



# Perioperative Medicine Summit

Evidence Based Perioperative Medical Care

## Debate in Perioperative Medicine: Are Glycohemoglobin Levels Indicated Prior to Surgery?

Moderator

Barbara Slawski, MD, MS, FACP, SFHM

Professor of Medicine and Orthopaedic Surgery;

Interim Chief, Division of General Internal Medicine;

Chief, Section of Perioperative and Consultative Medicine;

Department of Medicine, Medical College of Wisconsin

**David Baldwin, MD**  
Professor of Medicine  
Rush University Medical Center  
Chicago IL

**Steven L. Cohn, MD, FACP, SFHM**  
Medical Director, UHealth Preoperative Assessment  
Center (UPAC)  
Director, Medical Consultation Services  
University of Miami Hospital/Jackson Memorial Hospital  
Professor of Clinical Medicine  
University of Miami Miller School of Medicine

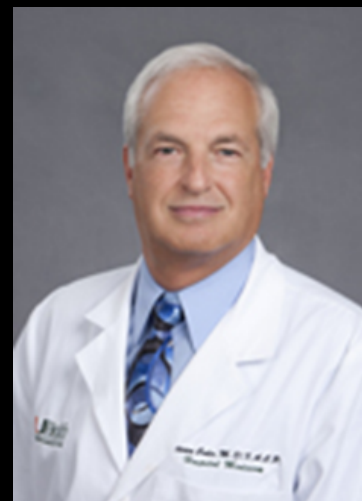
# Disclosures

David Baldwin

Research Grant Support

Novo-Nordisk

Boehringer Ingelheim



# DEBATE

The fine art of using the most words possible to not answer a direct question

A 58 year old woman presents for preoperative evaluation prior to total knee arthroplasty scheduled in 5 days. She cannot walk one block due to pain. She states she has been unable to lose weight or control her DM because she has knee pain and cannot exercise.

### Medical History:

- DM type 2 with peripheral neuropathy
- HTN
- OSA on CPAP

Medications: Metformin 1000mg BID, Losartan 50mg

Physical Exam: BP 164/84 P 72 BMI 44 Obese, antalgic gait

Labs: HbA1C= 8.4%, Cre 1.1 mg/dL, Glucose (random) 201 mg/dL

Would you delay this patient's surgery for glycemic control?



# Perioperative Medicine Summit

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Evidence Based Perioperative Medical Care

## The Case for Reasonable Control of Hyperglycemia Prior to Elective Surgery

David Baldwin MD  
Section of Endocrinology  
Rush University Medical Center

# Surgical Site Infections Following Colorectal Surgery in Patients with Diabetes: Association with Postoperative Hyperglycemia

- 149 patients
- 83% of patients only received sliding scale insulin
- 24% of patients had mean blood glucose > 200 mg/dl
- Surgical wound infections were defined by CDC criteria
- There were twice as many surgical wound infections in the patients with mean BG > 200 mg/dl as compared with < 200 mg/dl (p=0.02)

J Gastrointestinal Surg, 13:508-515, 2009

## The Effect of Diabetes Mellitus Surgical Site Infections after Colorectal and Noncolorectal General Surgical Operations

- Amer College Surgery QI data file 2005-2006
- 129,909 patients undergoing general surgery
- Diabetic non-colorectal surg: site infections 5.5%
- Non-diabetic non-colorectal infections 3.1%
- Diabetic colorectal infections were 15.4%
- Non-diabetic colorectal infections were 11.0%
- Colorectal patients with infection were twice as likely to return to the OR and length of stay was 3 days longer compared with non-infected

