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Perioperative Glucose Management

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HOSPITAL MEDICINE CLINICS CHECKLIST

1. Hyperglycemia in the inpatient setting is associated with poor clinical outcomes.
2. Patients with diabetes are more frequently hospitalized and more likely to undergo surgical procedures.
3. Perioperative hyperglycemia has been associated with increased morbidity, decreased survival, and increased resource utilization.
4. Current glycemic targets depend on the clinical status of patient. Target blood glucose in critically ill patients is 140-180 mg/dL (7.8-10.0 mmol/L). In non-critically ill patients targets are premeal blood glucose <140 mg/dL (7.8 mmol/L) and random blood glucose <180 mg/dL (10.0 mmol/L).
5. Assessment of preoperative diabetes regimens by considering degree of glycemic control including history of hypo- and hyperglycemia, type and duration of surgery, and dietary changes guides perioperative glycemic control regimens.
6. Obtaining a preoperative hemoglobin A1c can be helpful to determine baseline glycemic control, provided the patient has normal red blood cell kinetics and no recent blood transfusions.
7. Oral and non-insulin diabetes medications should be held until patient is eating normally and not expected to have further fluid shifts, IV contrast dye, or procedures.
8. Type 1 diabetes patients need basal (long-acting) insulin at all times, even when NPO. DKA can occur within 6 hours if basal insulin is held.
9. Prandial insulin should be held when patient is fasting.
10. Correctional insulin (supplemental or “sliding scale”) needs to be adjusted to the patient’s insulin sensitivity and should be given with meals if eating or Q4-6h if fasting, starting at blood sugars >150 mg/dL (8.3 mmol/L).
11. Patients on basal insulin at home usually need basal insulin in the hospital, with adjustments made depending on outpatient glycemic control, insulin sensitivity, medication changes, and dietary changes during hospitalization.
12. Insulin regimens involving long-acting basal insulin, short-acting insulin bolus with meals, and short-acting insulin to correct hyperglycemia independent of meals

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(basal-bolus-correctional) have been shown to be safe and effective in the perioperative patient to control glycemia and decrease complications.

DEFINITIONS

1. What is the perioperative period?

The perioperative period starts when the patient enters the hospital for surgery and lasts until the time the patient is discharged home. This period includes preoperative, intraoperative, and postoperative care.

2. What is the definition of hyperglycemia? hypoglycemia?

Hyperglycemia in the hospital setting has been defined by the American Diabetes Association (ADA) as any blood glucose level >140 mg/dL (7.8 mmol/L) (1).

Hypoglycemia in the hospital setting has been defined by the ADA as any blood glucose level <70 mg/dL (3.9 mmol/L). Severe hypoglycemia in hospitalized patients has been defined as <40 mg/dL (2.2 mmol/L), although cognitive impairment generally begins at ~ 50 mg/dL (2.8 mmol/L).

3. What is stress-induced hyperglycemia?

Stress hyperglycemia is a transient elevation in blood glucose that occurs during acute illness due to a surge in counter-regulatory hormones (glucagon, cortisol, epinephrine). This can occur in patients without diabetes, or as an exacerbation of hyperglycemia in subjects with established diabetes mellitus (2).

4. What is meant by basal, bolus (prandial), and correctional insulin?

Physiologic insulin secretion occurs as both continuous (basal) insulin secretion to cover basal metabolic insulin requirements and limit hepatic gluconeogenesis, and prandial bolus insulin secretion in response to carbohydrate ingestion.

Exogenous insulin can be given as basal, bolus (prandial), and correctional insulin regimens to mimic physiologic insulin secretion (Table 1).

- Basal insulins are long-acting and slowly absorbed; they continuously deliver insulin to suppress hepatic gluconeogenesis between meals and overnight.
- Prandial insulins are short or rapid-acting insulins given with meals to limit hyperglycemia and drive glucose into cells.
- Correctional insulin (a.k.a. supplemental or “sliding scale”) is short or rapid-acting insulin used to correct glucose excursions that occur independent of carbohydrate administration.

