Perioperative Risk of and Monitoring for Hyperglycemia in Spine Surgery

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Abstract

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Perioperative hyperglycemia occurs frequently among patients with and without diabetes and is associated with increased morbidity and mortality. The purpose of this study was to describe perioperative hyperglycemia and to evaluate potential factors associated with postoperative hyperglycemia in a retrospective cohort of patients admitted following planned spine surgery between April 2010 and October 2013. ***Methods:*** Data were collected from electronic medical records for variables including age, gender, ethnicity, insurance status, diabetes status, HbA1c, ASA class, type and duration of surgery, and estimated blood loss. Glucose data were retrieved for morning of surgery, intraoperatively and postoperatively. Log-linear regression was used to assess for associations with postoperative hyperglycemia. ***Results:*** Preoperative glucose screening occurred in 71% of those with diabetes and 7% of those without. Intraoperative glucose testing occurred in 81% of those with diabetes and 57% of those without. Postoperative monitoring occurred in 80% of those with diabetes and 74% of those without. Early postoperative hyperglycemia was identified in 65% of cases with diabetes and 6% of those without diabetes. Most cases (95%) of postoperative hyperglycemia were identified by

postoperative day two. Early postoperative hyperglycemia was independently associated with preoperative glucose ≥140mg/ml (RR 1.34) and A1c > 8 (RR 1.26) among those with diabetes. Among those without diabetes, early postoperative hyperglycemia was independently associated with procedure duration ≥6 hours (RR 6.20) and intraoperative glucose ≥180mg/dL (RR 3.53). Median length of stay for those with early postoperative hyperglycemia was 6.8 days compared to 4.2 days for those without hyperglycemia. Linear regression revealed that early postoperative hyperglycemia was independently associated with longer length of stay in this study sample ($p<.01$). ***Conclusion:*** In current practice, glucose is inconsistently and insufficiently monitored. Determining the appropriate frequency of monitoring and delineating risk predictors will be essential to improving identification of perioperative hyperglycemia and for targeting interventions. These results suggest that among those with diabetes, poor preoperative glucose control represents a target for intervention to reduce the risk of postoperative hyperglycemia and subsequent potential complications. Among those without diabetes, more thorough data is needed to inform best practices. However, these results suggest that procedure duration and intraoperative hyperglycemia are risk factors for patients without diabetes. Protocols that include preoperative screening and postoperative monitoring for the first 48 hours will identify the vast majority of patients who develop postoperative hyperglycemia.

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This work is dedicated to the woman who inspires me to work hard and always keep learning – thank you Mom for all you have taught me.

Introduction

Over 950,000 patients undergo spine surgery each year in the United States.[1] Data from the National Inpatient Sample show that rates of spinal fusion and laminectomy increased from 98.7 per 100 thousand in 1998 to 169.5 per 100 thousand in 2008.[2] One of every six patients undergoing spine surgery, or 158 thousand patients, experiences at least one complication.[3] The average incremental cost associated with complications following spine surgery is $30 thousand, ranging from $4 to $121 thousand depending on the severity of the complication.[4]

Postoperative complications occur more often among patients who have or develop hyperglycemia.[5-19] Complications associated with perioperative hyperglycemia include infection, need for re-operation, extended length of hospitalization, and death. An exposure-response relationship was observed in two studies where degree of hyperglycemia and complication rates were positively correlated.[9,13] In spine surgery, perioperative hyperglycemia and diabetes have been independently associated with increased risk of surgical site infection.[20-23]

Perioperative hyperglycemia is common, occurring in 30 to 40 percent of all surgical patients.[7,9,15] Evidence shows that as many as two-thirds of patients with diabetes develop perioperative hyperglycemia.[9,15] Reported rates of perioperative hyperglycemia among patients without diabetes are highly variable, ranging from as low as 13 to as high as 67 percent.[9,15,24] The definition of hyperglycemia, however, varies considerably in studies both in terms of the timing and frequency of glucose testing, which may contribute to the observed variation in these rates.

Understanding the epidemiology of perioperative hyperglycemia in the spine surgery population is crucial because it has the potential to specify targets for clinical intervention that will be necessary to reduce complication rates. Nonetheless, perioperative glucose monitoring for patients with diabetes is inconsistent.[25-27] Moreover, despite the fact that one-third of patients with perioperative hyperglycemia do not have diabetes,[9,15] little is known about the approaches to or consistency of glucose monitoring in this group. There is no guideline or clinical consensus regarding perioperative glucose monitoring in the United States. As a result clinical decisions are based on sporadic data points that may fail to detect hyperglycemia in the perioperative setting leading to missed opportunities to improve the quality of care and patient outcomes.

Understanding current practices with regard to screening and monitoring for hyperglycemia, delineating incidence and patterns of perioperative hyperglycemia, and identifying factors associated with hyperglycemia are thus needed to inform future interventions. In this study, I have undertaken a retrospective cohort evaluation of patients admitted for planned spine surgery. The specific study aims were to:

Aim 1. Describe current practices in preoperative screening and intra and postoperative monitoring for hyperglycemia.

Research Hypotheses: Patients are infrequently tested for glucose control preoperatively as evidenced by low rates of obtaining preoperative HbA1c or random blood glucose. Intra and postoperative monitoring for hyperglycemia will be more common in patients with diabetes compared to patients without diabetes. Patients with known risk factors are more likely to be screened and monitored pre and postopertatively.

Aim 2. Describe the incidence and patterns of perioperative hyperglycemia.

Research Hypothesis: Intra and postoperative hyperglycemia will occur in 20-30 percent of patients.

Aim 3. Identify factors associated with increased risk of early postoperative hyperglycemia among patients with and without diabetes.

Research Hypothesis: Specific patient and surgery characteristics will be associated with postoperative hyperglycemia

Aim 4. Explore for associations between patient factors, surgery factors, hyperglycemia and clinical outcomes.

Research Hypothesis: Specific patient and surgery characteristics and early postoperative hyperglycemia will be associated with length of stay and 30-day readmission.

Methods

Study Setting

This study was conducted at Harborview Medical Center (HMC) in Seattle, Washington. HMC is a 413-bed level-one trauma center owned by King County and operated by the University of Washington. HMC serves as the regional trauma and referral center for Washington, Alaska, Montana and Idaho. HMC is a primary site for major spine surgery within the UW medical care system, performing over 1000 spine surgeries annually. Nearly half of these patients are admitted on the morning of surgery from home; the other half of patients are inpatients or are transfer to surgery directly from the emergency department. Nearly two-thirds of spine surgeries at HMC result in hospitalization for a minimum duration of 48 hours.

Patients

Source and sampling method. All patients who underwent spine surgery at HMC between April 1, 2010 and October 31, 2013 were screened for inclusion.

Eligibility inclusion criteria. Patients admitted for planned spine surgery who required a minimum inpatient stay of 48 hours were considered for inclusion. Forty-eight hours represents the current Washington State quality postoperative reporting requirement for hyperglycemia. For this study, “planned” surgery is operationalized as surgery on an individual admitted on the

morning of surgery, excluding patients transferred to surgery from inpatient units or the emergency department.

Eligibilty exclusion criteria. Patients less than 18 years old were excluded from the study sample. Patients having a second surgery within the designated five-day study period were excluded because the study was dependent on examining five postoperative days of glucose data. For patients receiving more than one spine surgery during the 31-month study timeframe, only data related to the first surgery were included.

Study Oversight

The study procedures were approved by the University of Washington Institutional Review Board (IRB).

Data Collection

Source, protocol and data quality. Data were obtained from electronic medical records. Standard methods were used to extract data, based on fields rigorously defined by the Quality Improvement Program at the medical center.

Outcome and Risk Factor Assessments

The primary outcome was early postoperative hyperglycemia, defined by having two glucose measurements greater than 180mg/dL at least one of three designated postoperative times: postoperatively on the day of surgery, on postoperative day one (POD1), or on postoperative day two (POD2). Having two or more glucose values greater than 180mg/dL within 24 hours was adapted from the University Health Consortium's definition of inpatient hyperglycemia. Patients with insufficient glucose testing in these periods were categorized as having normal glucose for this analysis.

Risk factors and covariates included *patient demographic characteristics*: age, gender, race, insurance status; *physical factors*: American Society of Anesthesia (ASA) class, body mass index (BMI), history of diabetes (defined by at least one ICD-9 code for diabetes (250) within one year prior to admission), glucose on the morning of surgery, hemoglobin A1c (A1c) measured within six months of surgery; and *surgery factors*: procedure type and duration, and estimated blood loss. Postoperative data for steroid prescription and tube feedings were available and categorized as given if received by the patient between the end of surgery through postoperative day two.

Secondary outcomes included length of hospital stay (number of days from admission to discharge) and inpatient readmission within 30 days of discharge.

Analysis Plan

Statistical methods. Measures of central tendency and proportions were reported to describe the study sample. Patient and surgical characteristics were compared for patients with and without diabetes. Categorical variables were compared using Chi-Square analysis. Continuous variables were compared using the t-test for normal distributions and Mann-Whitney test for non-normal distributions.

Log-linear regressions were performed to provide an estimate of relative risk that is useful in interpreting findings in clinical practice. Full regression models were defined as those for which complete data (greater than 98 percent) were available. Reduced models were created by including only variables with significant associations at the level of alpha less than or equal to .05 in the bivariate or full model regressions. For log-linear regressions, a number of predictor variables were categorized into clinically relevant categories. Race was categorized as white or non-white. Insurance type was categorized based on higher (community, workers compensation) versus lower (government, uninsured) levels of coverage. ASA class was collapsed into two categories: low (classes I and II) and high (classes III and IV). A1c was categorized at less than or equal to 8 and greater than 8 for those with diabetes; this cut represents a clinical point above which glycemic control is considered poor. Among patients without diabetes, A1c was categorized as less than 5.7 versus greater than or equal to 5.7, the clinical cutoff for possible pre-diabetes. Procedure duration was categorized as less than 6 hours or greater than or equal to 6 hours. Estimated blood loss was categorized as less than or greater than or equal to 200cc. Preoperative hyperglycemia was defined based on what would be considered an elevated fasting glucose: greater than or equal to 140mg/dL for patients with diabetes and greater than or equal to

100mg/dL for patients without diabetes. Intraoperative hyperglycemia was defined as glucose greater than or equal to 180mg/dL for all patients.

Aim 1. *Describe current practices in preoperative screening and intra and postoperative monitoring for hyperglycemia.* Proportions of patients undergoing A1c and preoperative glucose screening were reported. Proportions of patients undergoing intraoperative glucose monitoring between the beginning and end of surgery were reported. Proportions of patients with postoperative glucose monitoring were reported for six distinct periods: postoperatively on the day of surgery (from end of surgery to midnight; denoted DOS), and for each subsequent 24 hour period, identified as postoperative day one through five and denoted POD1, POD2, POD3, POD4, POD5, respectively. Proportions of patients with no monitoring, a single measure of glucose, or two or more measures for each period were reported.

Separate analyses for patients with and without diabetes were undertaken to examine the associations of baseline factors with the occurrence of preoperative screening, intraoperative monitoring, and adequate postoperative monitoring. Among patients with diabetes, adequate postoperative screening was defined as having at least two glucose values on POD1 and POD2. Among those without diabetes, adequate screening was defined as having at least one glucose value on POD1 and POD2. Log-linear regression was used for both bivariate and multivariable analyses, and to compute the rate ratios and 95% confidence intervals.

Aim 2. *Describe the incidence and patterns of perioperative hyperglycemia.* Glucose levels were compared between patients with and without diabetes using the Mann-Whitney test. Proportions

of patients with preoperative and intraoperative hyperglycemia were reported. Among patients with diabetes, analysis was undertaken to identify factors associated with 1) presenting on the morning of surgery with a glucose greater than or equal to 140mg/dL, 2) presenting on the morning of surgery with a glucose greater than or equal to 180mg/dL and 3) developing intraoperative glucose greater than or equal to 180mg/dL. Among those without diabetes, analysis was undertaken to identify factors associated with presenting on the morning of surgery with a glucose level greater than or equal to 100mg/dL. The evaluation of factors associated with developing intraoperative glucose levels greater than or equal to 180mg/dL was limited due to the small event rate among patients without diabetes.