Am Surg 76:697-702, 2010

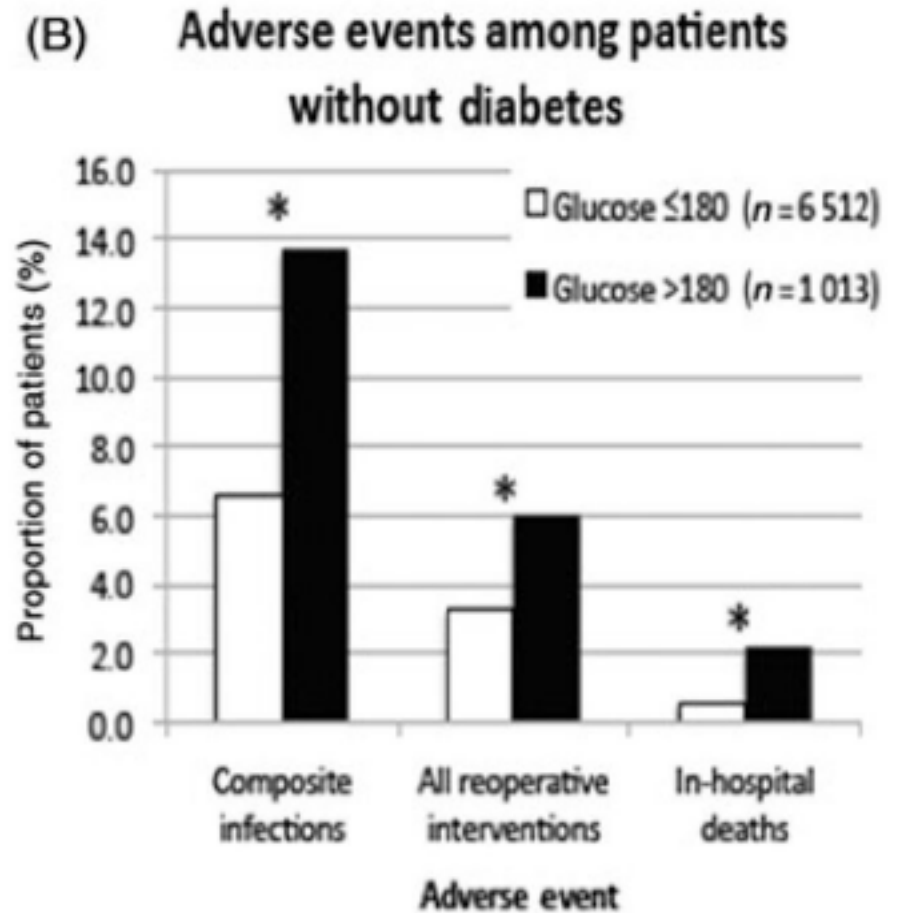
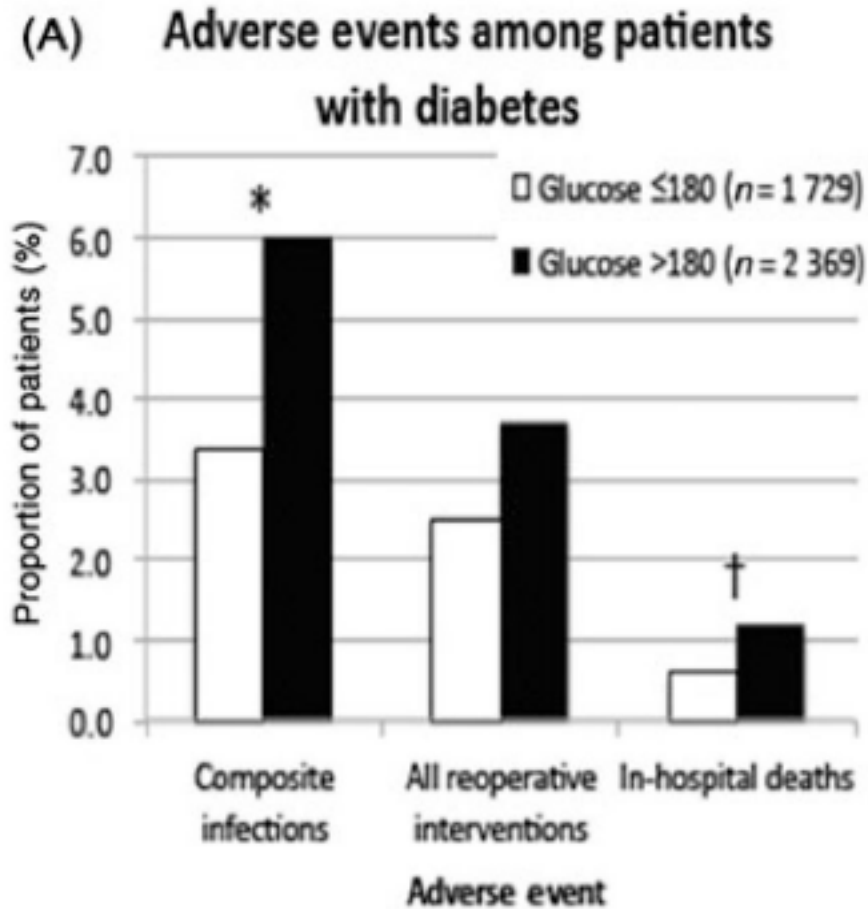


# Adverse Outcomes after General Surgery in Patients With and Without Diabetes

- Surgical Care and Outcomes Assessment- Washington State
- 11,633 cases, abdominal, vascular and spinal surgery had post-op BG levels
- 35 % of these patients had a history of diabetes
- Patients were stratified by the single highest blood glucose on POD 0, POD 1 and POD 2
- In multivariate analysis, patients with one blood glucose  $> 180$  mg/dl had an increased risk of infection OR 2.0
- Patients with blood glucose  $> 180$  mg/dl on all 3 days had a higher risk of infection OR 3.1 as compared with all blood glucoses  $< 180$  mg/dl
- Those patients who received treatment with insulin had the risk of infection decreased by 50%