EPIDEMIOLOGY

1. Does perioperative glycemic control affect clinical outcomes?

Perioperative hyperglycemia has been associated with increased morbidity, decreased survival, and increased resource utilization (3-5). Patients with uncontrolled diabetes have increased surgical complications, higher mortality, and longer lengths of stay (5-7).

Post-operative point-of-care (POC) glucose >200 mg/dL (11.1 mmol/L) has been associated with increased surgical site infections after colorectal procedures (8). Similar associations

have been seen after total joint arthroplasty, infra-inguinal vascular surgery, orthopedic spinal surgery, hepato-biliary-pancreatic surgery, and mastectomy (6, 9-12).

In intensive care patients, blood glucose levels >180 mg/dL (10 mmol/L) have been associated with impaired neutrophil function, increased risk for infection, longer hospital stay, and mortality in observational studies and randomized controlled trials (4). Intensive glycemic control with intravenous insulin therapy (target glucose <150 mg/dL [8.3 mmol/L]) has been associated with decreased mortality, sternal wound infections, and shorter length of stay after cardiothoracic surgery (13-15).

Although initial single-center studies in critically ill patients in the surgical intensive care unit (ICU) showed decreased morbidity and mortality in patients treated with intensive insulin therapy with tight glycemic control (goal 80-110 mg/dL [4.4-6.1 mmol/L]) (16), subsequent multicenter trials and meta-analyses failed to find a surgical site infection or mortality benefit of intensive insulin therapy to achieve tight glycemic control (target 92-125 mg/dL [5.1-6.9 mmol/L]) (17-19); moreover, it was difficult to achieve without hypoglycemia. As such, there is insufficient evidence to support tight (target 80-120 mg/dL [4.4-6.7 mmol/L]) glycemic control over conventional control (target <180 mg/dL [10.0 mmol/L]) in the perioperative period (20). A recent randomized controlled trial of a basal-bolus-correction insulin regimen in non-critically ill general surgery patients with known diabetes (RABBIT2-Surgery) showed improved glycemic control and decreased post-operative complications (i.e. wound infection) without increased risk for severe hypoglycemia (glucose <50 mg/dL [2.8 mmol/L]) (21).

2. What are risk factors for perioperative hyperglycemia?

Diabetes (known or undiagnosed), stress from acute illness, administration of medications (i.e. glucocorticoids, octreotide, vasopressors, immunosuppressants), and enteral or parenteral nutrition (4).

3. What are hidden sources of glucose to be mindful of during the perioperative period?

Intravenous medications mixed in dextrose (i.e. antibiotics, electrolytes, dextrose-containing intravenous fluids), clear liquid diet, enteral and parenteral nutrition, and peritoneal dialysate.

4. What are risk factors for perioperative hypoglycemia?

Hypoglycemia is a real risk in hospitalized patients, especially those treated with insulin, and is often the limiting factor in achieving adequate glycemic management (22). Factors that increase risk for hypoglycemia in the hospital include altered nutritional status, heart failure, renal or liver disease, malignancy, infection, and sepsis. Iatrogenic causes of hypoglycemia including sudden reduction in corticosteroid dose while on long-acting insulin, decreased oral intake, unexpected fasting (NPO) status, inappropriate timing of short- or rapid-acting insulin in relation to meals, decreased rate of intravenous dextrose infusions, and unexpected interruptions to enteral/parental nutrition.

HISTORY AND EXAMINATION

1. What information is needed to inform decisions regarding perioperative glycemic control?

- Preoperative diabetes history (type 1 vs. type 2 vs. other/surgical, previous hospitalization for diabetes)

- Outpatient treatment regimen (oral agents, insulin, non-insulin injectables)
- Preoperative glycemic control (HbA1c, frequency of hypoglycemia) to determine baseline glycemic control, insulin sensitivity, and potential for hypoglycemia unawareness
- Timing of surgery (scheduling patients with diabetes as the first case of the day facilitates glycemic management)
- Type and estimated duration of surgery and anesthesia
- Expected dietary changes (NPO, enteral or total parenteral nutrition) before and after surgery

2. What are symptoms of poor glycemic control?

- Hyperglycemia: polyuria, polydipsia, blurred vision, weight loss, fatigue
- Hypoglycemia: sympathoadrenal symptoms (shakiness, tachycardia, diaphoresis, etc.) and neuroglycopenic symptoms (confusion, behavior change, seizure, and coma). Assess for hypoglycemia unawareness (lack of symptoms when BG <70 mg/dL [3.9 mmol/L])

ADDITIONAL TESTING

1. What blood tests should be considered in the evaluation of preoperative patients with risk factors for perioperative hyperglycemia?

