

In the name of God

Management of Hyperglycemia in Hospitalized, Non-Critically ill Adults

Presenter:

Dr. Ameneh Ahmadi

26th Tir 1402



The NEW ENGLAND JOURNAL of MEDICINE

CLINICAL DECISIONS

INTERACTIVE AT [NEJM.ORG](https://www.nejm.org)

**Management of Hyperglycemia in Hospitalized,
Non–Critically Ill Adults**

September 15, 2022

2. Recommend stopping metformin and initiating insulin.

SILVIO E. INZUCCHI, M.D

Insulin therapy:

- In most instances, insulin is the preferred treatment for hyperglycemia in hospitalized patients.
- Such recommendations stem from the lack of **efficacy and safety** data in the inpatient setting for the use of non-insulin therapies, since studies of these agents have been performed primarily in the outpatient arena.

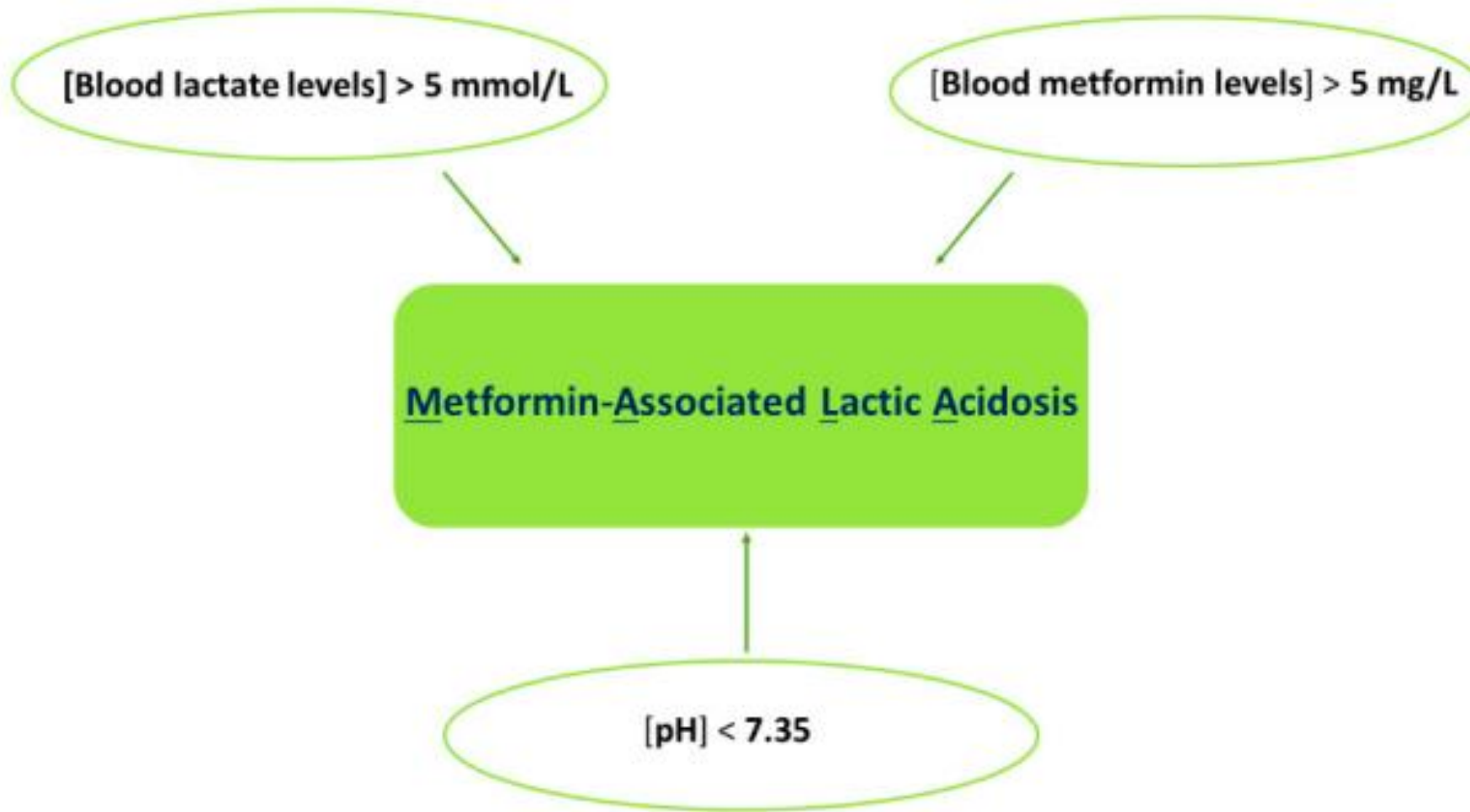
Insulin therapy:

- When they are at home, patients consume their usual home diets, whereas in hospital settings, nutritional intake is commonly impaired, which confers a predisposition to hypoglycemia.