Postoperative mean daily glucose levels were charted by postoperative period. Postoperative hyperglycemia was reported as 1) the proportion of hyperglycemic days, defined as having two or more glucose values greater than or equal to 180mg/dL, 2) the proportion of patients with two or more glucose values greater than or equal to 180mg/dL (presented for each postoperative time period), 3) the proportion of patients with early postoperative hyperglycemia, defined as having two or more glucose values greater than or equal to 180mg/dL postoperatively in at least one of the first three postoperative periods (DOS, POD1, POD2).

The number of patients presenting with or developing hypoglycemia were reported for preoperative, intraoperative and postoperative periods. Moderate hypoglycemia was defined as a glucose level 40 to 69mg/dL; severe hypoglycemia was defined as glucose level less than 40mg/dL.

Aim 3. *Identify factors associated with increased risk of early postoperative hyperglycemia among patients with and without diabetes.* In this analysis, all patients with inadequate testing were assumed to have normal glucoses. Separate analyses were undertaken for patients with and without diabetes. Study factors were tested for their association with early postoperative hyperglycemia. Log-linear regression was used for bivariate and multivariable analyses and to compute rate ratios and 95% confidence intervals.

Aim 4. *Explore associations of patient and surgery factors and hyperglycemia with clinical outcomes.* In the analysis of clinical outcomes, diabetes status (diabetic, no diabetes) was used. Length of stay (LOS) was skewed and thus transformed to log LOS; bivariate and multivariable linear regression were then conducted. Standardized beta coefficients and p-values were reported. Factors were tested for their association with 30-day readmission using log-linear bivariate and multivariable analyses. Frequency and proportions of death were reported.

Significance was determined at the level of alpha less than .05. All analyses were performed using SPSS software Version 19.0 (IBM Corp., Armonk, NY).

Results

Description of the Sample

Patient characteristics. Eleven-hundred-and-one patients were hospitalized for at least 48 hours following planned spine surgery between April 1, 2010 and October 31, 2013. Six of these patients were excluded from the study (five were under the age of 18 years, and one had two spine surgeries within five days). The remaining 1095 cases comprised the sample for this study (Figure 1).

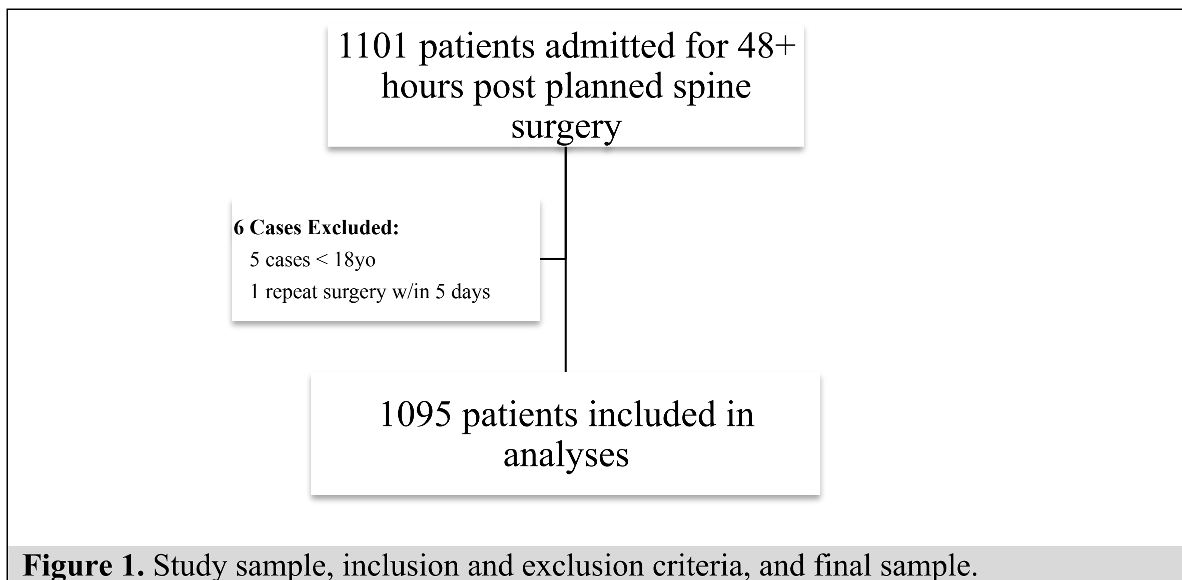

Figure 1. Study sample, inclusion and exclusion criteria, and final sample.

The mean age of the patient sample was 58 years (N=1095); 47 percent were female and 83 percent were white. Seventeen percent of cases had diabetes defined by at least one ICD9 code for diabetes in the twelve months prior to surgery. The majority of cases had health insurance, with 55 percent funded through Medicaid, Medicare or other state fiscal resources. Additional sample characteristics are described in Table 1.

Table 1. Baseline characteristics of patients (N=1095) undergoing planned spine surgery from April 2010 to October 2013					
Characteristic		**ALL N=1095**	**DM n =188**	**NDM n = 907**	**P-value**
Gender, % Female		46.8% (512)	42.6% (80)	47.6% (432)	.20 [X]
Age, mean SD		58 ±13	63±11	57±14	<.01[t]
	<40	10% (108)	2% (3)	12% (105)	<.01 [X]
	40-49	15% (165)	11% (20)	16% (145)	
	50-59	29% (317)	27% (50)	29% (267)	
	≥60	46% (505)	61% (115)	43% (390)	
Race, % (n)					<.01 [X]
	Asian	4.0% (44)	5% (10)	3.7% (34)	
	Black	6.6% (72)	12% (22)	5.5% (50)	
	Latino	2.7% (30)	5% (9)	2.3% (21)	
	Native American	1.8% (20)	2% (4)	1.8% (16)	
	White	82.6 (905)	75% (140)	84.3% (765)	
	Other	2.2% (24)	2% (3)	2.3% (21)	
Insurance Status, % (n)					.03 [X]
	Community/Workers Compensation	44% (480)	36% (67)	46% (413)	
	Medicare/Medicaid/State	55% (604)	64% (120)	53% (484)	
	Uninsured	1% (11)	.5% (1)	1.1% (10)	
ASA Class[a]					<.001 [X]
	I	4% (42)	0	5% (42)	
	II	54% (593)	32% (60)	59% (533)	
	III	40% (434)	64% (120)	35% (314)	
	IV	2% (21)	4% (7)	1.5% (14)	
BMI, median (IQR)[b]		28.0 (25,33)	33.0 (28,37)	27.4 (24,32)	<.001 [M]
	Underweight	0.5% (6)	0.5% (1)	0.6% (5)	<.001 [X]
	Normal	27% (291)	10% (19)	30% (272)	
	Overweight	34% (367)	23% (44)	36% (323)	
	Obese mod30-35	21% (227)	30% (56)	19% (171)	
	Severe35-40	10% (111)	17% (32)	9% (79)	
	Morbid >40	7% (80)	19% (35)	5% (45)	
Postoperative Steroids		11.2% (123)	11.7% (22)	11.1% (101)	.82 [X]
Postoperative Tube Feeds		2.4% (26)	1.6% (3)	2.5% (23)	.44 [X]

DM = Diabetes; NDM = No Diabetes.
[a] ASA missing 5 cases (1DM, 4NDM); [b] BMI missing 13 cases (1DM,12NDM)
[X] Chi-Square; [t] t-test; [M] Mann-Whitney

Surgical Characteristics. Sixty-four percent of surgeries involved fusion. The median duration of all surgeries was 5.8 hours (IQR 4.5, 7.9). Estimated blood loss (EBL) data were available for 943 cases. Median EBL was 250cc (IQR 100, 750). Table 2 describes specified surgical characteristics.

Table 2. Summary of surgical factors for patients (N=1095) undergoing planned spine surgery from April 2010 to October 2013.

Descriptor		ALL N=1095	DM n=188	NDM n=907	P-value
Procedure Duration					
	< 6 hours	52.8% (578)	45.2% (85)	54.4% (493)	.02 [X]
	≥6 hours	47.2% (517)	54.8% (103)	45.6% (414)	
Estimated Blood Loss [a]					
	< 200cc	40.5% (382)	39.4% (65)	40.7% (317)	.75 [X]
	> 200cc	59.5% (561)	60.6% (100)	59.3% (461)	
Spinal Fusion, % (n)		64% (704)	60% (112)	65% (592)	.14 [X]

DM = Diabetes; NDM = No Diabetes
[a] EBL missing 152 cases (DM23; NDM129)
[X] Chi-Square

Aim 1: Perioperative Glucose Screening

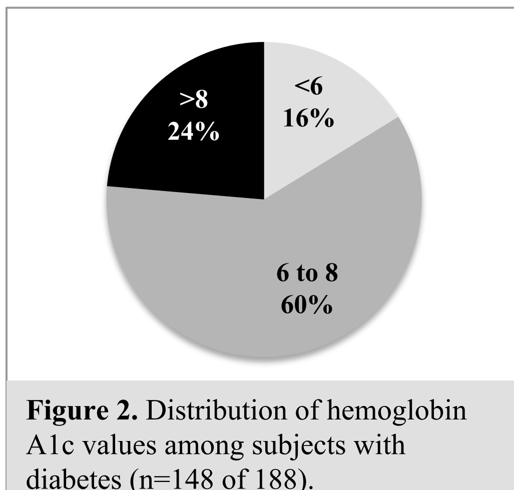

Figure 2. Distribution of hemoglobin A1c values among subjects with diabetes (n=148 of 188).

Screening patients with diabetes. Among the 188 cases with diabetes, baseline glucose control was assessed via A1c in 148 (79 percent). The mean A1c among cases with diabetes was 7.1 (± 1.3; range 4.1-11.2). Figure 2 shows the distribution of A1c values among those tested with diabetes. Glucose on the morning of surgery was tested in 133 of 188 (71 percent) of cases with diabetes. To determine what factors are associated with obtaining a screening glucose test on the morning of surgery, multivariable log-linear regression was undertaken (Table 3). Among cases with diabetes, cases of non-white race (RR 1.21 [95%CI 1.03, 1.43]; p=.02) and cases with A1c > 8 (RR 1.22 [95%CI 1.04, 1.44]; p=.02) were more likely to undergo glucose evaluation on the morning of surgery.

Table 3. Factors associated with preoperative glucose screening on the morning of surgery for patients with diabetes (N = 188).

DM	Bivariate RR (95%CI)	Multivariable Full RR (95%CI)	Multivariable Reduced RR (95%CI)
Number of cases	188	186	148
Gender, male v. female	0.92 (.77, 1.11)	1.04 (.86, 1.25)	
Age (for every 10 years)	0.94 (.86, 1.01)	0.97 (.88, 1.06)	
Race, nonwhite v. white	1.21 (1.01, 1.44)*	0.84 (.69, 1.02)	1.21 (1.03, 1.43)*
Insurance Status, C v. G	1.05 (.86, 1.28)	1.00 (.82, 1.25)	
ASA Class, high v. low[a]	1.05 (.85, 1.29)	0.94 (.76, 1.17)	
BMI (for each 5points)[b]	1.04 (.98, 1.10)	1.04 (.97, 1.11)	
Fusion, v. no fusion	0.91 (.75, 1.08)	1.01 (.83, 1.23)	
Duration, ≥6 v. <6hrs	0.89 (.74, 1.07)	1.10 (.90,1.35)	
EBL, ≥200 v. <200[c]	0.85 (.70, 1.03)		
A1c, >8 v. ≤8[d]	1.24 (1.05, 1.50)*		1.22 (1.04, 1.44)*

133 patients had a preoperative glucose test.
DM = Diabetes. Insurance Status: C = community and workers comp; G = government and uninsured.
[a]ASA missing in 1 case; [b]BMI missing in 1case; [c]EBL missing in 23 cases; [d]A1c missing in 40 cases.
For variables listed above the double line, > 98% of the cases had complete data and were included in full model.
*p <.05

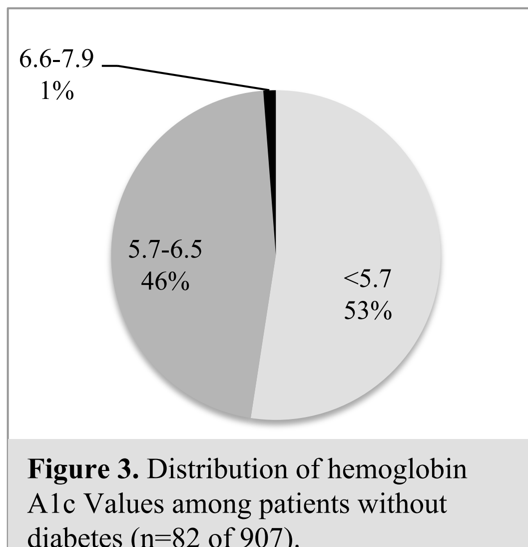

Figure 3. Distribution of hemoglobin A1c Values among patients without diabetes (n=82 of 907).

