

Perioperative Glucose Control in the Gastric Bypass Population: How Well Do We Do, How Well Do We Think We Do, and is it Predictable

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Abstract

Background: Bariatric patients are prone to insulin resistance and Postoperative Hyperglycemia (PH), which adversely affects postoperative care. Clinicians may underestimate PH on surgical wards. We aimed to characterize inpatient Blood Glucose (BG) control and identify predictors of PH after RYGB.

Methods: From a single University-based center, a retrospective review of 431 patients undergoing RYGB was performed. Postoperative inpatient BG control and diabetic therapy were characterized. Attending bariatric surgeons and surgical house staff were surveyed regarding inpatient BG management. BG management was compared, and predictors of PH were identified.

Results: PH (BG>180 mg/dL) was common particularly in patients with HbA1C>6.5%. From the observed sample, the mean postoperative BG was 133.5 ± 2.6 mg/dL, 167.0 ± 6.0 mg/dL, and 190.9 ± 9.2 mg/dL for each increasing HbA1c class, while physician perceived mean postoperative BG was 116.5 ± 7.9 mg/dL ($p<0.002$), 145.0 ± 9.3 mg/dL ($p<0.003$), and 182.8 ± 14.5 mg/dL ($p=ns$) respectively. However, physicians overestimated the incidence of PH. Postoperative hypoglycemia was rare and also overestimated by clinicians. Four independent predictors of PH were identified, including preoperative HbA1c, preoperative nonfasting BG, a laparoscopic procedure, and preoperative diabetes. PH (mean BG>180 mg/dL) was predicted with a sensitivity of 42%, a specificity of 95%, a PPV of 60%, NPV of 90% and an overall accuracy of 87%.

Conclusions: The incidence of PH is common after RYGB and may be overestimated, while mean postoperative BG may be underestimated. Postoperative hypoglycemia is rare and overestimated. Preoperative HbA1c and non-fasting BG help identify patients at greatest risk PH.

Keywords: Perioperative glucose; Control bariatric surgery; Gastric bypass; Postoperative hyperglycemia

Introduction

Postoperative Hyperglycemia (PH) is deleterious in a wide range of surgical patients as it increases morbidity and possibly mortality. Wound infections and other infectious complications are often associated with PH [1-12]. Improving glucose control may decrease postoperative morbidity [13,14]. However, in critically ill patients intensive insulin regimens have been associated with hypoglycemic events, a potentially deadly consequence [15].

Various organizations have recognized PH as an independent risk factor for surgical morbidity. Surgical Care Improvement Program (SCIP) and National Surgical Quality Improvement Program (NSQIP) have recommended that blood glucoses (BG) should be under 200 mg/dL [16]. American Association of Clinical Endocrinologists (AACE) and American Diabetes Association (ADA) have adopted more stringent recommendations, suggesting all inpatient BG should be below 180 mg/dL [17].

As morbid obesity and the insulin resistance/diabetes continuum are tightly linked, bariatric patients are particularly prone to PH [18-21]. In our data, we have confirmed that PH is an independent risk factor for wound infections and Acute Renal Failure (ARF) in bariatric patients undergoing Roux-en-Y Gastric Bypass (RYGB) [22].

According to recent estimates, approximately 220,000 bariatric surgery cases are performed yearly and are now some of the most common general surgical operations [23]. Also, the number of surgeons registered with the American Society for Metabolic and Bariatric Surgery (ASMBS) has doubled in a 6 year period [24]. With an increasing demand for weight loss surgery, more high volume surgical centers, and an expanding set of bariatric surgeons, inpatient bariatric

services tend to be quite busy. It remains unclear if clinicians are entirely aware of the frequency and severity of PH in RYGB populations.

Therefore, we characterized inpatient glycemic control and postoperative diabetic therapy after RYGB. In addition, we compared these results with clinician perceptions of inpatient glycemic control and postoperative insulin therapy. Finally, we aimed to identify independent risk factors of postoperative glycemic control in RYGB patients.

