Pre-operative glucose as a screening tool in patients without diabetes

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ABSTRACT

Background: Although hyperglycemia has been associated with poor post-operative outcomes, pre-operative hyperglycemia is not used as a screening tool in patients without diabetes. We evaluated pre-operative glucose as a marker for post-operative outcomes in patients without diabetes in order to assess its usefulness as a potential screening tool.

Materials and methods: Clinical characteristics for a sample of 6,683 patients without diabetes who underwent non-emergent vascular and general surgery were collected from the American College of Surgeons National Surgical Quality Improvement Program, Brigham and Women's Hospital database. Last glucose measured within 30 days prior to surgery was the main predictor variable with post-operative infection within 30 days as the primary outcome.

Results: For patients without known diabetes with pre-operative glucose of 100-139 mg/dL and 140-179 mg/dL, post-operative infection rates were significantly higher (9.33% and 10.16%, respectively) than that of patients with pre-operative glucose of 70-99 mg/dL (5.62%, $P < 0.001$). The risk-adjusted odds of post-operative infection increased by 40% (95% CI, 13%-72%) for each 40 mg/dL increase in pre-operative glucose over the range 70-179 mg/dL. Follow-up data demonstrated that 15% of patients with pre-operative glucose ≥ 100 mg/dL were diagnosed with diabetes within one year after surgery.

Conclusions: In patients without known diabetes, pre-operative glucose is a significant marker for post-operative complications even at moderate levels of hyperglycemia. Some of these patients likely had pre-diabetes or unrecognized diabetes at the time of surgery. Future studies are needed to determine whether such screening and follow-up of pre-operative hyperglycemia in all patients would be effective in lowering complication rates.

INTRODUCTION

Hyperglycemia in patients without known diabetes has been associated with poor clinical outcomes.¹⁻³ Reduced morbidity and mortality from improved glycemic control in surgical patients also support the association between hyperglycemia and post-operative outcomes.⁴⁻⁹ However, the risks of unrecognized hyperglycemia (in patients not known to have diabetes) prior to surgical operations remain unclear. Although Ramos et al. have investigated associations between post-operative hyperglycemia and post-operative complications,¹⁰ we were interested in using pre-operative blood glucose as a marker for post-operative complications in patients not known to have diabetes. These patients would not be expected to have HbA1c levels, making blood glucose screening a potentially useful tool to screen for post-operative risks and act as a gateway to connect these patients to short- and long-term monitoring and management of hyperglycemia.

Unrecognized pre-operative hyperglycemia is due to either undiagnosed diabetes, physiologic stress, or a combination, and may be a marker of poor outcomes or a primary pathologic process.^{4,10-12} Possible mechanisms linking hyperglycemia with worse outcomes (besides an undiagnosed illness causing physiologic stress) include derangements in leukocyte function, glycosylation and inactivation of immunoglobulins (leading to immune dysfunction), and collagen glycosylation (leading to poor healing from wounds and organ damage).¹³⁻¹⁶ However, since there are likely many confounding factors contributing to the relationship between pre-operative hyperglycemia and post-operative complications, we sought to assess pre-operative glucose as a marker, not as a causal determinant, of post-operative complications.

There have been a few studies investigating the link between pre-operative glucose levels and post-operative outcomes but the results have been mixed. Pre-operative hyperglycemia was

shown to be associated with increased hospital mortality in diabetic and non-diabetic patients.^{11,17} However, a study of surgical patients with aneurysmal subarachnoid hemorrhage showed that admission hyperglycemia was not associated with worse outcomes.¹⁸

Our study assesses pre-operative glucose as a marker for post-operative complications in a cohort of patients without known diabetes admitted for non-emergent non-cardiac surgery, which represents a unique chance to evaluate pre-operative screening for hyperglycemia in patients with lower levels of physiologic stress than previous study populations. Randomly tested glucose levels have been shown to be efficient in identifying pre-diabetic and undiagnosed diabetic patients.¹⁹ Moreover, once screened and identified, these patients represent a population for whom perioperative management of hyperglycemia could be initiated in an attempt to improve outcomes. We also examined the incidence of diagnosed diabetes in our study cohort at one year follow-up.

