Management of Inpatient Hyperglycemia in Special Populations

OVERVIEW

Inpatient Hyperglycemia and Poor Outcomes in Numerous Settings

Study	Patient Population	Significant Hyperglycemia-Related Outcomes
Pasquel et al, 2010	Total parenteral nutrition	↑ Mortality risk, pneumonia risk, ARF
Frisch et al, 2009	Noncardiac surgery	↑ Mortality risk, surgery-specific risk
Schlenk et al, 2009	Aneurysmal SAH	↑ Mortality risk; impaired prognosis
Palacio et al, 2008	All admitted patients, children's hospital	↑ ICU length of stay (LOS), ICU admissions
Bochicchio et al, 2007	Critically injured/trauma	↑ LOS, mortality risk, ventilator time, infection
Baker et al, 2006	Chronic obstructive pulmonary disease	↑ LOS, mortality risk, adverse outcomes
McAlister et al, 2005	Community-acquired pneumonia	↑ LOS, mortality risk, complications
Umpierrez et al, 2002	All admitted patients (87% non-ICU)	↑ LOS, mortality risk, ICU admissions ↓ Home discharges

Pasquel FJ, et al. *Diabetes Care*. 2010;33:739-741; Frisch A, et al. *Diabetes*. 2009;58(suppl 1):101-OR; Schlenk F, et al. *Neurocrit Care*. 2009;11:56-63; Palacio A, et al. *J Hosp Med*. 2008;3:212-217; Bochicchio GV, et al. *J Trauma*. 2007;63:1353-1358; Baker EH, et al. *Thorax*. 2006;61:284-289; McAlister FA, et al. *Diabetes Care*. 2005;28:810-815; Umpierrez GE, et al. *J Clin Endocrinol Metab*. 2002;87:978-982.

Current Recommendations for Hospitalized Patients

- All critically ill patients in intensive care unit settings
  - Target BG: 140-180 mg/dL
  - Intravenous insulin preferred
- Noncritically ill patients
  - Premeal BG: <140 mg/dL
  - Random BG: <180 mg/dL
  - Scheduled subcutaneous insulin preferred
  - Sliding-scale insulin discouraged
- Hypoglycemia
  - Reassess the regimen if blood glucose level is <100 mg/dL
  - Modify the regimen if blood glucose level is <70 mg/dL

BG, blood glucose.

Moghissi ES, et al. *Endocrine Pract.* 2009;15:353-369.
Umpierrez GE, et al. *J Clin Endocrinol Metab*. 2012;97:16-38.

PATIENTS RECEIVING ENTERAL NUTRITION

Enteral and Parenteral Nutrition

Provided to any patient who is malnourished or at risk for general malnutrition (ie, compromised nutrition intake in the context of duration/severity of disease)

Enteral

- For patients with intact gastrointestinal (GI) absorption

Short term

- Nasogastric (NG)
- Nasoduodenal
- Nasojejunal

Long term: (PEG)

- Gastrostomy
- Jejunostomy

Parenteral

- For patients with or at risk for deranged GI absorption (intestinal obstruction, ileus, peritonitis, bowel ischemia, intractable vomiting, diarrhea)

Short term: peripheral access (PPN)

Long term: central access (TPN)

Ukleja A, et al. *Nutr Clin Pract*. 2010;25:403-414.

Synchronization of Nutrition Support and Metabolic Control Is Important

- Nutrition support: to achieve a calorie target
  - Oral (standard and preferred)
  - Enteral (gastrostomy, postpyloric, jejunostomy tubes)
  - Parenteral (IV: peripheral, central)
- Metabolic control: to achieve a glycemic target
  - Insulin

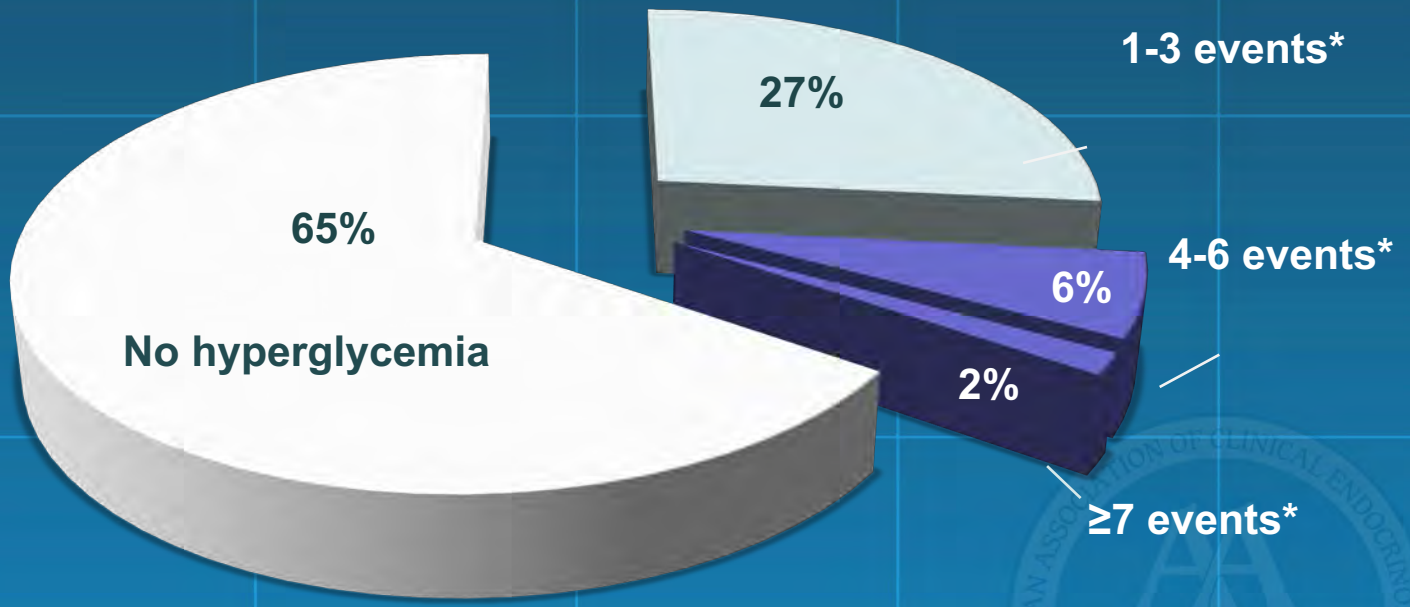
Nutrition Support + Metabolic Control = Metabolic Support

Enteral Nutrition and Hyperglycemia

- Continuous or intermittent delivery of calorie-dense nutrients
- Wide variety of schedules and formulas
- Altered incretin physiology (?)
- Increased risk of hyperglycemia
- Basal insulin should be ideal treatment strategy, but…
  - Concerns about potential hypoglycemia after abrupt discontinuation (eg, gastric residuals, tube pulled, etc)
- Combined basal-regular strategies may be optimal

Enteral Nutrition: Is It Diabetogenic?

Hyperglycemia Status



Patients in an acute care hospital on enteral feeding: mean age 76 years; 54.7% female; mean days EN 15 days.

*Blood glucose >200 mg/dL.

Pancorbo-Hidalgo PL, et al. *J Clin Nurs*. 2001;10:482-490.

Enteral Nutrition: Insulin Therapy Options

1. Basal (once or twice daily) + correction insulin
2. Basal + rapid acting every 6 hours + correction insulin

Variable Insulin Regimens Based on Different Types of Enteral Feeding Schedules

- Continuous EN
  - Basal: 40%-50% of TDD as long- or intermediate-acting insulin given once or twice a day
  - Short acting 50%-60% of TDD given every 6 h
- Cycled EN
  - Intermediate-acting insulin given together with a rapid- or short-acting insulin with start of tube feed
  - Rapid- or short-acting insulin administered every 4-6 hours for duration of EN administration
  - Correction insulin given for BG above goal range
  - Bolus enteral nutrition
    - Rapid-acting analog or short-acting insulin given prior to each bolus

BG, blood glucose; EN, enteral; TDD, total daily dose of insulin.