Patient/Subject and Methods

From a single institution with ASMBS and Surgical Review Corporation (SRC) center of excellence accreditation, a retrospective chart review was performed of 431 patients undergoing RYGB procedures during 2006 - 2009. IRB approval was obtained. Patients were excluded for age <18 and BMI<40 kg/m². In general, patients underwent a laparoscopic retrocolic, retrogastric RYGB.

Most patients were on at least an insulin sliding scale while Nil Per Os (NPO) with Finger Stick Blood Glucose (FSBG) analyses every four hours. Some patients however required insulin infusions, which

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prompted FSBS analyses every one hour. Postoperative inpatient BGs were recorded for each patient. According to AACE guidelines, patients were grouped based on preoperative Hemoglobin A1c (HbA1c) status.

A voluntary survey of attending bariatric surgeons, recent former chief residents, and advanced resident surgical house staff was performed with respect to inpatient BG control and diabetic management (Appendix). The retrospectively observed sample versus physician perceived survey of BG control and inpatient diabetic management strategies were compared. Continuous vs. continuous variables were compared via two-tailed student *t*-test. Continuous vs. dichotomous variables were compared via one sample *t*-test. Descriptive statistics were performed using Microsoft Excel (Microsoft, Redmond, WA) spreadsheets and GraphPad QuickCalc software (La Jolla, CA). Statistical significance was defined as $p < 0.05$. SAS 9.2 (SAS Institute Inc., Durham, NC) was used for multivariate modeling.

Next, 381 of 431 (88.4%) patients were included into the predictive modeling for PH. Patients were excluded if records were incomplete. Univariate predictors were identified and then included into the multivariable modeling if they were at least borderline statistically significantly ($p < 0.15$) related to postoperative BG. A stepwise backwards elimination approach was used by removing one variable at a time starting with the least significant (i.e. *p*-value closest to 1.0) until all remaining variables in the model were statistically significantly related to postoperative BG ($p < 0.05$).

Results

Of the 431 patients reviewed, 278 (64.5%) had HbA1c < 6.5% (group 1), while 88 (20.4%) were between 6.5%-7.9% (group 2) and 66 (15.3%) were > 7.9% (group 3). The preoperative HbA1c class and the observed mean postoperative glucose were positively correlated (data not shown). As defined by ACEE as BG > 180 mg/dL the incidence of PH, was quite frequent, particularly in group 2 (27.7%) and group 3 (47.8%) (Table 1). The vast majority of patients were on "lower" dose insulin sliding scales, and there little was documented record regarding why treatment decisions were made. Also, neither insulin sliding scale (mostly low dose) or Diabetic Management Service (DMS) consult appeared to significantly reduce the incidence of PH, while insulin drips did (data not shown).

18/24 (75%) physician surveys were completed and analyzed. The range of responses varied significantly. Clinicians appeared to overestimate the incidence of PH across HbA1c classes. However, clinicians may underestimate mean postoperative BG, particularly in the group 1 and group 2 (116.5 ± 7.9 mg/dL vs. 133.5 ± 2.6 mg/dL, $p < 0.002$) and (145.0 ± 9.3 mg/dL vs. 167.0 ± 6.0 mg/dL, $p < 0.003$) (Table 2 and Figure 1). Clinicians underestimated the observed percentage of patients treated with insulin sliding scales and those requiring insulin drips postoperatively (Table 2). Rates of hypoglycemia (BG < 70 mg/dL) were low throughout all HbA1c classes (Table 1), but clinicians highly overestimated the rates of hypoglycemia in all HbA1c groups (Figure 2). Finally, rates of severe hypoglycemia, as defined as BG < 50 mg/dL, were exceptionally rare in this population (0.00%-0.04%) (Table 1).