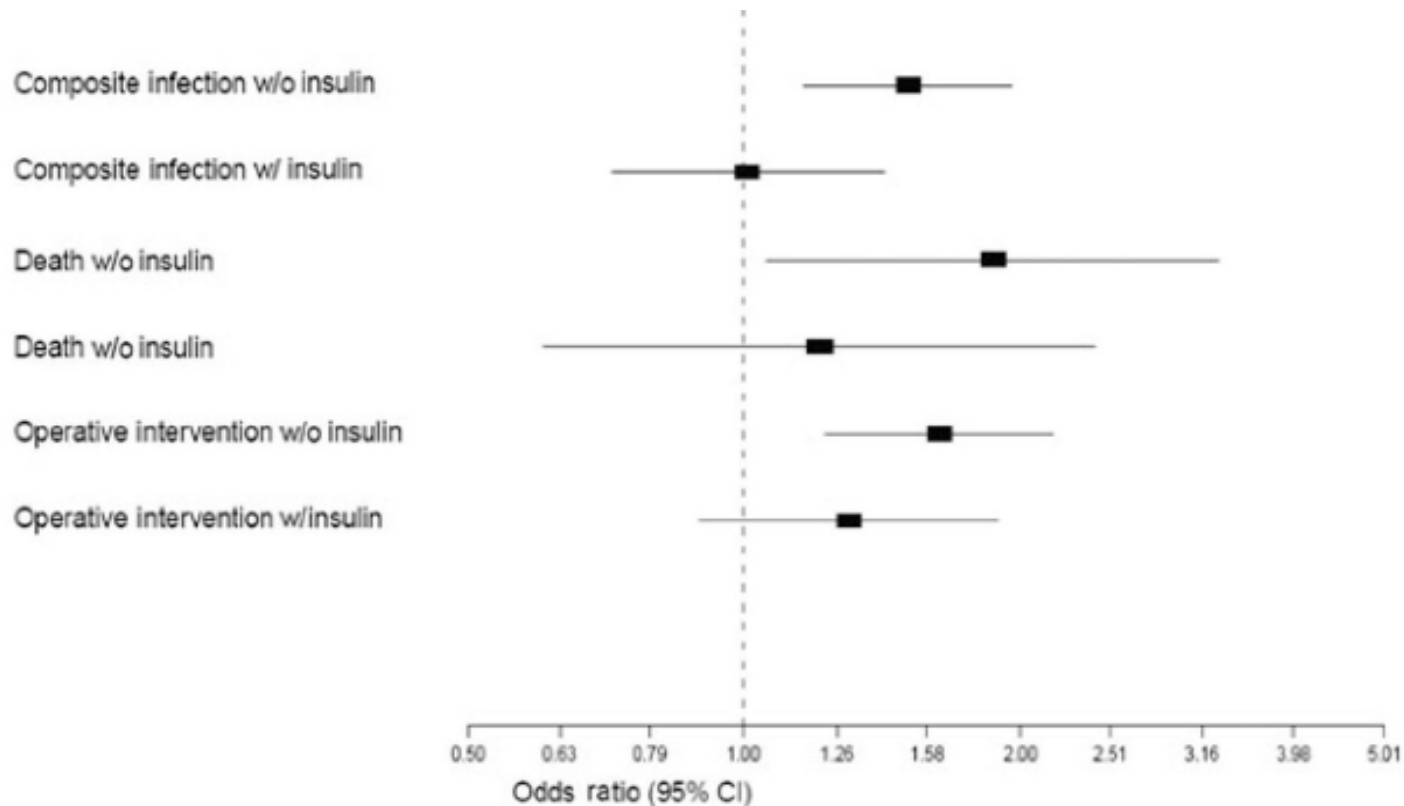
Kwon et al. *Annals of Surgery* 257: 8-14, 2013

# Adverse Outcomes after General Surgery in Patients With and Without Diabetes



Kwon et al. Annals of Surgery 257: 8-14, 2013

# Adverse Outcomes after General Surgery in Patients With and Without Diabetes



Kwon et al. *Annals of Surgery* 257: 8-14, 2013

# Surgical site infections after abdominal surgeries

- Single center study evaluated the association of HBA1C and major post-op complications
- 438 cases were chosen because they had a pre-op HBA1C
- 22% had a major complication
- HBA1C > 6.5% was significantly associated with the development of a major complication OR 1.95

J American Coll Surgeons. 221:854-861, 2015

# Hospital length of Stay after major non-cardiac surgeries in patients with diabetes

- National Surgical Quality Improvement Program database
- 449 cases were analyzed by HBA1C quartiles
  - < 6.5%
  - 6.5% - 8%
  - 8% -10%
  - > 10%
- When compared with age/sex/BMI matched controls, diabetic patients with HBA1C > 8% has a significantly longer length of stay, 7.9 days vs 5.2 days  $p < 0.001$
- Shouldn't we pay more attention to pre-operative HBA1C?

Diabetes Care 37:611-617, 2015

# Surgical Site Infection after Total Knee Arthroplasty

## in Patients with Diabetes

- 714 cases single center
- All patients had pre-op HBA1C and fasting blood glucose
- Mean HBA1C = 7%
- Multivariate analysis
- HBA1C > 8% was significantly associated with infection OR 6.1
- Fasting BG > 200 was significantly associated with infection OR 9.2
- Shouldn't these sub-groups of patients with poorly controlled diabetes be selected for delay of surgery and improvement of diabetic control?

Clinical Orthopedic Research. 473: 1726-1731, 2015

# HBA1C as a Marker for Surgical Complications after Total Joint Arthroplasty in Patients with Diabetes

- VA surgical quality improvement program database
- 6088 cases with diabetes and pre-op HBA1C
- 35% of patients had HBA1C > 7%
- There was a significant association between HBA1C and postoperative complications if HBA1C was > 7%.
- There was a steady linear increase in the risk of postoperative complications as the HBA1C increased from 7% to 8% to 9% etc.
- There was a significant association between pre-op HBA1C and the degree of postoperative hyperglycemia

Journal of Arthroplasty. Suppl 1:25-29, 2013

# Can Total Joint Arthroplasty Candidates with Diabetes and HBA1C > 7% be Improved if Surgery is Delayed?

- VA Palo Alto (Stanford University)
- A policy was established whereby patients with diabetes were only scheduled for joint arthroplasty if HBA1C was < 7%.
- 345/404 (85%) patients met this expectation and underwent surgery
- 59 (15%) patients had surgery delayed because HBA1C was > 7%
- 6% of total patients were never able to get their HBA1C < 7%
- If an HBA1C cut-off of 8% for delay of surgery had been used, 93% of patients would have been eligible for surgery without delay and only 2% of patients would have failed to meet that cut-off.
- Perhaps a HBA1C target of < 8% would better balance the risk vs access to a better quality of life.

