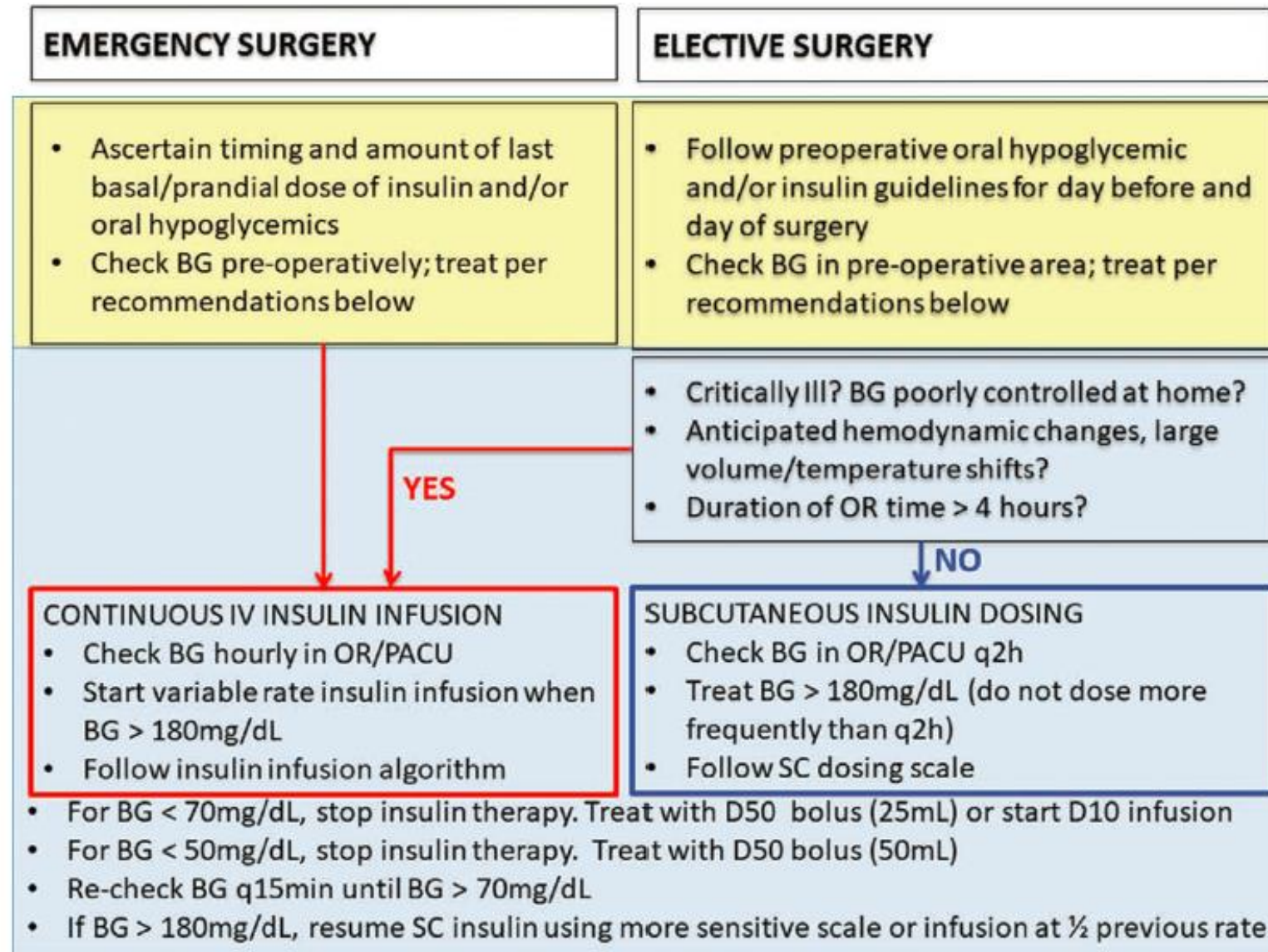
Perioperative adjustment of insulin

Insulin	Day before admission	Day of surgery		Whilst a VRIII is being used*
		Surgery in the morning	Surgery in the afternoon	
Once daily (e.g. Lantus®, Levemir®, Tresiba®, Insulatard®, Humulin I®, Insuman®)				
Evening	Reduce dose by 20%	Check blood glucose on admission	Check blood glucose on admission	Continue at 80% of usual dose
Morning	Reduce dose by 20%	Reduce dose by 20%; check blood glucose on admission	Reduce dose by 20%; check blood glucose on admission	Continue at 80% of usual dose
Twice daily				
Biphasic or ultra-long acting (e.g. Novomix 30®, Humulin M3®, Humalog Mix 25®, Humalog Mix 50®, Insuman® Comb 25, Insuman® Comb 50, Levemir®, Lantus®) by single injection, given twice daily	No dose change	Halve the usual morning dose; check blood glucose on admission; leave evening meal dose unchanged	Halve the usual morning dose; check blood glucose on admission; leave the evening meal dose unchanged	Stop until eating and drinking normally
Short-acting (e.g. animal neutral, Novorapid®, Humulin S®, Apidra®) and intermediate-acting (e.g. animal isophane, Insulatard®, Humulin I®, Insuman®) by separate injections, both given twice daily	No dose change	Calculate total dose of morning insulin(s); give half as intermediate-acting only in the morning; check blood glucose on admission; leave evening meal dose unchanged	Calculate total dose of morning insulin(s); give half as intermediate-acting only in the morning; check blood glucose on admission; leave evening meal dose unchanged	Stop until eating and drinking normally
Three to five injections daily	No dose change	Basal bolus regimens: Omit morning and lunchtime short-acting insulins; keep basal unchanged* Premixed morning insulin: Halve morning dose and omit lunchtime dose; check blood glucose on admission	Give usual morning insulin dose(s); omit lunchtime dose; check blood glucose on admission	Stop until eating and drinking normally

VRIII variable-rate intravenous insulin infusion

Barker et al. | Guidelines on peri-operative management of diabetes. Anaesthesia. 2015 ;70(12):1427-40.

Pre- and intraoperative testing and treatment algorithm



Perioperative phase management

► Type 2 diabetes treated with diet alone —

1. are managed by diet alone do not require any therapy perioperatively.