METHODS

Study cohort

The initial sample from the American College of Surgeons National Surgical Quality Improvement Program, Brigham and Women's Hospital (ACS NSQIP BWH) database contained 10,812 randomly selected patients who underwent non-emergent vascular and general surgery at BWH from 1/1/2005 to 4/5/2010. We excluded patients who had known diagnosis of diabetes or pre-operative sepsis. ACS NSQIP-defined variables such as demographics, surgical profile, pre-operative risk factors, pre-operative laboratory values, American Society of Anesthesiology (ASA) classification, principal Current Procedural Terminology (CPT) and International Classification of Diseases, 9th Edition, Clinical Modification (ICD-9 CM) codes, and operative

information were utilized to characterize patients. Individual medical record numbers were matched to the BWH laboratory database to determine pre-operative random glucose measurements. Post-operative insulin treatment was determined from BWH medical records. The primary independent variable for the study was defined as the last glucose (in the clinical lab or as point of care (POC) testing) measured within 30 days prior to surgery. The study was approved by the BWH/Partners Institutional Review Board.

Outcome measures

The primary outcome was post-operative infection rate as defined by the percentage with any occurrences from a composite list of post-operative infections within 30 days, based on NSQIP data and definition.²⁰ Post-operative infections have been associated with prolonged hospitalization, increased readmission, and increased cost.²¹ Following previous research,¹⁰ we used a composite of superficial incisional surgical site infection (SSI), deep incisional SSI, organ space SSI, wound disruption, graft/prosthesis/flap failure, pneumonia, urinary tract infection, sepsis, and septic shock. Secondary outcomes included the number of composite post-operative infections, and the rate and number of all NSQIP-identified post-operative complications including unplanned intubation, pulmonary embolism, on ventilator > 48 hrs, progressive renal insufficiency, acute renal failure, stroke, coma, peripheral nerve injury, cardiac arrest requiring cardio-pulmonary resuscitation, myocardial infarction, bleeding/transfusions, and deep vein thrombosis. In our one year follow-up, we classified patients as having had pre-diabetes at the time of surgery as those with evidence of diabetic diagnoses within the following year. Diabetic diagnosis was defined by retrospective review of hospital and outpatient records from the Partners Healthcare Clinical Data Repository using the following criteria: HbA1c ≥ 6.5 , billing

diagnosis of diabetes (ICD-9 CM 250.xx), use of anti-hyperglycemic medications, or outpatient problem of diabetes in the outpatient medical record.

Analysis and statistical methods

All statistical analyses were performed using Stata 12. Clinical characteristics of the patient population included in this study were described for the entire sample and as a comparison between patients who had any post-operative infection and those who did not. These comparisons were conducted with t-tests for samples of unequal variances or Fisher's exact test as appropriate. Next, post-operative infection rates were calculated for patient groups according to pre-operative glucose levels. Patients were classified into 5 groups based on clinically relevant cut-off points: pre-operative glucose <70 mg/dL, 70-99 mg/dL, 100-139 mg/dL, 140-179 mg/dL, and ≥ 180 mg/dL. The glucose level stratification was based on a composite of current ADA recommendations for diagnosis of pre-diabetes and diabetes including both random and fasting values. These are also cut points considered for treatment with insulin in the inpatient setting under various circumstances (e.g., ICU vs. ward vs. ward with risk factors for hypoglycemia). These stratifications were used in the first parts of our analyses to estimate any trends in the relationship, before we proceeded to using multivariable logistic regressions to model the incremental relationship and adjust for other risk factors. Likelihood ratio tests were used to determine overall differences among groups, and t-tests were used to determine differences between individual groups. The same analyses were performed for the secondary outcome measures. Before proceeding to logistic regression to assess pre-operative glucose as a screening tool while controlling for other clinical characteristics, an analysis for threshold and non-linear effects of pre-operative glucose on infection rates was conducted using a cubic spline model. One identified non-linear range (patients with pre-operative glucose ≥ 180 mg/dL) was then

assessed for confounding by indication by comparing post-operative insulin use using logistic regression.