A. Patient with known diabetes:

Preoperative assessment of glycemic control with preoperative hemoglobin A1C (HbA1c) or fasting blood glucose should be considered in all patients diagnosed with diabetes.

B. Patients without diabetes:

Screening for diabetes in high-risk patients with fasting blood glucose or HbA1c should be considered in those with risk factors.

United States Preventative Service Task Force (USPSTF) recommendations: Adults with blood pressure >135/80 mm Hg

ADA recommendations: Adults with BMI ≥ 25 kg/m² and have additional risk factors:

- physical inactivity
- first-degree relative with diabetes
- high-risk ethnicity
- h/o gestational diabetes or delivery of baby >9 lbs
- hypertension
- HDL <35 mg/dL or Triglycerides >250 mg/dL
- h/o polycystic ovarian syndrome
- history of cardiovascular disease
- history of impaired glucose tolerance or impaired fasting glucose.

In situations where preoperative glycemic testing was not obtained, consider checking a HbA1c in hyperglycemic inpatients without prior diagnosis of diabetes with fasting glucose

100 mg/dL (5.6 mmol/L) or random blood glucose 180 mg/dL (10 mmol/L), if not performed within the previous 3 months.

Note: HbA1c is not reliable in patients with altered red blood cell kinetics (e. g. hemolytic anemia, end-stage renal disease, thalassemia) or after blood transfusions. Point of care glucose testing before breakfast and dinner or before meals and at bedtime can help clarify the degree of hyperglycemia.

TREATMENT STRATEGIES

1. What are the goals of glycemic control in the peri-operative period?

ADA, American Association of Clinical Endocrinologists, and Society of Hospital Medicine (ADA/AACE/SHM) recommendations (4):

All patients with diabetes should have blood glucose monitoring

Blood glucose (BG) goals:

- Critically ill patients – start insulin therapy for persistent hyperglycemia with goal BG 140-180 mg/dL (7.8-10.0 mmol/L)
- Non-critically ill patients treated with insulin – premeal BG <140 mg/dL (7.8 mmol/L) and a random BG <180 mg/dL (10.0 mmol/L), provided these targets can be achieved safely.
 - If BG <100 mg/dL (5.6 mmol/L) reassess insulin regimen.
 - If BG <70 mg/dL (3.9 mmol/L), assess for factors related hypoglycemic event and modify insulin regimen.

2. When should an intravenous insulin infusion be considered?

- Type 1 diabetes patients who are NPO, perioperative, or in labor and delivery
- Any ICU patient with hyperglycemia (BG >180 mg/dL [10.0 mmol/L])
- Patients with acute myocardial infarction or acute coronary syndrome and significant hyperglycemia (BG >180 mg/dL [10.0 mmol/L])
- Patients with known diabetes s/p cardiac surgery
- Patients with diabetic ketoacidosis or hyperosmolar hyperglycemic syndromes
- Patients with poorly controlled blood glucose despite subcutaneous insulin administration

3. What insulin infusion protocol should be used?

There are multiple validated insulin infusion protocols (23-25). Insulin infusion protocols should be tailored to the capabilities and policies of the institution. A standardized and validated protocol should be used with appropriately trained staff. In light of recent data regarding tight glycemic control in the ICU setting (17), the recommended target glucose is 140-180 mg/dL (7.8-10.0 mmol/L).

4. What should be done with patients on insulin pumps?

Patients who use continuous subcutaneous insulin infusions via pump in the outpatient setting can continue their diabetes self-management in the hospital and perioperatively provided they have the mental and physical capacity to do so. Type and duration of surgery,

recovery from anesthesia, and availability of hospital personnel with expertise in insulin pump management all play a role in determining whether or not it is safe for the patient to continue insulin pump therapy in the hospital. The ADA advises that hospitals create policy and procedures delineating inpatient guidelines for pump therapy (1). Availability of hospital personnel with expertise in insulin pump therapy and daily documentation of basal rates and bolus doses are crucial to safe continuation of insulin pump therapy perioperatively.