2. Supplemental short- (eg, regular) or rapid acting (eg, lispro, aspart, or glulisine) insulin may be given as correction insulin in patients whose glucose levels rise over desired target.
3. It is administered every six hours.

Perioperative phase management

► Type 2 diabetes treated with oral hypoglycemic agents -

1. Sulfonylureas increase the risk of hypoglycemia.
2. Metformin is contraindicated in conditions that increase the risk of renal hypoperfusion, lactate accumulation, and tissue hypoxia.
3. Thiazolidinediones may worsen fluid retention and peripheral edema and could precipitate congestive heart failure.
4. Sodium-glucose cotransporter 2 (SGLT2) inhibitors increase the risk of hypovolemia. There have also been reports of acute kidney injury and euglycemic diabetic ketoacidosis
5. Dipeptidyl peptidase-4(DPP-4) inhibitors and GLP-1 analogs could alter gastrointestinal (GI) motility and worsen the postoperative state

Perioperative phase management

► Type 2 diabetes treated with oral hypoglycemic agents

1. Most patients with HbA1C <7.0 percent on oral agents will not need insulin for short surgical procedures.
2. Blood glucose should be monitored every two hours
3. For patients who develop hyperglycemia, supplemental short- or rapid-acting insulin is administered subcutaneously (typically every six hours)
4. Correction insulin is administered until the patient is eating and either can resume oral agents or a basal-bolus insulin regimen is initiated.
5. Most antidiabetic medications can be restarted after surgery when patients resume eating, with the exception of metformin, delayed in patients with suspected renal hypoperfusion

Perioperative phase management

- ▶ Type 1 or insulin-treated type 2 diabetes
- ▶ Short procedures
- ▶ Generally, patients on insulin can continue with subcutaneous insulin perioperatively for procedures that are not long and complex (eg, less than two hours).
- ▶ For minor, early morning procedures where breakfast is likely only delayed, patients may delay taking their usual morning (short- or rapid-acting insulin) insulin until after the surgery and before eating.
- ▶ Patients on once-daily, long-acting or basal insulin (eg, glargine, degludec) or continuous insulin infusion (insulin pump) may continue basal insulin without any change to their usual regimen.