Insulin and Enteral Therapy: Coverage Protocol if Tube Feeds Abruptly Stopped

1. Calculate total carbohydrate calories being given as tube feeds
2. Assess BG every 1 h
3. If BG <100 mg/dL, give dextrose as D5W or D10W IV
4. Continue dextrose for duration of action of administered insulin

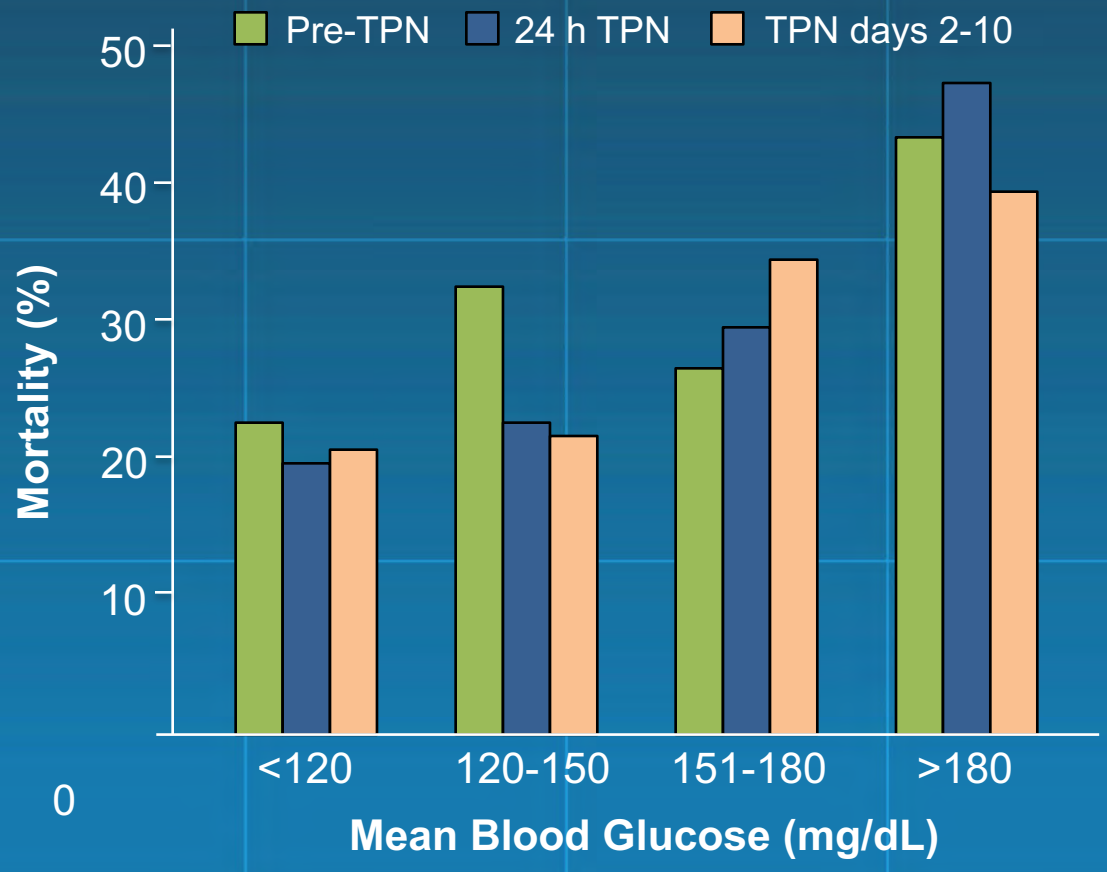
100 mL=5 g **100 mL=10 g**

- Example
  - Patient receiving 80 mL/h of Jevity™ enterally
  - Jevity = 240 mL/8 oz can, containing 36.5 g carb
  - 1 mL Jevity ≈0.15 g (150 mg) carbohydrate
  - @ 80 mL/h ≈12 g
  - Give 120 mL/h D10W or 240 mL/h D5W

PATIENTS RECEIVING PARENTERAL NUTRITION

Glycemia in Patients Receiving TPN

Mean BG and mortality rate in hospitalized patients on TPN



276 patients receiving TPN

Mean BG

- Pre TPN: 123 ± 33 mg/dL
- 24 h TPN: 146 ± 44 mg/dL
- TPN days 2-10: 147 ± 40 mg/dL

Pasquel FJ, et al. *Diabetes Care.* 2010; 33:739-741.

TPN, Glucose, and Patient Outcomes

Study	Cheung (2005)	Lin (2007)	Sarkisian (2009)	Pasquel (2010)
Hyperglycemia Definition (mg/dL)	>164*	>180**	≥180***	>180****
Mortality OR(95%CI)	10.90 (2.0-60.5)^	5.0 (2.4-10.6)^	7.22 (1.08-48.3)^	2.80 (1.20-6.80)^
Any Infection OR(95%CI)	3.9 (1.2-12.0)^	3.1 (1.5-6.5)^	0.9 (0.3-2.5)	NA
Cardiac OR(95%CI)	6.2 (0.7-57.8)	1.6 (0.3-7.2)	1.3 (0.1-12.5)	NA
Acute Renal Failure OR(95%CI)	10.9 (1.2-98.1)^	3.0 (1.2-7.7)^	1.9 (0.4-8.6)	2.2 (1.0-4.8)
Septicemia OR(95%CI)	2.5 (0.7-9.3)	NA	NA	NA
Any Complication OR(95%CI)	4.3 (1.4-13.1)^	5.5 (2.5-12.4)^	NA	NA

^ Significant at $P<0.05$.

* ORs are expressed using blood glucose <124 mg/dL as a reference category.

** ORs are expressed using blood glucose <110 mg/dL as a reference category.

*** ORs are expressed using blood glucose <180 mg/dL as a reference category.

**** ORs are expressed using blood glucose <120 mg/dL as a reference category as measured within 24 h of PN initiation.

Kumar PR, et al. *Gastroenterol Res Pract*. 2011;2011. doi:pii: 760720.

Parenteral Nutrition

- Continuous IV delivery of high concentrations of dextrose (20-25 gm/100 mL)
- No incretin stimulation of insulin secretion
- Hyperglycemia extremely common
- Basal insulin should be ideal treatment strategy, but...
  - Concerns about potential hypoglycemia after abrupt discontinuation (eg, technical issues with line)

Parenteral Nutrition: Insulin Therapy Options

1. Basal (once or twice daily) + correction insulin
2. Basal + rapid acting every 6 hours + correction insulin

Should You Stop Insulin Infusion and Put Insulin in the TPN?

Pros

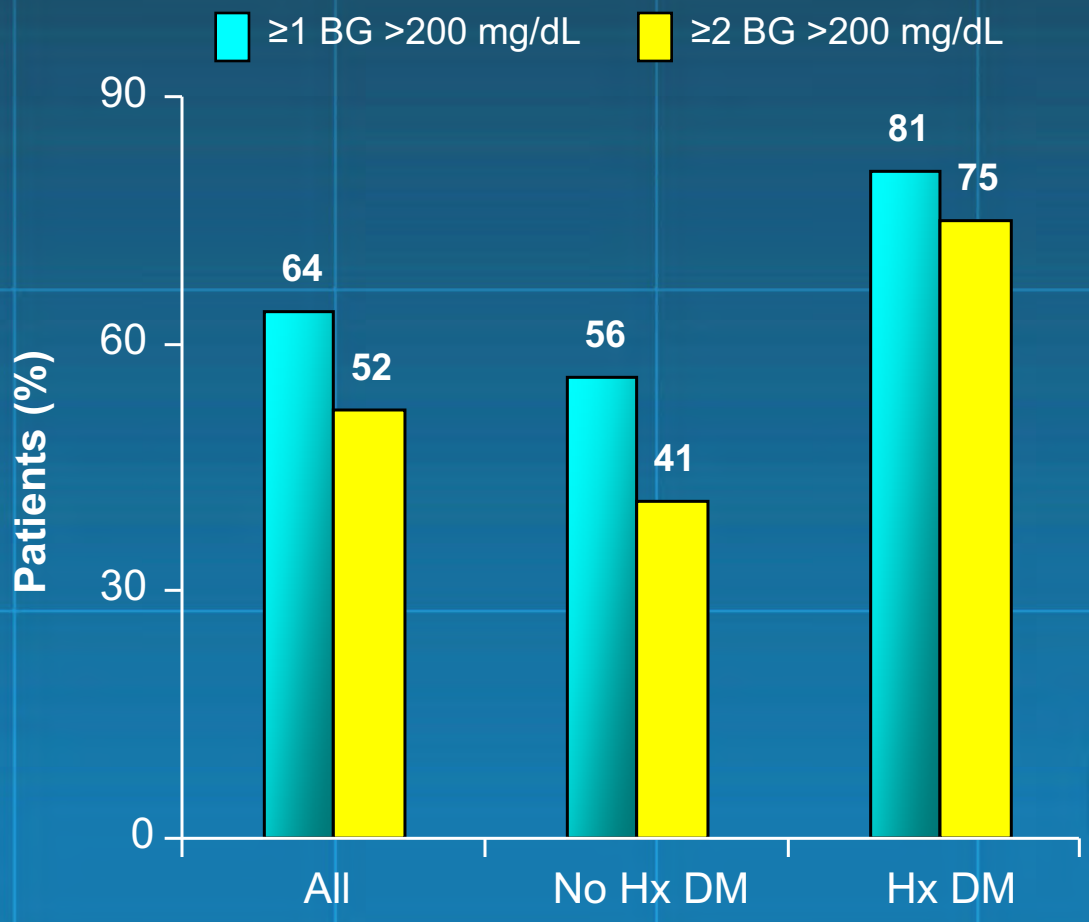
- Simplifies number of infusions/lines
- Easier if patient will be discharged on TPN

Cons

- Hard to predict insulin requirement
- Once it is in the bag, you cannot take it out

PATIENTS ON STEROIDS

Frequency of Hyperglycemia in Patients Receiving High-Dose Steroids



Donihi A, et al. *Endocr Pract.* 2006;12:358-262.

Steroid Therapy and Inpatient Glycemic Control

- Steroids are counterregulatory hormones
  - Impair insulin action (induce insulin resistance)
  - Appear to diminish insulin secretion
- Majority of patients receiving >2 days of glucocorticoid therapy at a dose equivalent to ≥40 mg/day of prednisone developed hyperglycemia
- No glucose monitoring was performed in 24% of patients receiving high-dose glucocorticoid therapy

Donihi A, et al. *Endocr Pract.* 2006;12:358-362.