After identifying a reliable range for logistic modeling, a multivariate model was used to estimate the relationship of pre-operative glucose as a marker for post-operative infection rate to assess the former as a potential screening tool when combined with other clinical characteristics. The risk adjusted logistic model controlled for age, gender, BMI, ASA classification, and type of surgery (gastric bypass, colectomy, hepatectomy, cholecystectomy, pancreatectomy, hernia, AAA, bypass graft). The same adjusted analysis was performed on the secondary outcomes. The 1-year follow-up data was used to identify patients within our study cohort who may have had pre-diabetes or undiagnosed diabetes prior to surgery. We analyzed the post-operative infection rates among these patients, and analyzed the relationship between pre-operative glucose and post-operative infection rates among pre-diabetic and non-pre-diabetic patients.

RESULTS

Of 10,812 patients with non-emergent surgery at BWH during the study period, 8,154 (75%) had a pre-operative glucose level within 30 days of surgery. We excluded 1,204 patients with a known diagnosis of diabetes and 267 patients with pre-operative sepsis, leaving 6,683 patients in the final study cohort. The study characteristics for the entire cohort are shown in Table 1. Overall, the mean age of the patients was 54.6 years and 34% were male. 6,037 (90%) underwent general surgery and 646 (10%) underwent vascular surgery. 2,524 (38%) had a body mass index (BMI) >30 and 69 (1%) were in ASA class 4 or 5. Patients with post-operative infection were more likely to be male, be older, have longer operation time, have higher pre-operative glucose, and have a diagnosis of diabetes within 1 year post surgery. The type of surgery and ASA classification prior to surgery were also significantly different between patients

with and without post-operative infection. The vast majority of pre-operative glucose measurements were from laboratory blood glucose testing, with 147 (2.2%) of the pre-operative glucose levels coming from POC measurements. The last pre-operative glucose measurements were taken on average 8 days prior to surgery, with 16% within 1 day and 29% within 3 days prior to surgery (Figure 1). Excluded patients were more likely to be older (55.4 vs. 54.6 years, $P<0.05$), have shorter operation time (121 vs. 141, $P<0.001$), shorter days of stay (3.5 vs. 4, $P<0.001$), and lower post-operative infection rate (4.8% vs. 6.7%, $P<0.001$). Of these, patients excluded due to lack of glucose measurement within 30 days prior to surgery were younger (53.6 vs. 54.6, $P<0.01$), more likely to have ASA classification of 1 or 2 (76.7% vs. 67.8%, $P<0.001$), had lower BMI (28 vs. 30, $P<0.001$), shorter days of stay (2 vs. 4, $P<0.001$), shorter length of operation (106 vs. 141 minutes, $P<0.001$), and lower post-operative infection rate (3.0% vs. 6.7%, $P<0.001$).

Comparison of post-operative outcomes by pre-operative glucose levels

Dividing the sample into five groups based on their pre-operative glucose levels, patients with glucose levels <70 mg/dL, 70-99 mg/dL, 100-139 mg/dL, 140-179 mg/dL, and ≥ 180 mg/dL had post-operative infection rates of 5.47%, 5.62%, 9.33%, 10.16%, and 6.67% respectively (Figure 2). Logistic likelihood ratio test on the primary outcome of post-operative infection rates showed significant differences among groups ($P<0.001$), with the 100-139 mg/dL and 140-179 mg/dL groups having significantly higher post-operative infection rates than the normo-glycemic group (70-99 mg/dL). The group with the highest pre-operative glucose (≥ 180 mg/dL) did not have a statistically significant difference in infection rates from the normo-glycemic group.

Similar trends were seen for total complication rates, mean number of infections and mean number of complications per patient. All three outcomes are more common with increasing levels of pre-operative glucose up to 180 mg/dL (Table 2).

Estimating the magnitude of effect of pre-operative glucose on post-operative outcomes

The cubic spline model (overlay in Figure 2) has flexibility to allow for possible threshold and non-linear effects. This model indicated non-linearity for patients with pre-operative glucose at the low extreme (<70 mg/dL) and the high extreme (≥ 180 mg/dL). Regarding potential confounding by indication in cases of extreme hyperglycemia (e.g., patients doing better because providers chose to treat these patients with insulin after noticing their hyperglycemia), we found that the odds of post-operative insulin treatment in the highest pre-operative glucose (≥ 180 mg/dL) group was 8.04 (95% CI, 3.57-18.10) times that of the rest of the patients in our sample ($P < 0.001$). Of note, in these 60 patients, 5% had ASA classification 1, 40% had ASA classification 2, 53% had ASA classification 3, 2% had ASA classification 4, and 60% went on to develop diabetes during the following year according to our records. Over the range of pre-operative glucose between 70 and 180 mg/dL, the cubic spline model indicated a continuous trend that could be well-estimated by logistic regression models. Therefore, to quantify the relationship of hyperglycemia as a marker of post-operative complications and minimize the effects of confounding by indication, we proceeded by focusing on the range of patients with pre-operative glucose ≥ 70 mg/dL and < 180 mg/dL (93% of the entire sample).

