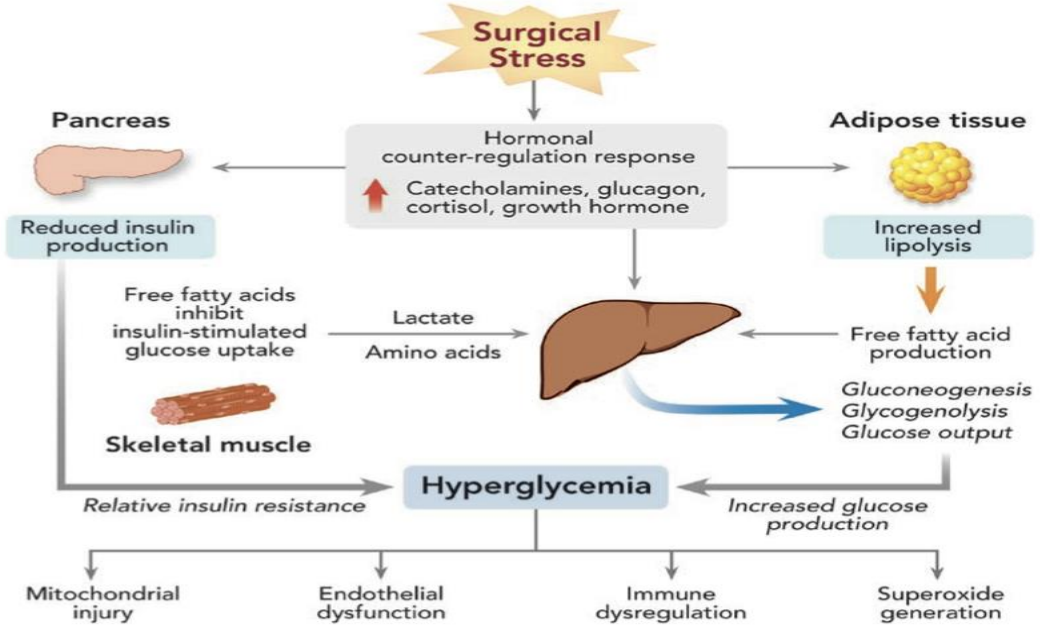
Perioperative Glycemic Control

R2 Chanathip Meerod
Lt.Col.Ekasak Chantrapannik

OUTLINE

- Metabolic consequences of surgical stress and anesthesia
- Preoperative evaluation of diabetic patient
- Preoperative glycemic management
- Perioperative glycemic control
- Diabetic crisis
- Postoperative glycemic management

Metabolic Sequences of Surgical Stress and Anesthesia



Elizabeth W. Duggan, Karen Carlson, Guillermo E. Umpierrez; Perioperative Hyperglycemia Management: **An Update**. *Anesthesiology* 2017; 126:547–560

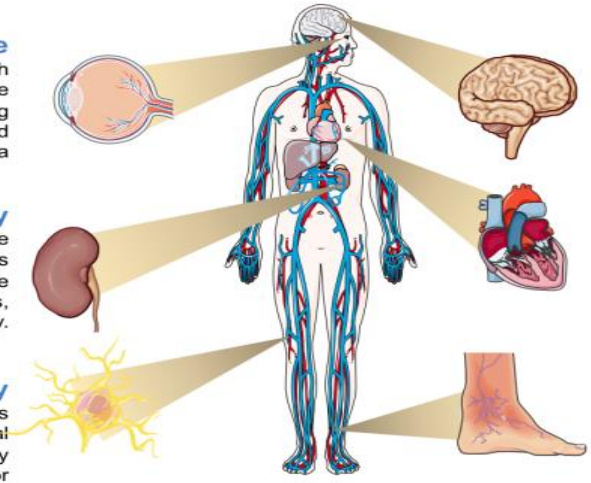
Major Complications of Diabetes

Microvascular

Eye
High blood glucose and high blood pressure can damage eye blood vessels, causing retinopathy, cataracts and glaucoma

Kidney
High blood pressure damages small blood vessels and excess blood glucose overworks the kidneys, resulting in nephropathy.

Neuropathy
Hyperglycemia damages nerves in the peripheral nervous system. This may result in pain and/or numbness. Feet wounds may go undetected, get infected and lead to gangrene.



Macrovascular

Brain
Increased risk of stroke and cerebrovascular disease, including transient ischemic attack, cognitive impairment, etc.

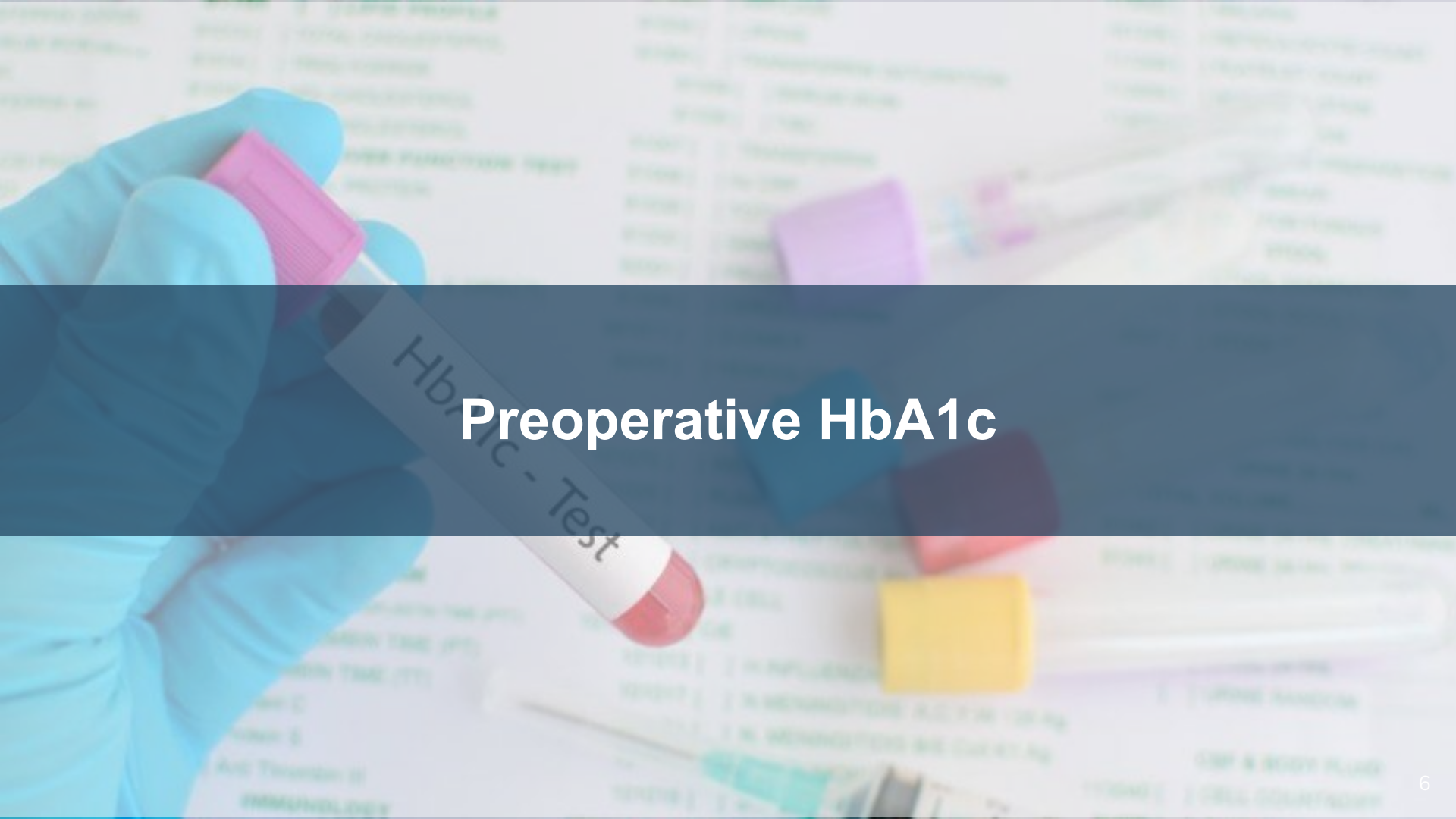
Heart
High blood pressure and insulin resistance increase risk of coronary heart disease

Extremities
Peripheral vascular disease results from narrowing of blood vessels increasing the risk for reduced or lack of blood flow in legs. Feet wounds are likely to heal slowly contributing to gangrene and other complications.