TES Guidelines for Glucose Control and Glucocorticoid Therapy

- The majority of patients (but not all) receiving high-dose glucocorticoid therapy will experience elevations in blood glucose, which are often marked
- Recommended approach
  - Blood glucose monitoring for patients with or without diabetes receiving glucocorticoid therapy
  - Patients without diabetes: may discontinue BG monitoring if BG remains <140 mg/dL without insulin therapy for 24-28 h
  - Use continuous insulin infusion for patients with severe and persistent BG elevations despite use of scheduled basal-bolus SC insulin

BG, blood glucose.

Umpierrez GE, et al. *J Clin Endocrinol Metab*. 2012;97:16-38.

Steroid Therapy and Glycemic Control Patients With and Without Diabetes

- Patients without prior diabetes or hyperglycemia or those with diabetes controlled with oral agents
  - Begin BG monitoring with low-dose correction insulin scale administered prior to meals
- Patients previously treated with insulin
  - Increase total daily dose by 20% to 40% with start of high-dose steroid therapy
  - Increase correction insulin by 1 step (low to moderate dose)

Adjust insulin as needed to maintain glycemic control (with caution during steroid tapers)

PATIENTS TAKING U-500 INSULIN

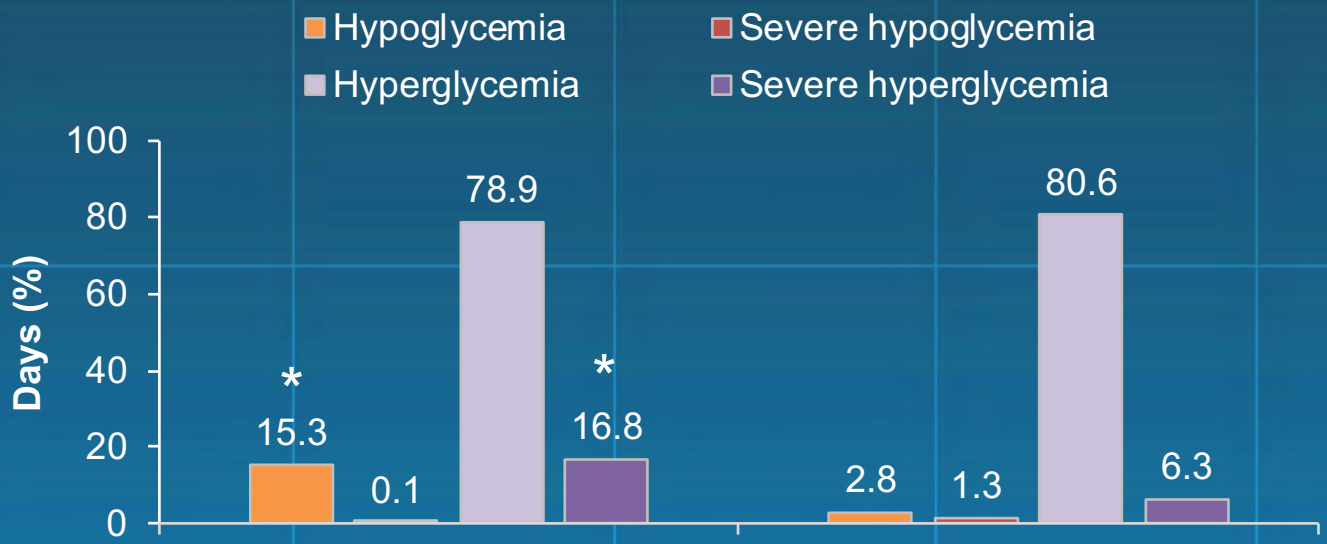
U-500 Insulin

- When daily insulin requirements exceed 200 units/day
  - Volume of U-100 injected insulin may be problematic
  - Use of U-500 insulin (5 times more concentrated than U-100 insulin) may be appropriate but switching to U-100 during hospital stay may prevent dosage errors
- Possible patients
  - Obstetrics patients
  - Patients receiving high-dose glucocorticoid therapy
  - Patients with type 2 diabetes, obesity, or severe insulin resistance

Kelly JL. *Am J Health-Syst Pharm*. 2010;67(suppl 8):S9-S16.

Use of U-500 vs U-100 in Hospital Setting

Retrospective Analysis



	Group A	Group B	
Median BG, mg/dL	237.6	207.9	*P*=0.48
Median daily insulin dose	200	35	*P*<0.001

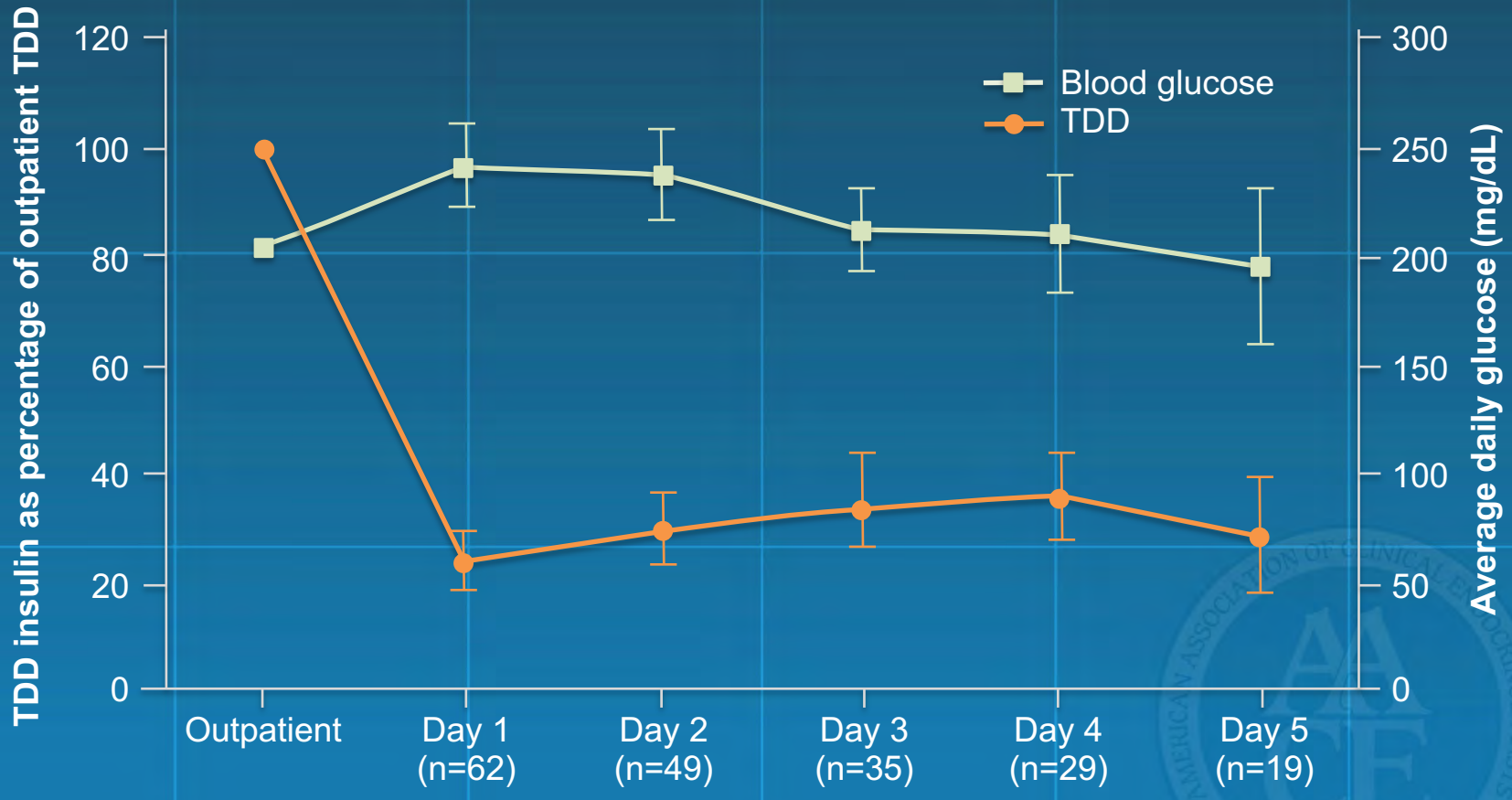
*$P<0.001$ vs Group B.

BG, blood glucose.

Tripathy PR, Lansang C. *Endocr Pract*. 2015:21:54-58.

Glycemic Control After Switching From U-500 to U-100

Retrospective Analysis



TDD, total daily dose of insulin.

Paulus AO, et al. *Endocr Pract*. 2016:22:1187-1191.