Noninsulin Agents: Why Not?

- Metformin

- Several conditions, common during hospitalization, are associated with the potential for **lactic acidosis**: hepatic failure, poor caloric intake, congestive heart failure, a hypoxic state, advanced age, and use of iodinated contrast media in the presence of one or more of them.



Lactic acidosis is associated with the use of metformin (MALA).

Noninsulin Agents: Why Not?

- Sulfonylureas
 - These medications can cause hypoglycemia, and unlike insulin, their dosing is less flexible, and onset and duration of action can be less predictable.
 - Considering the risk of **hypoglycemia** is increased in those with erratic or poor oral intake, or those with hepatic or renal impairment, all of which may be encountered more frequently in hospitalized patients, sulfonylureas are not considered preferred agents for inpatient glycemic control.

Noninsulin Agents: Why Not?

- Thiazolidinediones
 - These drugs are associated with **peripheral edema** and precipitation or exacerbation of heart failure.

Noninsulin Agents: Why Not?

- GLP-1 receptor agonists **decrease appetite**, which may not be desirable during recovery from illness.
- SGLT2 inhibitors induce a catabolic state, which could confer a predisposition to **euglycemic diabetic ketoacidosis**, and also may theoretically increase the risk of **urinary tract infection**, particularly under conditions of bladder catheterization.

Insulin Therapy

- Accordingly, it is advisable to stop metformin and use insulin instead to manage hyperglycemia for inpatients.
- Insulin remains the most flexible form of glucose-lowering therapy; it can be used in both basal and prandial components and can be adjusted frequently to meet the patient's metabolic needs.

Insulin Therapy

- Scheduled subcutaneous insulin therapy is the backbone of treatment for non–critically ill hospitalized patients with hyperglycemia.
- Components of insulin administration include.
 1. Sliding scale insulin (SSI)
 2. Correction insulin therapy
 3. Scheduled insulin therapy
 4. Basal bolus insulin (BBI)
 5. Carbohydrates counts (CC)

Insulin Therapy

- The **basal-bolus regimen** was recommended as the preferred regimen for the management of hyperglycemia and diabetes in hospital settings.
- This regimen involves the administration of basal insulin given once or twice daily, along with rapid-acting insulin before meals, plus corrective doses of subcutaneous rapid acting insulin for elevated glucose levels.
- The incidence of **mild hypoglycemia** with basal-bolus regimen is around **12% to 30%**.

Insulin Therapy

- For patients with **decreased oral intake or undergoing surgery**, a “basal-plus approach” is currently recommended by clinical guidelines.
- Patients with mild hyperglycemia (<180 mg/ dL) can be initially treated with less aggressive regimens (sliding scale)

Randomized Study of Basal-Bolus Insulin Therapy in the Inpatient Management of Patients With Type 2 Diabetes Undergoing General Surgery (RABBIT 2 Surgery)