5. What should be done with a patient's home oral diabetes medications?

There are no data on the safety and efficacy of oral diabetes medications and non-insulin injectable medications during hospitalization. As such, the recommendations have been to hold all oral agents and non-insulin injectables (Table 2) during hospitalization, especially in the perioperative setting given fluctuations in nutritional status and potential development of contraindications (i.e. imaging requiring radiocontrast dye) (4). For brief hospital stays in which the patient is eating normally and is not expected to have fluid shifts, it may be reasonable to continue oral agents.

6. What is the optimal perioperative glycemic control in non-critically ill patients?

For patients who take insulin at home, assessment of perioperative insulin dosing needs to take into consideration preoperative glycemic control (HbA1c, mean glucose), type of diabetes, complications (hypoglycemia unawareness, history of diabetic ketoacidosis), and timing of surgery (how long patient will be fasting).

As discussed in the "Definitions" section, insulin is physiologically secreted as continuous basal insulin to cover basal metabolic insulin requirements and suppress hepatic gluconeogenesis and ketosis and boluses of insulin in response to carbohydrate ingestion to limit post-prandial hyperglycemia.

- Type 1 diabetes patients have minimal to no native pancreatic insulin secretion and thus require physiologic replacement of insulin in both a basal and bolus fashion.
- Type 2 diabetes patients who require insulin may have some endogenous insulin secretion function, but in insufficient amounts (either due to insulin resistance or beta-cell insufficiency) to suppress hepatic gluconeogenesis and/or cover prandial carbohydrate loads.
- Understanding a patient's diabetes phenotype, home diabetes medication regimens, and baseline glycemic control are important to determine insulin needs and sensitivity in the hospital, especially in the perioperative period.

General recommendations for patients who take insulin prior to surgery:

- Type 1 diabetes patients need basal insulin at all times, even when NPO. Diabetic ketoacidosis (DKA) can occur within 6 hours if insulin is held.
- Patients on basal-bolus insulin regimens at home should be managed in the hospital as if they have type 1 diabetes, even if they are labeled as having type 2 diabetes.
- Hold prandial short-/rapid-acting insulin when NPO.
- Point-of-care blood glucose should be checked and documented every 4-6 hours while NPO.
- Correction (short-/rapid-acting) insulin should be given every 4-6 hours starting at blood sugars >150 mg/dL (8.3 mmol/L).

- Patients on basal insulin at home usually require some basal insulin in the hospital. The degree of dose adjustment depends on whether the long-acting insulin is thought to truly cover basal metabolic insulin requirement or to cover the basal metabolic requirement plus some component of nutritional requirement (Table 3).
- Correction insulin should be adjusted to the patient's insulin sensitivity.

For patients with type 2 diabetes on oral agents +/- insulin as an outpatient (Table 4), their non-insulin diabetes medications should be held and their blood sugars monitored before meals and bedtime if eating or every 4-6 hours if not eating. Given the association with hyperglycemia and worse perioperative outcomes, insulin should be used to achieve glycemic targets of pre-meal glucose <140 mg/dL (7.8 mmol/L) and random glucose <180 mg/dL (10.0 mmol/L). For patients with stress hyperglycemia or minimal hyperglycemia perioperatively, these goals may be achieved with correctional (sliding scale) insulin alone. For most patients with type 2 diabetes, this is best achieved with a basal-bolus-correctional insulin regimen. There is no one basal-bolus-correctional insulin protocol that fits every situation. A number of basal-bolus protocols have been reported in observational before-after studies and shown to be efficacious with regards to reaching glycemic targets (26-28).

A recently published randomized controlled trial of basal-bolus-correctional insulin regimens in non-critically ill general surgery patients with known diabetes (RABBIT2-Surgery) demonstrated improved glycemic control and decreased post-operative complications (i.e. infection) without increased risk for severe hypoglycemia (glucose < 50 mg/dL [2.8 mmol/L]) (21). This basal-bolus-correctional insulin protocol is detailed below and is a good starting point for initiating basal-bolus insulin regimens in non-critically ill perioperative type 2 diabetes patients.