The risk adjusted logistic model (Table 3) controls for basic clinical characteristics as well as disease severity, indicating a 40% (95% CI, 13%-72%) increase in the odds of infection for each 40 mg/dL in pre-operative glucose ($P = 0.002$). Figure 3 is a graphical representation of pre-operative glucose as a marker for post-operative infection rate after risk adjustment. The risk

adjusted models for each type of infection showed non-statistically significant trends for increased risk of infection with hyperglycemia, except for superficial SSI where the relationship was statistically significant (Table 4).

Similar results were demonstrated for the secondary outcome measures: 42% (95% CI, 21%-68%) increased odds of infection ($P<0.001$), 24 (95% CI, 5-43) more infections per 1000 patients ($P=0.014$), and 71 (95% CI, 35-107) more complications per 1000 patients ($P<0.001$) per 40 mg/dL increase in pre-operative glucose after risk adjustment.

One year follow-up on diabetic status

Of the entire study population, 547 patients (8.18%) were identified as diabetic one year later, including 314 patients (15.33%) of those with pre-operative glucose ≥ 100 mg/dL. This group of 547 will be identified below as “pre-diabetic” while the others are classified as “non-pre-diabetic”. Those who were (retrospectively) identified as pre-diabetic at the time of the operation had significantly higher infection rates (9.32%) than those who were not identified as diabetic one year later (6.52%, $P=0.012$).

Within the pre-diabetic group, there is no statistically significant relationship for pre-operative glucose as a marker of post-operative infection rate (6.6% increase in odds per 40 mg/dL increase in pre-operative glucose, 95% CI -36% to 78%). Within the much larger non-pre-diabetic group, there was a risk adjusted 41% increase in the odds of post-operative infection per 40 mg/dL increase in pre-operative glucose (95% CI 12% to 78%, $P=0.004$).

DISCUSSION

Our study shows that pre-operative blood glucose in patients without known diabetes can be a useful marker to screen for complications after non-emergent operations, even after

adjusting for basic clinical characteristics and disease severity. Though there likely are many confounding factors in this relationship, we were interested in pre-operative glucose as a screening tool instead of establishing any causal or independent relationship. Patients without “known diabetes” (as defined by NSQIP, i.e., anyone not taking oral hypoglycemic agents or insulin) may have had hyperglycemia due to undiagnosed diabetes, diabetes controlled by diet only, pre-diabetes, or illnesses causing physiologic stress. We excluded patients with known diabetes as treatment is likely to confound the findings and pre-operative testing is more common, and emergent cases, where pre-operative screenings may not be possible and physiological stress is often more apparent. Ramos et al. found that pre-operative glucose level did not predict post-operative infection if post-operative glucose level is known,¹⁰ however, our study is interested in proactive, pre-operative identification of patients at risk since this may lead to better intra- and post-operative care and may lead to diagnosis of underlying diabetes or pre-diabetes prior to surgery.

Our main results suggest that blood glucose should be considered as one of the pre-operative screening measures for patients without known diabetes, as a marker for worse post-operative outcomes and for identification of patients with pre-diabetes and undiagnosed diabetes. One of the most interesting findings of our study is the fact that patients with random mild hyperglycemia (pre-operative glucose level of 100-139 mg/dL), which many surgeons may accept as normal, did indeed have an increased risk of post-operative infections and other post-operative complications. We would recommend checking an HbA1c in these patients pre-operatively to identify patients with previously undiagnosed diabetes or pre-diabetes (HbA1c 5.8-6.4). Once these patients are identified, we recommend looking for possible sources of physiological stress (e.g., review of systems and physical exam for symptoms and signs of

infection, urinalysis and chest x-ray if warranted), close monitoring of glucose levels immediately before, during, and after surgery, a low threshold for treating with physiological doses of insulin (e.g., if glucose >140 mg/dL), and outpatient follow-up for the development of diabetes in the following year (e.g., HbA1c every 3 months). The number of patients in the group with pre-operative glucose >180 mg/dL was too small to show any significant difference in post-operative infection and complication rates. Treatment with insulin may have confounded the relationship between glucose levels and infection rates. Many likely had underlying physiological stress, although this is difficult to prove. Similarly, patients with pre-operative glucose <70 mg/dL did not have significant differences in post-operative complication rates, but did trend higher than patients with pre-operative glucose between 70-99 mg/dL, raising the implications of mild hypoglycemia as another possible area to investigate in further studies.