Journal of Arthroplasty. Suppl 1:25-29, 2013

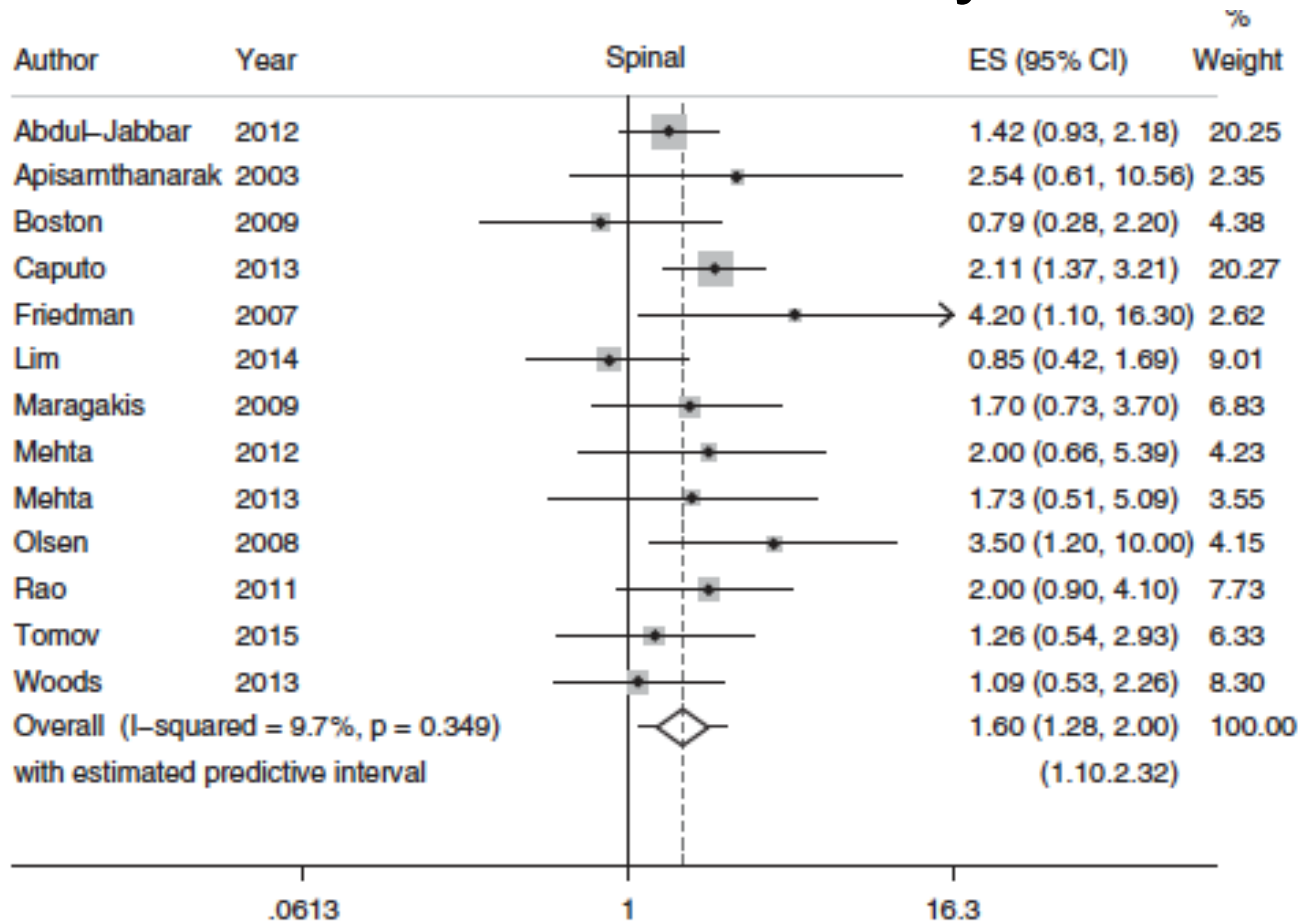


# Diabetes and the Risk of Surgical Site Infection: Meta Analysis

- 94 studies met criteria for analysis
- Surgical site infections were more common in patients with diabetes. The overall effect size for the association was OR 1.53.
- The association was higher for cardiac surgery as compared with other types of surgery OR 2.03.