Note: This protocol was implemented in patients with known diabetes, on no more than 0.4 units/kg insulin prior to admission, and excluded patients undergoing cardiac surgery, and those with clinically relevant hepatic disease, impaired renal function (serum creatinine ≥ 3.0 mg/dL), history of diabetic ketoacidosis, pregnancy, or altered mental status.

RABBIT2-Surgery Insulin Treatment protocol (21):

1. Discontinue oral antidiabetic drugs
2. Monitor blood glucose before each meal and at bedtime, or every 6 hours if patient not eating.
3. Basal-bolus therapy: Determine insulin total daily dose (TDD) = 0.5 unit/kg (0.3 unit/kg in patients ≥ 70 years of age and/or serum creatinine ≥ 2.0 mg/dL)
 - a. ½ TDD as long-acting insulin (i.e. glargine) once daily
 - b. ½ TDD as short- or rapid-acting insulin (i.e. glulisine) divided in three and given before meals. Dose held if NPO.
4. Supplemental insulin following a sliding scale for blood glucose >140 mg/dL (7.8 mmol/L) (Table 5).
5. Daily insulin adjustment based on fasting and pre-dinner blood sugars (Table 4).
6. How should hypoglycemia be treated?

It is important both to monitor and prevent hypoglycemia. Appropriate protocols should be established to recognize and treat hypoglycemia.

A protocol and order set for treatment of hypoglycemia should be ordered for any patient with diabetes, especially if on anti-hyperglycemic therapies (i.e. insulin, sulfonylureas). The hypoglycemia treatment orders should include:

- Threshold for treatment of hypoglycemia. BG <70 mg/dL (3.9 mmol/L) is used in many hospitals.
- If patient is alert and cooperative, give 15 g carbohydrates (i.e. 4 oz juice/soda, 3 crackers). Alert MD.
- If patient is not alert, give 25 gm IV dextrose (1 amp [50 cc] D50). In situations where there is no IV access, give 1 mg glucagon IM. Alert MD.
- For severe hypoglycemia (BG <50 mg/dL [2.8 mmol/L]), recurrent hypoglycemia, or association with long-acting insulin or sulfonylurea use, start continuous dextrose infusion (D5 or D10).
- Repeat blood glucose check 10-15 min intervals to assess response.
- Treatment goal is blood glucose >100 mg/dL (5.6 mmol/L).

After treatment, investigate cause and document the event and subsequent treatment adjustments.

8. When is it safe to use oral agents in surgical patients?

Once it is clear that no further procedures are planned and the patient is tolerating a normal diet, oral agents can be resumed. Caution is required in restarting metformin as contraindications may have developed since hospitalization (i.e. acute renal insufficiency, radiocontrast induced nephropathy) that may potentially increase the risk for lactic acidosis (29).

ADDITIONAL RESOURCES

- Society of Hospital Medicine Glycemic Control Resource Room - <http://www.hospitalmedicine.org/ResourceRoomRedesign/GlycemicControl.cfm>
- Diabetes Facts and Guidelines – Yale Diabetes Center - http://endocrinology.yale.edu/patient/50135_Yale%20National%20F.pdf
- AACE/ADA inpatient guidelines - <http://alt.aace.com/pub/pdf/guidelines/InpatientGlycemicControlConsensusStatement.pdf>

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REFERENCES

1. Standards of medical care in diabetes--2011. Diabetes care. Jan; 2011 34(Suppl 1):S11–61. [PubMed: 21193625]
2. Dungan KM, Braithwaite SS, Preiser JC. Stress hyperglycaemia. Lancet. May 23; 2009 373(9677): 1798–807. [PubMed: 19465235]
3. Economic costs of diabetes in the U.S. In 2007. Diabetes Care. Mar; 2008 31(3):596–615. [PubMed: 18308683]
4. Moghissi ES, Korytkowski MT, DiNardo M, Einhorn D, Hellman R, Hirsch IB, et al. American Association of Clinical Endocrinologists and American Diabetes Association consensus statement on inpatient glycemic control. Diabetes Care. Jun; 2009 32(6):1119–31. [PubMed: 19429873]