Screening patients without diabetes. A1c was available in 82 of 907 (9 percent) of cases without diabetes. The mean A1c among those tested was 5.6 (± 0.4; range 4.6-6.6). Figure 3 shows the distribution of A1c results. Among the 907 cases without known diabetes, glucose on the morning of surgery was checked in 65 cases (7 percent). To determine what factors are associated with obtaining a screening glucose test on the morning of surgery, multivariable log-linear regression was undertaken (Table 4). Among cases without diabetes, older patients (RR 1.24 for every 10 years [95%CI 1.02, 1.50]; p=.03) and those with higher ASA class (RR 1.77 [95%CI 1.07, 2.92]; p=.03) were more likely to undergo glucose screening on the morning of surgery. There was a trend toward higher likelihood of glucose testing among non-white race category.

Table 4. Factors associated with preoperative glucose screening on the morning of surgery among patients without diabetes (N=907).

NDM	Bivariate RR (95%CI)	Multivariable Full RR (95%CI)	Multivariable Reduced RR (95%CI)
Number of cases	907	891	907
Gender, male v. female	1.00 (.62, 1.59)	1.08 (.67, 1.74)	
Age (for every 10 years)	1.28 (1.07, 1.51)*	1.23 (1.02, 1.55)*	1.24 (1.02, 1.50)*
Race, nonwhite v. white	1.48 (.84, 2.60)	1.80 (1.00, 3.23)*	1.70 (.95, 3.03)
Insurance Status, C v. G	1.34 (.83, 2.17)	1.07 (.63, 1.83)	
ASA Class, high v. low[a]	2.05 (1.28, 3.27)*	1.60 (.97, 2.63)	1.77 (1.07, 2.92)*
BMI (for each 5points)[b]	1.14 (.98, 1.33)	1.15 (.98,1.36)	
Fusion, v. no fusion	1.50 (.88, 2.57)	1.40 (.77, 2.52)	
Duration, ≥ 6 v. < 6hrs	1.39 (.87, 2.22)	1.14 (.69, 1.88)	
EBL, ≥ 200 v. < 200[c]	1.02 (.61, 1.69)		
A1c, ≥ 5.7 v. < 5.7[d]	1.10 (.35, 3.52)		

65 patients had a preoperative glucose test.
NDM = No Diabetes. Insurance Status: C = community and workers comp; G = government and uninsured.
[a]ASA missing in 4 cases; [b]BMI missing in 12 cases; [c]EBL missing in 129 cases; [d]A1c missing in 825 cases.
For variables listed above the double line, > 98% of the cases had complete data and were included in full model.
*p <.05

Intraoperative Monitoring. Six-hundred-ninety-seven of 1095 cases (61 percent) had at least one glucose test. Eighty-one percent of those with diabetes and 57 percent of those without diabetes had at least one intraoperative glucose test. (Figure 4)

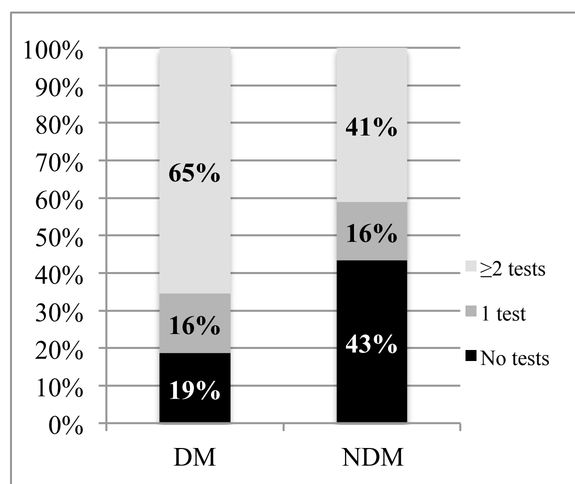

Figure 4. Proportion of patients with intraoperative glucose test.
DM = diabetes, NDM = no diabetes.

Among cases with diabetes, intraoperative glucose testing was associated with spinal fusion (RR 1.24 [95%CI 1.02, 1.51]; p =.03), and procedure duration greater than 6 hours (RR 1.35 [95%CI 1.11, 1.65]; p<.01) (Table 5). These factors were also associated with intraoperative testing among cases without diabetes. Other factors associated with glucose testing among the cases without diabetes included age, white race, ASA class and EBL (Table 6).

Table 5. Factors associated with intraoperative glucose monitoring among patients with diabetes (N=188).

DM	Bivariate RR (95%CI)	Multivariable Full RR (95%CI)	Multivariable Reduced RR (95%CI)
Number of cases	188	186	165
Gender, male v. female	1.06 (.92, 1.22)	1.05 (.93, 1.19)	
Age (for every 10 years)	1.06 (.99, 1.13)	1.02 (.95, 1.09)	
Race, nonwhite v. white	1.00 (.85, 1.17)	1.08 (.92, 1.26)	
Insurance Status, C v. G	1.11 (.95, 1.29)	1.05 (.90, 1.22)	
ASA Class, high v. low[a]	1.02 (.88, 1.19)	0.98 (.85, 1.13)	
BMI (for each 5points)[b]	1.00 (.95, 1.05)	1.00 (.96, 1.05)	
Fusion, v. no fusion	1.48 (1.24, 1.77)*	1.28 (1.08, 1.51)*	1.24 (1.02, 1.51)*
Duration, ≥ 6 v. < 6hrs	1.60 (1.35, 1.90)*	1.48 (1.25, 1.75)*	1.35 (1.11, 1.65)*
EBL, ≥ 200 v. < 200[c]	1.42 (1.18, 1.72)*		1.10 (.90, 1.36)
A1c, > 8 v. ≤ 8[d]	1.01 (.86, 1.18)		
Preop Glucose ≥ 140mg/dL[e]	0.97 (.82, 1.14)		

153 patients had at least one intraoperative glucose test.
DM = Diabetes. Insurance Status: C = community and workers comp; G = government and uninsured.
[a]ASA missing in 1 case; [b]BMI missing in 1 case; [c]EBL missing in 23 cases; [d]A1c missing in 40 cases; [e]Preoperative glucose missing in 55 cases.
Variables listed above the double line have > 98% complete data and were included in full model.
*p <.05

Table 6. Factors associated with intraoperative glucose monitoring among patients without diabetes (N=907).

NDM	Bivariate RR (95%CI)	Multivariable Full RR (95%CI)	Multivariable Reduced RR (95%CI)
Number of cases	907	891	776
Gender male v. female	0.98 (.87, 1.09)	1.02 (.93, 1.12)	
Age (for every 10 years)	1.14 (1.09, 1.19)*	1.06 (1.02, 1.10)*	1.05 (1.01, 1.09)*
Race nonwhite v. white	0.66 (.53, .81)*	0.83 (.70, .97)*	0.82 (.68, .98)*
Insurance Status, C v. G	1.20 (1.06, 1.35)*	1.04 (.94, 1.14)	1.00 (.90, 1.11)
ASA Class high v. low[a]	1.60 (1.40, 1.74)*	1.29 (1.18, 1.42)*	1.34 (1.21, 1.48)*
BMI (for each 5points)[b]	1.03 (.99, 1.07)	1.01 (.97, 1.04)	
Fusion, v. no fusion	1.95 (1.67, 2.29)*	1.43 (1.24, 1.64)*	1.32 (1.12, 1.57)*
Duration ≥ 6 v. < 6hrs	3.00 (2.61, 3.45)*	2.59 (2.25, 2.99)*	2.13 (1.82, 2.50)*
EBL ≥ 200 v. < 200[c]	2.78 (2.30, 3.36)*		1.59 (1.29, 1.95)*
A1c ≥ 5.7 v. < 5.7[d]	0.70 (.53, .94)*		
Preoperative Glucose ≥ 100mg/dL[e]	0.84 (.59, 1.20)		

514 patients had at least one intraoperative glucose test.
NDM = No Diabetes. Insurance Status: C = community and workers comp; G = government and uninsured.
[a]ASA missing in 4 cases; [b]BMI missing in 12 cases; [c]EBL missing in 129 cases; [d]A1c missing in 825 cases; [e]Preoperative glucose missing in 842 cases.
For variables listed above the double line, > 98% of the cases had complete data and were included in full model.
*p < .05

Postoperative Monitoring. In each of the six postoperative periods, glucose was tested at least once in the majority of cases that remained hospitalized from POD1 through POD5 (Figure 5).

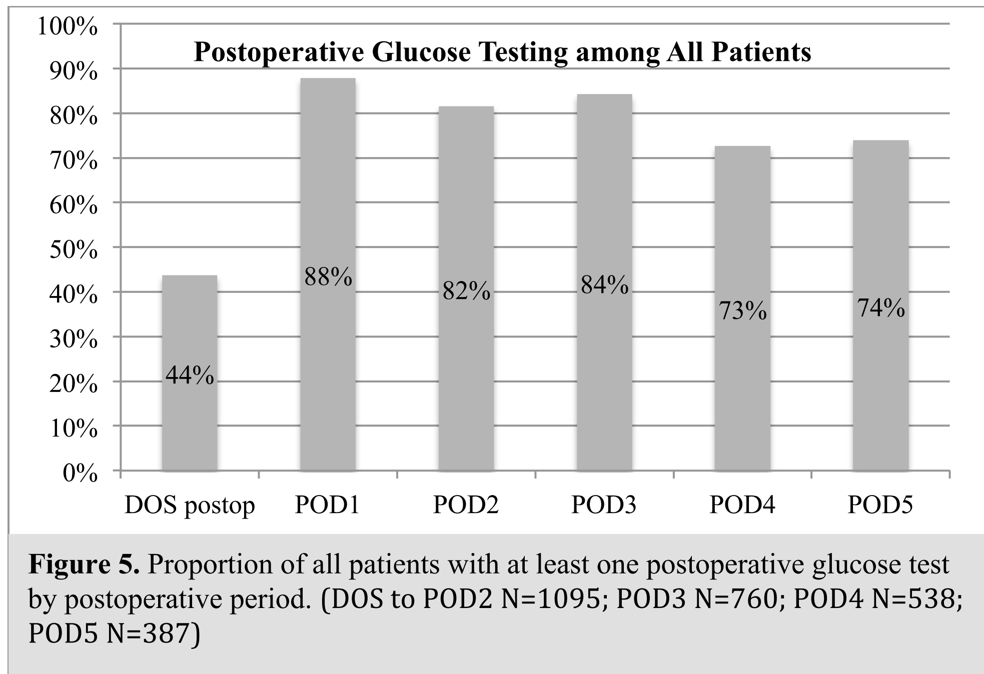

Figure 5. Proportion of all patients with at least one postoperative glucose test by postoperative period. (DOS to POD2 N=1095; POD3 N=760; POD4 N=538; POD5 N=387)

Three of 188 cases with diabetes had no glucose test performed on POD1 and seven had no test on POD2. Testing two or more times occurred for 158 cases on POD1 and POD 2 (Figure 6). Testing two or more times on *both* POD1 and POD2 occurred among 151 of 188 cases with diabetes (80 percent). Cases that had at least two glucose tests on both POD1 and POD2 compared to those with less frequent testing were more likely to have an ASA classification of III or IV and a surgical procedure duration greater than 6 hours in a multivariable model with all predictors included (N=186). In a multivariable model using the subsample of cases that had A1c data available (N=125), intraoperative glucose and A1c were significantly associated with postoperative monitoring, but ASA classification and surgical duration were not (Table 7).