Preoperative Evaluation Of Diabetic Patient

- Level of glycemic control (BGL / HBA1c)
- Type and dose of antidiabetic drug
- Hospital admissions for glycemic control
- Hypoglycemia related information
  (occurrence & frequency , hypoglycemia manifestation , BGL which hypoglycemia occur)
- Ability of patients to monitor BGL , understand and manage BGL

Society for Ambulatory Anesthesia Consensus Statement on Perioperative Blood Glucose Management in Diabetic Patients Undergoing Ambulatory Surgery, Anesthesia & Analgesia: December 2010 - Volume 111 - Issue 6 - p 1378-1387



Preoperative HbA1c

Elevated Preoperative Hemoglobin A1c Level is Associated With Reduced Long-Term Survival After Coronary Artery Bypass Surgery

Michael E. Halkos, MD, Omar M. Lattouf, MD, PhD, John D. Puskas, MD, Patrick Kilgo, MS, William A. Cooper, MD, Cullen D. Morris, MD, Robert A. Guyton, MD, and Vinod H. Thourani, MD

- 3201 patients undergoing primary , elective CABG
- January 2002 to December 2006

Table 2. Unadjusted Kaplan-Meier Survival Estimates: Effect of Hemoglobin A1c (HbA1c) and Diabetes Mellitus on Survival

Subgroup	1-Year Survival	3-Year Survival	5-Year Survival	Log-Rank *p* Value
All patients				
HbA1c < 7.0 (n = 2,360)	0.968	0.922	0.876	0.001
HbA1c ≥ 7.0 (n = 841)	0.948	0.888	0.823	
Yes, diabetes (n = 1,285)	0.953	0.877	0.811	<0.001
No, diabetes (n = 1,916)	0.969	0.937	0.898	
Diabetic patients				
HbA1c < 7.0 (n = 538)	0.954	0.859	0.801	0.37
HbA1c ≥ 7.0 (n = 747)	0.952	0.890	0.819	
Insulin control (n = 399)	0.930	0.838	0.783	0.006
Noninsulin control (n = 886)	0.963	0.894	0.824	

GYNECOLOGIC ONCOLOGY

Preoperative HBA1c and risk of postoperative complications in patients with gynaecological cancer

C. Iavazzo[1] · M. McComiskey[1] · M. Datta[1] · M. Ryan[1] · J. Kiernan[1] · B. Winter-Roach[1] · R. Slade[1] · M. Smith[1]

- prospective cohort study 1 August 2012 through 31 August 2014

Table 2 Broken down by HBA1c status alone (p value compared to HBA1c <42 mmol/mol cohort)

	HBA1c (mmol/mol)			
	<42 ($n = 225$)	42–47 ($n = 44$)	48–64 ($n = 23$)	>64 ($n = 8$)
Mean BMI (kg/m^2)	28.7	32.0 ($p = 0.002$)*	34.0 ($p = 0.008$)*	34.7 ($p = 0.09$)
Mean length of stay (days)	6.0	8.9 ($p = 0.30$)	7.3 ($p = 0.33$)	5.8 ($p = 0.89$)
Infective complications (%)	38/225 (16.9)	10/44 (22.7) ($p = 0.35$)	10/23 (43.5) ($p = 0.002$)*	3/8 (37.5) ($p = 0.13$)
Non-infective complications (%)	25/225 (11.1)	10/44 (22.7) ($p = 0.04$)*	6/23 (26.1) ($p = 0.04$)*	1/8 (12.5) ($p = 0.90$)
Re-admission (%)	10/225 (4.4)	2/44 (4.5) ($p = 0.98$)	4/13 (30.8) ($p = 0.01$)*	2/8 (25) ($p = 0.01$)*

* Statistically significant ($p < 0.05$)

Original Article Clinics in Orthopedic Surgery 2013;5:118-123 • http://dx.doi.org/10.4055/cios.2013.5.2.118

Relations between Long-term Glycemic Control and Postoperative Wound and Infectious Complications after Total Knee Arthroplasty in Type 2 Diabetics

Hyuk-Soo Han, MD, Seung-Baik Kang, MD

Department of Orthopedic Surgery, Seoul Metropolitan Government Seoul National University Boramae Medical Center, Seoul, Korea

Table 3. Logistic Regression Analysis of Preoperative Variables with Wound Complications

Factor	Adjusted odds ratio (95% CI)
Body mass index	0.89 (0.35–1.28)
Hypertension	1.00 (0.94–1.05)
Volume of blood transfusion	0.99 (0.97–1.01)
Antibiotics-impregnated cement	0.70 (0.00–181.86)
Operation time	1.01 (1.00–1.03)
Hemoglobin A1c ≥ 8%	6.07 (1.12–33.0)

- 167 TKAs performed in 115 patients with T2DM
- Retrospectively reviewed
- January 2001 through March 2007

PAPER

Long-term Glycemic Control and Postoperative Infectious Complications

Annika S. Dronge, MD; Melissa F. Perkal, MD; Sue Kancir, RN; John Concato, MD, MPH; Michaela Aslan, PhD; Ronnie A. Rosenthal, MS, MD

- Retrospective observational study
- Veterans Affairs Connecticut Healthcare
- Jan 1 2000, through Sep 30,2003

Table 5. Logistic Regression Analysis of Preoperative Variables

Factors	Unadjusted OR (95% CI)	*P* Value	Adjusted OR (95% CI)	*P* Value
Age	1.04 (1.01-1.06)	.01	1.03 (1.00-1.06)	.03
Race	1.59 (0.83-3.05)	.16		
ASA class	3.06 (1.80-5.22)	<.001	1.87 (1.02-3.41)	.04
ADL assessment	2.68 (1.58-4.57)	<.001	1.83 (0.98-3.44)	.06
Case status	2.11 (1.26-3.55)	.005	1.78 (0.99-3.19)	.05
Operation length	1.00 (1.00-1.01)	.003	1.004 (1.002-1.007)	<.001
Wound classification	1.62 (1.01-2.60)	.05	1.80 (1.06-3.05)	.03
Diabetic therapy	1.26 (0.79-2.03)	.33		
HbA_{1c}	1.95 (1.16-3.27)	.02	2.13 (1.23-3.70)	.007

A1c	Average BGL
5.0	95
6.0	125
7.0	155
8.0	185
9.0	215
10.0	245
11.0	275

Estimated BGL

BGL = (HbA1c - 2) x 30

Preoperative HbA1c

- Indicator of blood glucose control over previous 3 months
- Correlates with perioperative morbidity and mortality in diabetics and non-diabetics
- Consider checking for BMI ≥ 30 kg/m² and age ≥ 40
- Target ≤ 8.5% (elective surgery)
  - higher values for patients at risk of hypoglycemia
- HbA1c < 7% associated with decrease infectious complication