There has been controversy regarding perioperative glycemic control.²²⁻²⁶ Some evidence supports implementing glycemic control prior to surgery,^{27,28} which suggests that delaying surgery for better glycemic control in the cases of elective surgeries may be a useful option. A randomized prospective study would be needed to address the best course of action once patients without known diabetes are pre-operatively screened for glucose. Regardless of the causal factors, our findings raise the possibility that pre-operative hyperglycemia is a modifiable risk marker, for which monitoring and management may improve post-operative outcomes.

Upon follow-up, those who were pre-diabetic at the time of surgery had worse post-operative outcomes than those who were not, further emphasizing the need for identifying those who are pre-diabetic prior to surgery (e.g., with an HbA1c measurement) and may be at increased risk for post-operative complications. These patients may also need long-term surveillance and management. Increasing pre-operative glucose in those who did not go on to

develop diabetes, i.e., those who possibly had “stress” hyperglycemia,^{1,2} was associated with increasing risks of post-operative infection, showing that there may be an important pathophysiologic process requiring further investigation and treatment. Our sample size did not give us enough power to estimate this effect in those with pre-diabetes and we cannot exclude the possibility that those who were pre-diabetic also suffered from stress as a cause of their hyperglycemia, at least in part. In patients with pre-operative glucose ≥ 100 mg/dL, 15% were diagnosed with diabetes over the next year, but 85% were not, suggesting that stress hyperglycemia may be far more common than undiagnosed diabetes, at least within the limits of our ability to detect diabetes on follow-up.

In comparison, reports utilizing pre-operative HbA1c found increased risk of deep sternal wound infection after CABG when controlling for diabetes diagnosis,²⁹ higher post-operative complications after colorectal surgery in patients without known diabetes,³⁰ increased 30-day morbidity in patients without diabetes undergoing vascular surgery,³¹ but no association with post-operative infection risk in non-diabetic cardiac surgery patients,³² with increased HbA1c levels. The patients included in our study had no known diabetes, and HbA1c measurements were not available. We also feel that glucose would be useful to identify patients with recent hyperglycemia (i.e., due to physiological stress). We advocate for a policy to routinely measure pre-operative glucose and identify patients with poor glucose control so that follow-up HbA1c testing and other interventions could be initiated prior to surgery as this practice is not yet a routine pre-operative screening tool at many hospitals. In patients with a diagnosis of diabetes, studies have been mixed, showing that pre-operative hyperglycemia is not associated with mortality or infection rates in non-cardiac surgery,^{9,17} but also that increased pre-operative glucose is associated with higher mortality in patients undergoing non-cardiac non-vascular

surgery,¹¹ and that operative day hyperglycemia is associated with SSI after colectomy for cancer.³³

Our study had several limitations. Due to the retrospective nature of its design, 2,658 patients did not have a record of blood glucose measurement within 30 days prior to their operations and so could not be included in the study. Our conclusions are based on patients who did have a pre-operative glucose measurement. Physicians may have had clinical reasons for not ordering pre-operative glucose for some patients, likely because they did not believe these patients would be at risk for hyperglycemia. However, though not routine, glucose testing is often obtained pre-operative evaluation, as witnessed by the fact that 75% of our cohort did have a pre-operative glucose value and that most glucose values were still normal. Thus, while there may be some bias in the absolute proportion of patients in our cohort found to have hyperglycemia (22% instead of 31% if all untested patients had normo-glycemia), it is unlikely that the relationship between pre-operative glucose levels and outcomes is substantially different in the minority of patients without pre-operative glucose readings. One might argue that the exclusion of these patients from the study limits the generalizability of the findings to these healthiest of patients, but their exclusion does not bias our regression coefficients. Our findings in fact suggest that excluded patients had fewer risk factors for hyperglycemia, better clinical outcomes, and were less likely to have post-operative infections, thus would strengthen our conclusions if they had been included. In terms of data gathering, as glucose levels were randomly obtained we cannot distinguish which of the hyperglycemic group actually had what would be considered normal post-prandial values. If anything, this would bias our findings towards the null. In addition, ACS NSQIP does not capture a small number of patients with diabetes controlled on diet only (i.e., who should not have been included in the study); it is