Perioperative phase management

- ▶ Short procedures -breakfast and lunch missed
- ▶ short-acting (eg, regular) or rapid-acting (eg, lispro, aspart, glulisine) insulin are omitted on the morning of surgery.
- ▶ For patients taking two types of insulin (intermediate or long and rapid or short-acting) only in the morning, one-half to two-thirds of their usual total morning insulin dose is given.
- ▶ For patients who take insulin (intermediate or long and rapid or short-acting) two or more times per day, one-third to one-half of the total morning dose is given.
- ▶ Patients on continuous insulin infusion may continue with their usual basal infusion rate assuming that the catheter and pump can remain safely in place during the procedure.

Perioperative phase management

- ▶ Short procedures -breakfast and lunch missed
- ▶ Dextrose containing IV solution (D5 with either water or with one-half isotonic saline) at a rate of 75 to 125 cc/hour to avoid the metabolic changes of starvation.
- ▶ Blood sugars to be checked every hour and more frequently if blood glucose is <100 mg/dL or if the rate of fall is rapid.
- ▶ For patients who develop hyperglycemia, supplemental short- or rapid-acting insulin may be administered subcutaneously, based on frequently measured glucose levels.

Perioperative phase management

- ▶ **Long and complex procedures**
- ▶ **IV insulin** – Intravenous (IV) insulin is usually required for long and complex procedures like coronary artery bypass graft, renal transplant, or prolonged neurosurgical operations).
- ▶ Generally, insulin infusions should be started early in the morning prior to surgery to allow time to achieve glycemic control.
- ▶ Glucose checks should be, at minimum, every one to two hours (even shorter intervals may be required if blood glucose levels are <100 mg/dL).

Management of insulin therapy for patients undergoing short fasting period (up to a missed meal)

Type of insulin	Previous day	Day of surgery	
		Morning surgery	Afternoon surgery
Continuous subcutaneous insulin infusion (pump)	Maintain basal infusion or reduce 20–30% of baseline if history of frequent hypoglycemia		
Long-acting or basal insulin (glargine, detemir)	Morning application: maintain dose Night application: maintain dose or reduce 20–30% ^b	Morning application ^a : Maintain dose or reduce 20–30% if history of frequent hypoglycemia. Check blood glucose at admission	
Intermediate-acting insulin (NPH)	Morning application: maintain dose Night application: maintain dose or reduce 20–30% ^b	Reduce morning dose by 50% ^a ; check blood glucose at admission; keep evening dose unchanged after surgery (if already fed)	
Pre-mixed insulin	Maintain dose	Reduce morning dose intermediate insulin to 50%; omit the dose of fast/short-acting insulin. Check blood glucose at admission. Keep evening dose unchanged after surgery (if already fed)	
Fast-acting or short-acting insulin analogs	Maintain dose	Hold dose	Hold dose

^a On the day of surgery, the morning insulin should be given upon arrival at the health center.

^b History of hypoglycemia during dawn/morning.

Alberti Glucose Insulin Potassium infusion

The GIK infusion is an alternative IV insulin regimen when a VRIII is not feasible. It provides substrate, IV insulin and electrolytes via a single infusion.

The original GIK regimen was published by Alberti and Thomas in 1979. It provides a safe and effective method of giving substrate, IV insulin in the same infusion. Alterations of the original regimen remain in use today.^[28,29,30]

The original GIK regimen uses a bag containing 500 mL 10% dextrose and adds:

- 10 U short-acting insulin
- 10 mL 10% KCl.

The infusion runs at a fixed rate of 100 mL/h, providing 2 U insulin per hour.

CBG is measured 1 - 2-hourly. To increase or decrease the insulin infusion rate by 1 U/h the insulin content of the bag is changed up or down by 5 U. A new bag must be mixed each time it is decided to adjust the insulin infusion rate.

Problems with the GIK infusion are:

- labour intensive and wasteful when multiple bag changes are needed
- maintenance at 100 mL/h exceeds current standards for care of surgical patients
- 500 mL 10% dextrose bags are not available at all locations
- 10% dextrose water is not an acceptable maintenance fluid
- risk of DKA in type 1 DM if GIK infusion is stopped.