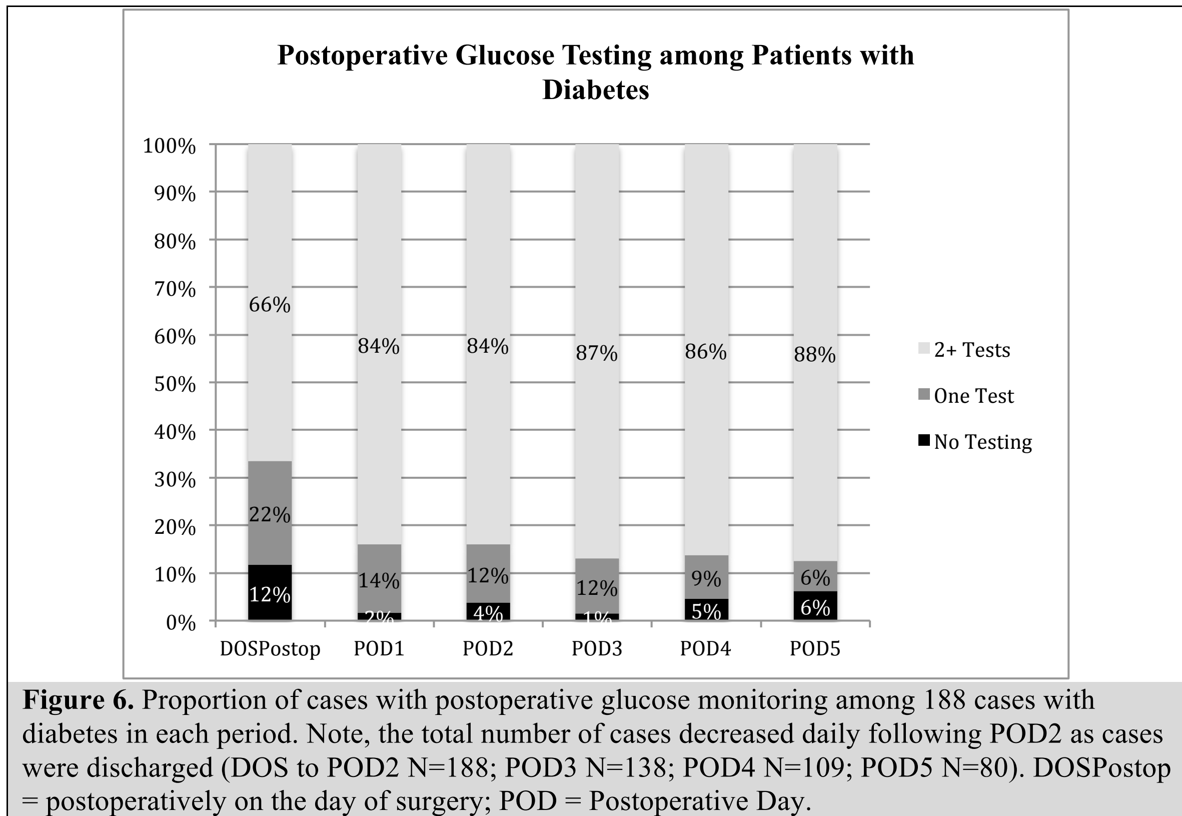

Figure 6. Proportion of cases with postoperative glucose monitoring among 188 cases with diabetes in each period. Note, the total number of cases decreased daily following POD2 as cases were discharged (DOS to POD2 N=188; POD3 N=138; POD4 N=109; POD5 N=80). DOSPostop = postoperatively on the day of surgery; POD = Postoperative Day.

Table 7. Factors associated with postoperative adequate glucose monitoring among cases with diabetes (N=188).

DM	Bivariate RR (95%CI)	Multivariable Full RR (95%CI)	Multivariable Reduced RR (95%CI)
Number of cases	188	186	125
Gender, male v. female	0.95 (.83, 1.10)	0.97 (.85, 1.11)	
Age (for every 10 years)	1.00 (.99, 1.01)	0.99 (.92, 1.06)	
Race, nonwhite v. white	1.02 (.87, 1.19)	1.02 (.86, 1.22)	
Insurance Status, C v. G	1.05 (.90, 1.23)	1.00 (.85, 1.17)	
ASA Class, high v. low*	1.22 (1.01, 1.46)*	1.21 (1.01, 1.46)*	1.12 (.98, 1.29)
BMI (for each 5points)*	1.03 (.98, 1.08)	1.01 (.96, 1.06)	
Fusion, v. no fusion	0.95 (.82, 1.09)	0.90 (.77, 1.05)	
Duration, ≥6 v. <6hrs	1.15 (.99, 1.34)	1.19 (1.00, 1.40)*	1.04 (.93, 1.17)
EBL, ≥200 v. <200*	1.05 (.89, 1.24)		
A1c, > 8 v. ≤ 8*	1.14 (1.07, 1.22)*		1.09 (1.02, 1.16)
Preoperative Glucose ≥ 140mg/dL	1.04 (.93, 1.17)		
Intraoperative Glucose ≥180mg/dL	1.20 (1.08, 1.33)*		1.08 (1.02, 1.14)

A minimum of two glucose values on both POD1 and POD2 were tested in 151 patients.
DM = Diabetes. Insurance Status: C = community and workers comp; G = government and uninsured. POD = Postoperative Day.
[a]ASA missing in 1 case; [b]BMI missing in 1 case; [c]EBL missing in 23 cases; [d]A1c missing in 40 cases; [e]Preoperative glucose missing in 55 cases; [f]intraoperative missing in 35..
For the variables listed above the double line, > 98% of the cases had complete data and were included in full model.
*p <.05

The majority of cases without diabetes had at least one glucose test in each period POD1 through POD5 (Figure 7). Among cases without diabetes, 674 of the 907 cases (74 percent) had at least one glucose tested on *both* POD1 and POD2. Sixty-four cases (7 percent) had at least two glucoses tested on both days. Having at least one glucose test on both POD1 and POD2 was associated with an intraoperative glucose level greater than or equal to 180mg/dl (RR 1.13, p<.01) and higher ASA classification (RR 1.12, p<.01) (Table 8). Testing twice daily on both POD1 and POD2 occurred in 7 percent of cases without diabetes.

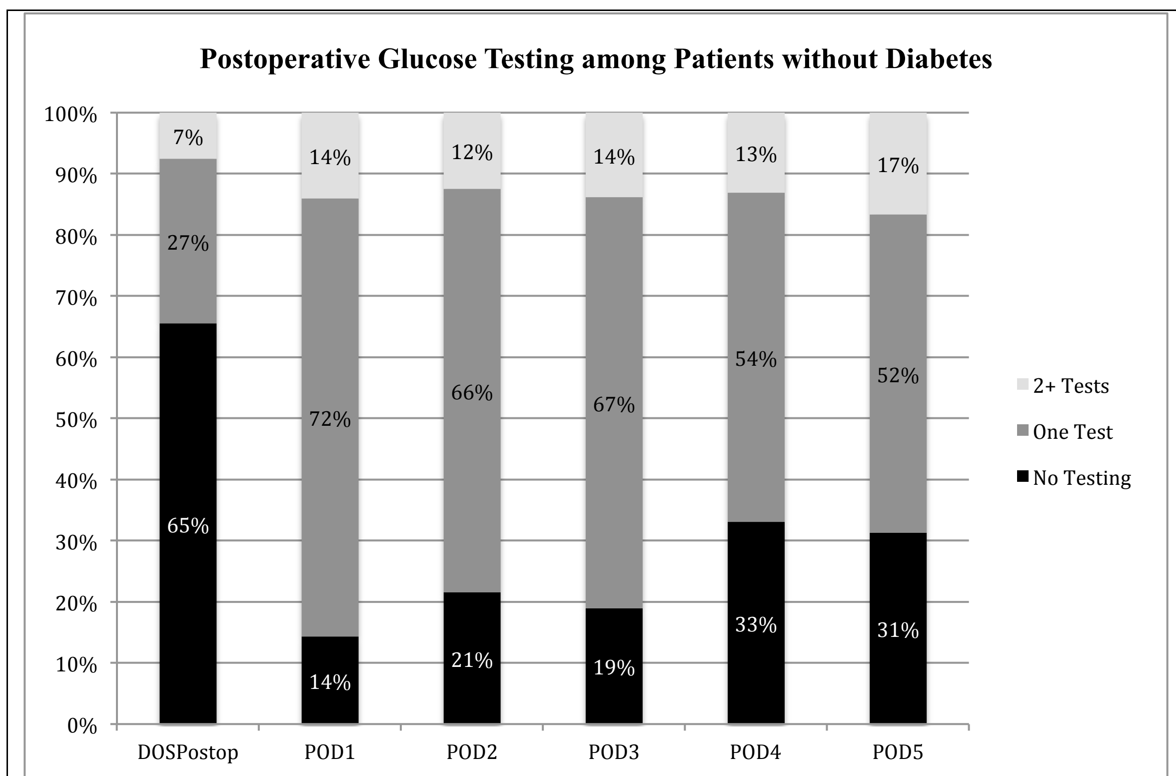

Figure 7. Proportion of cases with postoperative glucose monitoring among 907 cases without diabetes in each period. Note, the total number of cases decreased daily following POD2 as cases were discharged (DOS to POD2 N=907; POD3 N=622; POD4 N=429; POD5 N=307). DOSPostop = postoperatively on the day of surgery; POD = Postoperative Day.

Table 8. Factors associated with undergoing postoperative glucose tested among those without diabetes (N=907).

NDM	Bivariate RR (95%CI)	Multivariable Full RR (95%CI)	Multivariable Reduced RR (95%CI)**
Number of cases	907	891	428
Gender, male v. female	0.95 (.88, 1.02)	0.96 (.89, 1.04)	
Age (for every 10 years)	1.01 (1.01, 1.01)*	1.08 (1.05, 1.12)*	1.02 (.99, 1.05)
Race, nonwhite v. white	0.96 (.86, 1.07)	1.07 (.96, 1.19)	
Insurance Status, C v. G	1.07 (.99, 1.15)	0.97 (.89, 1.05)	
ASA Class, high v. low[a]	1.26 (1.17, 1.35)*	1.15 (1.07, 1.24)*	1.12 (1.03, 1.22)*
BMI (for each 5points)	1.01 (.98, 1.04)	1.01 (.98, 1.04)	
Fusion, v. no fusion	1.2 (1.10, 1.31)*	1.10 (1.00, 1.20)*	1.01 (.91, 1.13)
Duration, ≥6 v. <6hrs	1.32 (1.22, 1.42)*	1.24 (1.15, 1.35)*	1.07 (.96, 1.18)
EBL, ≥200 v. <200[b]	1.32 (1.20, 1.45)*		1.11 (.97, 1.27)
A1c, ≥ 5.7 v. < 5.7[c]	0.81 (.67, .97)*		
Preoperative Glucose ≥100mg/dL[d]	0.90 (.70, 1.15)		
Intraoperative glucose ≥180mg/dL[e]	1.19 (1.14, 1.23)*		1.13 (1.04, 1.23)*

674 patients had glucose tested on both POD1 and POD2.
NDM = No Diabetes. Insurance Status: C = community and workers comp; G = government and uninsured. POD = Postoperative Day.
[a]ASA missing in 4 cases; [b]BMI missing in 12 cases; [c]EBL missing in 129 cases; [d]A1c missing in 825 cases; [e]Preoperative glucose missing in 842 cases; [f]Intraoperative glucose missing in 393.
For the variables listed above the double line, > 98% of the cases had complete data and were included in full model.
*p < .05
**A1c not included in reduced model as 46 cases had available data.