unlikely that these patients substantially altered our findings. The severity and physiological stress of our patients were not completely adjusted for in our study by the ASA classification and type of surgery, as the acute physiology score was not readily available in the databases we used. In terms of follow-up data, since the pre-operative and follow-up data were obtained from the Partners Clinical Data Repository, we may have underestimated the proportion of patients with diagnosed diabetes within one year. Lastly, the generalizability of our results may be limited as our study was conducted at a large academic medical center. Nevertheless, our sample is drawn from a large urban teaching hospital with a diverse patient population. In future studies, we hope to include multi-site prospective analyses and greater sample size for sub-group analyses and with more complete follow-up on diabetic status.

In conclusion, we found that in patients not known to have diabetes, increasing random pre-operative glucose is a marker for worsening post-operative outcomes, an effect that holds true after adjusting for other clinical screening measures and over even mild to moderate degrees of hyperglycemia. Whether pre-operative hyperglycemia is a marker for other factors that influence post-operative outcomes or is an independent factor, pre-operative glucose remains a metric that is easily obtainable and actionable. Our results suggest that blood glucose measurements should be taken routinely for patients without known diabetes prior to non-emergent surgery. For those noted to be hyperglycemic, future studies may indicate delaying surgery to improve glycemic control, perioperative glucose monitoring and treatment, a search for previously unknown causes of physiologic stress, as well as follow up with patients after surgery for the development of diabetes mellitus. We recommend that future studies should use prospective methods and randomized multi-centered controlled trials to test for the effectiveness

of pre-operative screening for hyperglycemia as a way to improve patient outcomes in the immediate post-operative period and beyond.

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Table 1 – Clinical characteristics of the study participants

Variable	All	Patients with post-operative infection	Patients without post-operative infection	P value
N	6,683	451 (6.7)	6,232 (93.3)	
Male	2,276 (34.1)	212 (47.0)	2,064 (33.1)	<0.001
Mean age, years	54.6 ± 15.9	57.3 ± 16.1	54.5 ± 15.9	<0.001
Mean BMI	30.4 ± 9.7	29.6 ± 8.8	30.5 ± 9.7	0.062
Race				
American Indian/ Alaskan Native	3 (0.04)	0	3 (0.05)	0.738 (F test)
Asian	93 (1.4)	7 (1.6)	86 (1.4)	
Black/African American	507 (7.6)	27 (6.0)	480 (7.7)	
Native Hawaiian/ Pacific Islander	2 (0.03)	0	2 (0.03)	
White	5,297 (79.3)	365 (80.9)	4,932 (79.1)	
Hispanic	400 (6.0)	31 (6.9)	369 (5.9)	
Type of surgery				
Gastric Bypass	1,227 (18.4)	51 (11.3)	1,176 (18.9)	<0.001 (F test)
Colectomy	1,400 (20.9)	169 (37.5)	1,231 (19.8)	
Hepatectomy	109 (1.6)	21 (4.7)	88 (1.4)	
Cholecystectomy	346 (5.2)	12 (2.7)	334 (5.4)	
Pancreatectomy	116 (1.7)	23 (5.1)	93 (1.5)	
Hernia	246 (3.7)	13 (2.9)	233 (3.7)	
Amputation	39 (0.6)	0	39 (0.6)	
AAA	82 (1.2)	4 (0.9)	78 (1.3)	
Bypass graft	51 (0.8)	8 (1.8)	43 (0.7)	
Length of Stay, days	4.4 ± 7.3	12.6 ± 12.0	3.8 ± 6.5	<0.001
Mean Op Time, minutes	141 ± 100	217 ± 128	136 ± 95	<0.001
ASA Classification				
1	362 (5.4)	10 (2.2)	352 (5.6)	<0.001 (F test)
2	4,170 (62.4)	205 (45.5)	3,965 (63.6)	
3	2,076 (31.1)	229 (50.8)	1,847 (29.6)	
4	68 (1.0)	7 (1.6)	61 (1.0)	
5	1 (0.01)	0	1 (0.02)	
None	6 (0.09)	0	6 (0.1)	
Pre-operative glucose within 30 days, mg/dL	94.9 ± 22.4	99.3 ± 23.3	94.6 ± 22.3	<0.001
Diagnosis of diabetes within 1 year	547 (8.18)	51 (11.3)	496 (8.0)	0.029