GUILLERMO E. UMPIERREZ, MD, DAWN SMILEY, MD

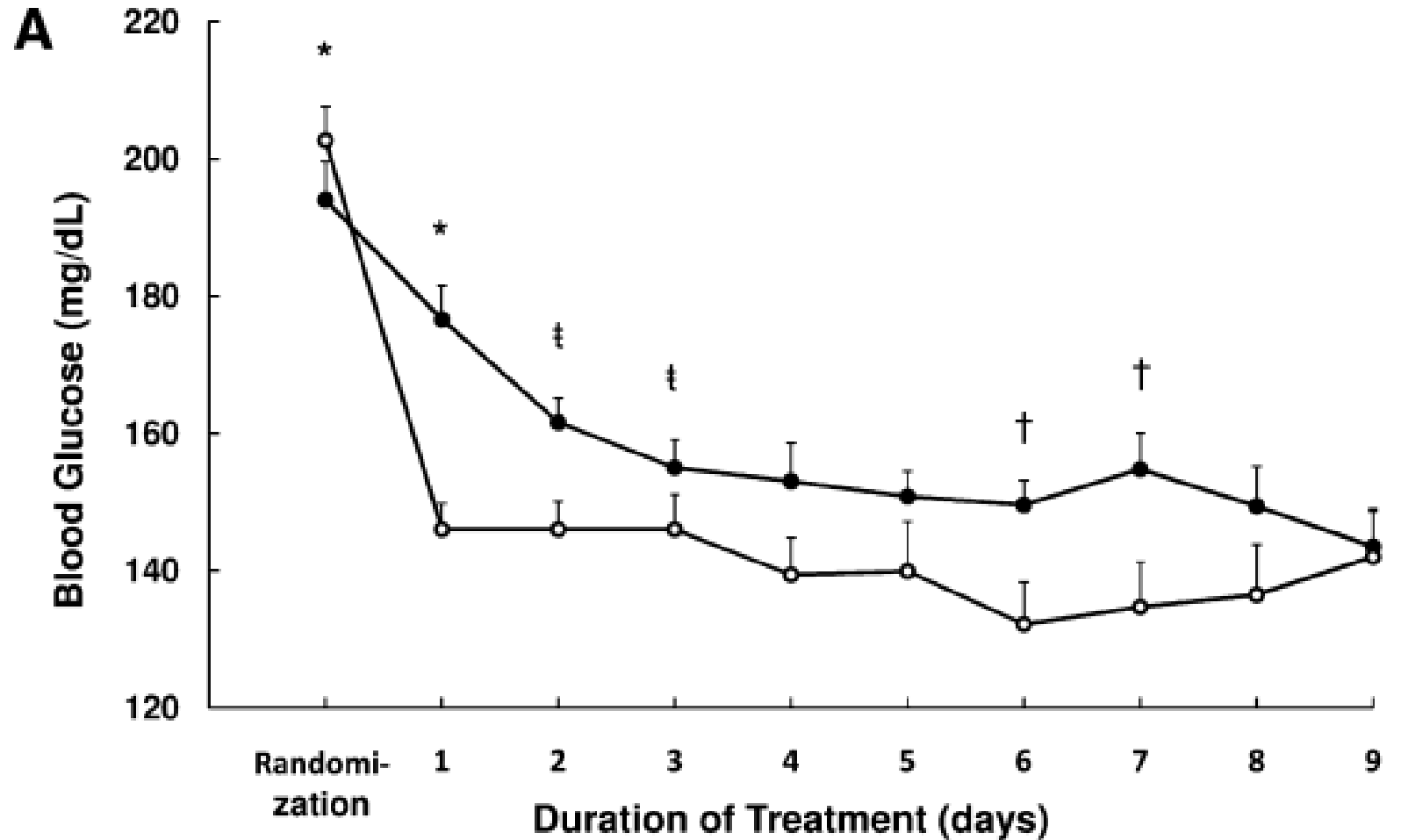
DIABETES CARE, VOLUME 34, FEBRUARY 2011

- This RCT compared the safety and efficacy of a basal-bolus insulin regimen with glargine once daily and glulisine before meals
- (n = 104) to sliding scale regular insulin four times daily (n = 107) in patients with type 2 diabetes mellitus undergoing general surgery.
- Outcomes: included differences in daily blood glucose and a composite of postoperative complications including wound infection, pneumonia, bacteremia, and respiratory and acute renal failure.

Clinical characteristics on admission, type of surgery, and blood glucose values during treatment.