Aim 2: Perioperative Hyperglycemia

Preoperative hyperglycemia. Among the 18 percent of cases who had glucose testing between midnight and the initiation of surgery the next day, the median glucose was 118mg/dL (IQR 100,152). Median glucose was higher among cases with known diabetes than those without (137 v. 100 mg/dL; M-W=1332, p<.001).

Sixty-four of 133 cases with diabetes with glucose tested (48 percent) had a preoperative glucose value greater than or equal to 140mg/dL on the morning of surgery. Twenty-nine of the 133

cases (22 percent) had a preoperative glucose value greater than or equal to 180mg/dL. Presenting on the morning of surgery with a glucose value greater than or equal to 140mg/dL was associated with race (proportionately more frequent among whites) in a multivariable analysis. In a sub-analysis of cases that had A1c data available (N=112), increasing BMI and A1c greater than 8 were associated with increased risk of preoperative glucose value greater than or equal to 140mg/dL (Table 9). Preoperative glucose value greater than or equal to 180mg/dL on the morning of surgery was associated with A1c greater than 8 in a bivariate analysis (RR 3.33 (95% CI 1.7, 6.52); $p<.01$) (Table 10).

Of 65 cases without diabetes that had preoperative glucose tested, four (6 percent) had a glucose level greater than or equal to 126mg/dL. No case without diabetes presented with a preoperative glucose level greater than or equal to 180mg/dL. Fifteen of the 65 cases with testing (23 percent) were found to have a blood sugar in a range normally consistent with the condition impaired fasting glucose (100-125mg/dL). Presenting with an elevated glucose level greater than or equal to 100mg/dL preoperatively was associated with age in the bivariate analysis (Table 11).

Intraoperative hyperglycemia. Of the 667 cases with glucose tested in the operating room, the median glucose level was 108mg/dL (IQR 97,124). Glucose values were significantly higher among cases with diabetes than those without (129 v. 106mg/dL; M-W = 21087, $p<.001$).

Forty-one cases (4 percent) had at least one intraoperative glucose value that was greater than or equal to 180mg/dL. Twenty-one cases had two or more glucose values that were greater than or equal to 180mg/dL during surgery. Of the 41 cases with glucose values greater than or equal to 180mg/dL, 32 (86 percent) had known diabetes and nine (14 percent) did not have diabetes (X^2=75.06; $p<.001$) (Table 12).

Table 9. Factors associated with presenting on the morning of surgery with elevated glucose ≥140mg/dL among cases with diabetes that had preoperative glucose measured (N=133).			
DM	Bivariate RR (95%CI)	Multivariable Full RR (95%CI)	Multivariable Reduced RR (95%CI)
Number of cases with testing	133	132	112
Gender, male v. female	0.96 (.68, 1.37)	0.96 (.67, 1.38)	
Age (for every 10 years)	0.90 (.78, 1.04)	0.96 (.82, 1.12)	
Race, nonwhite v. white	0.61 (.38, .99)*	0.62 (0.38, 1.00)*	0.56 (.34, .91)
Insurance Status, C v. G	0.83 (.58, 1.17)	0.95 (0.65, 1.40)	
ASA Class, high v. low[a]	1.04 (.70, 1.54)	1.05 (.68, 1.63)	
BMI (for each 5points)	1.17 (1.05, 1.31)*	1.14 (1.00, 1.30)	1.16 (1.03, 1.29)*
Fusion, v. no fusion	0.85 (.60, 1.21)	1.00 (.64, 1.43)	
Duration, ≥6 v. <6hrs	0.82 (.75, 1.17)	0.76 (.52, 1.13)	
EBL, ≥200 v. <200[b]	1.15 (.78, 1.71)		
A1c, > 8 v. ≤ 8[x]	1.74 (1.23, 2.46)*		1.80 (1.29, 2.51)*

64 patients with testing available presented with glucose level ≥140mg/dL.
DM = Diabetes. Insurance Status: C = community and workers comp; G = government and uninsured.
[a]ASA missing in 1 case; [b]EBL missing in 18 cases; [c]A1c missing in 21 cases.
For variables listed above the double line, > 98% of the cases had complete data and were included in full model.
*p <.05

Table 10. Factors associated with presenting on the morning of surgery with elevated glucose ≥180mg/dL among cases with diabetes that had preoperative glucose measured (N=133).		
DM	Bivariate RR (95%CI)	Multivariable Full RR (95%CI)
Number of cases with testing	133	132
Gender, male v. female	1.13 (.59, 2.18)	1.18 (.59, 2.36)
Age (for every 10 years)	0.99 (.96, 1.01)	0.88 (.65, 1.19)
Race, nonwhite v. white	0.50 (0.21, 1.22)	0.48 (.19, 1.18)
Insurance Status, C v. G	1.01 (.51, 1.98)	1.30 (.61, 2.78)
ASA Class, high v. low[a]	1.18 (.57, 2.45)	1.14 (.49, 2.65)
BMI (for each 5points)	1.21 (.97, 1.51)	1.15 (.89, 1.47)
Fusion, v. no fusion	0.92 (.48,1.76)	0.97 (.47, 1.99)
Duration, ≥6 v. <6hrs	0.99 (.52,1.89)	0.84 (.41, 1.73)
EBL, ≥200 v. <200[b]	0.83 (.42,1.66)	
A1c, > 8 v. ≤ 8[c]	3.32 (1.70, 6.52)*	

29 patients with testing available presented with glucose level ≥180mg/dL.
DM = Diabetes. Insurance Status: C = community and workers comp; G = government and uninsured.
[a]ASA missing in 1 case; [b]EBL missing in 18 cases; [c]A1c missing in 21 cases.
For variables listed above the double line, > 98% of the cases had complete data and were included in full model.
*p <.05

Table 11. Associations with glucose level ≥100mg/dL on the morning of surgery among those without diabetes that had preoperative glucose measured (N=65). 19 patients presented with preoperative glucose level ≥100mg/dL.

NDM	Bivariate RR (95%CI)**
Number of cases with testing	65
Gender, male v. female	1.60 (.95, 2.67)
Age (for every 10 years)	**1.03 (1.01, 1.05)** *
Race, nonwhite v. white	0.81 (.42, 1.56)
Insurance Status, C v. G	0.85 (.53, 1.37)
ASA Class, high v. low	0.91 (.57, 1.47)
BMI (for each 5points)	1.00 (.83, 1.19)
Fusion, v. no fusion	0.71 (.44, 1.13)
Duration, ≥6 v. <6hrs	0.91 (.57, 1.47)
EBL, ≥200 v. <200[a]	0.78 (.46, 1.31)
A1c, ≥ 5.7 v. < 5.7[b]	3.00 (.45, 19.93)

NDM = No Diabetes. Insurance Status: C = community and workers comp; G = government and uninsured.
[a]EBL missing in 8 cases; [c]A1c missing in 55 cases.
For variables listed above the double line, > 98% of the cases had complete data and were included in full model.
*p <.05
** Multivariable models not performed as 65 with available data.

Table 12. Proportion of cases with intraoperative hyperglycemia (glucose level ≥180mg/dL) among those with glucose testing (N=667).

	Normal Glucoses	One glucose ≥180mg/dL	Two or more glucoses ≥180mg/dL
Diabetes, % (n)	79% (121)	7% (11)	14% (21)
No Diabetes, % (n)	98% (505)	1.2% (6)	0.6% (3)

Intraoperative hyperglycemia was associated with an A1c greater than 8 and a preoperative glucose level greater than or equal to 140mg/dL in cases with diabetes (Table 13). Among the 514 patients without diabetes who had intraoperative glucose values tested, only nine had values greater than or equal to 180mg/dL. None of these cases had a preoperative glucose level greater than 100mg/dL.

Postoperative hyperglycemia. Mean daily glucose levels were higher among cases with diabetes than cases without diabetes. In both groups, the mean daily glucose level was highest on POD1 and decreased through POD3 leveling off on POD4 and POD5 (Figure 8).

Table 13. Associations with intraoperative hyperglycemia among cases with diabetes that had testing available (N=153).

DM	Bivariate RR (95%CI)	Multivariable Full RR (95%CI)	Multivariable Reduced RR (95%CI)
Number of cases with testing	153	151	97
Gender, male v. female	1.17 (.62, 2.21)	1.12 (.60, 2.11)	
Age (for every 10 years)	0.98 (.96, 1.01)	0.82 (.61, 1.09)	
Race, nonwhite v. white	0.54 (.22,1.30)	0.48 (.20, 1.14)	
Insurance Status, C v. G	0.83 (.44, 1.57)	1.35 (.53, 2.04)	
ASA Class, high v. low[a]	1.13 (.56, 2.26)	1.35 (.63, 2.87	
BMI (for each 5points) [b]	1.04 (.83, 1.32)	0.99 (.78, 1.27)	
Fusion, v. no fusion	0.76 (.41, 1.43)	0.93 (.49, 1.78)	
Duration, ≥6 v. <6hrs	0.66 (.36, 1.22)	0.65 (0.35, 1.20)	
EBL, ≥200 v. <200[c]	0.96 (.48, 1.95)		
A1c, > 8 v. ≤ 8[d]	3.94 (2.15, 7.22)*		1.75 (1.03, 3.00)*
Preoperative glucose ≥140mg/dL[e]	14.53 (3.63, 58.20)*		10.69 (2.68, 42.61)*
Preoperative glucose ≥180mg/dL[e]	4.87 (2.63, 9.03)*		

32 patients had one or more intraoperative glucose values ≥180mg/dL.
Diabetes. Insurance Status: C = community and workers comp; G = government and uninsured.
[a]ASA classification missing in 1 case; [b]BMI missing in 1 case; [c]EBL missing in 19 cases; [d]A1c missing in 27 cases; [e]Preoperative glucose missing in 45 cases.
For variables listed above the double line, > 98% of the cases had complete data and were included in full model.
*p <.05

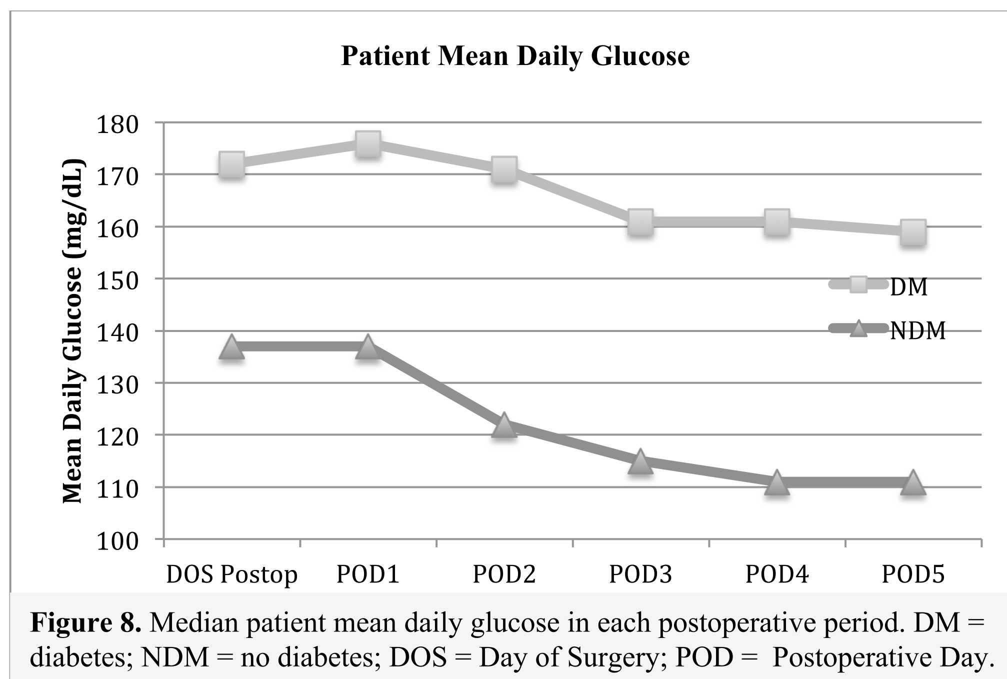

Figure 8. Median patient mean daily glucose in each postoperative period. DM = diabetes; NDM = no diabetes; DOS = Day of Surgery; POD = Postoperative Day.