PATIENTS ON INSULIN PUMP THERAPY

Insulin Pump Therapy

- Electronic devices that deliver insulin through a SC catheter
  - Basal rate (variable) + bolus delivery for meals
- Used predominately in type 1 diabetes
- “Pumpers” tend to be fastidious about their glycemic control
  - Often reluctant to yield control of their diabetes to the inpatient medical team
- Hospital personnel typically unfamiliar with insulin pumps
  - Hospitals do not stock infusion sets, batteries, etc, for insulin pumps (multiple models available from different manufacturers

The Challenge of Insulin Pump Use in the Hospital

- If patient is clinically stable, awake, alert, and able to independently manage his/her pump, continuation of pump therapy should be considered
  - But…many medical-legal issues!
  - And…many obstacles to safe pump therapy in the hospital (trained personnel, equipment, alarms, documentation, etc)
- Therefore, all hospitals should have a policy for the safe use of insulin pumps at their facilities

Insulin Pump Policy: Main Elements

- Patient qualifications for self-management (normal mental status, able to control device, etc)
- Pump in proper functioning order and supplies stocked by patient/family
- Signed patient contract/agreement
- Order set entry
- Documentation of doses delivered (pump flow sheet)
- Ongoing communication between patient and RN
- Policies regarding procedures, surgeries, CTs, MRIs, etc

AACE Position on CSII in the Hospital

- Patients who use CSII outside the hospital may use it inside if:
  - Patient has the mental and physical capacity to use CSII for self-management
  - Hospital personnel with CSII expertise are available
  - Nurses document basal and bolus doses at least daily
- Specialist responsible for ambulatory CSII management should be contacted to make decisions about infusion rate adjustments

A formal inpatient insulin pump protocol reduces confusion and treatment variability

CSII, continuous subcutatneous insulin infusion.

Grunberger G, et al. *Endocr Pract*. 2014;20:463-489.

Inpatient Insulin Pump Therapy: A Single Hospital Experience

- N=65 patients (125 hospitalizations)
- Mean age: 57 ± 17 y
- Diabetes duration: 27 ± 14 y
- Pump use: 6 ± 5 y
- A1C: 7.3% ± 1.3%
- Length of stay: 4.7 ± 6.3 days

- Pump therapy continued 66%
- Endocrine consults in 89%
- Consent agreements in 83%
- Pump order sets completed in 89%
- RN assessment of infusion site in 89%
- Bedside insulin pump flow sheets in only 55%
- Mean BG 175 mg/dL (same as off pump)
- No AEs (1 catheter kinking)

Nassar AA, et al. *J Diabetes Sci Technol*. 2010;4:863-872.

A Validated Inpatient Insulin Pump Protocol

- Physician order set
  - Consult diabetes service/endocrinologist
  - Discontinue all previous insulin orders
  - Check capillary blood glucose frequency
  - Patient to self-administer insulin via pump
  - Patient to document all BG and basal/bolus rates
  - Insulin type order for pump: rapid-acting analog (lispro, aspart, glulisine)
  - Set target BG range
  - Implement hypoglycemia treatment protocol

Noschese ML, et al. *Endocr Pract*. 2009;15:415-424.

A Validated Inpatient Insulin Pump Protocol

Basal Insulin Rates

Start Time	Stop Time	Basal Rate Units/h
12 am	1 am	0.7
1 am	2 am	0.7
2 am	3 am	0.7
3 am	4 am	0.7
4 am	5 am	1.0
5 am	6 am	1.0
6 am	7 am	1.0
7 am	8 am	1.0
8 am	9 am	1.0
9 am	10 am	1.0
10 am	11 am	0.9
11 am	12 pm	0.9
12 pm	1 pm	0.9
1 pm	2 pm	0.9
2 pm	3 pm	0.9
3 pm	4 pm	0.7
4 pm	5 pm	0.7
5 pm	6pm	0.9
6pm	7 pm	0.9
7 pm	8 pm	0.9
8 pm	9 pm	0.9
9 pm	10 pm	0.9
10 pm	11 pm	0.7
11 pm	12 am	0.7

Patient to self-administer insulin via SC insulin pump and document all basal rates

Noschese ML, et al. *Endocr Pract*. 2009;15:415-424.

A Validated Inpatient Insulin Pump Protocol

Meal boluses based on:

Carbohydrate count

Breakfast ___ u/per _____gram

Lunch ___ u/per _____gram

Supper ___ u/per _____gram

Snacks ___ u/per _____gram

or

Fixed doses

___ u at Breakfast

___ u at Lunch

___ u at Supper

___ u with Snacks

Correction boluses: _____ unit(s) for every ____mg/dL over ____ mg/dL (target glucose)

Noschese ML, et al. *Endocr Pract*. 2009;15:415-424.

A Validated Inpatient Insulin Pump Protocol

Hospitalizations After Implementation of an Inpatient Insulin Pump Protocol (IIPP)

	Mean BG (mg/dL)	*P* value
Group 1 - IIPP+DM consult (n=34)	173 ±43	NS
Group 2 - IIPP alone (n=12)	187 ±62	
Group 3 - Usual care (n=4)	218 ±46	

- More inpatient days with BG >300 mg/dL in Group 3 ($P<0.02$.)
- No differences in inpatient days with BG <70 mg/dL
- 1 pump malfunction; 1 infusion site problem; no SAEs
- 86% of pumpers expressed satisfaction with ability to manage DM in the hospital

Noschese ML, et al. *Endocr Pract*. 2009;15:415-424.

Clinical Outcomes with Inpatient CSII

Systematic Review
(N=11 Studies*; 624 Patients)

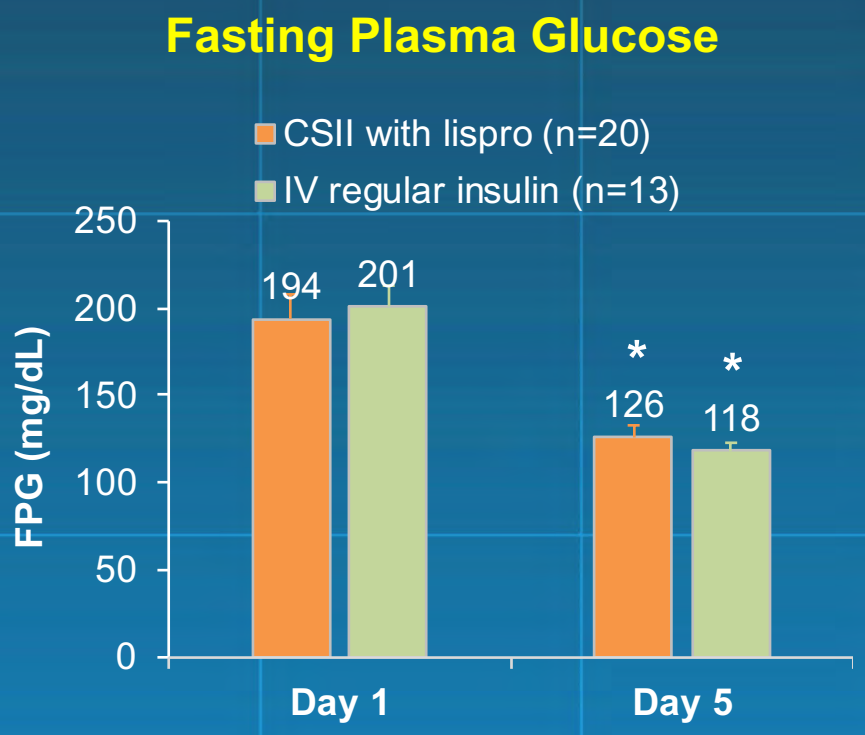
Inpatient mortality	None reported (only 1 study assessed mortality in 253 patients over 1000 patient-days)
Hyperglycemia	Trend toward less hyperglycemia with CSII
Hypoglycemia	Trend toward more hypoglycemia with CSII
Length of stay	Shorter stay with continued CSII (4.5 days) vs suspended CSII or IV infusion (7 days)
Average blood glucose	CSII continued: 175 mg/dL; suspended CSII or IV infusion: 178 mg/dL

*9 retrospective; 2 prospective, including 1 randomized, controlled study.

CSII, continuous subcutaneous insulin infusion; IV, intravenous.

Anstey J, et al. *Diabet Med*. 2015;32:1278-1288.

Efficacy of CSII in Hospitalized Patients with Type 2 Diabetes



*P<0.05 vs day 1.

BG, blood glucose; CBG, capillary blood glucose; CSII, continuous subcutaneous insulin infusion; IV, intravenous.

Boullu-Sanchis S, et al. *Diabetes Metab*. 2006;32:350-357.

- No significant differences between treatment groups in
  - Mean daily CBG levels
  - Percent of preprandial CBG values in the target range
  - Daily standard deviation of BG on day 5
- Insulin dose lower in CSII group (P<0.05)
- Hypoglycemia
  - CSII: 0.06 events/patient per day
  - IV insulin: 0.015 events/patient per day
  - Between group difference not statistically significant
  - No severe hypoglycemia reported in either group

Results of an Inpatient CSII Protocol

	IDS + IPP	IPP	No IDS/IPP
N (% female)	34 (32)	12 (50)	4 (75)
Age	48±15	51±16	36±12
LOS (days)	9.8±15.4	5.2±6.2	3±1.5
CSII use (days)	5.4±7.1	3.2±2.9	3±1.5
Mean CBG (mg/dL)	173±43	187±62	218±46
Patient days with			
≥1 CBG <70	21	10	20
All CBG 70-180	25	24	24
≥1 CBG 181-300	56	55	73
≥1 CBG >300	22	7	60

IDS, inpatient diabetes service; IPP, inpatient pump protocol.

Noschese ML, et al. *Endocr Pract.* 2009;15:415-424.