Infection Control and Hospital Epidemiology. 37: 88-99, 2016

# Diabetes and the Risk of Surgical Site Infection: Meta Analysis



Infection Control and Hospital Epidemiology. 37: 88-99, 2016

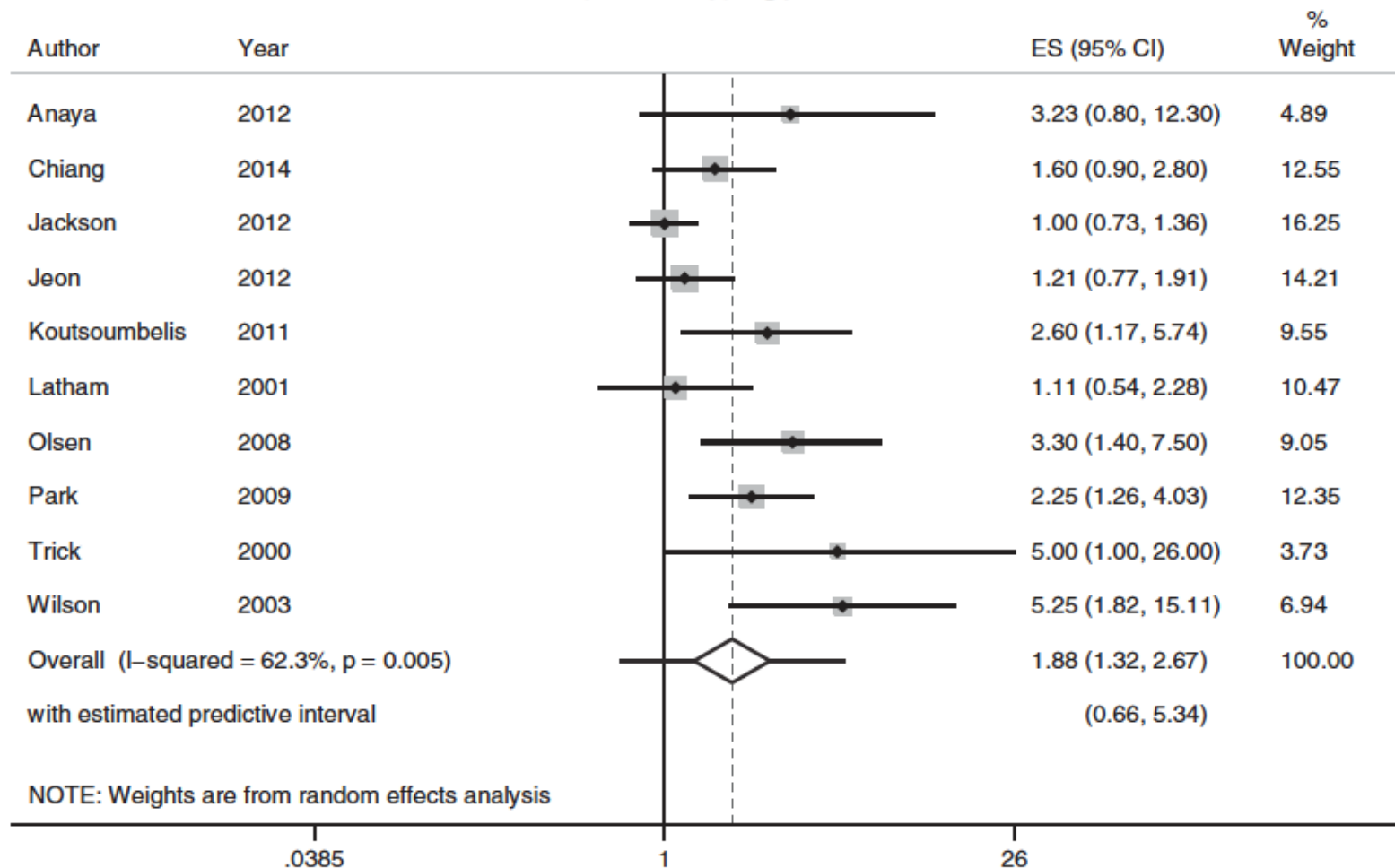
# Diabetes and the Risk of Surgical Site Infection: Meta Analysis

Surgery Type	No. of Studies	Pooled Estimate	95% Prediction Interval
Gynecological	6	1.61	1.15–2.24
Colorectal	7	1.16	0.93–1.44
Arthroplasty	6	1.26	1.01–1.66
Breast	5	1.58	0.91–2.72
Cardiac	15	2.03	1.13–4.05
Spinal	14	1.66	1.10–2.32
Other/Multiple surgery types combined	37	1.46	1.07–2.00

Infection Control and Hospital Epidemiology. 37: 88-99, 2016

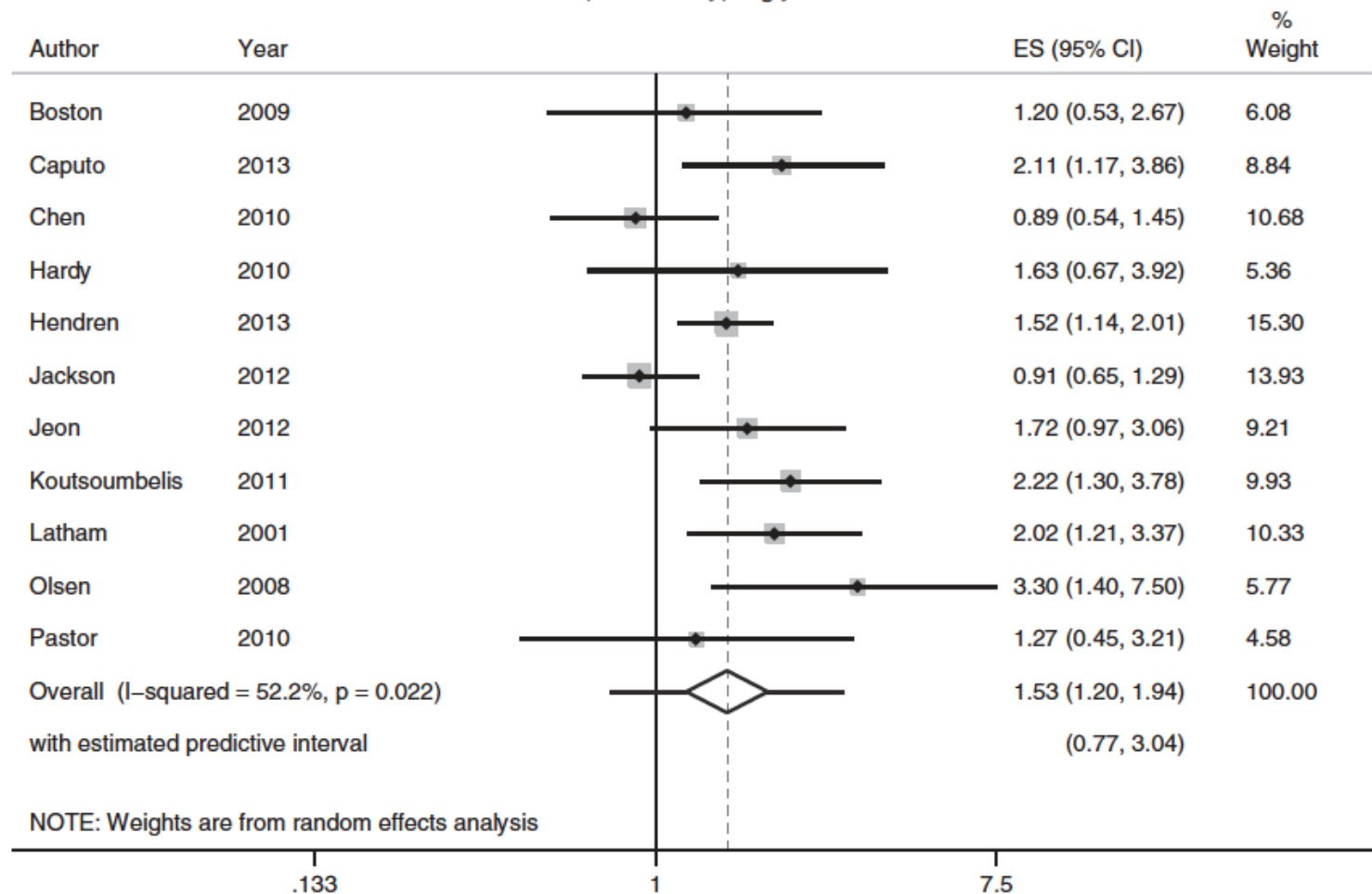
# Diabetes and the Risk of Surgical Site Infection: Meta Analysis