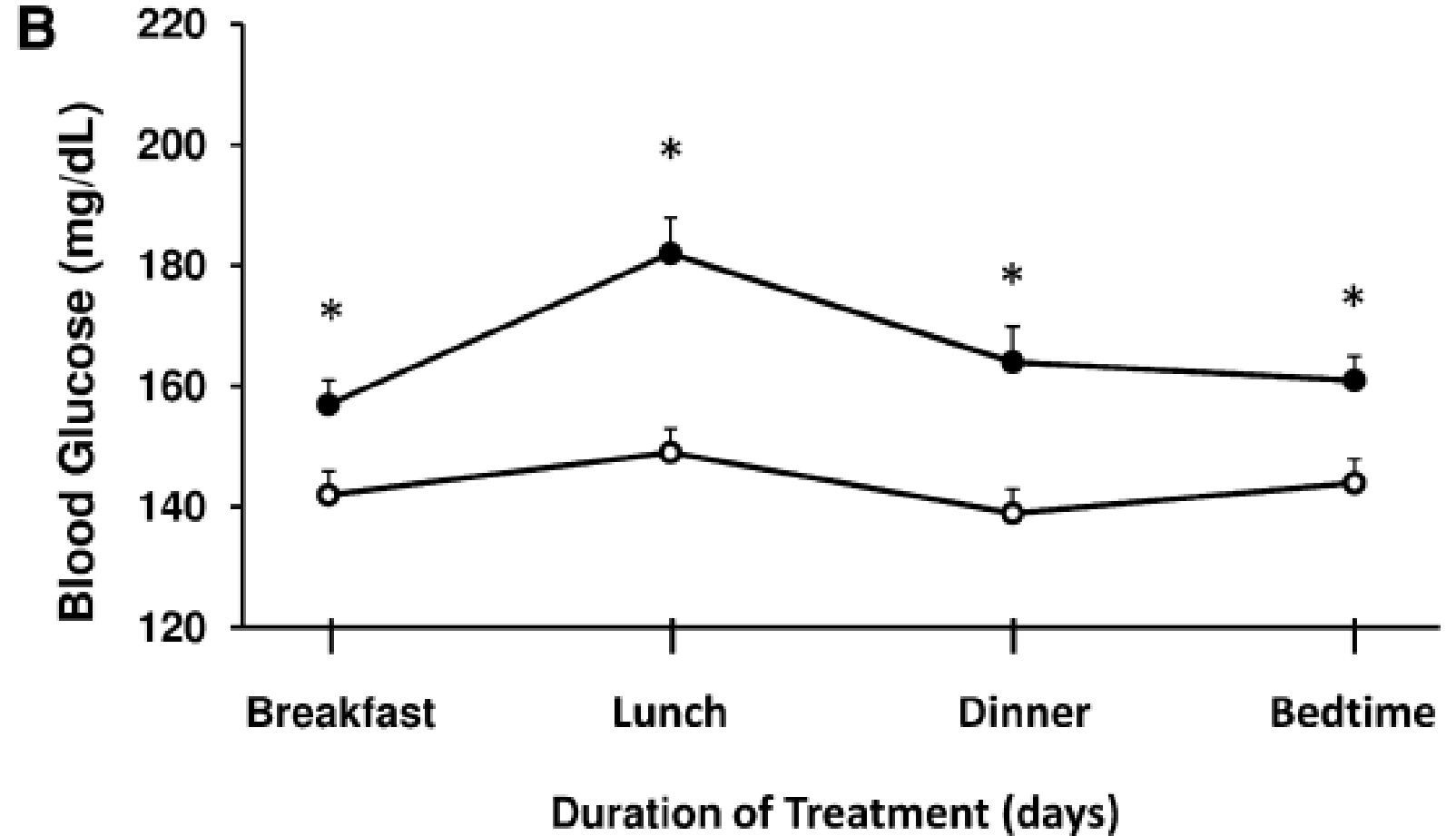
	All	SSI	Basal-bolus insulin	P value
Number of patients	211	107	104	NS
Male/female	107/104	53/54	54/50	NS
Race (white/black/other)	75/117/19	40/59/8	35/58/11	NS
Age (years)	58 ± 11	57 ± 10	58 ± 12	NS
BMI (kg/m ²)	31.3 ± 8.0	32.2 ± 8.5	30.3 ± 7.4	NS
Body weight (kg)	90.5 ± 24.1	93.1 ± 25.6	87.9 ± 22.2	NS
Duration diabetes mellitus (years)	6.5 ± 6.3	6.8 ± 6.3	6.3 ± 6.2	NS
Serum creatinine (mg/dL)	0.9 ± 0.3	0.9 ± 0.3	1.0 ± 0.3	NS
Diabetic treatment on admission				
Diet alone	17	11	6	NS
Oral agents	153	80	73	NS
Insulin alone	22	11	11	NS
Insulin + oral agents	20	11	9	NS
Type of surgery				
Cancer	76	40	36	NS
Gastrointestinal/genitourinary benign	59	28	31	NS
Vascular	31	15	16	NS
Trauma	38	20	18	NS
Others	7	5	2	NS
BG values				
Admission (mg/dL)	190 ± 92	184 ± 80	197 ± 104	NS
Randomization	198 ± 54	194 ± 56	202 ± 51	NS
Presurgery (mg/dL)	178 ± 71	181 ± 72	174 ± 70	NS
Postsurgery (mg/dL)	198 ± 53	195 ± 52	201 ± 55	NS
After 2nd day of Rx	159 ± 42	172 ± 46	145 ± 32	<0.001
BG values after 24-h treatment, % readings				
<140 mg/dL	41.9 ± 30.9	31.2 ± 28	52.9 ± 30.1	<0.001
70–140 mg/dL	41.6 ± 30.3	31.7 ± 28.1	51.8 ± 29.2	<0.001
>180 mg/dL	28.1 ± 30.7	35.3 ± 33.5	20.5 ± 25.5	<0.001