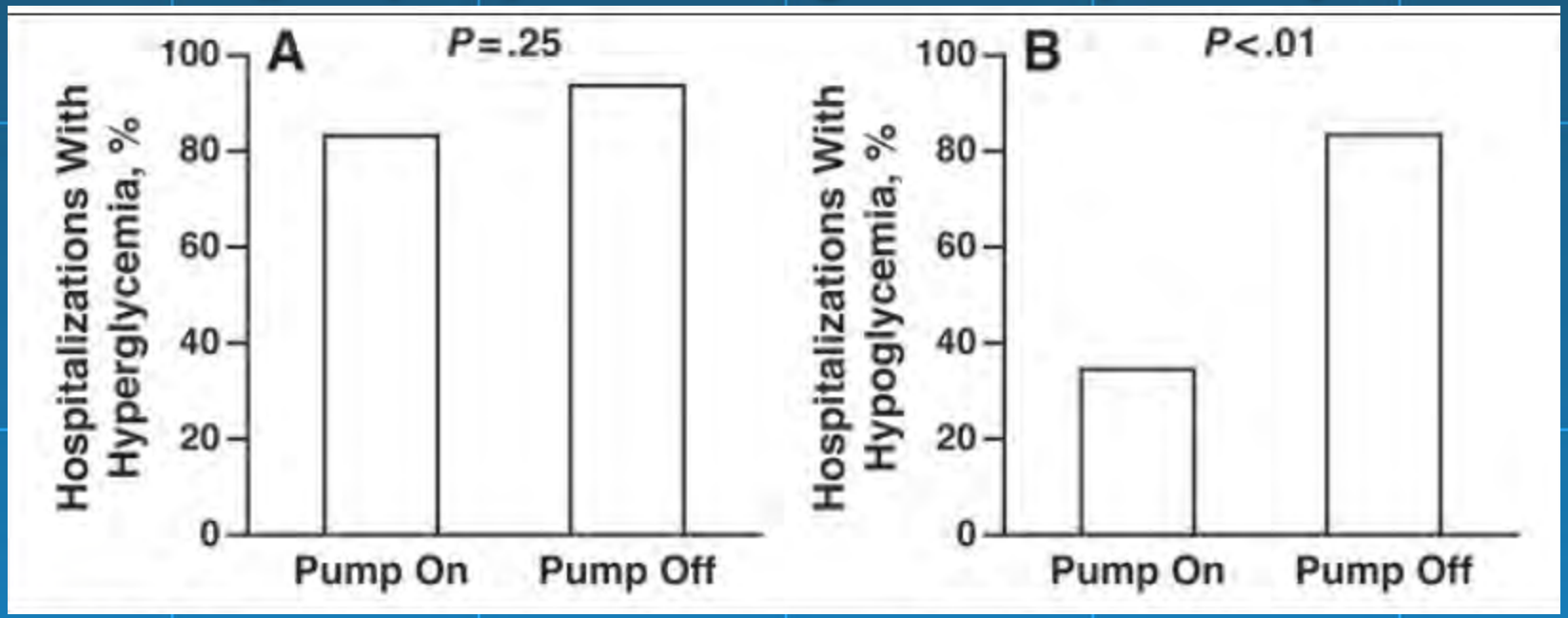
Inpatient CSII Therapy in Patients Treated With Insulin as Outpatients

- Patients completing questionnaire (n=17) reported a high degree of satisfaction with their ability to continue CSII therapy in the hospital
- There were 2 CSII related adverse events
  - 1 infusion site problem
  - 1 pump malfunction

Noschese ML, et al. *Endocr Pract.* 2009;15:415-424.

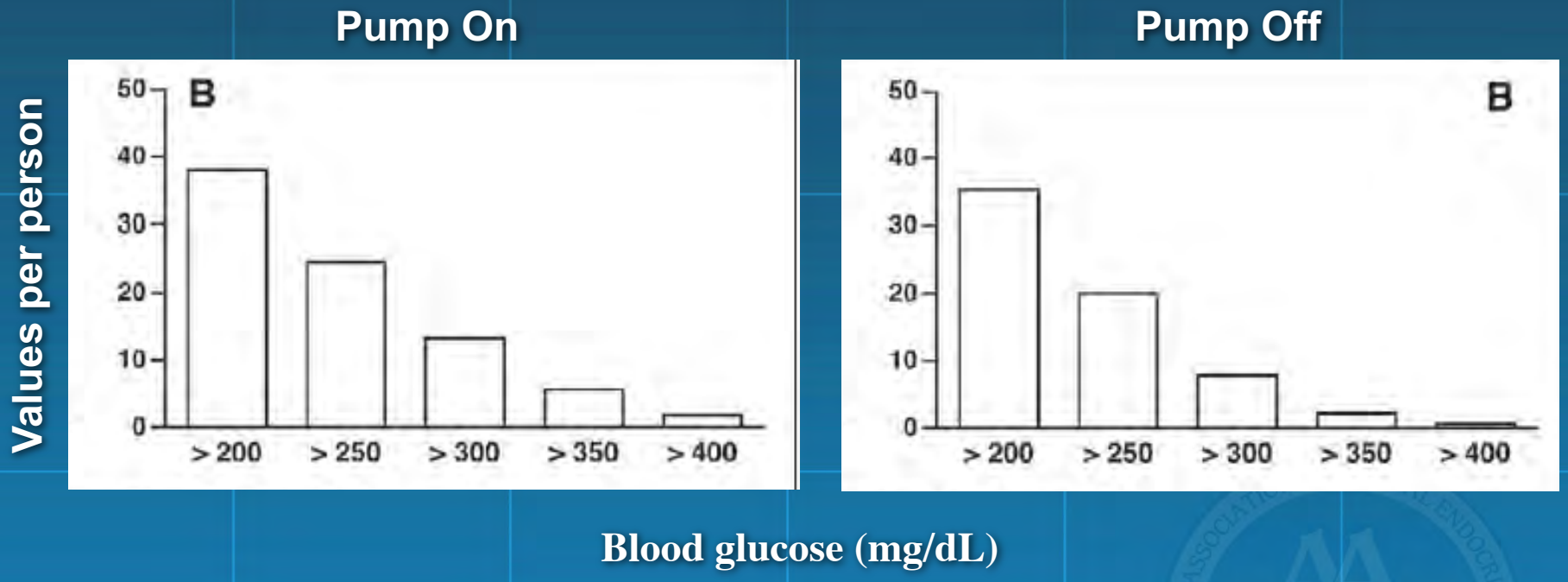
Inpatient CSII Therapy

Prevalence of hyperglycemia and hypoglycemia in inpatients who continued (pump on) or discontinued (pump off) CSII during their hospital stay



Bailon RM, et al. *Endocr Pract.* 2009;15:24-29.

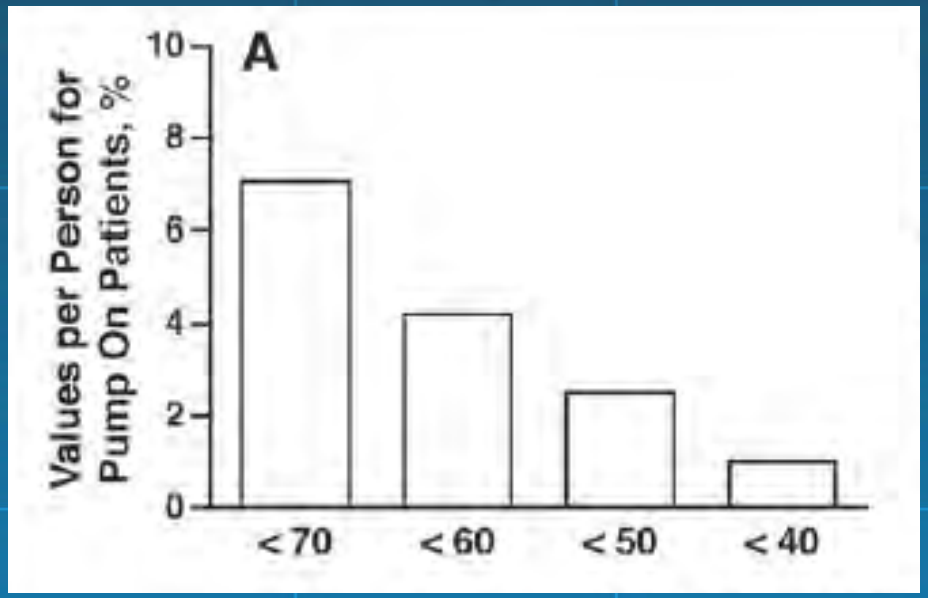
Hyperglycemic Events in Patients Continuing or Stopping CSII Therapy During Their Hospital Stays