Postoperative hyperglycemic days. In this sample ten percent of all postoperative hospital days met the specific definition criteria for “hyperglycemic days”. A hyperglycemic day was defined as having two or more glucose values greater than or equal to 180mg/dL within the postoperative period. Days without at least two glucose measurements were considered to be normal glycemic days. Glucose testing was performed at least twice per day on 25 percent of days. Testing at least two times a day was more common in cases with diabetes than in cases without diabetes (81 percent v. 12 percent) (Figure 9).

Evidence of any postoperative hyperglycemia. One hundred and seventy-eight of the 1095 cases (16 percent) developed postoperative hyperglycemia—defined as two or more glucose values greater than or equal to 180mg/dL in at least one postoperative period. Postoperative hyperglycemia was more common among cases with diabetes than cases without diabetes (65 v. 6 percent; $p < .001$, chi-square). Fifty-five of the 178 cases (31 percent) that developed hyperglycemia were patients without diabetes.

Of the subset of cases with at least two glucoses tested daily, on average 53 percent of cases with diabetes and 16 percent of cases without diabetes experienced hyperglycemia in at least one period (Figure 10).

Early Postoperative Hyperglycemia. Of the 178 cases that developed hyperglycemia, 169 (95 percent) were identified within the first two days of surgery. Postoperative hyperglycemia was identified on or before POD2 in 120 of 123 cases of cases with diabetes (98 percent) and in 49 of

55 cases without diabetes (89 percent. Only three cases with diabetes and six cases without diabetes developed new hyperglycemia on or after POD3. (Figure 11)

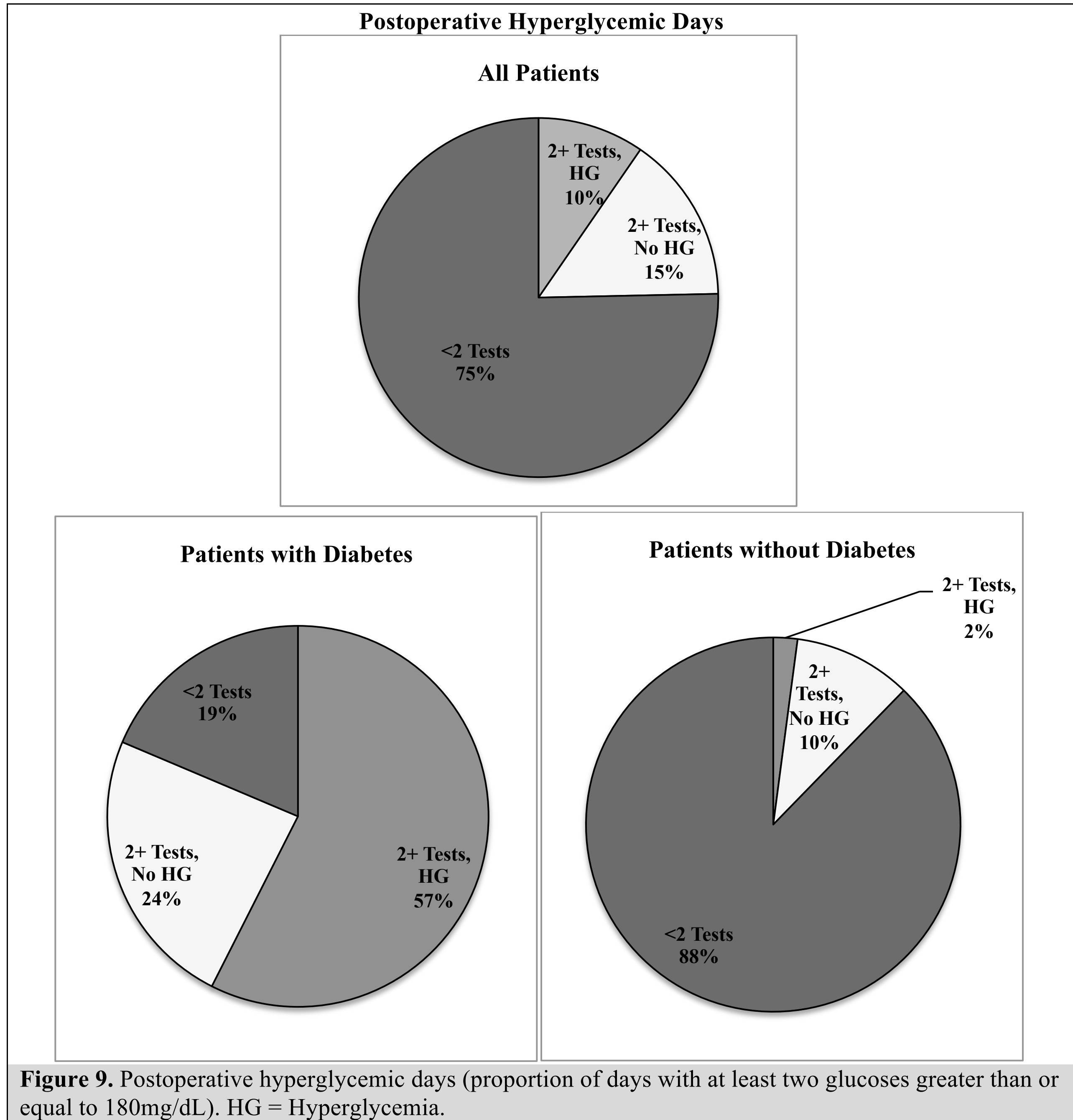

Figure 9. Postoperative hyperglycemic days (proportion of days with at least two glucoses greater than or equal to 180mg/dL). HG = Hyperglycemia.

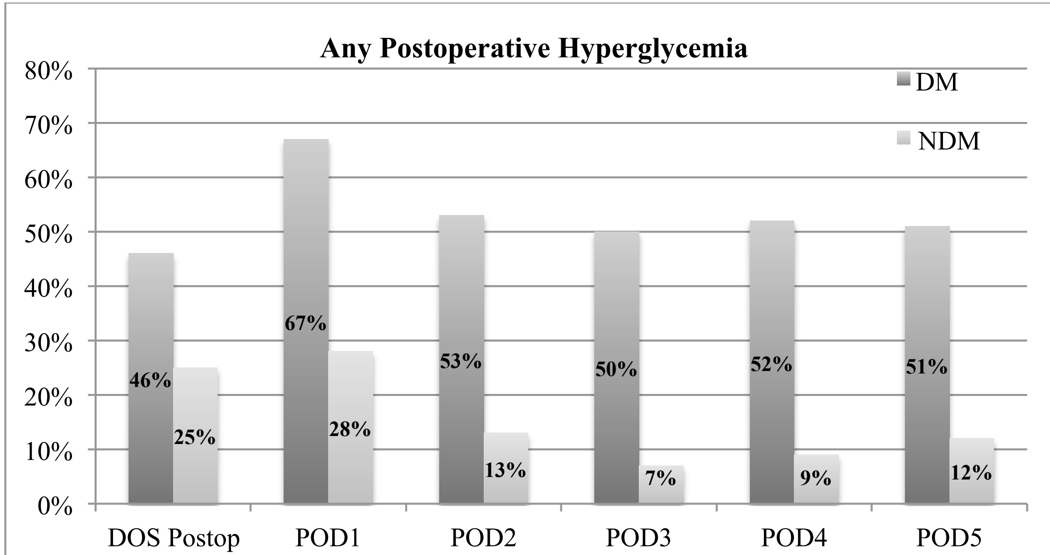

Figure 10. Proportion of patients with at least two results per period who had two or more glucoses ≥ 180mg/dL. DM = diabetes; NDM = no diabetes; DOS = Day of Surgery; POD = Postoperative Day.

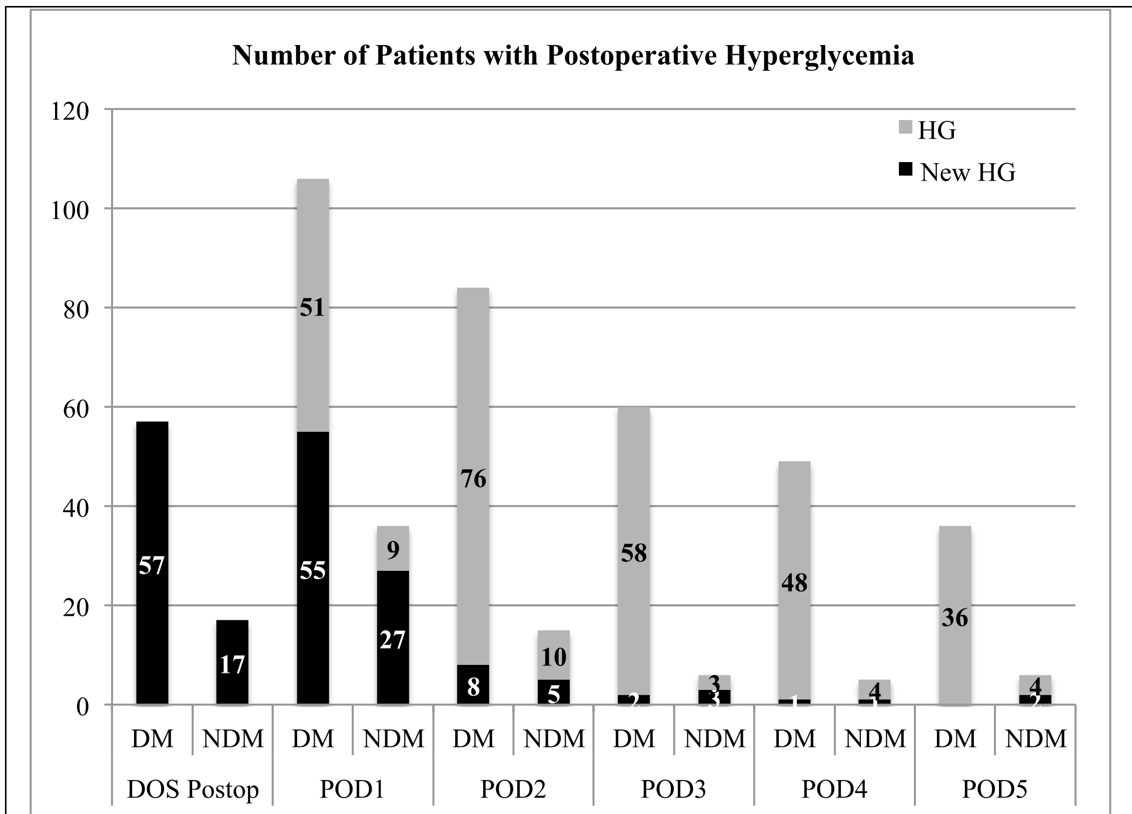

Figure 11. Number of cases with two glucose measurements ≥180mg/dL in each period. Black represents new case in a given period. Grey represents cases with hyperglycemia on previous days in addition to current period. DM = diabetes; NDM = no diabetes; DOS = day of surgery; POD = postoperative day; HG = hyperglycemia.

Hypoglycemia. Hypoglycemia was infrequent in all periods. Preoperatively, only two cases presented with glucose values less than 70mg/dL; both were cases without diabetes who had a glucose level of 68mg/dL (normal for patients without diabetes). Intraoperatively, 12 cases had a glucose value less than 70mg/dL (11 were cases without diabetes; 1 with diabetes). No cases pre- or intra-operatively developed severe hypoglycemia (glucose value less than 40mg/dL). Postoperatively, 11 cases developed hypoglycemia (glucose value between 40 and 69mg/dL) from the end of surgery through POD5. Nine events were in patients with diabetes, two events occurred in patients without diabetes. Severe hypoglycemia occurred postoperatively in one case. This patient had diabetes and developed a glucose level of 35mg/dL on POD1 while on long acting and prandial subcutaneous insulin. Glucose was promptly administered intravenously and the glucose level normalized within minutes.

