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The impact of preoperative carbohydrate loading on patients with type II diabetes in an enhanced recovery after surgery protocol

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ABSTRACT

Background: We aimed to determine the effects of preoperative carbohydrate-loading (CHO) as part of an enhanced recovery after surgery (ERAS) pathway on patients with/without type II diabetes (DMII).
Methods: Retrospective review of ERAS patients with CHO, including 80 with DMII, 275 without DMII in addition to 89 patients with DMII from the previous (non-ERAS) year. Outcomes included glucose-levels, insulin requirements, and complications. Logistic regression was used to determine the association of any complication with perioperative glucose control variables.
Results: Among ERAS versus non-ERAS patients with DMII, there were significant differences in median preoperative (142 mg/dL versus 129.5 mg/dL, $p = 0.017$) and postoperative day-1 glucose levels (152 mg/dL, versus 137.5 mg/dL, $p = 0.004$). There were no differences in insulin requirements, hypoglycemic episodes, or complications. Complications were not associated with Hgb-A1C%, home DMII-medications, or preoperative glucose measurement on logistic regression.
Conclusions: Patients with DMII tolerated CHO without increasing insulin requirements or substantially affecting glucose levels or complications.

Introduction

Traditional surgery practices have emphasized preoperative fasting, ensuring an empty stomach upon anesthesia induction. However, preoperative fasting and the physiologic stress of operations are sufficient to adversely alter metabolism, deplete carbohydrate (CHO) reserves, and promote insulin-resistance.[1] Insulin-resistance manifests with enhanced hepatic gluconeogenesis and glycogenolysis and impaired peripheral insulin-dependent glucose uptake.[2] Insulin-resistance is associated with increases in morbidity, mortality, and length of stay and can be attenuated by minimizing the physiologic stress of surgery, providing adequate pain relief, and minimizing fasting time.[2,3]

Enhanced Recovery After Surgery (ERAS) pathways are multimodal patient care protocols that minimize physiologic stress responses to operations.[4] Several randomized controlled trials have demonstrated that ERAS protocols reduce lengths of hospital stay by up to 30% and postoperative complications by as much as 50%.[3–5] These protocols span phases of care and have numerous components that hasten postoperative recovery. ERAS pathways incorporate prophylactic anti-emetic medications, multimodal analgesia with less reliance upon narcotics, reduced amounts of intravenous fluid, and preoperative CHO-loading, all of which decrease postoperative nausea and emesis and promote the return of gut function.[4]

The usage of preoperative CHO-loading has also been associated with a reduction of physiologic stress and insulin-resistance. In patients without diabetes, CHO-loading beverages have resulted in an improvement of perioperative glycemic control with a diminished likelihood of hyperglycemia, preserved lean body mass, maintenance of muscle strength, and neutral nitrogen balance.[6] However, the practice of preoperative CHO-loading in patients with type II diabetes mellitus (DMII) remains unsettled due to concerns about hyperglycemia-related complications. The aim of this study is to evaluate the clinical effects of CHO-consumption in

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an ERAS protocol among patients with DMII. We hypothesized that ERAS patients with DMII would not have higher glucose levels, increased insulin requirements, or more complications as a result of CHO-consumption.

Materials and methods

This is an Institutional Review Board-approved retrospective chart review of patients managed under the ERAS protocol during its first year of implementation (10/1/15–9/30/16) with documented consumption of the preoperative CHO beverage. ERAS patients during this time included those undergoing intraabdominal operations cared for by surgeons in the Sections of Colon and Rectal Surgery, Surgical Oncology, and Bariatrics/Minimally Invasive Surgery. The types of operations included in the ERAS protocol include elective colonic and/or bowel resections, stoma creation or reversal, roux-en-y gastric bypasses, and gastric, pancreatic, and liver resections. At their Pre-Procedure Clinic visit, all ERAS patients at our institution receive a 32-ounce bottle of Gatorade,® containing 55 g of carbohydrates. Patients are instructed to drink half of the bottle on the evening before the operation and the other half on the morning of surgery. Our ERAS protocol allows consumption of clear liquids until 2 h prior to the operation. Consumption of preoperative Gatorade® is documented in nursing flowsheets in the preoperative holding area. Since inception of the ERAS program at our institution, patients with DMII have intentionally received preoperative CHO-loading. On the other hand, patients with type I diabetes mellitus are excluded from this component of ERAS.

Patients with diet-controlled DMII were excluded from the study due to inconsistent perioperative glucose monitoring in this patient population. Patients were also excluded if they received scheduled antiemetics in the postoperative period. While ERAS patients routinely receive intraoperative prophylaxis against postoperative nausea and vomiting, the administration of postoperative anti-emetic medications (ondansetron, metoclopramide, and scopolamine patches), was captured as a surrogate measure of postoperative ileus.

Patient demographics, including age, sex, and body mass index (BMI) were collected. Operative variables of interest included operating room time, surgery specialty, operative approach (laparoscopic/open), and American Society of Anesthesiologists (ASA) classification.

Among patients with DMII, preoperative hemoglobin A1C (Hgb A1c), number of oral hypoglycemic medications, and daily insulin dosage were collected. The total number of home diabetes medications is reported as a sum of all agents, including subcutaneous insulin, non-insulin subcutaneous hypoglycemic injections, and oral hypoglycemic medications.