There appeared to be many potential predictors of elevated mean PH in univariate modeling. Of note, age, ASA class and the other components of metabolic syndrome including hypertension and hyperlipidemia were associated with elevated mean PH, while BMI was not. However, only four of the predictors remained significant after multivariable modeling. These predictors included preoperative HbA1c, preoperative random glucose, preoperative DM, and surgery

	HbA1c Class		
	< 6.5%	6.5 %-7.9%	> 8%
Mean Postoperative BS (mg/dL)	133.5	167.1	190.9
# Patients	N = 278	N = 88	N = 66
# FSBS	n = 5439	n = 2445	n = 2082
BG (mg/dL)			
< 50	0.02%	0.04%	0.00%
50-70	0.26%	0.41%	0.53%
70-180	90.86%	71.82%	51.68%
180-350	8.66%	27.16%	45.68%
> 350	0.20%	0.57%	2.11%
Total	100.00%	100.00%	100.00%

Table 1: The incidence of hypo- and hyperglycemia after gastric bypass in three different HbA1c classes.

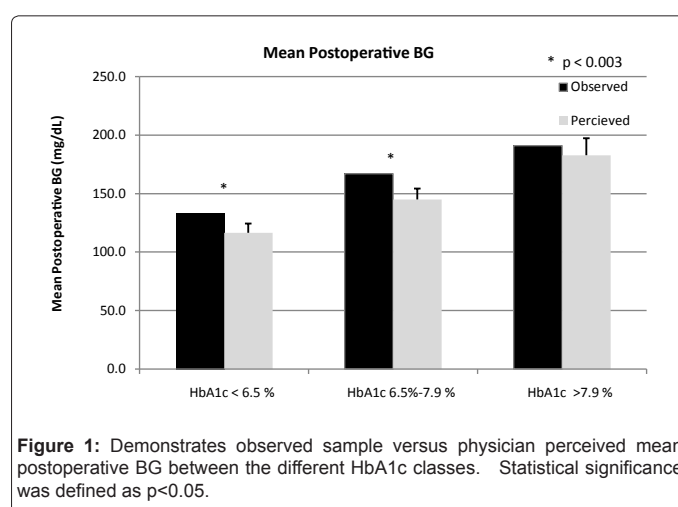


Figure 1: Demonstrates observed sample versus physician perceived mean postoperative BG between the different HbA1c classes. Statistical significance was defined as $p < 0.05$.

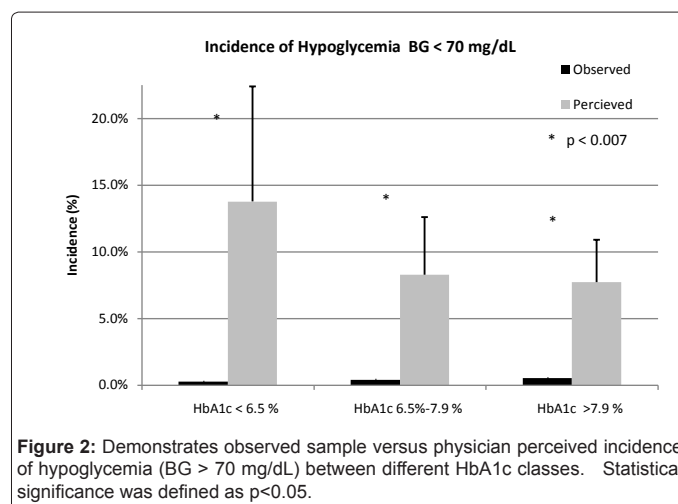


Figure 2: Demonstrates observed sample versus physician perceived incidence of hypoglycemia (BG < 70 mg/dL) between different HbA1c classes. Statistical significance was defined as $p < 0.05$.

type (laparoscopic vs. open RYGB) (Table 3). An equation for estimating mean postoperative BG was constructed from the multivariable model:

$$\text{Estimated mean postoperative BG (mg/dL)} = 81.3 + 7.7(\text{Baseline HbA1c (\%)}) + 0.16(\text{Preoperative BG (mg/dL)}) + 9.6(\text{Baseline DM}) - 12.2(\text{Laparoscopic Surgery})$$