5. Umpierrez GE, Isaacs SD, Bazargan N, You X, Thaler LM, Kitabchi AE. Hyperglycemia: an independent marker of in-hospital mortality in patients with undiagnosed diabetes. *J Clin Metab Endocrinol.* Mar; 2002 87(3):978–82.
6. Marchant MH Jr, Viens NA, Cook C, Vail TP, Bolognesi MP. The impact of glycemic control and diabetes mellitus on perioperative outcomes after total joint arthroplasty. *J Bone Joint Surg Am.* Jul; 2009 91(7):1621–9. [PubMed: 19571084]
7. Gandhi GY, Nuttall GA, Abel MD, Mullany CJ, Schaff HV, Williams BA, et al. Intraoperative hyperglycemia and perioperative outcomes in cardiac surgery patients. *Mayo Clin Proc.* Jul; 2005 80(7):862–6. [PubMed: 16007890]
8. McConnell YJ, Johnson PM, Porter GA. Surgical site infections following colorectal surgery in patients with diabetes: association with postoperative hyperglycemia. *J Gastrointest Surg.* Mar 13.2009 (3):508–15. [PubMed: 19002535]
9. Malmstedt J, Wahlberg E, Jorreskog G, Swedenborg J. Influence of perioperative blood glucose levels on outcome after infrainguinal bypass surgery in patients with diabetes. *Br J Surg.* Nov; 2006 93(11):1360–7. [PubMed: 16779879]
10. Olsen MA, Nepple JJ, Riew KD, Lenke LG, Bridwell KH, Mayfield J, et al. Risk factors for surgical site infection following orthopaedic spinal operations. *J Bone Joint Surg Am.* Jan; 2008 90(1):62–9. [PubMed: 18171958]
11. Ambiru S, Kato A, Kimura F, Shimizu H, Yoshidome H, Otsuka M, et al. Poor postoperative blood glucose control increases surgical site infections after surgery for hepato- biliary-pancreatic cancer: a prospective study in a high-volume institute in Japan. *J Hosp Infect.* Mar; 2008 68(3): 230–3. [PubMed: 18294725]
12. Vilar-Compte D, Alvarez de Iturbe I, Martin-Onraet A, Perez-Amador M, Sanchez-Hernandez C, Volkow P. Hyperglycemia as a risk factor for surgical site infections in patients undergoing mastectomy. *Am J Infect Control.* Apr; 2008 36(3):192–8. [PubMed: 18371515]
13. Furnary AP, Gao G, Grunkemeier GL, Wu Y, Zerr KJ, Bookin SO, et al. Continuous insulin infusion reduces mortality in patients with diabetes undergoing coronary artery bypass grafting. *TJ Thorac Cardiovasc Surg.* May; 2003 125(5):1007–21.
14. Furnary AP, Wu Y. Clinical effects of hyperglycemia in the cardiac surgery population: the Portland Diabetic Project. *Endocr Pract.* Jul-Aug;2006 12(Suppl 3):22–6. [PubMed: 16905513]
15. Furnary AP, Zerr KJ, Grunkemeier GL, Starr A. Continuous intravenous insulin infusion reduces the incidence of deep sternal wound infection in diabetic patients after cardiac surgical procedures. *Ann Thorac Surg.* Feb; 1999 67(2):352–60. discussion 60-2. [PubMed: 10197653]
16. van den Berghe G, Wouters P, Weekers F, Verwaest C, Bruyninckx F, Schetz M, et al. Intensive insulin therapy in the critically ill patients. *N Engl J Med.* Nov 8; 2001 345(19):1359–67. [PubMed: 11794168]
17. Finfer S, Chittock DR, Su SY, Blair D, Foster D, Dhingra V, et al. Intensive versus conventional glucose control in critically ill patients. *N Engl J Med.* Mar 26; 2009 360(13):1283–97. [PubMed: 19318384]
18. Kansagara D, Fu R, Freeman M, Wolf F, Helfand M. Intensive insulin therapy in hospitalized patients: a systematic review. *Ann Intern Med.* Feb 15; 2011 154(4):268–82. [PubMed: 21320942]
19. Preiser JC, Devos P, Ruiz-Santana S, Melot C, Annane D, Groeneveld J, et al. A prospective randomised multi-centre controlled trial on tight glucose control by intensive insulin therapy in adult intensive care units: the Glucontrol study. *Intensive Care Med.* Oct; 2009 35(10):1738–48. [PubMed: 19636533]
20. Kao LS, Meeks D, Moyer VA, Lally KP. Peri-operative glycaemic control regimens for preventing surgical site infections in adults. *Cochrane Database Syst Rev.* 2009; (3):CD006806. [PubMed: 19588404]
21. Umpierrez GE, Smiley D, Jacobs S, Peng L, Temponi A, Mulligan P, et al. Randomized study of basal-bolus insulin therapy in the inpatient management of patients with type 2 diabetes undergoing general surgery (RABBIT 2 surgery). *Diabetes Care.* Feb; 2011 34(2):256–61. [PubMed: 21228246]
22. Cryer PE. Hypoglycaemia: the limiting factor in the glycaemic management of Type I and Type II diabetes. *Diabetologia.* Jul; 2002 45(7):937–48. [PubMed: 12136392]