American diabetic association : diabetic care 2020;43:s193-202

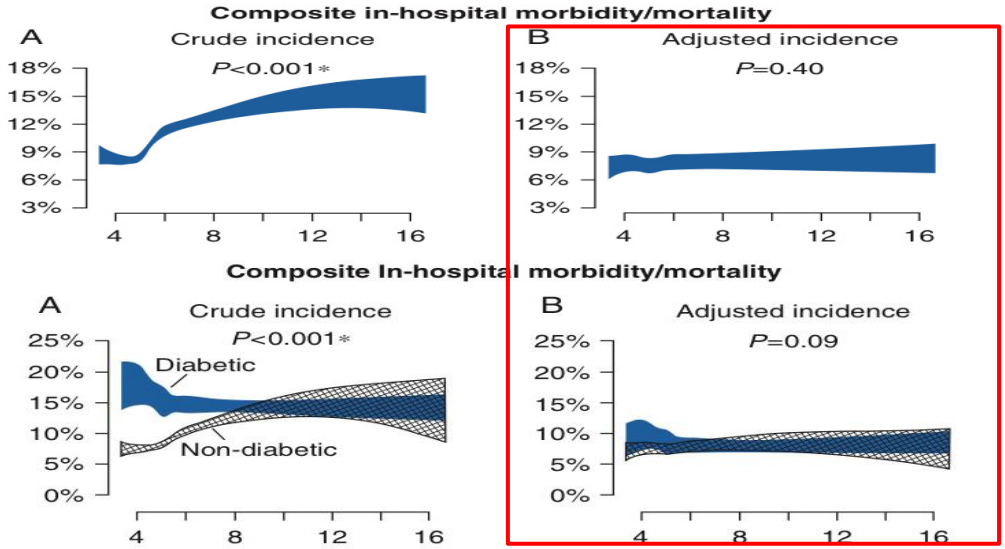
Preoperative BGL

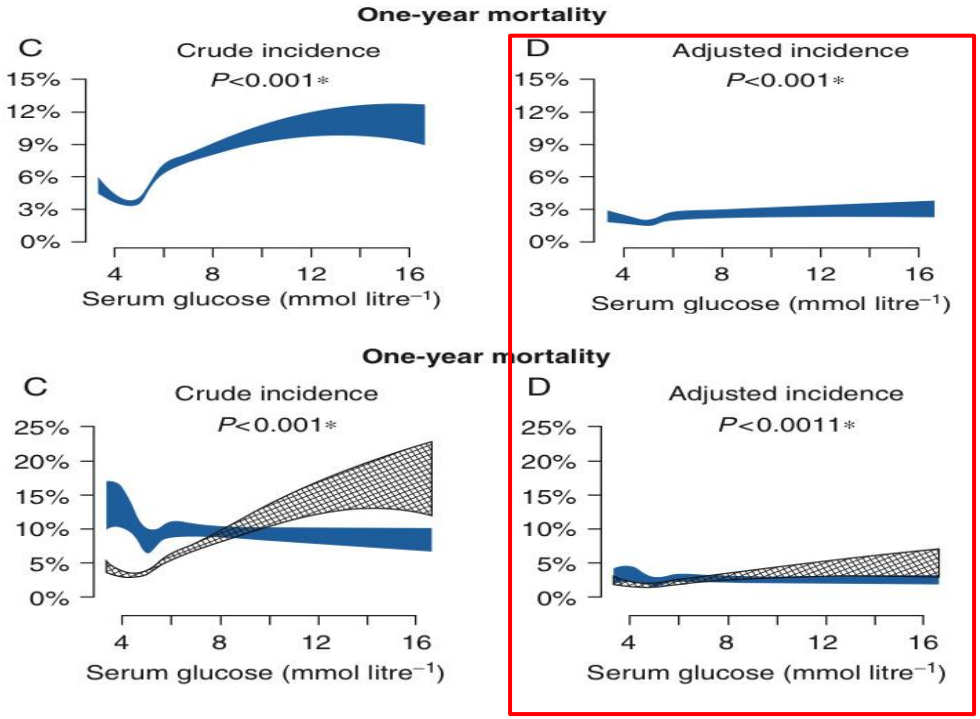
British Journal of Anaesthesia **112** (1): 79–88 (2014)
Advance Access publication 5 September 2013 · doi:10.1093/bja/aet297

BJA

Preoperative blood glucose concentrations and postoperative outcomes after elective non-cardiac surgery: an observational study†

B. B. Abdelmalak[1,2]*, J. Knittel[3], J. B. Abdelmalak[4], J. E. Dalton[5,2], E. Christiansen[4], J. Foss[1], M. Argalious[1], R. Zimmerman[6] and G. Van den Berghe[7]




One-year mortality
C
Crude incidence
P<0.001*
15%
12%
9%
6%
3%
0%
4
8
12
16
Serum glucose (mmol litre⁻¹)
D
Adjusted incidence
P<0.001*
15%
12%
9%
6%
3%
0%
4
8
12
16
Serum glucose (mmol litre⁻¹)
One-year mortality
C
Crude incidence
P<0.001*
25%
20%
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Serum glucose (mmol litre⁻¹)
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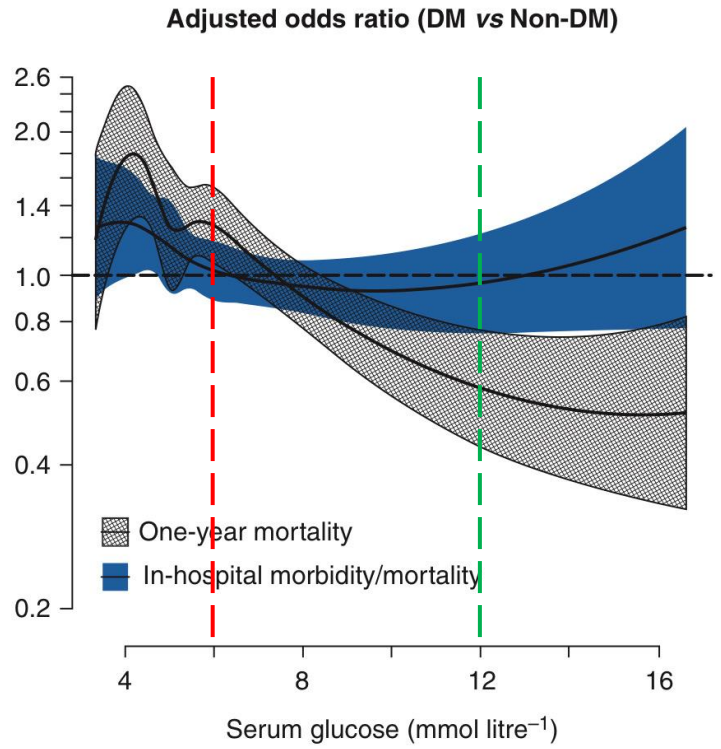
Serum glucose (mmol litre⁻¹)



- Diagnosed diabetes patients and preoperative euglycemia had worse1 yr. mortality than those with out diabetes in same BG

  [95% CI of 1.27(1.06,1.53) at 108 mg/dl , P=0.003]

- Hyperglycemic patients with DM displayed a significantly lower 1 yr. mortality than hyperglycemic patient without DM

  [95% CI of 0.58(0.44,0.77) at 216 mg/dl , P<0.001]

Surgical Neurology International

OPEN ACCESS

Editor-in-Chief: James I. Ausman, MD, PhD University of California, Los Angeles, CA, USA

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Original Article

Preoperative hyperglycemia and complication risk following neurosurgical intervention: A study of 918 consecutive cases

Matthew C. Davis, John E. Ziewacz[1,2], Stephen E. Sullivan[3], Abdulrahman M. El-Sayed[3,4,5]