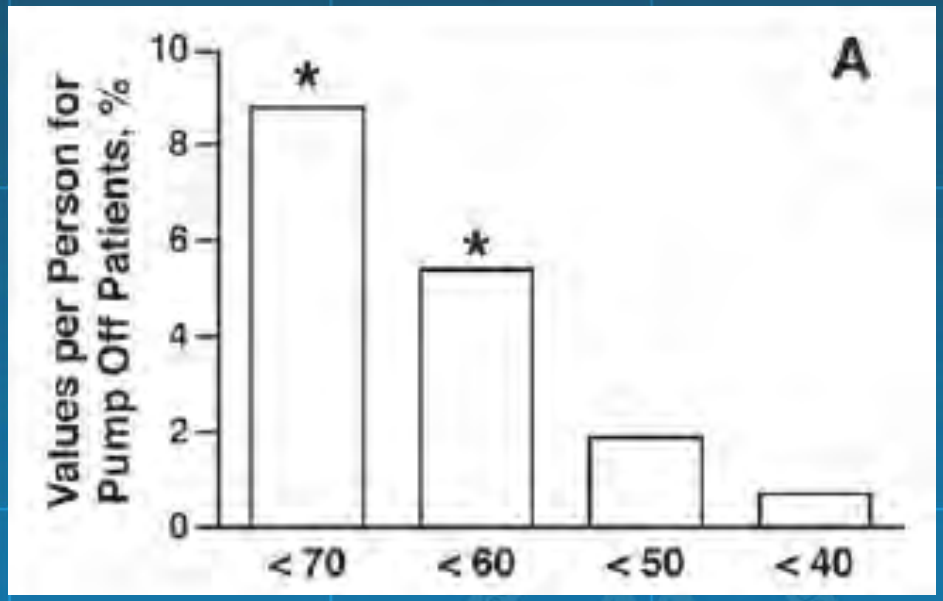
Bailon RM, et al. *Endocr Pract.* 2009;15:24-29.

Hypoglycemic Events in Patients Continuing or Stopping CSII Therapy During Their Hospital Stays

Pump On



Pump Off

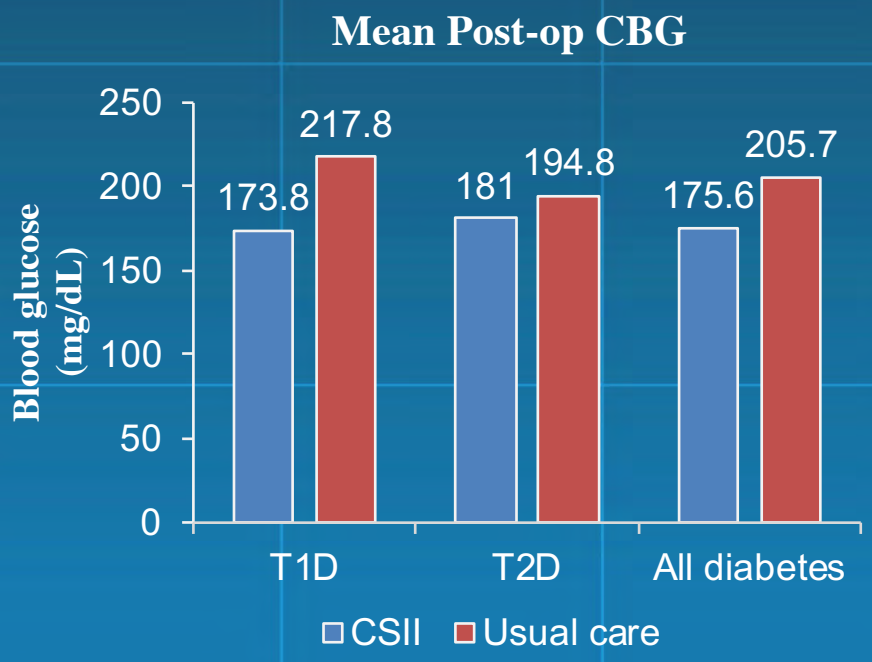


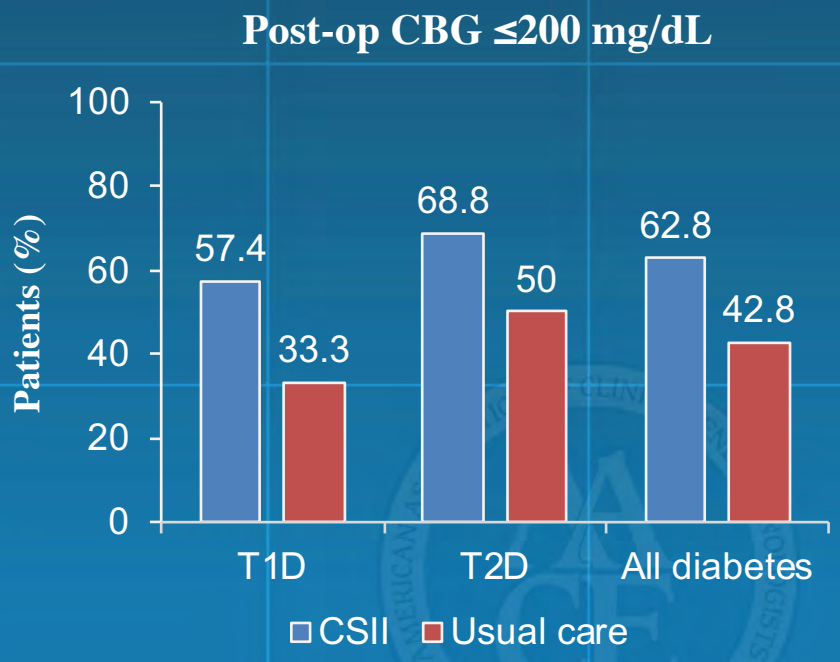
Blood glucose (mg/dL)

Bailon RM, et al. *Endocr Pract.* 2009;15:24-29.

Blood Glucose Levels with Peri-operative CSII

Patients with Diabetes Undergoing Same-Day Surgery (N=49)





CBG, capillary blood glucose; CSII, continuous subcutatneous insulin infusion.

Sobel SI, et al. *Endocr Pract*. 2015;21:1269-1276.

Inpatient Management of Hyperglycemia: Managing Safety Concerns

- Both undertreatment and overtreatment of hyperglycemia create safety concerns
- Areas of risk
  - Changes in carbohydrate or food intake
  - Changes in clinical status or medications
  - Failure to adjust therapy based on BG patterns
  - Prolonged use of SSI as monotherapy
  - Poor coordination of BG testing with insulin administration and meal delivery
  - Poor communication during patient transfers
  - Errors in order writing and transcription

PERIOPERATIVE RECOMMENDATIONS

Pre-Op Recommendations for Patients Admitted Day of Surgery: Patients on Noninsulin Agents

- Withhold noninsulin agents the morning of surgery
- Insulin is necessary to control glucose in patients with BG >180 mg/dL during surgery
- Noninsulin agents can be resumed postoperatively when:
  - Patient is reliably taking PO
  - Risk of liver, kidney, and heart failure are lower

Pre-op Recommendations for Insulin Treated Patients

- Morning of surgery
  - Give 50-75% of home basal insulin dose (NPH/glargine/detemir)
  - Do NOT give prandial insulin
  - Give correction for hyperglycemia
  - For prolonged procedures initiate insulin infusion

Pre-op Recommendations: Patients Using Insulin Pump

- Discontinue insulin pump and change to IV insulin according to patient's current basal rate
  - If basal rate <1 unit/h, start IV insulin at 0.5 units/h
  - If basal rate 1-2 units/h, start IV insulin at 1 units/h
  - Monitor BG hourly, with titration per insulin infusion protocol
- For brief surgical procedures in which the pump insertion site is not in surgical field, may consider continuing pump therapy
  - Reduce basal rate by 20% (eg, 1 u/h changes to 0.8 u/h)
  - Remove pump and initiate insulin infusion if patient becomes hemodynamically unstable
- Hypoglycemia and hyperglycemia treated in manner similar to that of patients receiving SC insulin pre-op