## Preoperative Hyperglycemia



# Diabetes and the Risk of Surgical Site Infection: Meta Analysis

Postoperative Hyperglycemia



Infection Control and Hospital Epidemiology. 37: 88-99, 2016

# Conclusions

- Pre-operative hyperglycemia is highly associated with post-operative hyperglycemia
- Both are associated with an increased risk of post-op infections after a wide variety of surgeries
- All patients with a h/o diabetes or a random pre-op blood glucose > 140 mg/dl should have pre-op HBA1C measured
- Correct uncontrolled hyperglycemia before the OR
- Reduce your patient's risk of infection
- Conserve your hospital's financial resources

# HbA1c and Orthopedic Surgery

Steven L. Cohn, MD, FACP, SFHM



# The Questions

- ⊙ Is an elevated HbA1c predictive of postop complications?
  - Is there a specific cutoff level?
  - Which complications?
- ⊙ Is an elevated glucose predictive of postop complications?
  - Is there a specific cutoff level?
  - Is it preop, intraop, postop, highest, average?
- ⊙ Is there any correlation between HbA1c and periop glucoses?
- ⊙ Will active interventions improve outcomes?
- ⊙ **Do we have any answers???** **What is the evidence???**



# THIS IS WHAT IT'S LIKE TO LEARN ENDOCRINOLOGY

SO  $17\alpha$ -HYDROXYLASE ACTS ON PROGESTERONE WHICH BECOMES  $17\alpha$ -HYDROXY PROGESTERONE WHICH CAN EITHER GET  $21$ -HYDROXYLASE TO BECOME  $11$ -DEOXYCORTISOL OR GET  $17,20$ -LYASE TO BECOME ANDROSTENEDIONE.



I'M  
CONFUSED.



OH, SORRY. IT'S A LITTLE  
TRICKY AT FIRST. BUT I  
BROUGHT ALONG THIS  
HELPFUL DIAGRAM.





**CAUTION**

**BE WARY OF THESE  
RECOMMENDATIONS!**

## Why order a HbA1c preop?

- ⦿ Findings from various studies show that HbA1c can Dx previously unknown DM, predict periop insulin sensitivity, preop glucose, increased postop glucose and complications (colorectal), UTI (ortho), long-term mortality (CABG), short-term morbidity (vasc).
- ⦿ Many other studies have found no association with HbA1c and increased infections, other postop complications, and death.

## My Opinion

- ⦿ Hyperglycemia, either preop or postop, is associated with increased risk of some complications.
- ⦿ HbA1c is a poor marker for complications:
  - Not necessarily correlated with preop glucose
  - No cutoff that is prohibitive or clearly associated with increased risk

# The impact of preoperative testing for blood glucose concentration and haemoglobin A1c on mortality, changes in management and complications in noncardiac elective surgery: a systematic review.

Bock et al, Eur J Anaesthesiol. 2015

- ⦿ Preop HbA1c not required in nondiabetic pts
- ⦿ Vasc and ortho surgery carry an elevated risk justifying preop testing for blood glucose or HbA1c as a screening tool.

# Is Hemoglobin A1c or Perioperative Hyperglycemia Predictive of Periprosthetic Joint Infection or Death Following Primary Total Joint Arthroplasty?

Chrastil et al. J Arthroplasty. 2015

- VA VINCI database – 13,272 pts with DM
  - Well-controlled (HbA1c <7%; n=8237; 62%) vs poorly controlled (HbA1c  $\geq$ 7%; n=5035; 38%)
- **HbA1c $\geq$ 7: No increased risk of infection** (HR=0.86;p=.23)
  - Increased risk of 2-year mortality (HR=1.3;p=.01)
- Preop hyperglycemia (>194mg/dL):increased risk of PJI (HR=1.44;p=.008)

# Surgical outcomes of total knee replacement according to diabetes status and glycemic control, 2001 to 2009.

Adams et al. J Bone Joint Surg Am. 2013

- Kaiser Permanente TJR Registry (TKR: n=40,491)
  - 7567 (18.7%) had DM
- No association between DM (<7 or ≥7%) vs no DM for risk of deep infection, revision, or VTE (also MI and all-cause rehospitalization)

	No DM	DM HbA1c<7 (OR; 95%CI)	DM HbA1c≥7 (OR; 95%CI)
Deep infection	-	OR 1.31 0.92-1.86	OR 0.55 0.29-1.06
Revision arthroplasty	-	OR 1.32 0.99-1.76	OR 1.03 0.68-1.54
DVT or PE	-	OR 0.84 0.60-1.17	OR 0.70 0.43-1.13

# Diabetes mellitus, hemoglobin A1C, and the incidence of total joint arthroplasty infection.

Iorio et al. J Arthroplasty. 2012

- Lahey Clinic TJA database: 3468 pts; 4241 TJA
- 46 infections – 4-fold higher risk with DM
  - 12 (3.4%) in DM; 34 (.87%) non-DM ( $p < .00001$ )
- No correlation with HbA1c (<7 vs >7%);  $p = .293$



# Diabetes mellitus, hyperglycemia, hemoglobin A1C, and the risk of prosthetic joint infections in total hip and knee arthroplasty.