If deemed appropriate for the location, the local multidisciplinary team must adapt the GIK regimen to suite their context and address the concerns mentioned. Involve specialist input.

GIK = glucose-insulin-potassium; IV = intravenous; VRIII = variable rate intravenous insulin infusion; CBG = capillary blood glucose; DKA = diabetic ketoacidosis; DM = diabetes mellitus.

Variable Continuous insulin infusion recommendation

BG mg/dl (mM)	If BG Increased from Previous Measurement	BG Decreased from Previous Measurement by Less Than 30mg/dl	BG Decreased from Previous Measurement by Greater Than 30mg/dl
> 241 (13.4)	Increase rate by 3 U/h	Increase rate by 3 U/h	No change in rate
211–240 (11.7–13.4)	Increase rate by 2 U/h	Increase rate by 2 U/h	No change in rate
181–210 (10–11.7)	Increase rate by 1 U/h	Increase rate by 1 U/h	No change in rate
141–180 (7.8–10)	No change in rate	No change in rate	No change in rate
110–140 (6.1–7.8)	No change in rate	Decrease rate by ½ U/h	Hold insulin infusion
100–109 (5.5–6.1)	1. Hold insulin infusion 2. Recheck BG hourly 3. Restart infusion at ½ the previous infusion rate if BG > 180mg/dl (10mM)		
71–99 (3.9–5.5)	1. Hold insulin infusion 2. Check BG every 30 minutes until BG > 100mg/dl (5.5mM) 3. Resume BG checks every hour 4. Restart infusion at ½ the previous infusion rate if BG > 180mg/dl (10mM)		
70 (3.9) or lower	If BG = 50–70 (2.8–3.9mM), 1. Give 25ml D50 2. Repeat BG checks every 30 min until BG > 100mg/dl (5.5mM) If BG < 50mg/dl (2.8mM), 1. Give 50ml D50 2. Repeat BG every 15 min until > 70mg/dl (3.9mM) 3. When BG > 70mg/dl, check BG every 30 min until > 100 mg/dl (5.5mM). Repeat 50ml D50 dose if BG < 50mg/dl a second time and start D10 infusion 4. After BG > 100mg/dl (5.5mM), resume hourly BG check Restart infusion at ½ the previous infusion rate if BG > 180mg/dl (10mM)		

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Post operative management Diabetes mellitus

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Post operative phase

- ▶ Metformin should not be restarted in patients with renal insufficiency, significant hepatic impairment, or congestive heart failure
- ▶ Sulfonylureas stimulate insulin secretion and may cause hypoglycemia; they should be started only after eating has been well established.
- ▶ A step-up approach can be used for patients on high-dose sulfonylureas, starting at low doses and adjusting them until the usual dose is reached.
- ▶ Thiazolidinediones should not be used if patients develop congestive heart failure or fluid retention, or if there are any liver function abnormalities

Post operative phase

- ▶ If an insulin infusion has been used, it should be continued in patients who do not resume eating postoperatively.
- ▶ Once solid food is tolerated, the patient can be switched to subcutaneous insulin, and then the insulin infusion can be discontinued.
- ▶ Because of the short half-life of intravenous (IV) regular insulin, the first dose of subcutaneous insulin must be given before discontinuation of the IV insulin infusion.
- ▶ If intermediate or long-acting insulin is used, it should be given two to three hours prior to discontinuation
- ▶ Short - or rapid-acting insulin should be given one to two hours prior to stopping the infusion

Post operative phase

- ▶ Patients on subcutaneous insulin in the early postoperative phase, before alimentation is restarted, should continue this treatment along with IV dextrose to prevent hypoglycemia.
- ▶ Once the patient is able to tolerate food, outpatient or other insulin regimens can be titrated back.

Summary

- ▶ Hyperglycemia is a common finding in surgical patients during the perioperative period.
- ▶ Factors for poor glycemic control include counter regulatory hormones, insulin resistance, decreased glucose uptake, immune suppression, activation of cytokines
- ▶ Hyperglycemia in the perioperative period is associated with increased morbidity and increased resource utilization.
- ▶ Optimal glucose management in the perioperative period contributes to reduced morbidity.