Medication Adjustment Before Surgery

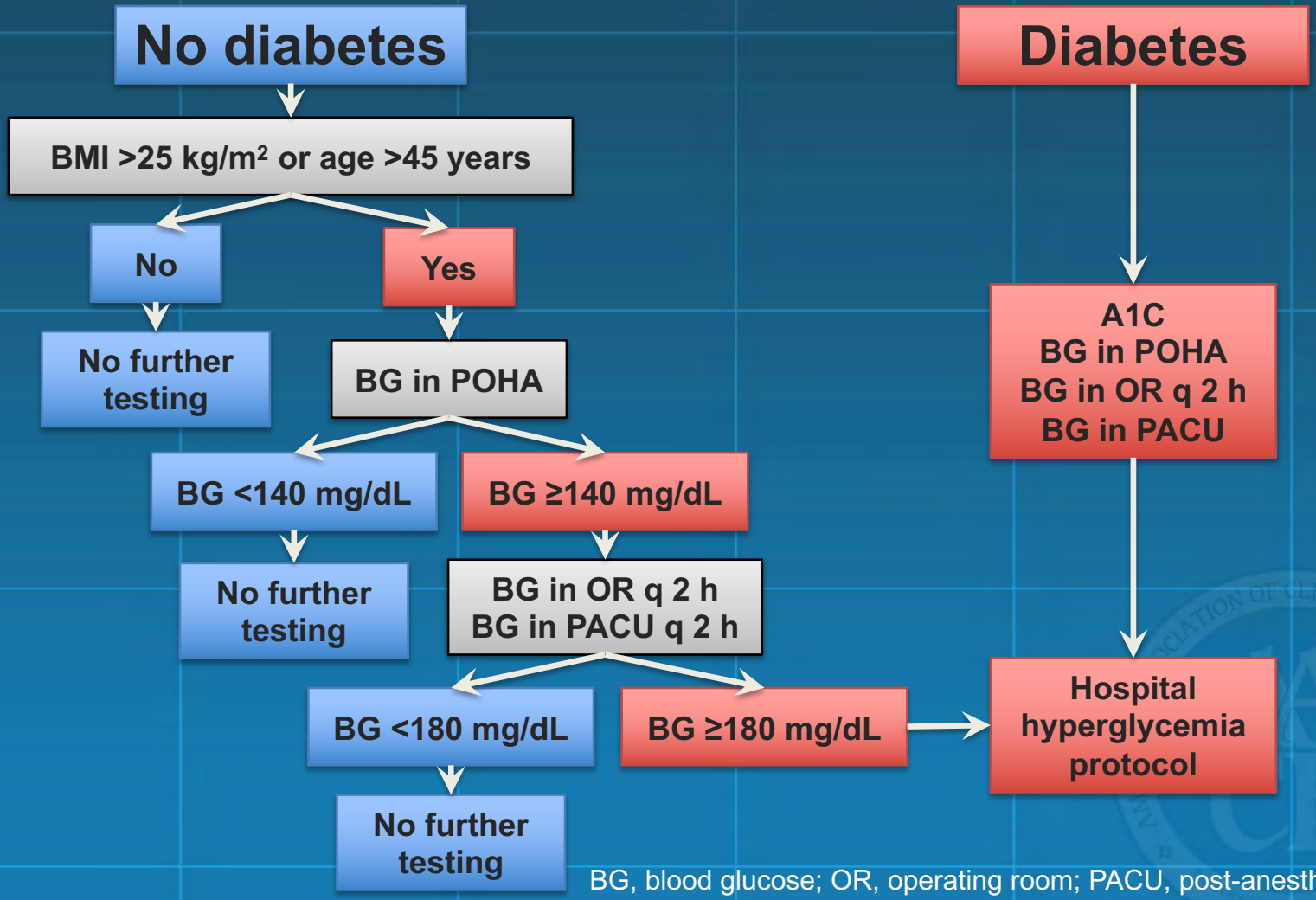
Emory University Protocol

Oral agents	Detemir or glargine	NPH or premixed insulin	Short or rapid-acting insulin	Noninsulin injectable agents
Day before surgery				
AM: usual dose PM: usual dose	AM: usual dose PM: 80% of usual dose	AM: usual dose PM: 80% of usual dose	AM: usual dose PM: usual dose	AM: usual dose PM: usual dose
Day of surgery				
Hold	80% of usual dose	50% of usual dose if BG >120 mg/dL	Hold if nothing by mouth	Hold

Duggan EW, et al. *Curr Diab Rep*. 2016;16:34.

Day-of-Surgery Glucose Monitoring

Emory University Protocol

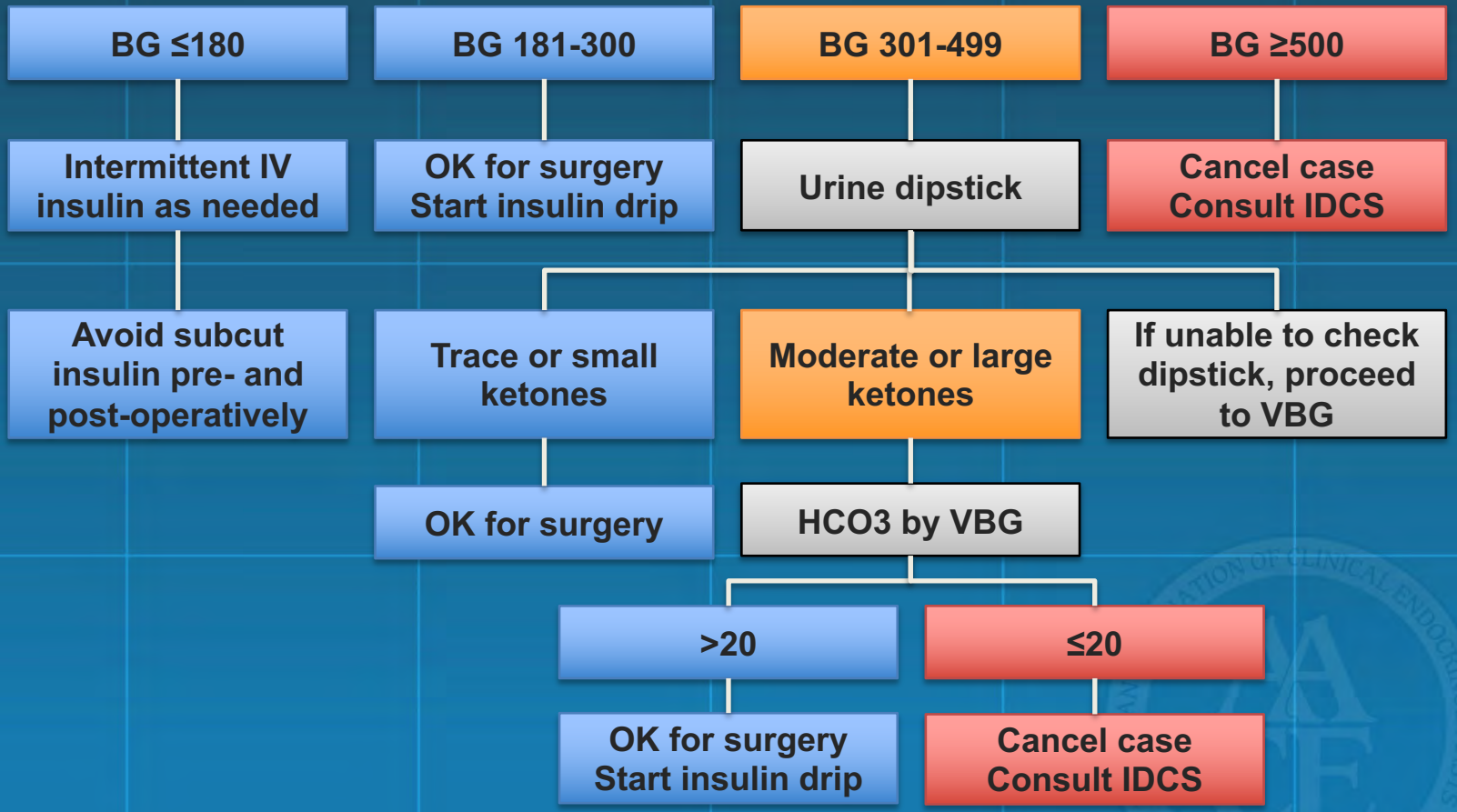


BG, blood glucose; OR, operating room; PACU, post-anesthesia care unit; POHA, pre-operative holding area.

Duggan EW, et al. *Curr Diab Rep*. 2016;16:34.