A: Glucose levels during basal-bolus and SSI treatment. Changes in blood glucose concentration after the 1st day of treatment with basal-bolus with glargine once daily plus glulisine before meals (○) and with SSI 4-times daily (●)



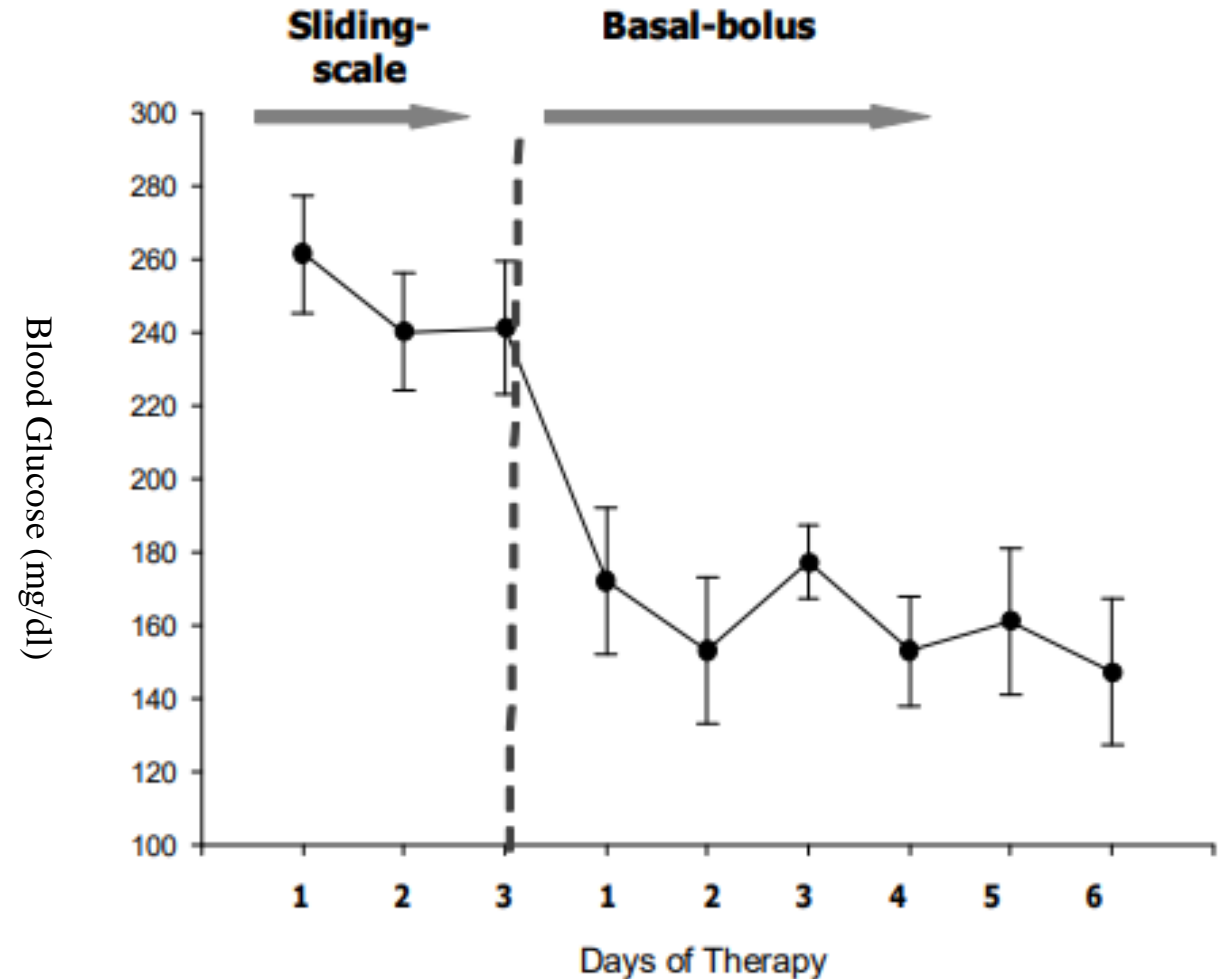
Patients treated with insulin glargine and glulisine had better glycemic control than SSI ($P < 0.001$)