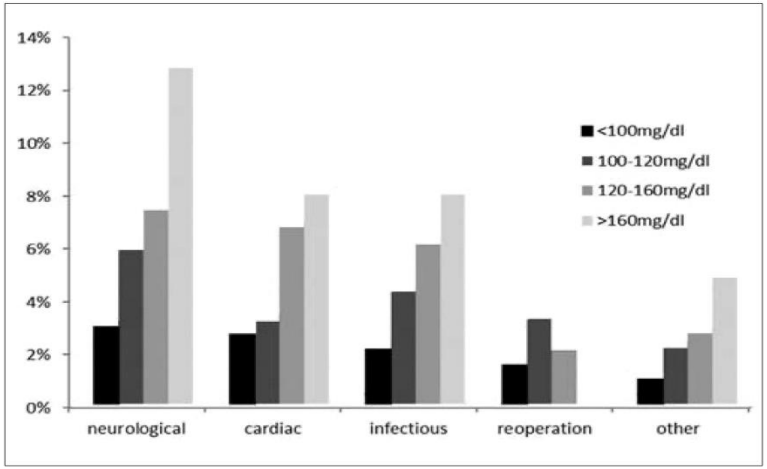

Figure 1: 30-day postoperative complication rates as a function of preoperative blood glycemia values among 918 neurosurgical patients at the University of Michigan Hospitals

- 918 craniotomy or spine-related neurosurgical cases
- University of Michigan Hospital

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Preoperative hyperglycemia and complication risk following neurosurgical intervention: A study of 918 consecutive cases

Matthew C. Davis, John E. Ziewacz[1,2], Stephen E. Sullivan[3], Abdulrahman M. El-Sayed[3,4,5]

Table 2: Analysis of variance between explanatory covariates and post-surgical hospital and intensive care unit stay among 918 patients undergoing neurosurgical intervention at the University of Michigan Hospitals

Patient descriptives	Intensive care unit stay			Hospital stay		
	Days	SD	*P*	Days	SD	*P*
Total	2.0	4.6		6.6	9.4	
Pre-op glucose			<0.001			<0.001
<100	1.2	2.9		5.2	8.6	
100–120	2.0	4.3		6.9	9.3	
121–160	3.7	6.7		9.4	10.5	
>160	4.3	7.6		10.5	11.3	

Preoperative BGL

- Correlates with postoperative morbidity and mortality in diabetics and non-diabetics
- One year mortality was significantly related to preoperative blood glucose
- Preoperative BGL > 120 mg/dl was associated with increased length of stay
- Optimize preoperative BGL : 6 – 12 mmol/L (108 - 216 mg/dl)

Perioperative Morbidity And Mortality Of Hyperglycemia

- Cardiac complication
- Infection , delay wound healing
- Sepsis and multiorgan failure
- Ketoacidosis and hyperosmolar state
- Increasing hospital length of stay & ICU admission
- Overall healthcare costs

CLINICAL CONCEPTS AND COMMENTARY

Jerrold H. Levy, M.D., F.A.H.A., F.C.C.M., Editor

Perioperative Hyperglycemia Management

An Update

Elizabeth W. Duggan, M.D., Karen Carlson, M.D., M.B.A., Guillermo E. Umpierrez, M.D., C.D.E.

This article has been selected for the ANESTHESIOLOGY CME Program. Learning objectives and disclosure and ordering information can be found in the CME section at the front of this issue.

Society for Ambulatory Anesthesia Consensus Statement on Perioperative Blood Glucose Management in Diabetic Patients Undergoing Ambulatory Surgery

Girish P. Joshi, MB, BS, MD, FFARSCI,* Frances Chung, MD, FRCPC,† Mary Ann Vann, MD,‡ Shireen Ahmad, MD,§ Tong J. Gan, MD, FRCA,‖ Daniel T. Goulson, MD,¶ Douglas G. Merrill, MD,# and Rebecca Twersky, MD, MPH**

Systematic review of the literature : the protocol recommended by Cochrane collaboration

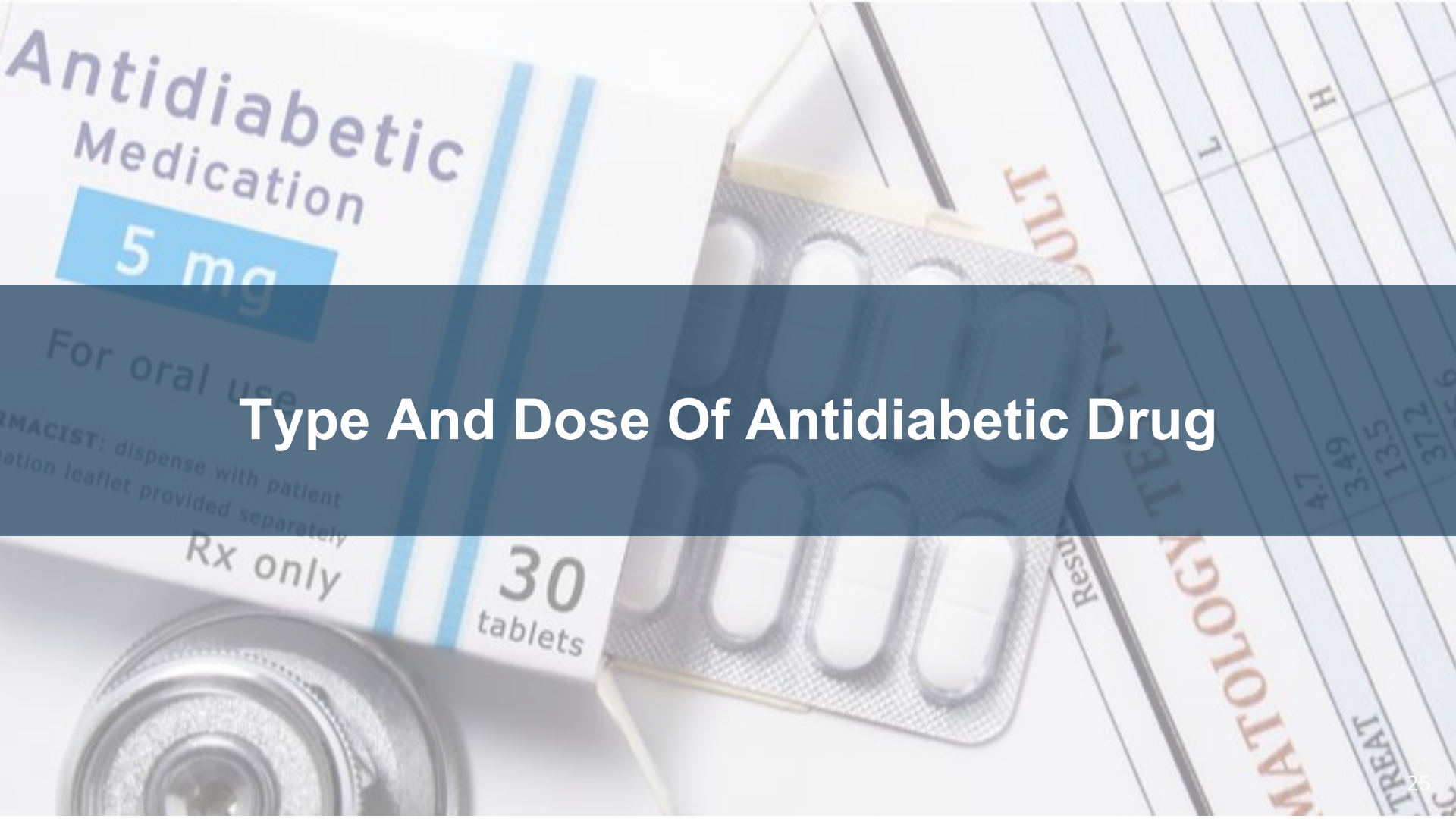
- **Meta-analysis guide-lines** [*1 systematic review , 9 trials , 5 RCT*]

Table 1. Level of Evidence

Category 1	High-level evidence (i.e., high-powered randomized clinical trials or meta-analyses), and the panel has reached uniform (near unanimous) consensus.
Category 2A	Lower-level evidence (phase II or large cohort studies), but despite the absence of higher-level studies, there is uniform consensus that the recommendation is appropriate. It is assumed that these recommendations may be modified as higher-level evidence becomes available.
Category 2B	Lower-level evidence, and there is nonuniform consensus that the recommendation should be made. This suggests to the practitioner that there could be more than one approach to the question in statement.
Category 3	A major disagreement among the panel members. The level of evidence is not pertinent in this category, because experts can disagree about the significance of high-level trials. This category directs the practitioners that there is a major interpretation issue in the data and directs them to the manuscript for an explanation of the controversy.