Kremers et al. J Arthroplasty. 2015

- 20,171 TJA
- Higher risk of infection with DM, DM meds, periop hyperglycemia
  - Attenuated after adjustment for BMI, type of surgery, ASA, operative time
- No association with HbA1c

# Preoperative hyperglycemia predicts infected total knee replacement.

Jansen et al. Eur J Intern Med. 2010

- HbA1c  $\geq 6.5\%$  predicted postop PJI within 1 yr after TKR
  - OR 1.60; CI 1.09-1.37 per 1% unit increase
  - PPV 2.84%; accuracy 55.1%
- But A1c was anytime from 1 yr preop to 3 mos postop & only 381 pts with A1c data

The effect of glucose metabolism markers on the 1-year postoperative prosthetic joint infection rate.

		n	Infections		Univariate regression	
			%	95% CI	HR	95% CI
Plasma glucose	Per 1 mmol/l <sup>2</sup> increase	1565	-	-	1.14	1.01-1.29
	<6.1 mmol/l	910	0.44	0.17-1.12	1	
	6.1-6.9 mmol/l	324	0.93	0.32-2.69	2.10	0.47-9.39
	$\geq 7.0$ mmol/l	331	2.42	1.23-4.70	5.65	1.70-18.77
Glycosylated hemoglobin	Per 1%-unit unit increase	381	-	-	1.61	1.12-2.29
	Normal, <6.5%	205	0		(p = 0.015) <sup>b</sup>	
	Increased, $\geq 6.5\%$	176	2.84	1.22-6.48		

# Preoperative A1C and clinical outcomes in patients with diabetes undergoing major noncardiac surgical procedures.

Underwood et al, Diabetes Care, 2014

- Higher rate of complications with DM.
- Study suggests **A1C > 8%** is associated with poor surgical outcomes (longer LOS).
  - However, **A1C < 6.5%** also had higher LOS!
  - 65% of pts with DM did not have A1C within 3 mos
  - Too few events to evaluate for death, infection, or readmission rate.

**Table 2—Patient characteristics and surgical outcomes by A1C category**

Characteristics	Control subjects (N = 888)	A1C ≤ 6.5% (N = 109)	A1C > 6.5–8% (N = 202)	A1C > 8–10% (N = 91)	A1C > 10% (N = 47)
Surgery (vascular)	128 (14)	30 (28)*	41 (20)	29 (32)*	14 (30)
Hospital LOS (days)	5.2 ± 5.3	8.3 ± 7.4*	5.3 ± 5.6	7.9 ± 7.0*	6.8 ± 6.7
Postoperative acute renal failure	3 (0.3)	1 (0.9)	0 (0)	0 (0)	0 (0)
Death within 30 days	0 (0)	9 (8)	6 (3)	3 (3)	1 (2)
Wound class (dirty)	0 (0)	12 (11)	18 (9)	11 (12)	3 (6)

# Elevated postoperative blood glucose and preoperative hemoglobin A1C are associated with increased wound complications following total joint arthroplasty.

Stryker et al. J Bone Joint Surg Am. 2013

- 1702 pts – TJA; 237 with 30 day complications
  - Results based on only 30 pts with wound infections and matched controls
  - Increased risk with mean **postop gluc >200** or **HbA1c>6.7**

TABLE I Non-Matched Demographic Characteristics			
	Study Group	Control Group	P Value
BMI* (kg/m <sup>2</sup> )	37.2 ± 8.5 (22.6 to 60.5)	34.9 ± 8.3 (20 to 56.1)	0.19
Overall operative time* (min)	129 ± 39 (57 to 191)	120 ± 45 (59 to 199)	0.42
Mean blood glucose* (mg/dL)	217 ± 42 (134 to 292)	185 ± 33 (116 to 236)	<0.01
Maximum blood glucose† (mg/dL)	272 (225 to 336)	227 (184 to 268)	0.02
Hemoglobin A1C* (%)	6.8 ± 0.8 (5.2 to 7.9)	6.4 ± 0.8 (5.0 to 8.6)	0.11

\*The values are given as the mean and the standard deviation, with the range in parentheses. †The values are given as the median, with the 25th to 75th percentiles in parentheses.

TABLE II Laboratory Value Odds Ratios			
Laboratory Study	Threshold	Odds Ratio (95% CI)	P Value
Mean blood glucose	200 mg/dL	3.75 (1.25 to 11.22)	0.02
Maximum blood glucose	260 mg/dL	3.0 (0.97 to 9.30)	0.08
Hemoglobin A1C	6.7%	9.0 (1.14 to 71.20)	0.03

# Do Glycemic Markers Predict Occurrence of Complications After Total Knee Arthroplasty in Patients With Diabetes?

Hwang et al. Clin Orthop Relat Res. 2014

- Single center (Korea) – 462 pts; 714 TKRs
- **HbA1c  $\geq 8\%$  and/or FBG  $\geq 200\text{mg}$**  was associated with superficial surgical site infections (no deep infections)
  - HbA1c was only moderately correlated with FBG & PPG2
  - May be considerable disparity between acute and chronic markers which should be considered separately

# Hemoglobin A1C as a marker for surgical risk in diabetic patients undergoing total joint arthroplasty.

Harris et al. J Arthroplasty. 2013

- VA retrospective cohort study – 6088 pts; TJA
- Risk of complications increased linearly through a threshold of 7%
  - Any complication ( $\text{HbA1c} \geq 7\%$ ): adj OR 1.22 (1.01-1.47)
    - Only significant for UTI and ARF

**“Before delaying surgery to achieve better diabetic control, surgeons and patients should weigh the estimated risks of TJA against the potential benefits.”**

**Many diabetic total joint arthroplasty candidates are unable to achieve a preoperative hemoglobin A1c goal of 7% or less.**

Giori et al. J Bone Joint Surg Am. 2014

- 404 diabetic pts – TJA
  - 59 cases delayed for HbA1c>7%
  - Only 35 pts (59%) achieved this goal - mean time 8 months!