B: Glucose levels before meals and bedtime. Premeal and bedtime glucose levels were higher throughout the day in the SSI group (●) compared with basal-bolus regimen (○).



Premeal glucose levels before meals and at bedtime were significantly higher in the SSI group compared with basal bolus regime.

Thirteen patients (12%) treated with SSI remained with BG > 240 mg/dL despite increasing the SSI dose to the maximal or insulin resistant scale.



Treatment Failure with Sliding Scale Insulin

Table 2—Composite hospital complications and outcomes composite hospital complications

	All	SSI	Basal-bolus insulin	P value
Wound infections	14	11	3	0.050
Pneumonia	3	3	0	0.247
Acute respiratory failure	6	5	1	0.213
Acute renal failure	15	11	4	0.106
Bacteremia	3	2	1	0.999
Number of patients with complications	35	26	9	0.003
Mortality	2	1	1	NS
Postsurgery ICU admission (%)	16	19.6	12.5	NS
Length of stay (days)				
ICU	2.51 ± 1.90	3.19 ± 2.14	1.23 ± 0.60	0.003
Hospital	6.8 ± 8.9	6.3 ± 5.6	7.23 ± 11.39	NS

Table 3—Hypoglycemic events

Variable	All	SSI	Basal-bolus insulin	P value
Number of patients	211	107	104	
Number of BG tests	3,778	1,826	1,952	
BG <40 mg/dL				
Number of patients (%)	4 (3.8)	0 (0)	4 (3.8)	0.057
Number of events	4	0	4	
Number of readings (%)	0.10	0	0.20	
BG <60 mg/dL				
Number of patients (%)	14 (6.6)	2 (1.9)	12 (11.5)	0.005
Number of events	17	2	15	
Number of readings (%)	0.45	0.11	0.77	
BG <70 mg/dL				
Number of patients (%)	29 (0.8)	5 (4.7)	24 (23)	<0.001
Number of events	44	6	38	
Number of readings (%)	1.16	0.33	1.95	

- Basal-bolus treatment with glargine once daily plus glulisine before meals improved glycemic control and reduced hospital complications compared with SSI in general surgery patients.
- Basal-bolus insulin regimen is preferred over SSI in the hospital management of general surgery patients with type 2 diabetes.

Randomized Study Comparing a Basal-Bolus With a Basal Plus Correction Insulin Regimen for the Hospital Management of Medical and Surgical Patients With Type 2 Diabetes

Basal Plus Trial

GUILLERMO E. UMPIERREZ, MD- DAWN SMILEY, MD

Diabetes Care 36:2169–2174, 2013

- Prospective multicenter trial randomized
- 375 patients with T2D treated with diet, oral antidiabetic agents, or low-dose insulin (≤ 0.4 units/kg/day) to receive a basal-bolus regimen with glargine once daily and glulisine before meals, a basal plus regimen with glargine once daily and supplemental doses of glulisine, and sliding scale regular insulin (SSI).

Primary outcome of the study was difference in glycemic control, as measured by mean daily BG concentration, among patients treated with basal-bolus, basal plus, and SSI regimens.

Secondary outcomes included differences between treatment groups in any of the following measures: number of hypoglycemic events (BG <70 and <40 mg/dL) after the first day of treatment, number of episodes of hyperglycemia (BG >200 mg/dL) after the first day of treatment, TDD of insulin, hospital stay, and hospital complications.