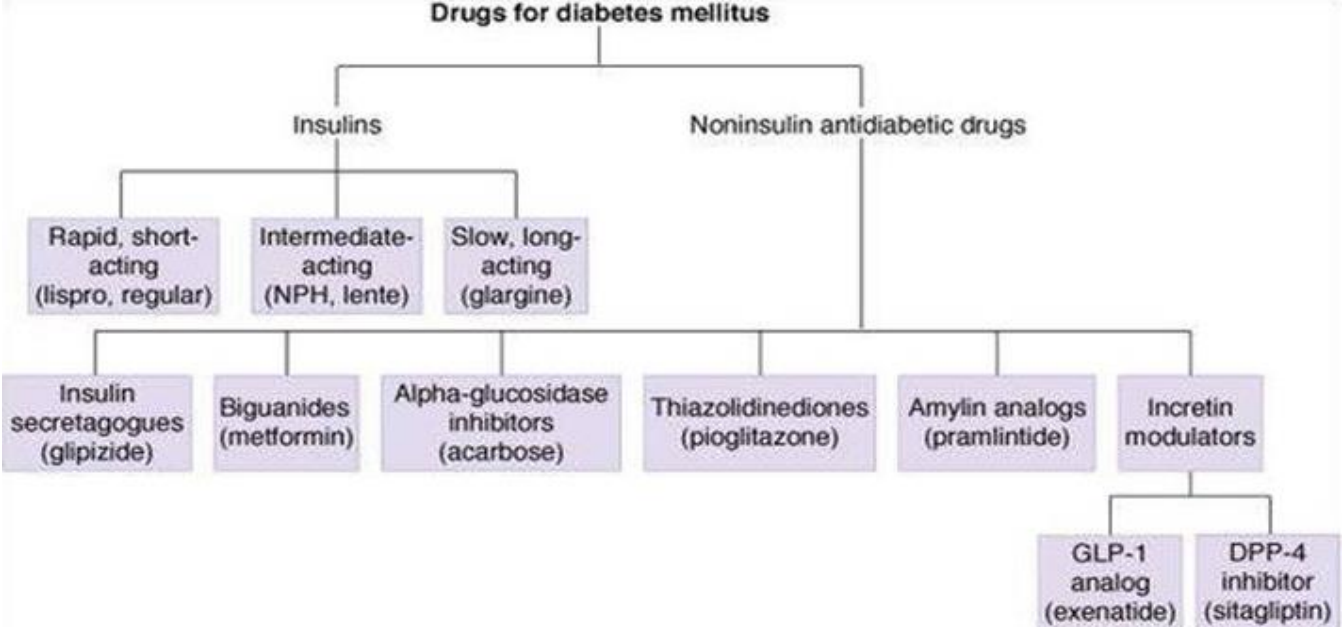
Specific considerations in diabetic outpatients

- **First case of the day**
  Minimize starvation time
- **Adequate preoperative hydration**
  Consumption of water until 2 hr. before surgery
- **Optimize intraoperative hydration**
  Crystalloid 20-40 ml/kg bolus if no contraindication
- **Aggressive PONV prophylaxis**
  dexamethasone 4 mg is safe (2A)
- **Prompt return to their meal and normal dosing regimen**



Type And Dose Of Antidiabetic Drug

Oral and non-insulin injectable anti-diabetic medications



Oral And Non-insulin Injectable Anti-diabetic Medications

Drug class: generic (trade name)	Mechanism of action	Half-life (hours)	Adverse effects
Biguanides Metformin (Glucophage) Metformin extended release	Decrease hepatic gluconeogenisis, increase insulin sensitivity.	6–18 24	Diarrhea, nausea, vomiting, lactic acidosis (avoid in renal & liver disease, congestive heart failure).
Sulphonylureas Chlorpropamide (Diabenese) Tolbutamide (Orinase) Glimepride (Amaryl) Glipizide (Glucotrol) Glyburide (DiaBeta, Micronase)	Stimulate insulin secretion, decrease insulin resistance.	2–10	Hypoglycemia (caution in elderly & renal disease). Gastrointestinal disturbance.
Meglitinides Repaglinide (Prandin) Nateglinide (Starlix)	Stimulate pancreatic insulin secretion.	1	Hypoglycemia, but less common in comparison with sulfonylureas.
Thiazolidindiones Rosiglitazone (Avandia) Pioglitazone (Actos)	Regulate carbohydrate and lipid metabolism, reduce insulin resistance and hepatic glucose production.	3–8	Fluid retention, increased cardiac risk including congestive heart failure. Hepatotoxicity.
Alpha-glucosidase inhibitors Acarbose (Precose) Miglitol (Glyset)	Reduce the intestinal absorption of ingested glucose.	2–4	Gastrointestinal irritation, flatus.
Dipeptidyl peptidase-4 (DPP-4) inhibitors Sitagliptin (Januvia) Saxagliptin (Onglyza)	Reduces breakdown of gastrointestinal hormone-incretins (glucagon-like peptide type-1, enhance insulin secretion, decrease glucagon.	8–14	Infection.

Society for Ambulatory Anesthesia Consensus Statement on Perioperative Blood Glucose Management in Diabetic Patients Undergoing Ambulatory Surgery, Anesthesia & Analgesia: December 2010 - Volume 111 - Issue 6 - p 1378-1387

Oral And Non-insulin Injectable Anti-diabetic Medications

Table 3. Noninsulin Injectables

Drug class: generic (trade name)	Mechanism of action	Half-life (hours)	Adverse effects
Exenatide (Byetta)	Synthetic form of exendin 4, which has actions similar to glucagon-like peptide type-1 (GLP-1). Suppresses glucagon secretion and hepatic glucose production. Suppresses appetite. Delays gastric emptying.	6–10	Nausea, vomiting, weight loss, hypoglycemia when combined with sulfonylureas.
Pramlintide (Symlin)	Synthetic form of amylin, a naturally occurring peptide that is cosecreted with insulin by beta cells. Suppresses postprandial glucagon secretion and hepatic glucose production. Enhances the effects of insulin. Suppresses appetite. Delays gastric emptying.	2–4	Nausea, vomiting, weight loss, hypoglycemia with insulin.

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Metformin : Preoperative Management

- **Metformin can be taken the day before surgery**

SAMBA consensus statement : Joshi GP , et al.Anest Analg 2010;111:1378-87 (2A)
Joint British diabetes societies guideline

- **Metformin may be discontinued 24-48 hr. before surgery in renal impairment (GFR<45ml/min) who might receive IV contrast**

Chan NN,Fether MD.Metformin and perioperative risk. Br J Anaesth 1999;83:540-1
FDA drug safety : http://WWW.fda.gov/drugs/drugsafety/ucm493244.htm

Metformin : Preoperative Management

- **Metformin is not associated with increased risk perioperative lactic acidosis**

SAMBA consensus statement : Joshi GP , et al.Anest Analg 2010;111:1378-87 (2)
Risk of fatal and nonfatal lactic acidosis with metformin in T2DM. Cochrane database syst Rev 2010 Jan 20

- **Oral antidiabetics and noninsulin injectables should not be taken on the day of surgery until normal food intake is resumed**

SAMBA consensus statement : Joshi GP , et al.Anest Analg 2010;111:1378-87 (2A)

- **Sulfonylurea and insulin secretagogues be discontinued the day of surgery**

American diabetes association. Standards of medical care in diabetes-2009
SAMBA consensus statement : Joshi GP , et al.Anest Analg 2010;111:1378-87 (2A)

Metformin : Preoperative Management

Recent Metformin Ingestion Does Not Increase In-Hospital Morbidity or Mortality After Cardiac Surgery

Andra I. Duncan, MD*
Colleen G. Koch, MD, MS*
Meng Xu, MS†
Mariel Manlapaz, MD*
Brian Batdorf, DO, PhD*
Grzegorz Pitas, MD*
Norman Starr, MD*

BACKGROUND: Perioperative treatment of type 2 diabetes with metformin, an oral hypoglycemic drug, is thought to increase the risk of life-threatening postoperative lactic acidosis. In contrast, metformin improves serum glucose control and has beneficial cardiovascular effects, which may decrease the risk of adverse outcomes. In this investigation we sought to determine the influence of metformin treatment on mortality and morbidity compared with treatment with other oral hypoglycemic drugs in diabetic patients undergoing cardiac surgery.