23. Inzucchi SE. Clinical practice. Management of hyperglycemia in the hospital setting. *N Engl J Med.* Nov 2; 2006 355(18):1903–11. [PubMed: 17079764]
24. Wilson M, Weinreb J, Hoo GW. Intensive insulin therapy in critical care: a review of 12 protocols. *Diabetes Care.* Apr; 2007 30(4):1005–11. [PubMed: 17213376]
25. Ahmann AJ, Maynard G. Designing and implementing insulin infusion protocols and order sets. *J Hosp Med.* Sep; 2008 3(5 Suppl):42–54. [PubMed: 18951382]
26. Guerra YS, Das K, Antonopoulos P, Borkowsky S, Fogelfeld L, Gordon MJ, et al. Computerized physician order entry- based hyperglycemia inpatient protocol and glycemic outcomes: The CPOE-HIP study. *Endocr Pract.* May-Jun;2010 16(3):389–97. [PubMed: 20061296]
27. Maynard G, Lee J, Phillips G, Fink E, Renvall M. Improved inpatient use of basal insulin, reduced hypoglycemia, and improved glycemic control: effect of structured subcutaneous insulin orders and an insulin management algorithm. *J Hosp Med.* Jan; 2009 4(1):3–15. [PubMed: 19140173]
28. Schnipper JL, Ndumele CD, Liang CL, Pendergrass ML. Effects of a subcutaneous insulin protocol, clinical education, and computerized order set on the quality of inpatient management of hyperglycemia: results of a clinical trial. *J Hosp Med.* Jan; 2009 4(1):16–27. [PubMed: 19140191]
29. Bailey CJ, Turner RC. Metformin. *N Engl J Med.* Feb 29; 1996 334(9):574–9. [PubMed: 8569826]

Table 1

Different types of insulin and their characteristics

Long-acting (Basal)	Onset	Peak	Duration	Comments
Glargine (Lantus)	1-3 h	Minimal	24 h	
Detemir (Levemir)	1-3 h	Minimal	18-24 h	
NPH (Humulin N, Novolin N)	90 min	4-12 h	18-28 h	May be pre-mixed with short-acting insulins (regular, aspart, lispro) in 70/30, 75/25 and 50/50 ratios (% NPH/%short-acting)
Short-acting (Bolus/Prandial/Correctional)				
Regular (Humulin R, Novolin R)	30 min	2-4 h	5-8 h	
Aspart (Novolog)	10-20 min	1-3 h	3-5 h	
Lispro (Humalog)	10-20 min	1-3 h	3-5 h	
Glulisine (Apidra)	5-15 min	45-75 min	2-4 h	