Table 1—Clinical characteristics of study patients

Variable	Basal-bolus	Basal plus	SSI	P value
No. of patients	144	133	74	
Sex				0.96
Male	86 (60)	78 (59)	44 (59)	
Female	58 (40)	55 (41)	30 (41)	
Age (years)	58.7 ± 11	58.6 ± 13	58.7 ± 12	0.99
BMI (kg/m ²)	32.6 ± 8	33.0 ± 9	32.6 ± 9	0.96
Body weight (kg)	96 ± 24	98 ± 28	95 ± 29	0.74
Duration of diabetes (years)	9.9 ± 8	7.6 ± 7	8.4 ± 7	0.02
Admission service				0.91
Medicine	82 (56)	76 (51)	40 (54)	
Surgery	64 (44)	57 (43)	34 (46)	
Hospital stay (days)	5.9 ± 5	6.0 ± 6	5.5 ± 5	0.67
Admission diabetes therapy				0.002
Diet alone	18 (12)	10 (8)	15 (20)	
Oral agents	99 (68)	98 (74)	54 (73)	
Insulin alone	20 (14)	15 (11)	0 (0)	
Insulin with oral agents	9 (6)	10 (8)	5 (7)	

outcomes

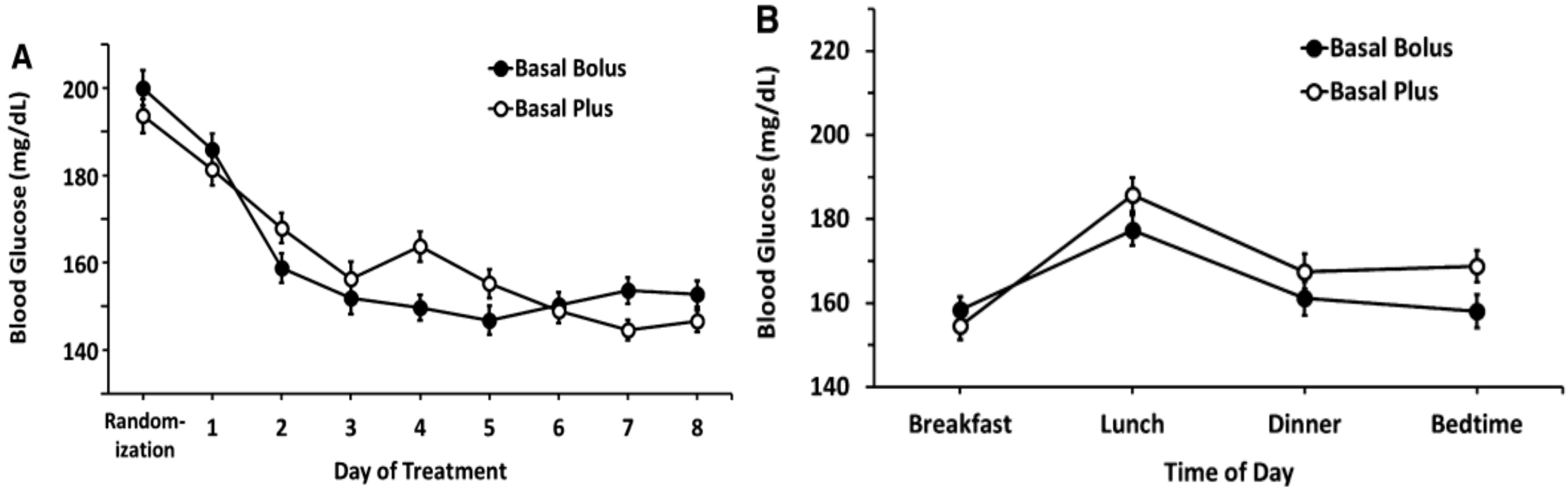
Glycemic control, insulin therapy, and hospital complications in patients treated with basal-bolus, basal plus, and SSI regimens

	Basal-bolus	Basal plus	SSI	P value*
Glycemic control				
HbA _{1c} (%)	8.7 ± 2.5	8.3 ± 2.3	8.0 ± 2.1	0.09
Admission BG (mg/dL)	210 ± 89	207 ± 83	185 ± 72	0.12
Randomization BG (mg/dL)	200 ± 49	194 ± 45	187 ± 43	0.13
Mean BG after first day of therapy	156 ± 36	163 ± 37	172 ± 41	0.046
BG readings after 24 h of treatment				
BG readings 70–140 mg/dL (%)	42 ± 30	37 ± 29	32 ± 32	0.045
BG readings >140 mg/dL (%)	56 ± 31	62 ± 30	68 ± 32	0.019
BG readings >180 mg/dL (%)	27 ± 28	33 ± 31	38 ± 35	0.12
Treatment failures				
Treatment failures	0 (0)	3 (2)	14 (19)	<0.001
Day of treatment failure	—	3.3 ± 0.6	1.9 ± 1	0.036
Daily insulin				
Total insulin (units/day)	32.2 ± 16	27.3 ± 11	8.2 ± 5	<0.001
Total insulin (units/kg/day)	0.34 ± 0.2	0.29 ± 0.1	0.1 ± 0.1	<0.001
Total glargine insulin (units/day)	21.1 ± 9	22.1 ± 8	8.2 ± 5	0.21
Total glulisine insulin (units/day)	17.1 ± 9	9.3 ± 6	—	<0.001
Total regular insulin (units/day)	—	—	8.2 ± 5	