METHODS: In this retrospective investigation, 1284 diabetic patients, with recent oral hypoglycemic ingestion (presumed to be 8–24 h preoperatively), underwent cardiac surgery from 1994–2004. Propensity scores were calculated from a logistic model which included baseline characteristics and perioperative variables. Four-hundred-forty-three (85%) of the metformin-treated patients were matched on nearest propensity score using greedy matching techniques with 443 nonmetformin-treated patients. Postoperative outcomes were compared between matched metformin- and nonmetformin-treated patients.

RESULTS: In-hospital mortality, cardiac, renal, and neurologic morbidities were similar between groups. Metformin-treated patients had less postoperative prolonged tracheal intubation [OR (95% CI), 0.3 (0.1, 0.7), $P = 0.003$], infection [0.2 (0.1, 0.7), $P = 0.007$] and overall morbidities [0.4 (0.2, 0.8), $P = 0.005$].

CONCLUSIONS: These data suggest that recent metformin ingestion is not associated with increased risk of adverse outcome in cardiac surgical patients. Alternatively, metformin treatment may have beneficial effects.

(Anesth Analg 2007;104:42–50)

Preoperative Oral Antidiabetic Management

Table 2. Oral Medication Use the Day Before and Day of Surgery

Oral Medication for Elective Surgery	Day Before Surgery	Day of Surgery if Normal Oral Intake Anticipated Same Day and Minimally Invasive Surgery	Day of Surgery if Reduced Postoperative Oral Intake or Extensive Surgery, Anticipated HD Changes and/or Fluid Shifts
Secretagogues	Take	Hold	Hold
SGLT-2 Inhibitors	Hold	Hold	Hold
Thiazolidinediones	Take	Take	Hold
Metformin	Take*	Take*	Hold
DPP-4 Inhibitors	Take	Take	Take

*Hold if patient having a procedure with intravenous contrast dye administration, particularly in those with glomerular filtration rate < 45 ml/min.[56]

DPP = dipeptidyl peptidase-4; HD = hemodynamic; SGLT = sodium glucose cotransporter-2.

Preoperative insulin therapy based on patient status

- **History of hypoglycemia at night or morning**
- **Insulin and oral antidiabetic combination (intermediate acting insulin)**
- **Tight glycemic control or wide range of daily blood glucose with complex insulin regimen**
- **Patient's ability to check blood glucose and follow instruction**
- **Time of surgery & expected time to return regular diet**

Joshi GP , et al.Anest Analg 2010;111:1378-87

Pharmacology of insulin

Drug class: generic (trade name)	Onset	Peak effect	Duration
Short acting and rapid acting			
Regular (Novolin R, Humulin R)	30–60 minutes	2–4 hours	6–8 hours
Lispro (Humalog)	5–15 minutes	30–90 minutes	4–6 hours
Aspart (Novolog)	5–15 minutes	30–90 minutes	4–6 hours
Glulisine (Apidra)	5–15 minutes	30–90 minutes	4–6 hours
Intermediate acting			
NPH (Novolin N, Humulin N-NF)	2–4 hours	4–10 hours	10–16 hours
Zinc insulin (Lente)	2–4 hours	4–10 hours	12–20 hours
Extended zinc insulin (Ultralente)	6–10 hours	10–16 hours	18–24 hours
Long acting (peakless)			
Glargine (Lantus)	2–4 hours	None	20–24 hours
Detemir (Levemir)	2–4 hours	None	20–24 hours
Mixed insulins (NPH + regular)			
70% NPH/30% regular (Novolin 70/30, Humulin 70/30)	30–90 minutes	Dual	10–16 hours
50% NPH/50% regular (Humulin 50/50)	30–90 minutes	Dual	10–16 hours
Mixed insulins (intermediate-acting + rapid-acting analogs)			
70% Aspart Protamine suspension/30% Aspart (Novolog mix 70/30)	5–15 minutes	Dual	10–16 hours
75% Lispro Protamine suspension/25% Lispro (Humalog mix 75/25)	5–15 minutes	Dual	10–16 hours
50% Lispro Protamine suspension/50% Lispro (Humalog mix 50/50)	5–15 minutes	Dual	10–12 hours

Society for Ambulatory Anesthesia Consensus Statement on Perioperative Blood Glucose Management in Diabetic Patients Undergoing Ambulatory Surgery, Anesthesia & Analgesia: December 2010 - Volume 111 - Issue 6 - p 1378-1387

Pharmacology of insulin

Insulin type	onset	Peak effect	duration
Ultra-short acting Lispro , Aspart , Glulisine	5-15 min	30-90 min	4-6 hr.
Short acting Regular (HR)	30-60 min	2-4 hr.	6-8 hr.
Intermediate-acting NPH(HN), Lente	2-4 hr.	4-10 hr.	10-16 hr.
Long-acting Glargine, Detemir	2-4 hr.	none	20-24 hr.

Joshi GP , et al.Anest Analg 2010;111:1378-87

Preoperative insulin management

Table 5. Instructions to Patient Regarding Preoperative Insulin and Noninsulin Injectable Administration

Insulin regimen	Day before surgery	Day of surgery	Comments
Insulin pump	No change	No change	Use "sick day" or "sleep" basal rates.
Long-acting, peakless insulins	No change	75%–100% of morning dose	Reduce nighttime dose if history of nocturnal or morning hypoglycemia. On the day of surgery, the morning dose of basal insulin may be administered on arrival to the ambulatory surgery facility.
Intermediate-acting insulins	No change in the daytime dose. 75% of dose if taken in the evening	50%–75% of morning dose	See the comments for long-acting insulins.
Fixed combination insulins	No change	50%–75% of morning dose of intermediate-acting component	Lispro-protamine only available in combination; therefore use NPH instead, on day of surgery. See the comments for long-acting insulins.
Short- and rapid-acting insulin	No change	Hold the dose	
Noninsulin injectables	No change	Hold the dose	

Society for Ambulatory Anesthesia Consensus Statement on Perioperative Blood Glucose Management in Diabetic Patients Undergoing Ambulatory Surgery, Anesthesia & Analgesia: December 2010 - Volume 111 - Issue 6 - p 1378-1387

Preoperative insulin management

Type of insulin	Day before surgery	Day of surgery	Comment
Insulin pump	No change	No change	Use six day or sleep rate
Long-acting	No change	75%-100% AM	PM dose 80% if history of nocturnal or morning hypoglycemia
Intermediate-acting	No change in AM dose 75% PM dose	50-75% AM	AM dose may be given on arrival to facility
Fixed combination	No change	50-75% AM	Lispro-protamine available in combination, use NPH
Short/Ultra-short acting	No change	Hold the dose	

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Goal of intraoperative glycemic control