In accordance with AACE/ADA guidelines which defined inpatient hyperglycemia as BG > 180 mg/dL, a 2 × 2 table of observed sample versus model predicted mean postoperative BG was constructed for this

Postoperative Variable	Observed n = 431 sampled patients		Perceived n = 18 physician surveys		P-Value
	Mean	95% CI	Mean	95% CI	
Mean Postoperative BG					
HbA1c < 6.5%	133.5	(130.9 - 136.2)	116.5	(108.6 - 124.4)	0.002
HbA1c 6.5%-7.9%	167.1	(161.0 - 173.2)	145.0	(135.7 - 154.3)	0.003
HbA1c > 7.9%	190.9	(181.7 - 200.1)	182.8	(168.3 - 197.3)	0.410
% of patients with mean postoperative BG >200 mg/dL					
HbA1c < 6.5%	1.8%		15.8%	(3.1% - 28.6)	0.046
HbA1c 6.5%-7.9%	15.7%		29.3%	(16.8% - 41.8%)	0.047
HbA1c > 7.9%	40.9%		41.8%	(29.0% - 54.6%)	0.892
% of patients on insulin sliding scale					
HbA1c < 6.5%	77.0%		68.3%	(54.0% - 82.7%)	0.236
HbA1c 6.5%-7.9%	95.7%		80.0%	(71.1% - 88.9%)	0.003
HbA1c > 7.9%	100.0%		86.9%	(78.8% - 95.1%)	0.006
% on Insulin Drip					
HbA1c < 6.5%	12.0%		5.7%	(2.8% - 8.5%)	<0.001
HbA1c 6.5%-7.9%	27.2%		14.4%	(7.8% - 21.0%)	0.002
HbA1c > 7.9%	48.5%		34.4%	(21.0% - 47.9%)	0.055
% with DMS Consult					
HbA1c < 6.5%	7.8%		12.9%	(3.2% - 22.5%)	0.315
HbA1c 6.5%-7.9%	36.9%		28.5%	(16.6% - 40.4%)	0.184
HbA1c > 7.9%	58.1%		58.8%	(44.8% - 72.8%)	0.953
% on Preoperative Insulin					
HbA1c < 6.5%	2.9%		19.4%	(10.5% - 28.3%)	0.002
HbA1c 6.5%-7.9%	29.3%		35.4%	(26.9% - 44.0%)	0.180
HbA1c > 7.9%	54.5%		63.1%	(51.0% - 75.2%)	0.182
Incidence of Hyperglycemia (> 200 mg/dL)					
HbA1c < 6.5%	4.6%		16.1%	(5.9% - 26.4%)	0.037
HbA1c 6.5%-7.9%	17.3%		29.5%	(18.1% - 40.9%)	0.046
HbA1c > 7.9%	35.7%		46.9%	(35.6 - 58.3%)	0.063
Incidence of Hypoglycemia (< 70 mg/dL)					
HbA1c < 6.5%	0.3%		13.8%	(5.2% - 22.4%)	0.006
HbA1c 6.5%-7.9%	0.4%		8.3%	(3.9% - 12.6%)	0.002
HbA1c > 7.9%	0.5%		7.7%	(4.5% - 10.9%)	<0.001

Table 2: The observed sample versus the physician perceived postoperative BG and inpatient BG management between different HbA1c classes.

model. The model demonstrated a sensitivity of 42.0% and a specificity of 95.0%. Also, the model had a positive predictive value (PPV) of 60.0% and a negative predictive value (NPV) of 90%. The overall incidence of mean postoperative BG > 180 mg/dL was approximately 17%, while the overall accuracy was 87.0% for the model ($R^2=50.5\%$).