outcomes

Glycemic control, insulin therapy, and hospital complications in patients treated with basal-bolus, basal plus, and SSI regimens

	Basal-bolus	Basal plus	SSI	<i>P</i> value*
Complications				
Wound infections	1(1)	3 (3)	1 (1)	0.54
Pneumonia	3 (2)	0 (0)	0 (0)	0.24
Acute respiratory failure	1(1)	2 (2)	0 (0)	0.61
Acute renal failure	9 (7)	8 (7)	3 (4)	0.84
Bacteremia	7 (5)	4 (3)	3 (4)	0.78
Mortality	0 (0)	3 (2)	0 (0)	0.11
Hypoglycemic events				
BG tests per patient during study period	14.8 ± 11	14.3 ± 10	11.4 ± 9	0.044
Patients at <70 mg/dL	23 (16)	17 (13)	2 (3)	0.009
BG readings <70 mg/dL (%)	1.7 ± 5.3	1.1 ± 3.7	0.4 ± 2.2	0.019
Patients at <60 mg/dL	12 (8)	7 (5)	1 (1)	0.11
BG readings <60 mg/dL (%)	0.7 ± 3.4	0.4 ± 1.7	0.2 ± 1.5	0.12
Patients at <40 mg/dL	1 (1)	1 (1)	0 (0)	0.76
BG readings <40 mg/dL (%)	0.1 ± 0.8	0.1 ± 0.6	0 ± 0.0	0.76



Differences in glycemic control in medical and surgical patients with T2D treated with basal-bolus (●) and basal plus (○) regimens.

A: Mean daily BG levels. B: Mean BG levels before meals and bedtime

- The use of a basal plus regimen with glargine once daily plus corrective doses with glulisine insulin before meals resulted in glycemic control similar to a standard basal bolus regimen.
- The basal plus approach is an effective alternative to the use of a basal-bolus regimen in general medical and surgical patients with T2D.

ADA Recommendations

Basal insulin or a basal plus bolus correction insulin regimen is the preferred treatment for non critically ill hospitalized patients with poor oral intake or those who are taking nothing by mouth.

A

An insulin regimen with basal, prandial, and correction components is the preferred treatment for most non critically ill hospitalized patients with adequate nutritional intake.

A

Use of a correction or supplemental insulin without basal insulin (often referred to as a sliding scale) in the inpatient setting is discouraged.

A

CLINICAL SCENARIO

- A 72-year-old woman with a body-mass index of 35 and a 5-year history of type 2 non–insulin-dependent diabetes mellitus without complications presents to the emergency department with fevers, cough, and decreased oral intake.
- On arrival, she has a temperature of 38.1°C; her oxygen saturation is 88% while she is breathing ambient air, and she is given supplemental oxygen.



CLINICAL SCENARIO

- Her condition is hemodynamically stable.
- Laboratory tests are performed and show a neutrophil-predominant leukocytosis. Blood lactate and liver enzyme levels are within normal limits.
- A chest radiograph reveals an opacity in the left lower lobe, and intravenous antibiotics are initiated for treatment of community-acquired pneumonia.



CLINICAL SCENARIO

- She is admitted to your general medicine service for further care.
- On admission, you confirm her home medications, which include metformin, 500 mg twice a day. Her last glycated hemoglobin measurement in clinic 2 months ago was 7.7%.



CLINICAL SCENARIO

- You view her laboratory results and note a fasting glucose level of 175 mg/dl and a creatinine level of 0.9 mg/dl, which was similar to the level 2 months previously.
- She appears tired but is alert and oriented and is breathing comfortably.
- You notice that she has finished only about **a quarter of the food on her lunch tray.**



The question here is whether this specific patient's metformin regimen, which had been maintaining reasonable glycemic control before admission, should be continued during her hospitalization.

Thank you for your attention!