Data are presented as mean ± standard deviation or n (%) unless otherwise indicated.

Table 2 – Outcome comparisons among patient groups by pre-operative glucose levels

Patient groups by pre-operative glucose levels	<70 mg/dL (N=384)	70-99 mg/dL (N=4251)	100-139 mg/dL (N=1801)	140-179 mg/dL (N=187)	≥180 mg/dL (N=60)	
Infection rate	5.47%	5.62%	9.33%	10.16%	6.67%	P<0.001
Complication rate	10.68%	10.84%	17.93%	20.32%	13.33%	P<0.001
Infections (per 1,000)	68	70	113	123	66	P<0.001
Complications (per 1,000)	148	163	291	353	233	P<0.001

Table 3 – Adjusted logistic model of pre-operative glucose, over the range of 70-179 mg/dl, as a marker of post-operative infection

Variable	OR (95% CI)	P value
Pre-operative glucose (per 40 mg/dL)	1.40 (1.13–1.72)	0.002
Age (per year)	0.99 (0.99–1.00)	0.169
Male	1.40 (1.14–1.72)	0.001
BMI (per unit)	1.02 (1.00–1.03)	0.042
ASA Class (per increase in category)	1.90 (1.58–2.29)	<0.001
Gastric bypass	0.63 (0.40–1.00)	0.052
Colectomy	2.56 (2.02–3.24)	<0.001
Hepatectomy	3.94 (2.33–6.66)	<0.001
Cholecystectomy	0.75 (0.40–1.41)	0.368
Pancreatectomy	4.11 (2.43–6.95)	<0.001
Hernia	1.00 (0.54–1.85)	0.994
AAA	0.52 (0.16–1.69)	0.275
Bypass graft	2.99 (1.35–6.60)	0.007

BMI: body mass index; ASA: American Society of Anesthesiology; AAA: abdominal aortic aneurysm.

Table 4 – Adjusted logistic models of pre-operative glucose, over the range of 70-179 mg/dl, as a marker of each category of post-operative infection

Category of post-operative infection*	Pre-op glucose (per 40 mg/dL) OR (95% CI)	P value
Superficial incisional SSI	1.56 (1.16–2.10)	0.003
Deep incisional SSI	1.17 (0.34–4.02)	0.802
Organ space SSI	1.57 (0.97–2.53)	0.065
Wound disruption	1.18 (0.97–3.04)	0.726
Graft/prosthesis/flap	0.68 (0.97–4.24)	0.676
Pneumonia	1.17 (0.70–1.96)	0.549
Urinary tract infection	0.53 (0.28–1.02)	0.057
Sepsis	1.46 (0.97–2.19)	0.068
Septic shock	0.85 (0.41–1.79)	0.677

* All models adjusted for age, gender, BMI, ASA classification, type of surgery (gastric bypass, colectomy, hepatectomy, cholecystectomy, pancreatectomy, hernia, AAA, bypass graft).

Figure 1 – Distribution of last glucose measured pre-operatively by days from start of operation (ex. measurements within 24 hours prior to the start of operation fall between -1 and 0).

Figure 2 – Percent of patients without known diabetes with any post-operative infections grouped by clinically relevant cut-off points for last glucose levels measured within 30 days prior to surgery. Number of patients in each group is listed along with the percent infection rate. Overlying cubic spline model is shown. * p-value < 0.05 compared with pre-operative glucose 70-99 mg/dL; *** p-value < 0.001 compared with pre-operative glucose 70-99 mg/dL.

Figure 3 – Pre-operative glucose level as a marker for post-operative infection, over the range of 70-179 mg/dl, adjusted for age, gender, BMI, ASA classification, and type of surgery using multivariable logistic model.