Aim 3. Factors Associated with Early Postoperative Hyperglycemia

Early postoperative hyperglycemia is defined as having two or more glucose values greater than or equal to 180mg/dL in at least one period between DOS, POD1 and POD2. For this analysis, cases were required to have had at least two glucose measurements in the specified period in order to define hyperglycemia. Cases with insufficient glucose testing were considered to have normal glucose.

Patients with diabetes. Of the 188 cases with known diabetes, 123 (65 percent) developed early postoperative hyperglycemia. A bivariate log-linear regression revealed that A1c and measures

of preoperative and intraoperative glucose were significantly associated with occurrence of postoperative hyperglycemia. In the multivariable analysis, each 10 years of preoperative glucose value greater than or equal to 140mg/dL (RR 1.26 [95%CI 1.12, 1.42]; p<.01) and A1c value greater than 8 (RR 1.34 [95%CI 1.11, 1.60]; p<.001) were associated with early postoperative hyperglycemia (Table 14).

Table 14. Factors associated with early postoperative hyperglycemia among patients with diabetes (N=188).

DM	Bivariate RR (95%CI)	Multivariable Full RR (95%CI)	Multivariable Reduced RR (95%CI)
Number of cases	188	186	112
Gender, male v. female	1.00 (.81, 1.25)	0.99 (.79, 1.23)	
Age (for every 10 years)	1.05 (.95, 1.15)	1.06 (.95, 1.19)	
Race, nonwhite v. white	0.93 (.72, 1.21)	0.97 (.74, 1.28)	
Insurance Status, C v. G	0.89 (.72, 1.11)	0.83 (.65, 1.06)	
ASA Class, high v. low[a]	1.23 (.95, 1.59)	1.26 (.97, 1.64)	
BMI (for each 5points)[b]	0.98 (.91, 1.07)	0.99 (.91, 1.08)	
Fusion, v. no fusion	0.98 (.79, 1.22)	1.02 (.80, 1.30)	
Duration, ≥6 v. <6hrs	0.94 (.76, 1.16)	0.91 (.71, 1.17)	
EBL, ≥200 v. <200[c]	1.14 (.88, 1.48)		
A1c, > 8 v. ≤ 8[d]	1.51 (1.32, 1.72)*		1.26 (1.12, 1.42)*
Preoperative Glucose ≥ 140mg/dL[e]	1.46 (1.19, 1.80)*		1.34 (1.11, 1.60)*
Preoperative Glucose ≥ 180mg/dL[e]	1.35 (1.14, 1.58)*		
Intraoperative Glucose ≥ 180mg/dL[f]	1.72 (1.46, 2.04)*		0.92 (.75, 1.13)

123 patients had early postoperative hyperglycemia.
DM = Diabetes. Insurance Status: C = community and workers comp; G = government and uninsured.
[a]ASA classification missing in 1 case; [b]BMI missing in 1 case; [c]EBL missing in 23 cases; [d]A1c missing in 40 cases; [e]Preoperative glucose missing in 55 cases; [f]Intraoperative glucose missing in 35 cases.
For variables listed above the double line, > 98% of the cases had complete data and were included in full model.
*p <.05

Patients without diabetes. Forty-nine of the 907 cases without known diabetes (5 percent) developed early postoperative hyperglycemia. Factors associated with postoperative hyperglycemia among those without diabetes in the reduced multivariable model, included duration greater than 6 hours (RR 6.20 [95%CI 1.49, 25.83]; p=.01) and intraoperative glucose greater than or equal to 180mg/dL (RR 3.53 [95%CI 1.14, 10.92]; p=.03) (Table 15).

Table 15. Factors associated with early postoperative hyperglycemia among cases without diabetes (N=907).

NDM	Bivariate RR (95%CI)	Multivariable Full RR (95%CI)	Multivariable Reduced RR (95%CI)
Number of cases with testing	907	891	428
Gender, male v. female	0.81 (.47, 1.39)	0.85 (.49, 1.46)	
Age (for every 10 years)	1.50 (1.22, 1.85) *	1.31 (1.01, 1.71) *	1.07 (.78, 1.48)
Race, nonwhite v. white	1.05 (.50, 2.20)	1.63 (.80, 3.32)	
Insurance Status, C v. G	1.90 (1.05, 3.43) *	1.25 (.65, 2.41)	1.78 (.79, 4.03)
ASA Class, high v. low[a]	2.92 (1.65, 5.16) *	1.92 (1.03, 3.58) *	1.53 (.73, 3.21)
BMI (for each 5points) [b]	1.05 (.86, 1.28)	1.04 (.86, 1.27)	
Fusion, v. no fusion	1.64 (.87, 3.10)	0.99 (.52, 1.90)	
Duration, ≥6 v. <6hrs	7.14 (3.25, 15.73) *	7.24 (3.03, 17.31) *	6.20 (1.49, 25.83) *
EBL, ≥200 v. <200[c]	3.99 (1.56, 10.19) *		1.20 (.38, 3.75)
A1c, ≥ 5.7 v. < 5.7[d]	0.63 (.34, 1.11)		
Preoperative Glucose ≥ 100mg/dL[e]	1.46 (.26, 8.14)		
Intraoperative Glucose ≥ 180mg/dL[f]	5.47 (2.49, 12.03) *		3.53 (1.14, 10.92) *

49 patients without diabetes developed early postoperative hyperglycemia.
NDM = No diabetes. Insurance Status: C = community and workers comp; G = government and uninsured.
[a]ASA classification missing in 4 cases; [b]BMI missing in 12 cases; [c]EBL missing in 129 cases; [d]A1c missing in 825 cases; [e]Preoperative glucose missing in 842 cases; [f]Intraoperative glucose missing in 393 cases.
For variables listed above the double line, > 98% of the cases had complete data and were included in full model.
*p <.05

Aim 4. Factors Associated with Clinical Outcomes

Length of stay (LOS). Median LOS was 4.3 days (IQR 3.2,6.5). Median LOS was longer for patients with diabetes than for patients without diabetes (5.2 v. 4.3 days; M-W = 75581, p=.01). LOS was also longer for those with postoperative hyperglycemia (6.8 v. 4.2 days; M-W = 56437, p<.001). To test for associations with LOS, stepwise linear regression was undertaken. Early postoperative hyperglycemia was associated with LOS when controlling for diabetes status, patient and surgical characteristics (p<.01; see Table 16).

Table 16. Factors associated with length of stay. The log LOS was used in this analysis given that LOS data are skewed.

Log LOS	Bivariate		Multivariable	
	B_s	p-value	B_s	p-value
Number of cases	1095		929	
Early Postoperative Hyperglycemia	.17	<.01	.10	<.01
Diagnosis of Diabetes, DM v. NDM	.07	.02	-.06	.12
Gender, v. Female	-.00	<.01	-.08	<.01
Age, (for every 10 years)	.22	<.01	.10	<.01
Race, nonwhite v. white	-.02	.01	-.03	.31
Insurance Status, C v. G	.02	<.01	.07	.01
ASA Class, high v. low [a]	.26	<.01	.15	<.01
BMI (for each 5points) [b]	.05	.08	.01	.72
Fusion, v. no fusion	.23	<.01	.10	<.01
Duration, ≥6 v. <6hrs	.45	<.01	.29	<.01
Postop Steroids	.01	.68	.02	.41
Postop Tube Feeds	.26	<.01	.21	<.01
EBL > 200cc v. <200cc [c]	.26	<.01	.10	<.01
A1c <6, 6-8, >8 [d]	-.20	<.01		
Preop Glucose ≥140mg/dL [e]	.12	.09		
Intraop Glucose ≥ 180mg/dL [f]	.05	.20		

DM = Diabetes; NDM = No diabetes. Insurance Status: C = community and workers comp; G = government and uninsured. Bs – Standardized beta coefficient; C - community and workers comp; G - government and uninsured
[a]ASA classification missing in 5 cases; [b]BMI missing in 13 cases; [c]EBL missing in 152 cases; [d]A1c missing in 865 cases; [e]Preoperative glucose missing in 897 cases; [f]Intraoperative glucose missing in 428 cases.
*p <.05

Readmission at 30 days. Ninety-three of 1095 patients (nine percent) were readmitted to HMC within 30 days of discharge. In bivariate analysis, cases with diabetes were more likely to be readmitted compared to cases without diabetes (12 v. 8 percent; RR 1.58 [95%CI 1.01, 2.47]; p=.04). There was not a significant difference in readmission rates between cases with and without postoperative hyperglycemia (10 v. 8 percent; RR 1.23 [95%CI 0.74, 2.02]; p=.43). In the full multivariable log-linear regression, duration of surgery and gender were associated with 30-day readmission but not diabetes. In the reduced model, duration but not female gender remained associated (Table 17).

Table 17. Factors associated with 30-day readmission.			
30-Day Readmission	Bivariate RR (95%CI)	Multivariable Full RR (95%CI)	Multivariable Reduced RR (95%CI)
Number of cases	1095	1095	1095
Diagnosis of Diabetes, DM v. NDM	1.58 (1.01, 2.47) *	1.67 (.89, 3.11)	1.55 (.99, 2.42)
Postoperative Hyperglycemia	1.23 (.74, 2.02)	0.83 (.41, 1.68)	
Gender, v. Female	0.69 (.49, 1.03)	0.65 (.44, .97) *	0.68 (.46, 1.00)
Age, (for every 10 years)	0.99 (.85, 1.15)	0.92 (.78, 1.08)	
Race, nonwhite v. white	0.77 (.44, 1.36)	0.79 (.45, 1.38)	
Insurance Status, C v. G	1.03 (.69, 1.53)	0.96 (.64, 1.44)	
ASA Class, high, v. low [a]	1.37 (.93, 2.01)	1.25 (.80, 1.94)	
BMI (for each 5points)[b]	1.04 (.91, 1.20)	0.98 (.86, 1.12)	
Fusion, v. no fusion	1.11 (.74, 1.68)	0.89 (.58, 1.38)	
Duration, ≥6 v. <6hrs	1.69 (1.14, 2.52) *	1.76 (1.15, 2.72) *	1.66 (1.11, 2.47) *
Postop Steroids	1.64 (.99, 2.72)	1.51 (.89, 2.56)	
Postop Tube Feeds	.09 (.24, 3.47)	0.73 (.17, 3.12)	
EBL, > 200cc v. <200cc [c]	1.31 (.85, 2.03)		
A1c >8 [d]	0.24 (.34, 1.74)		
Preoperative Glucose ≥ 140mg/dL	1.23 (.57, 2.66)		
Intraoperative Glucose ≥180mg/dL	1.29 (.55,3.05)		

DM = Diabetes; NDM = No diabetes. Insurance Status: C = community and workers comp; G = government and uninsured.
[a]ASA classification missing in 5 cases; [b]BMI missing in 13 cases; [c]EBL missing in 152 cases; [d]A1c missing in 865 cases; [e]Preoperative glucose missing in 897 cases; [f]Intraoperative glucose missing in 428 cases.
For variables listed above the double line, > 98% of the cases had complete data and were included in full model.
*p <.05

Death. Eleven of the 1095 cases (1 percent) died. Six of the 907 cases without diabetes died, compared to 5 of the 188 cases with diabetes (0.5 v. 2.7 percent; p=.01, chi-square). Seven of the 926 without postoperative hyperglycemia and four of the 169 with postoperative hyperglycemia died (0.8 v. 2.4 per 100; p=.05, chi-square).

Discussion

The primary aims of this study were to describe current practice in screening and monitoring for perioperative hyperglycemia and to describe the incidence of and factors associated with postoperative hyperglycemia for patients with and without diabetes admitted for planned spine surgery. In general, screening and monitoring for hyperglycemia among spine surgery patients in this study sample was suboptimal. One in six patients had postoperative hyperglycemia; the majority of cases with hyperglycemia (95 percent) were identified within 48 hours of surgery.