- **Maintain of intraoperative blood glucose levels**
  - well controlled DM : BGL 140- 180 mg/dl or 10 mmol/L (2A)

  - poorly controlled DM : BGL maintained around their preoperative baseline (2A)

  - start insulin therapy for persistent hyperglycemia BGL > 180 mg/dl
  : the joint British diabetes societies guideline

- **Avoid hypoglycemia**
  - avoid aggressive strategies
  (altered counterregulatory response resulting hypoglycemic symptom)

Joshi GP , et al.Anest Analg 2010;111:1378-87

Goal of intraoperative glycemic control

- **Minimized interrupt of patient's therapy**
- **Optimal blood glucose monitoring**

- Checked on the patients arrival to before surgery and before discharge (2A)

- Intraoperative performed every 1-2 hr. (duration of procedure, type of insulin)

- Poor controlled DM : maintain BGL at preoperative rather than temporarily normalizing it

- **Prompt resumption of enteral intake and antidiabetic therapy**

Joshi GP , et al.Anest Analg 2010;111:1378-87

Perioperative insulin administration

- **Type of insulin**
  Regular insulin VS rapid-acting insulin

- **Route of insulin administration**
  Subcutaneous VS intravenous

- **Dosing schedule**
  Sliding scale
  Rules of 1500/1800

Joshi GP , et al.Anest Analg 2010;111:1378-87

Intraoperative insulin

Rapid-acting insulin

- Short duration procedure (< 4 hr.)
- Ambulatory setting : rapid-acting insulin preferred over RI (2A)
- BG testing should occur at least 2 hr.
- Rapid-acting should not be dosed more frequently than 2 hr. to minimize risk of insulin stacking

Regular insulin

- Operative time > 4 hr.
- Anticipated hemodynamic changes, significant fluid shifts, changes in temperature

Joshi GP , et al.Anest Analg 2010;111:1378-87

Route of administration

- **Subcutaneous rapid-acting insulin provide similar control as IV infusion RI (2A)**

  Umpierrez : Am J Med 2004 ; Diabetes care 2004

- **IV infusion RI used to maintain BG in critically ill patients**

- **Subcutaneous route for noncritical patients**

  (concern about stacking of repeated doses mar result hypoglycemia)

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Dosing schedule

- **Sole use of sliding scale, without considering insulin resistance is strongly discouraged**
- **Assumes similar insulin sensitivities or no change in insulin sensitivity during different stages of acute illness**
- **Correction-dose based on total daily dose or body weight**

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Dose determination

- Insulin dose = BGL – 100 / insulin sensitivity factor
- Insulin sensitivity factor : how much blood glucose decrease for each unit of bolus insulin
- ISF = 1500 / TDD (regular insulin)
  = 1800 / TDD (rapid-acting insulin)

Joshi GP , et al.Anest Analg 2010;111:1378-87

Calculation

RI regimen : premeal [4U - 4U - 4U] – 13 U basal

TDD = 4U+4U+4U+13U = 25 U

ISF for RI = 1500/25 = 60

1 U of RI ↓ BS 60 mg/dl

ISF for rapid acting = 1800/25 = 72

1 U of rapid acting ↓ BS 72 mg/dl

Insulin therapy in naïve patients

- **Insufficient evidence of literature to guidance**
- **Insulin therapy may be considered in BGL increased significantly (severe dehydration , DKA , HHS)**
- **Caution in ambulatory surgery patients**
- **Required close monitoring**

Joshi GP , et al.Anest Analg 2010;111:1378-87

Subcutaneous insulin scale

Table 5. Correctional Subcutaneous Insulin Scale Day of Surgery and Postoperative Surgical Ward Care

Blood Glucose mg/dl (mM)	Insulin Sensitive* Age > 70 yr, GFR < 45 ml/min, No History of Diabetes	Usual Insulin	Insulin Resistant* BMI > 35 kg/m2, Home TDD Insulin > 80 U, Steroids > 20 mg Prednisone Daily
141–180 (7.7–10)	0	2	3
181–220 (10–12.2)	2	3	4
221–260 (12.2–14.4)	3	4	5
261–300 (14.4–16.6)	4	6	8
301–350 (16.6–19.4)	5	8	10
351–400 (19.4–22.2)	6	10	12
> 400 (> 22.2)	8	12	14

*If the patient falls into more than one insulin treatment group, choose the category with the lowest correctional dose to minimize the risk of hypoglycemia.

BMI = body mass index; GFR = glomerular filtration rate; TDD = total daily dose.

Elizabeth W. Duggan, Karen Carlson, Guillermo E. Umpierrez; Perioperative Hyperglycemia Management: **An Update**. *Anesthesiology* 2017; 126:547–560

Continuous intravenous insulin infusion

- **Continuous insulin infusion provides the best glucose control**

- **Independent adjustment of both insulin and glucose infusions based on hourly blood glucose**
  - Looks complicated but it is easy
  - Safe and effective

- **Indications**
  - Critically ill, major or trauma surgery, cardiac surgery
  - Patients with acute MI or cardiogenic shock
  - Pregnancy with type I DM
  - Emergency surgery in diabetic crisis

Variable continuous rate insulin infusion

- Patients who will miss more than one meal
- Type 1 DM undergoing surgery who have not received background insulin
- Poor controlled DM (HbA1c > 8.5%)
- Diabetes patients requiring emergency surgery

Variable continuous rate insulin infusion

BG mg/dl (mM)	If BG Increased from Previous Measurement	BG Decreased from Previous Measurement by Less Than 30 mg/dl	BG Decreased from Previous Measurement by Greater Than 30 mg/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

Elizabeth W. Duggan, Karen Carlson, Guillermo E. Umpierrez; Perioperative Hyperglycemia Management: **An Update**. *Anesthesiology* 2017; 126:547–560

Variable continuous rate insulin infusion

BG mg/dl (mM)	If BG Increased from Previous Measurement	BG Decreased from Previous Measurement by Less Than 30 mg/dl	BG Decreased from Previous Measurement by Greater Than 30 mg/dl
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 > 180 mg/dl (10 mM)		1
71–99 (3.9–5.5)	1. Hold insulin infusion 2. Check BG every 30 minutes until BG > 100 mg/dl (5.5 mM) 3. Resume BG checks every hour 4. Restart infusion at ½ the previous infusion rate if BG > 180 mg/dl (10 mM)		2
70 (3.9) or lower	If BG = 50–70 (2.8–3.9 mM), 1. Give 25 ml D50 2. Repeat BG checks every 30 min until BG > 100 mg/dl (5.5 mM) If BG < 50 mg/dl (2.8 mM), 1. Give 50 ml D50 2. Repeat BG every 15 min until > 70 mg/dl (3.9 mM) 3. When BG > 70 mg/dl, check BG every 30 min until > 100 mg/dl (5.5 mM). Repeat 50 ml D50 dose if BG < 50 mg/dl a second time and start D10 infusion 4. After BG > 100 mg/dl (5.5 mM), resume hourly BG check Restart infusion at ½ the previous infusion rate if BG > 180 mg/dl (10 mM)		3

Elizabeth W. Duggan, Karen Carlson, Guillermo E. Umpierrez; Perioperative Hyperglycemia Management: **An Update**. *Anesthesiology* 2017; 126:547–560

Fluid management

- **Hartmann's solution – safe for DM patients and not clinically significant hyperglycemia**

- **Aim - provide glucose substrate to prevent proteolysis, lipolysis, ketogenesis**
  - optimize intravascular volume status and maintain plasma electrolyte

5% glucose in 0.45% saline + KCL 0.15% (20 mEq) or KCL 0.3% (40 mEq)
(depend on presence of hypokalemia)

Rate = patient's usual maintenance requirements
(25-50 ml/kg/day or 83 ml/hr. for 70-kg patient)