Discussion

Clearly, PH affects surgical outcomes in a wide array of specialties, including general surgery. Despite frequent use of insulin sliding scales, insulin infusions, and DMS consults, PH was unfortunately still alarmingly common in the RYGB population. Also, it was potentially underestimated by clinicians on the busy surgical wards. Additionally, hypoglycemic events in this population were relatively uncommon and were far overestimated. These findings may be related to in the early postoperative period. A more standardized and aggressive treatment strategy may improve optimal postoperative BG homeostasis after RYGB.

Multiple univariate risk factors were associated with elevated mean PH, most of which were related to age, overall health (ASA class), and their diabetic parameters. Interestingly, BMI has no effect on PH, which suggests this issue is more related to insulin resistance and pancreatic reserve, and not necessarily their severity of obesity. Although not entirely unexpected, our multivariable findings demonstrated that elevated preoperative HbA1c, elevated preoperative BG, and baseline

DM to be strong risk factors for PH after RYGB. Also, having a laparoscopic procedure was protective of PH, likely as a result of less physiologic stress and decreased postoperative pain. This simple model may help distinguish RYGB patients at highest risk of PH from those with the lowest risk of PH. Our data is similar to postoperative cardiac surgery patients in that HbA1c and DM are predictors of higher postoperative BG [25]. Other recent literature cardiovascular surgery identified predictors of postoperative PH after, but they presumptively excluded diabetics and HbA1c from the model [26]. The authors here found age, BMI, and male gender among others to be predictors of PH, while preoperative BG was not. More recently, Kwon et al. found multiple potential univariate predictors of PH in general surgery patients, including age, BMI, DM, bariatric surgery, and surgical approach (laparoscopic vs. open). However, the scope of the study was outcomes after surgery and not necessarily predictors of PH [12]. As BG control is a quality measure, there will need to be more literature predicting PH in surgical patients.

Our multivariable model has important limitations and is not all inclusive yet. First, it contains 381 patients, which is relatively small for predictive modeling. This predictive dataset lacks specific Insulin Resistance (IR) measurements, such as preoperative serum insulin levels and HOMA-IR calculations, C-peptide levels, and number of years with diagnosis of DM. Future studies will need to incorporate this data into predictive BG models after RYGB. Therefore, it will be important to