Table 2

Outpatient non-insulin diabetes medications

Class	Name	Mechanism of Action	Contraindications to use
Biguanide	metformin (Glucophage)	Inhibits liver gluconeogenesis	IV contrast use, renal insufficiency, liver failure, GI intolerance, severe CHF
Sulfonylurea	glipizide (Glucotrol), glyburide (Micronase/Diabeta/Glynase), glimepiride (Amaryl), tolbutamide (Orinase)	K-ATP Channel mediated insulin release	Hypoglycemia, Renal insufficiency
Thiazolidinediones	pioglitazone (Actos)	PPAR-gamma mediated insulin sensitizer	Liver failure, renal insufficiency, CHF
Meglitinides	nateglinide (Starlix), repaglinide (Prandin)	K-ATP channel mediated insulin secretion	Liver failure
DPP4 inhibitors	sitagliptin (Januvia), linagliptin (Tradjenta), saxagliptin (Onglyza)	Inhibits breakdown of GLP-1, GIP and other DPP4 substrates	Renal insufficiency
Alpha-glucosidase inhibitors	acarbose (Precose), miglitol (Glyset)	Inhibits carbohydrate absorption in gut	GI disease/obstruction, liver disease, (Ineffective when fasting)
Amylin analogues	pramlintide (Symlin)	Slows digestion, suppresses glucagon release	Fasting
GLP-1 agonist and analogues	exenatide (Byetta), liraglutide (Victoza), exenatide extended release (Bydureon)	GLP-1-mediated insulin secretion, glucagon suppression, slowed gut transit	Fasting

Table 3

Practical tips for basal insulin adjustment

Home basal insulin regimen	Recommended preoperative adjustments
NPH sc bid	Continue or reduce bedtime dose slightly. Morning NPH should be reduced by 50% the morning of surgery and when NPO.
Long-acting insulin (glargine or detemir)	Determine whether the patient becomes hypoglycemic if a meal is skipped (a marker for tight glycemic control). If not, consider reducing the dose by 20-25% the evening prior to surgery. If so, then reduce by 50%.

Table 4

Type 2 diabetes patients on oral agents +/- insulin

- Hold non-insulin diabetes medications
- Monitor blood sugars before meals and bedtime if eating or every 4-6 hours if not eating
- Glycemic target of pre-meal glucose <140 mg/dL (7.8 mmol/L) and random glucose <180 mg/dL (10.0 mmol/L)
- Consider a basal-bolus-correction insulin regimen in most patients with type 2 diabetes
- For patients with minimal hyperglycemia or stress hyperglycemia, correctional (sliding scale) insulin may be adequate

Table 5

RABBIT2-Surgery sliding scale varied based on insulin sensitivity and nutritional status. If patient is eating, then follow “Usual” column and give supplemental rapid-acting insulin before each meal and at bedtime. If not eating, then follow the “insulin sensitive” column and give supplemental rapid-acting insulin every 6 hours. The “insulin sensitive” column may be halved for patients with type 1 diabetes.

Blood Glucose (mg/dL)	Insulin sensitive*	Usual	Insulin resistant
141-180	2	4	6
181-220	4	6	8
221-260	6	8	10
261-300	8	10	12
301-350	10	12	14
351-400	12	14	16
>400	14	16	18

* Give half of the insulin sensitive doses for lean patients with type 1 diabetes, or type 1 diabetes with hypoglycemia unawareness. Dosing may be increased as needed.

Table 6

RABBIT2-Surgery once daily insulin adjustment recommendations

	Recommended Insulin adjustment
Fasting and pre-dinner BG 100-140 mg/dL without hypoglycemia	No change
Fasting and pre-dinner BG 140-180 mg/dL without hypoglycemia	Increase TDD by 10% ($\frac{1}{2}$ of increase in basal, $\frac{1}{2}$ of increase in prandial dose)
Fasting and pre-dinner BG >180 mg/dL without hypoglycemia	Increase TDD by 20% ($\frac{1}{2}$ of increase in basal, $\frac{1}{2}$ of increase in prandial dose)
Fasting and pre-dinner BG 70-99 mg/dL without hypoglycemia	Decrease TDD by 10% ($\frac{1}{2}$ of decrease in basal, $\frac{1}{2}$ of decrease in prandial dose)
If any hypoglycemia (BG <70 mg/dL)	Decrease TDD by 20% ($\frac{1}{2}$ of decrease in basal, $\frac{1}{2}$ of decrease in prandial dose)