Fluid management

Patients requiring a VRIII

- Hartmann's solution
- Isotonic crystalloid solution
  (optimize intravascular volume)

Patients not requiring a VRIII

- Avoid glucose containing solutions unless BGL is low
- Requires postoperative fluids > 24 hr.
  ; VRIII + Hartmann's solution

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

Perioperative hypoglycemia management

- **Hypoglycemia unawareness :** hypoglycemia associated autonomic failure due to defective glucose counter regulation

- **Symptoms :** sweating, palpitation, weakness, confusion, loss of conscious brain damage or death

- **BGL** : symptomatic hypoglycemia BGL< 55 mg/dl
- : generally considered alert < 70 mg/dl

- **Treatment**
  - **symptomatic hypoglycemia :** consumption of 10-25 g of glucose (clear liquid)
  - **Inpatient :** 50% dextrose 20-50 ml IV (10-25 gm of glucose)
  - Monitor BGL q 15 min until normoglycemia, then hourly

Joshi GP , et al.Anest Analg 2010;111:1378-87

Diabetic crisis

Table 49.3 Diagnostic criteria in DKA and HHS

Finding	Mild DKA	Moderate DKA	Severe DKA	HHS
Plasma glucose (mg/dL)	>250	>250	>250	>600
Arterial pH	7.25–7.30	7.00–7.24	<7.00	>7.30
Serum HCO_3^- (mEq/L)	15–18	10–15	<10	>15
Serum or urine ketones	Positive	Positive	Positive	Small
Beta-hydroxybutyrate	High	High	High	Normal or high
Effective serum osmolality[a] (mOsm/kg)	Variable	Variable	Variable	>320
Anion gap[b]	Upper limits of normal or > normal	>Normal	Significantly > normal	Variable
Sensorium	Alert	Alert or drowsy	Stupor/coma	Stupor/coma

[a]Effective serum osmolality = 2 × measured Na^+ (mEq/L) + BUN (mg/dL)/2.8 + glucose (mg/dL)/18, >320–330 mOsm/kg associated with neurologic deterioration

[b]Anion gap = $(Na^+ + K^+) - (Cl^- + HCO_3^-)$

Diagnostic criteria

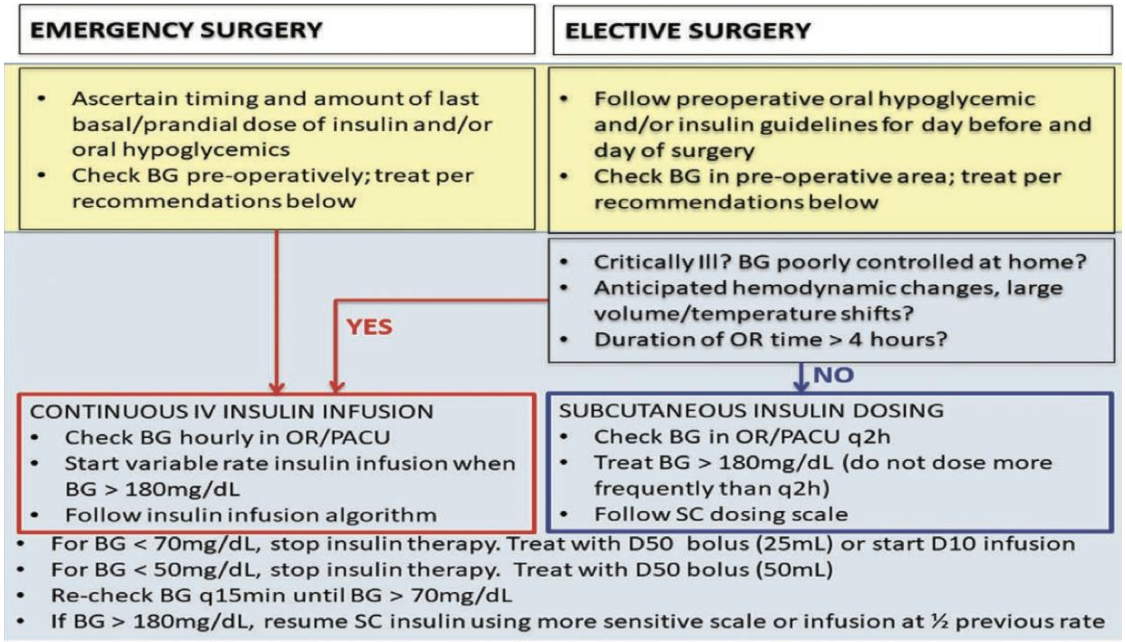
- Serum blood glucose > 250 mg/dl
- Ketonemia > 3 mmol/L or significant ketonuria (2+)
- Serum HCO_3<15 / arterial pH <7.3

Treatment guideline for perioperative DKA & HHS

General derangement	Specific guidelines
Hypovolemia	Use 0.9 % NS (if serum osmolality↑↑, consider .45 % NS)
	Rapid bolus followed by infusion at 250–1,000 cc/h
	Titrate to hemodynamic stability and UOP
	Caution in patients with depressed cardiac function
Electrolytes	Expect ↓Na^+, Mg^{++}, Ca^{++}, PO_4^{3-}, K^+
	Monitor q30–60 min
	Replace K^+ once UOP adequate and serum K^+ <5 mEq/L
Hyperglycemia	Start with regular insulin 10 units IV
	Infusion rate = (last serum glucose/100) units/h
	Add dextrose 5 % to fluids once glucose <250 mg/dL
Acidosis	Treat underlying DKA, hypovolemia, and renal failure
	Consider HCO_3^- if pH <7.15, hypotension refractory to volume

NS normal saline, *UOP* urine output

Emergency surgery VS Elective surgery



Duggan et al. : Anesthesiology 2017;126:547-60

Postoperative Management: Ambulatory Surgery

- **What is the optimal blood glucose level in PACU ?**

  Observe for an appropriate period after the last dose of insulin

  (rapid acting : 1.5 hr. , RI : 2-4 hr.)

- **Advice for glucose control after discharge home**

  Resume routine insulin therapy after oral intake

  Perform frequent postoperative blood glucose monitoring

Postoperative Management: Hospitalized Patients

- **Oral antidiabetic drugs are not recommended due to limited data on safety and efficacy**
- **Insulin should be administered , insulin dosage based on glycemic fluctuations**

status	Type of insulin	Insulin sensitive (U/kg/day)	Usual (U/kg/day)	Insulin resistance (U/kg/day)
NPO/poor intake	Basal(long acting)	0.1-0.15	0.2-0.25	0.3
Normal oral intake	Basal + rapid-acting	0.1-0.15	0.2-0.25	0.3
Correctional (BG>180mg/dl)	Rapid-acting	Dose based on BGL *(subcutaneous insulin scale day of surgery)*		

Duggan et al. : Anesthesiology 2017;126:547-60

Transition from IV infusion to subcutaneous insulin

- **Continue insulin infusion until patient can oral intake**
- **Continue insulin infusion at least 2 hr. after the first subcutaneous insulin injection**
- **Type 2 DM**
  - Do not use basal alone with *HbA1c > 8.5% on 2 or more oral agents*
  - Do not switch to oral agents alone *unless very low insulin infusion rates needed*
- **TDD based on the last 8 hr. of patient's insulin infusion**
  - basal insulin (70%) : long acting
  - prandial insulin (30%) for each meal : rapid-acting

Duggan et al. : Anesthesiology 2017;126:547-60

Take Home Messages

- *Clarify goals of preoperative evaluation and patient instructions for antidiabetic therapy*
- *Do not stop oral antidiabetics and non-insulin injectables day before surgery but withhold them on the day of surgery*
- *Optimize preoperative BGL : 6 – 12 mmol/L (108 - 216 mg/dl)*
- *Maintain BGL 140-180 mg/dl*
- *Frequent monitoring*
- *Follow up patients placed on insulin in the hospital*