Potential Risk Factors for Postoperative Blood Glucose		Univariate Postoperative Blood Glucose			
		Correlation (p)	Mean(SD)	p-value	
Demographics					
Age (years)		0.180		0.0002	†
Sex	Male (n = 92)		151.8 (38.4)	0.4292	
Race	Female (n = 339)		148.5 (34.0)		
	Nonwhite (n = 113)		146.5 (31.9)	0.3321	
ASA Class	White (n = 318)		150.2 (36.0)		
	1 or 2 (n = 95)		135.2 (22.8)	0.0001	†
	3 (n = 289)		151.1 (35.7)		
	4 (n = 14)		159.3 (30.6)		
Baseline BMI (kg/m²)		0.037		0.4460	
Smoking Status	Nonsmoking (n = 378)		149.6 (34.7)	0.6637	
	Smoking (n = 50)		147.3 (37.1)		
Lab Analysis					
Baseline Creatinine (mg/dL)		0.088		0.0687	†
Baseline HbA1c (%)		0.657		<0.0001	†*
Preoperative BG (mg/dL)		0.613		<0.0001	†*
Operation					
Surgery type	Open (n = 51)		164.7 (42.4)	0.0007	†*
	Laposcopic (n = 379)		147.2 (33.4)		
Roux limb length (cm)		0.057		0.3204	
Comorbidities					
Baseline Diabetes	No DM (n = 188)		130.6 (19.9)	<0.0001	†*
	DM (n = 243)		163.6 (37.2)		
Baseline Hyperlipidemia	No Hyperlipidemia (n = 197)		145.6 (35.3)	0.0477	†
	Hyperlipidemia (n = 234)		152.3 (34.4)		
Baseline Hypertension	No HTN (n = 123)		141.2 (35.0)	0.0026	†
	HTN (n = 308)		152.4 (34.5)		
Baseline Osteoarthritis	No OA (n = 40)		158.0 (46.4)	0.8227	
	OA (n = 155)		156.3 (42.5)		
Baseline Obstructive Sleep Apnea	No Sleep apnea (n = 193)		147.8 (35.2)	0.4448	
	Sleep apnea (n = 238)		150.4 (34.8)		
Baseline Venous Stasis Disease	No Venous stasis (n = 190)		155.4 (42.6)	0.0121	
	Venous stasis (n = 5)		204.3 (44.6)		
Baseline Degenerative Joint Disease	No DJD (n = 187)		155.0 (42.2)	0.0105	
	DJD (n = 8)		194.8 (52.7)		
Diabetic Parameters					
Baseline HbA1c > 6.5%	< 6.5% (n = 276)		133.5 (22.8)	<0.0001	
	>= 6.5% (n = 155)		177.2 (35.3)		
Baseline HbA1c > 8%	< 8% (n = 365)		141.7 (28.5)	<0.0001	
	>= 8% (n = 66)		190.9 (38.1)		
Preoperative Insulin	No (n = 359)		143.5 (32.5)	<0.0001	†
	Yes (n = 72)		177.6 (32.9)		
Preoperative Insulin > 100units/day	Yes (n = 392)		145.7 (33.1)	< 0.0001	
	No (n = 20)		190.6 (24.9)		
Oral Diabetic Medications	0 (n = 343)		143.5 (31.5)	<0.0001	†
	1 (n = 63)		168.6 (38.4)		
	2+ (n = 25)		178.1 (39.8)		
Oral Diabetic Medication > 1	No (n = 343)		143.5 (31.5)	<0.0001	
	Yes (n = 88)		171.3 (38.8)		
Oral Diabetic Medication > 2	No (n = 406)		147.4 (33.9)	<0.0001	
	Yes (n = 25)		178.1 (39.8)		
Other					
Baseline BMI > 50 (mg/m²)	No (n = 230)		150.5 (35.6)	0.4006	
	Yes (n = 201)		147.7 (34.2)		
Baseline BMI > 60 (mg/m²)	No (n = 364)		149.7 (34.7)	0.5096	
	Yes (n = 67)		146.6 (36.7)		
One FSBG > 200 mg/dL	No (n = 222)		127.3 (15.5)	<0.0001	
	Yes (n = 209)		172.5 (34.8)		
Two FSBG's > 180 mg/dL	No (n = 219)		126.7 (15.0)	<0.0001	
	Yes (n = 212)		172.5 (34.4)		
† originally included in the multivariable model					
* significant in the final model					

Table 3: The univariate and multivariable risk factors of elevated mean postoperative BG after gastric bypass.

augment and validate our current predictive model. Despite limitations, PH appears to be reasonably predictable preoperatively.

Admittedly, there are several other limitations to this study. First, the sampled data was collected retrospectively from 2006-2009, while physicians were surveyed in 2011. Also, they were asked to reflect about their time on the bariatric wards, but were not necessarily on the bariatric service at time of survey. More optimally, the clinicians would have been surveyed simultaneously to the hospital course of these patients. However, at our institution these results have raised awareness of a potential discrepancy between perceived and observed glucose control. It has sparked prospective study designs and more aggressive treatment protocols for the RYGB patients. Also, our study is from a single high volume center of excellence, but may lack generalizability as BG management strategies may be different at other institutions. Finally, our data lacks any outpatient BG data in the first weeks postoperatively as their blood glucose metabolism is rapidly changing.

Conclusion

In conclusion, PH clearly increases morbidity and potentially mortality in various surgical patients including RYGB patients [1-11,22]. Improving glycemic control in RYGB patients is important, as it may improve postoperative morbidities such as wound infection and ARF22. This may have implications in reducing excess hospital cost and improving patient outcomes. As BG management is a recognized quality measure, there will be increasing surveillance and scrutiny of inpatient PH. Therefore, increased clinician awareness and predictive models are vital for improving outcomes in these patients on busy surgical wards.

Disclosures

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