The following discussion details key findings and their interpretation related to each of the primary aims (Aims 1-3) within the context of current evidence. Research and clinical implications are discussed. The discussion focuses first on patients with diabetes and then on patients without diabetes. Subsequently, findings and interpretations related to the exploratory aim of associations with clinical outcomes (Aim 4) are discussed, followed by discussion of strengths and limitations of the study.

Patients with Diabetes

In this study sample postoperative hyperglycemia was observed in nearly two-thirds of patients with diabetes. This is consistent with rates observed in previous reports. [7,9,15] Hyperglycemia has been consistently associated with increased rates of complications and death among surgical patients.[5-19] Perioperative treatment of hyperglycemia with insulin has been associated with

decreasing morbidity and mortality.[9,28,29] One in ten patients in the study sample was a patient with diabetes who developed postoperative hyperglycemia. This high frequency coupled with the known benefits of insulin administration stresses the need for improved systems to provide early identification and efficient intervention.

Monitoring for postoperative hyperglycemia was not universal in this study sample; though 98 percent of the cases had at least one glucose test on postoperative day one, only 80 percent had at least two tests on both postoperative day one and postoperative day two. Similar rates were observed in two prior studies evaluating the frequency of glucose testing in the post-anesthesia care unit (87 and 96 percent).[26,27] What defines adequate monitoring to detect clinically significant postoperative hyperglycemia remains unknown. The majority of studies linking postoperative hyperglycemia to worse outcomes have been retrospective and, unfortunately, many of these have not reported frequency of glucose testing. Insufficient testing could significantly bias results. Currently there is no consensus on what is the most appropriate timing or frequency for postoperative testing. Understanding what represents adequate testing is an underdeveloped area of research. Research is needed to inform the development of such a consensus statement regarding best practice and to improve clinical monitoring nationwide.

Similarly, there is no consensus statement in the United States regarding frequency of intraoperative glucose testing. The National Health Service (NHS) in Britain recommends minimally testing every hour for all patients with diabetes.[30] In the present study, intraoperative monitoring was performed for a larger proportion of patients than previously reported in the other two studies: 81 percent compared to 33 and 60 percent.[26,27] One possible explanation for

this is the longer more complex nature of the spine surgeries examined in the present study. Among those with diabetes in this study sample, the median surgical duration was six hours, yet the median frequency of glucose testing was two tests per case. Though perhaps ideal, hourly glucose testing is intensive and may not be convenient for all operating rooms. As with postoperative monitoring, additional research will be needed to determine what frequency of intraoperative testing represents sufficient monitoring.

The NHS also recommends checking glucose prior to induction in all patients with diabetes.[30] In the study sample, only 71 percent of patients had glucose tested prior to anesthesia. This rate was somewhat lower than in previous studies of elective orthopaedic cases where 89 and 94 percent were found to have preoperative glucose testing.[26,27] One explanation is that clinical practice likely varies significantly between individual hospitals. Across these studies, one in three to one in sixteen patients with diabetes are not undergoing glucose testing on the morning of surgery, which is a significant missed opportunity to identify patients at increased risk for complications and death.

In the present study, one quarter of the patients presented with elevated glucose on the morning of surgery; one in five patients had intraoperative hyperglycemia. Having an A1c value greater than 8 was associated with both; this may represent a subset of patients who would benefit from more frequent glucose monitoring. Additionally, body mass index was associated with elevated preoperative glucose. Targeting preoperative glucose testing for patients with higher body mass index may be another intervention approach. Preoperative elevated glucose was associated with both intraoperative and postoperative hyperglycemia, yet intraoperative hyperglycemia was not

independently associated with postoperative hyperglycemia. One implication is that increasing preoperative screening should take precedence over intraoperative monitoring if resources are limited.

Findings from this study suggest that patients with diabetes who are older, those with A1c values greater than 8, and those with preoperative glucose values greater than 140mg/dL are more likely to develop postoperative hyperglycemia. These factors may also represent important indicators for increased perioperative glucose monitoring.

Patients without Diabetes

In this study sample postoperative hyperglycemia was observed in 6 percent of patients without diabetes. This rate is lower than those observed in previous reports,[9,15,24] due most likely to this study's more strict definition of postoperative hyperglycemia, which required a minimum of two glucose values greater than or equal to 180mg/dL in any single period including postoperatively on the day of surgery or postoperative days one or two.

Monitoring for postoperative hyperglycemia among patients without diabetes in this study was less frequent than for patients with diabetes. While 74 percent of patients without diabetes had a single glucose test on both postoperative day one and postoperative day two, only seven percent had at least two glucose tests on both days. Having only a single glucose test could lead to failure to identify hyperglycemia—especially if the single test is not postprandial. Testing only fasting

glucose levels could miss postprandial hyperglycemia that indicates impaired glucose tolerance—a likely mechanism of postoperative hyperglycemia among those without diabetes. A previous study found that 89 percent of patients without diabetes had one postoperative glucose test but only 42 percent had more than one test during the entire postoperative stay.[31] In that study, the majority of postoperative glucose values available were collected from routine chemistry panels and not from bedside point-of-care testing. In the present study sample, glucose testing could not be differentiated as part of the routine postoperative chemistry panel versus targeted monitoring for hyperglycemia with point-of-care testing. Routine chemistry testing in the hospital setting may be done for reasons other than to evaluate glucose; thus hyperglycemia even if present could go unrecognized clinically. Compared to patients with diabetes, the occurrence of hyperglycemia in patients without diabetes is associated with up to two times the risk of complications and mortality.[7,9,15] The lack of adequate evidence in the field indicates a clear need for research to identify which patients without diabetes would benefit from glucose testing and what frequency of testing would be optimal. With such information, clinical protocols can be developed

Intraoperative monitoring of glucose occurred in more than half of patients without diabetes in this study sample, though only nine of the 514 patients without diabetes who had glucose tested during surgery had intraoperative hyperglycemia. The median frequency of intraoperative glucose testing was one test per surgery. Thus, it remains unclear if the low rate of observed hyperglycemia represents truly low occurrence or simply a lack of adequate monitoring and detection. The observed low rate of intraoperative hyperglycemia precluded meaningful assessment of factors associated with intraoperative hyperglycemia.

Similarly, preoperative screening for hyperglycemia was infrequent and thus limiting meaningful analysis. However, elevated glucose levels normally considered to be consistent with impaired fasting glucose and diabetes were identified in 29 percent of patients tested on the morning of surgery. Patients in this tested group were older and more likely to be classified with high ASA, thus the findings may represent an overestimate of elevated preoperative glucose compared to a more general patient population. One previous prospective study, however, reported even greater rates of elevated preoperative glucose levels (47 percent) in patients without known diabetes.[32] Additionally, in the present study only 65 patients had preoperative glucose screening and thus findings may not necessarily reflect a broader population. Focusing research efforts to screen all patients preoperatively would provide a more comprehensive understanding of whether preoperative glucose levels are associated with increased risk of postoperative hyperglycemia and potentially allow for profiling risk of postoperative hyperglycemia based on preoperative glucose levels.

Currently, there is no universal standard for frequency of glucose testing among patients without diabetes despite the fact that postoperative hyperglycemia in these patients is associated with even greater risks than postoperative hyperglycemia in patients with diabetes. Three recent studies have demonstrated that compared to patients with diabetes, mortality is two to five times higher among patients without diabetes who develop hyperglycemia.[7,9,15] One study demonstrated that as level of glucose increased the odds of mortality increased more rapidly among those without compared to those with diabetes.[7] Significant work remains to be done to determine who is at risk for postoperative hyperglycemia and what represents sufficient preoperative, intraoperative and postoperative glucose monitoring among patients without

diabetes. The findings from the present study suggest that surgical duration greater than six hours and intraoperative hyperglycemia are associated with postoperative hyperglycemia and thus may represent reasonable clinical targets among spine surgery patients without diabetes for increased frequency of perioperative monitoring.

Strengths and Limitations

This research provides new and highly relevant evidence for health care practice. First, it distinguishes hyperglycemia occurring pre-, intra- and post-operatively whereas prior studies have typically omitted some or grouped these time frames together. Moreover, the postoperative study period spanned five days whereas many prior studies have been limited in terms of postoperative follow-up days. This revealed that the timing of new episodes of hyperglycemia in relation to postoperative day could be identified. The current analyses suggest that the occurrence of hyperglycemia is observable in over 95 percent of patients within the first two postoperative days. Second, this research is the first to evaluate clinical linkages with postoperative hyperglycemia among patients undergoing spine surgery—which has significantly high rates of complications. Such linkages will be able to serve as targets for increased monitoring and implementation of therapeutic interventions to reduce the risk of associated complications. Third, this study describes current clinical practice in terms of the frequency and timing of screening and monitoring for hyperglycemia. In doing so this study identified gaps in the research and clinical literature that impact both the quality of available evidence and clinical care.

The interpretation of the findings, however, needs to be considered within the context of the study limitations. First, this was a retrospective evaluation; thus, the type and range of available data was limited to that collected primarily for clinical and administrative purposes. To determine potential risk for perioperative hyperglycemia among patients without diabetes, it will be necessary to have additional information about other critical risk factors for diabetes including hypertension, history of gestational diabetes and family history of diabetes, not available in the dataset. Second, the diagnosis of diabetes was based on ICD-9 coding alone. However, the observed 17 percent of patients with diabetes based on this definition was consistent with previous reports showing a range of 12.5 to 25 percent of hospitalized patients having a diagnosis of diabetes.[33] Third, this was a single center study that reflects clinical practice limited to this center. Study of other settings will be needed to determine if the results are generalizable. Fourth, there was a relatively large amount of missing data, especially for preoperative glucose values among patients without diabetes. Patients with glucose testing may represent a sicker subset and thus results may not be generalizable to a broader population. The decision to group those without testing among the normal glucose group in the analyses may have biased results toward finding no difference. Missing data also impeded the ability to identify patients with possible unrecognized diabetes or prediabetes despite that these are common in the general population. Moreover, lack of preoperative data precluded the determination of association of elevated preoperative glucose levels and postoperative hyperglycemia. This underscores the need for more comprehensive evaluations of perioperative glucose as well as the need for identification of minimal levels of testing necessary to reduce the probability of missed hyperglycemia.

In summary, more comprehensive glucose screening and monitoring is needed for all patients perioperatively. Though rates of postoperative glucose testing were high, not all patients had testing. In this study sample, if all patients had postoperative glucose testing, an additional one in ten patients with diabetes and one in 20 patients without diabetes may have been identified as having postoperative hyperglycemia—potentially placing these individuals at unrecognized and increased risk for complications and death. Compared to postoperative rates of glucose monitoring, preoperative and intraoperative glucose testing was even less frequent. Notably, among patients who had any glucose testing, generally only one or two glucose tests were performed in a period. It is unclear what proportion of patients would have been identified with hyperglycemia if more frequent testing occurred. Currently, no evidence exists that informs what frequency of testing is sufficient to detect hyperglycemia. Significant research is needed to determine best practices for who and how often to monitor patients pre-, intra- and postoperatively.

Given that the vast majority of patients with postoperative hyperglycemia were identified by postoperative day two in this study, it would be logical, clinically feasible, and cost sensitive to increase glucose monitoring during the first two postoperative days for all patients. Findings suggest that among patients with diabetes, clinical targets for increased monitoring include: patients with an A1c value greater than 8, patients with preoperative glucose values greater than or equal to 140mg/dL, and older patients. Increased monitoring among patients without diabetes could be targeted for patients undergoing surgeries greater than six hours in duration. Moreover, increased intraoperative monitoring among patients without diabetes may lead to fewer missed cases of postoperative hyperglycemia. To substantially advance knowledge in this area, more

research is needed to determine if preoperative elevated glucose aids in identifying patients without diabetes at increased risk for postoperative hyperglycemia. Without more thorough and comprehensive glucose testing, clinical decisions will continue to rely upon sporadic and incomplete data potentially placing patients at increased risk for suffering complications and death.

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