Peri-operative Diabetes Management

Brigham and Women's Hospital Protocol
Procedures >1 Hour

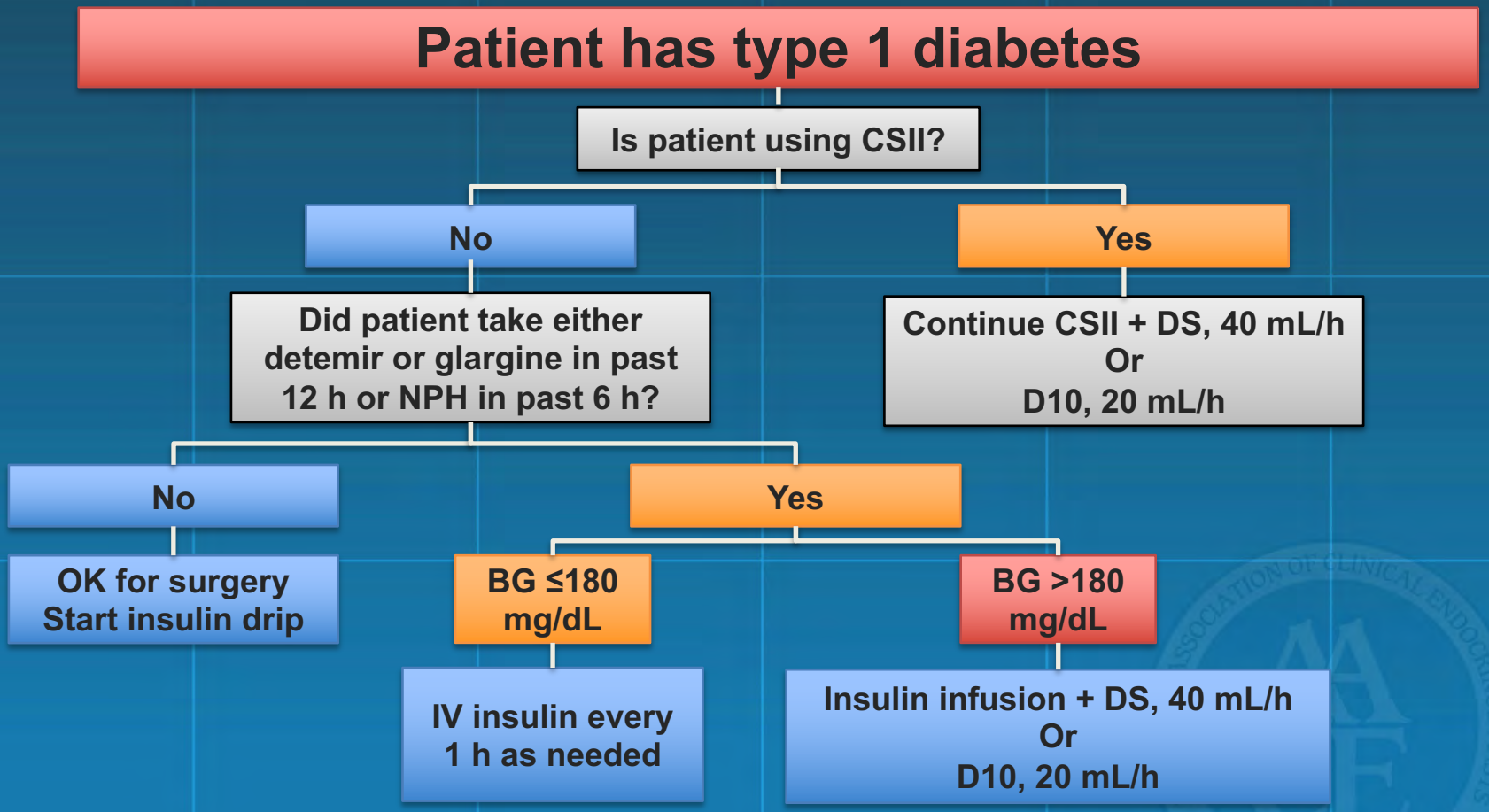


BG, blood glucose; HCO3, bicarbonate; IDCS, inpatient diabetes consult service; IV, intravenous; VBG, venous blood gas.

Arnold LM, et al. *Endocr Pract*. 2016:Nov 7 [Epub ahead of print]

Peri-operative Diabetes Management

Brigham and Women's Hospital Protocol
Procedures >1 Hour

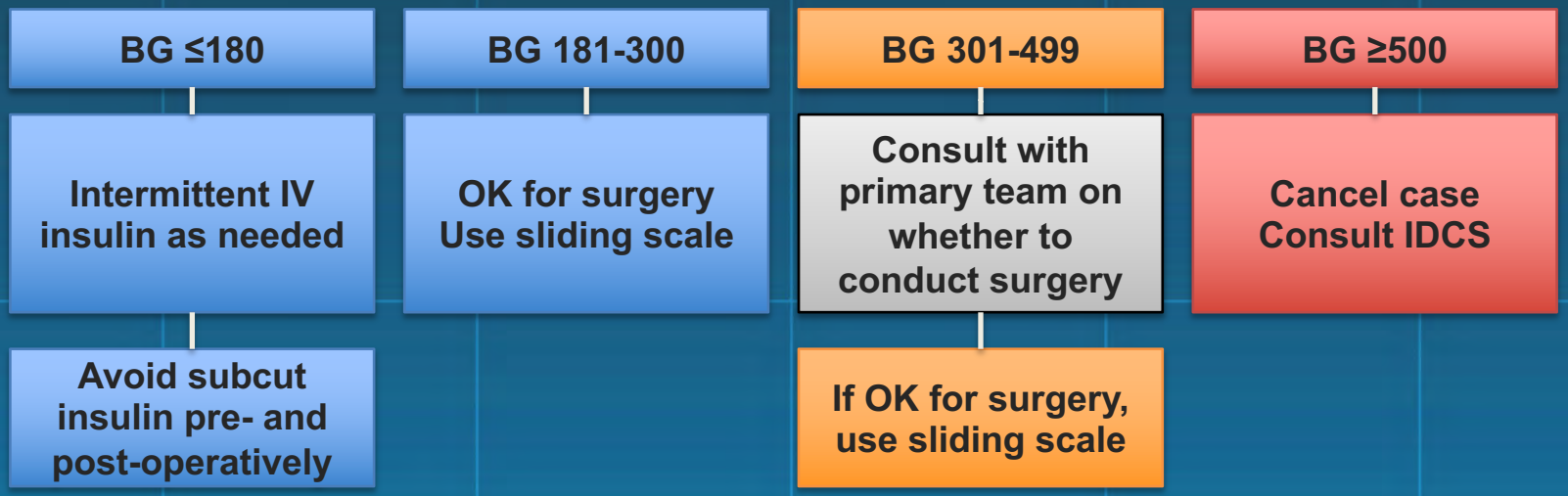


BG, blood glucose; CSII, continuous subcutaneous insulin infusion; D10, dextrose 10%; DS, dextrose solution; IV, intravenous.; NPH, Neutral Protamine Hagedorn.

Arnold LM, et al. *Endocr Pract*. 2016:Nov 7 [Epub ahead of print]

Peri-operative Diabetes Management

Brigham and Women's Hospital Protocol
Procedures ≤1 Hour



BG (mg/dL)	Regular insulin IV push (units)
≤180	0
181-230	2
231-280	3
281-330	4
331-499	5
>499	Call physician

BG, blood glucose; HCO3, bicarbonate; IDCS, inpatient diabetes consult service; VBG, venous blood gas.

Arnold LM, et al. *Endocr Pract*. 2016:Nov 7 [Epub ahead of print]

PATIENTS RECEIVING AN ORGAN TRANSPLANT

Risk Factors for Post–Organ Transplant Hyperglycemia

Traditional Risk Factors

- Age
- Gender
- BMI
- Non-white ancestry/ethnicity
- Hepatitis C infection
- Family history of diabetes
- Pre-existing diabetes

Risk Factors Unique to Organ Transplantation

- HLA subtype mismatch
- Deceased donor organs
- Male donors
- Cytomegalovirus
- Diabetogenic effects of immunosuppressive therapy

HLA, human leukocyte antigen.

Sadhu A, et al. In: *Managing Diabetes and Hyperglycemia in the Hospital Setting: a Clinician's Guide*. Draznin B, ed. Alexandria, VA: American Diabetes Association; 2016:157-166.

Post-Transplantation Glucose Control Challenges

- Immunosuppressive therapy
  - Corticosteroids increase hepatic gluconeogenesis, peripheral tissue insulin resistance, and insulin secretion from β-cells
  - Calcineurin inhibitors inhibit insulin secretion from β-cells and promote β-cell apoptosis
  - Mammalian target of rapamycin (mTOR) inhibitors decrease insulin secretion and β-cell mass, particularly in the hyperglycemic state
- Unpredictable post-transplant organ function
  - Altered medication pharmacokinetics after renal transplantation
  - Increased gluconeogenesis and glycogenolysis after liver transplant
  - Altered metabolic control due to delays or changes in allograft function

Sadhu A, et al. In: *Managing Diabetes and Hyperglycemia in the Hospital Setting: a Clinician's Guide*. Draznin B, ed. Alexandria, VA: American Diabetes Association; 2016:157-166.

Post-Transplantation Glucose Control Challenges

Immunosuppressive therapy	• Corticosteroids
	  • Increase hepatic gluconeogenesis and peripheral insulin resistance
	  • Reduce insulin secretion from β-cells
	• Calcineurin inhibitors
	  • Inhibit insulin secretion from β-cells
	  • Promote β-cell apoptosis
	• mTOR inhibitors: decrease insulin secretion and β-cell mass, particularly in the hyperglycemic state

Post-transplantation organ function	• Altered medication pharmacokinetics after renal transplantation • Increased gluconeogenesis and glycogenolysis after liver transplant • Altered metabolic control due to delays or changes in allograft function
Nutritional status	• Inconsistent calorie absorption due to GI side effects of immunosuppressive drugs

GI, gastrointestinal; mTOR, mammalian target of rapamycin.

Sadhu A, et al. In: *Managing Diabetes and Hyperglycemia in the Hospital Setting: a Clinician's Guide*. Draznin B, ed. Alexandria, VA: American Diabetes Association; 2016:157-166.

Post-Transplantation Treatment Recommendations

Glucose targets	• Initial blood glucose target: <180 mg/dL, avoid blood glucose <70 mg/dL

Therapy	• IV regular insulin during immediate post-transplantation period (48-96 h after heart, lung, or liver transplant)
	• Transition to subcutaneous insulin when postoperative progress and nutrition are stable and steroids are decreased
	  • NPH preferred basal insulin because its pharmacodynamics mimic effect of prednisone and methylprednisone on glucose
	  • Peak effect 4-8 h after administration, 12-16 h duration of action
	• Use rapid acting insulin analog for prandial glucose control

IV, intravenous; NPH, Neutral Protamine Hagedorn.

Sadhu A, et al. In: *Managing Diabetes and Hyperglycemia in the Hospital Setting: a Clinician's Guide*. Draznin B, ed. Alexandria, VA: American Diabetes Association; 2016:157-166.

Summary

- Hyperglycemia is associated with adverse clinical outcomes in the hospital setting, both in critically ill and noncritically ill patients
- National organizations have promoted safe and achievable glucose targets for inpatients
- Special considerations are necessary for patients
  - On enteral or parenteral nutrition
  - Receiving steroids
  - Using insulin pumps
- Established pre-op procedures are also important to optimize glucose control during surgery