**Achieving a goal of <7% may not be possible for many diabetic patients, and this requirement may risk access to TJA and potentially alter quality of life.**

# Perioperative Hyperglycemia and Risk of Adverse Events Among Patients With and Without Diabetes.

Kotagal et al. Ann Surg. 2015

- 40,836 pts – 19% with DM
  - 47% had periop glucose test; 18% of them >180
- DM pts had higher rate of adverse events (12% vs 9%)
- After adjustment, pts with hyperglycemia had a higher rate vs normal BG
- **This increased risk of hyperglycemia was only significant for non-diabetic pts**
  - ?underuse of insulin
  - Higher levels of stress in non-DM



# Systematic review of the impact of HbA1c on outcomes following surgery in patients with diabetes mellitus.

Rollins et al. Clin Nutr. 2015

- 20 studies – 19,515 pts with DM
- **No significant differences based on preop glycemic control on:**
  - 30-day mortality, CVA, VTE, readmission, ICU LOS
- **No link between preop HbA1c and:**
  - AKI, dysrhythmia, non-SSI infection, LOS
- Highly variable regarding MI, SSI, reoperation

# Joint British Diabetes Societies. NHS Diabetes guideline for the perioperative management of the adult patient with diabetes.

Dhatariya et al. Diabet Med. 2012

- ⦿ There is evidence that good control preop, as measured by HbA1c, is associated with improved outcomes after a range of noncardiac procedures.
- ⦿ “There is insufficient evidence to recommend an upper limit of HbA1c prior to elective surgery, and the risks associated with poor glycemic control should be balanced against the necessity for surgery.”
- ⦿ “An upper limit between **8-9% is acceptable**. For those at high risk of hypoglycemia a higher target may be appropriate.”

# Why I wouldn't order HbA1c preop?

- ⦿ Poor and conflicting evidence as to whether HbA1c predicts various outcomes: death, SSI, etc.
- ⦿ Unclear which is more important or a better predictor of complications – HbA1c, FBS on AM of surgery, intraop glucose, immediate postop glucose (1<sup>st</sup> 24 hrs), highest glucose, higher average glucose
- ⦿ Outcome is affected by type of surgery, type and intensity of insulin, and fluid Rx
- ⦿ **Too many variables – not enough evidence!**

**“Let My Patient Go!”**



# Rebuttals

David Baldwin

The Diabetologist's Perspective

# Preoperative Assessment of the Patient with Diabetes

Always check HBA1C if a current value is not available. Do it in real-time during your office visit, it's a golden opportunity for face-to-face planning.

- HBA1C 6% = average blood glucose 126 mg/dl
- HBA1C 7% = average blood glucose 154 mg/dl
- HBA1C 8% = average blood glucose 183mg/dl
- HBA1C 9% = average blood glucose 212 mg/dl
- HBA1C 10% = average blood glucose 240 mg/dl

In office HBA1C  
\$7.00 and 7 minutes per test  
Very Easy to Perform and Highly Accurate



# The Rush Protocol for Pre-operative Evaluation of Diabetes Control

- Which patients with diabetes need special attention for pre-operative clearance
  - HBA1C is greater than 8 % (mean glucose 180-210)
  - At Rush a pre-op AM glucose > 300 is a hard stop for OR
  - Who is at risk to have the AM of surgery blood glucose level > 300 mg/dl
    - Fasting AM home blood glucose readings > 200 mg/dl
    - Random home or pre-op lab glucose readings > 200 mg/dl
- These patients will benefit from more attention



# The Rush Protocol for Pre-operative Evaluation of Diabetes Control

- Currently HBA1C is our best metric for diabetes care
- A patient with HBA1C of 8.2% on 2-3 oral agents who is otherwise vigorous deserves to benefit from insulin therapy
- Pre-operative evaluation is a golden opportunity to help patients to improve their diabetes care
- Every week we see patients in our clinic who are waiting for surgery and we are able in most to rapidly initiate or titrate insulin therapy to move blood glucoses in the 200-300's to the 100-200 range.
- Immediately post-op we will be working hard to maintain all blood glucose levels between 100-180 using insulin therapy.
- The better the pre-op outpatient glucose control, the more success we will have in delivering the best postoperative outcomes

Thank-you

david\_baldwin@rush.edu

# Rebuttals

Steven Cohn

A 58 year old woman presents for preoperative evaluation prior to total knee arthroplasty scheduled in 5 days. She cannot walk one block due to pain. She states she has been unable to lose weight or control her DM because she has knee pain and cannot exercise.

Medical History:

- DM type 2 with peripheral neuropathy
- HTN
- OSA on CPAP

Medications: Metformin 1000mg BID, Losartan 50mg

Physical Exam: BP 164/84 P 72 BMI 44 Obese, antalgic gait

Labs: HbA1C= 8.4%, Cre 1.1 mg/dL, Glucose (random) 201 mg/dL

Would you delay this patient's surgery for glycemic control?

1. Yes
2. No