The primary outcomes of interest were perioperative glucose levels and insulin requirements, with the development of postoperative complications as a secondary outcome. At our institution, a multidisciplinary pathway guides the management of patients with diabetes throughout their perioperative care. Glucose levels are checked by bedside (point-of-care) fingerstick monitors in the preoperative holding area, and patients with a glucose >180 mg/dL are treated with intravenous insulin, either as an infusion or with intermittent injections. Postoperative glucose levels are measured immediately on arrival to the post-anesthesia care unit (PACU) and continued on a routine schedule before meals and at bedtime. The perioperative glucose measurements, intraoperative insulin infusion requirement, postoperative subcutaneous insulin dosage, episodes of hypoglycemia, postoperative Endocrinology service consultations, and anti-emetic medication administration were collected for patients with DMII. Glucose measurements and insulin dosing are reported as daily medians.

ERAS patients with DMII were compared to those without DMII. In addition, a third group consisted of patients with DMII who had undergone similar operations during the year that immediately preceded ERAS implementation (10/1/14–9/30/15). Demographic and perioperative variables were compared among the three groups using ANOVA, as were lengths of stay and complications (classified by the Clavien Dindo Classification system) occurring within 30 days of discharge.[7,8] Differences between ERAS and historical patients with DMII were evaluated using Chi square tests for categorical variables and Kruskal Wallis tests for continuous variables. Binary logistic regression was used to assess the association of having any complication, adjusting for perioperative glucose control variables among patients with DMII. Statistical significance was defined as $p < 0.05$.

Results

Among all ERAS patients, 355 met inclusion criteria, including 80 patients with DMII and 275 patients without diabetes. Eighty-nine patients with DMII from the previous (non-ERAS) year were included for comparison. ERAS patients, with and without DMII, were similar to each other and to historical patients with DMII with regard to sex, BMI, operation duration, surgery specialty, or laparoscopic technique (Table 1). ERAS patients with DMII and historical patients with DMII were older than ERAS patients without diabetes ($p < 0.001$). The ASA distribution differed among the three groups, as patients with DMII had higher ASA classifications ($p < 0.001$). Baseline diabetes-specific variables were also similar between ERAS and historical patients with DMII (Table 2). There were no differences in hemoglobin A1C levels, the number of preoperative DMII medications (both subcutaneous and oral), or home insulin dosing.

Perioperative glucose measurements and insulin dosing for the two groups of patients with DMII are presented in Table 3. There were two timepoints when median glucose levels were higher among ERAS patients with DMII than those with DMII in the historical cohort – in the preoperative holding area (142 mg/dL, range 66–392, versus 129.5 mg/dL, 82–316, $p = 0.017$), and on postoperative day (POD) 1 (152 mg/dL, range 84–323, versus 137.5 mg/dL, 86–279, $p = 0.004$), respectively. Even though these values are statistically significant, the numerical differences are modest, and glucose levels at all other times were comparable. Furthermore, insulin dosing in the operating room (0 units (U), range 0–16.5U, vs 0U, 0–19.2U, $p = 0.63$) and on POD 1 (4U, range 0–75U, versus 0U, 0–79U, $p = 0.09$) did not differ significantly between ERAS and historical groups of patients with DMII. Rates of intraoperative insulin infusion utilization were also similar between ERAS and historical groups of patients with DMII (11.3% versus 14.6%, $p = 0.65$). The number of patients who experienced episodes of hypoglycemia (glucose <70 mg/dL) was low in both the ERAS and historical groups of patients with DMII (7.5% versus 5.6%, $p = 0.76$). In addition, the frequency of inpatient Endocrinology consultations was also similar between the two groups (41.3% versus 37.1%, $p = 0.64$).

Outcomes for all 3 groups are presented in Table 4 and are comparable. The incidence of any complication was numerically highest in the historical DMII group (27%) compared to ERAS patients without DMII (21.1%) and those with DMII (20%), although these values did not significantly differ ($p = 0.65$). Among patients with complications, the majority were Clavien-Dindo Grades I and II. The administration of anti-emetic agents was used as a surrogate for postoperative ileus. Both groups of ERAS patients, those with and without DMII, received a median of 0 doses of anti-emetic medications (range 0–9 among patients without DMII and 0–5 in those with DMII), compared to a median of 1 dose (0–13) in historical patients with DMII ($p > 0.99$). Median length of stay was 2

Table 1
Demographics and operative variables.

	ERAS Patients without DMII (n = 275)	ERAS Patients with DMII (n = 80)	Historical Patients with DMII (n = 89)	p value
Time Period	10/1/15–9/30/16	10/1/15–9/30/16	10/1/14–9/30/15	
Median age in years (range)	43 (21–89)	48 (20–86)	51 (25–93)	< **0.001**[a]
Female, % (n)	74.9 (206)	78.8 (63)	74.2 (66)	0.74
BMI, kg/m2, (range)	39.5 (16.7–81.4)	38.6 (19.8–69.5)	40.5 (20.7–59.3)	0.37
Operative Duration, hours (range)	3.02 (1.50–11.10)	3.18 (1.67–10.80)	2.7 (1.70–11.60)	0.09
Specialty, % (n)				0.20
Bariatric	62.9 (173)	71.3 (57)	67.4 (60)	
Colorectal	25.8 (71)	13.8 (11)	23.6 (21)	
Surgical Oncology	11.3 (31)	15 (12)	9.0 (8)	
Laparoscopic, % (n)	83.6 (230)	90 (72)	93.3 (83)	0.08
ASA Classification, % (n)				< **0.001**[a]
1	0.4 (1)	0 (0)	0 (0)	
2	51.6 (142)	22.5 (18)	38.2 (34)	
3	47.6 (131)	76.3 (61)	60.7 (54)	
4	0.4 (1)	1.3 (1)	1.1 (1)	

BMI = Body mass index.
ASA = American Society of Anesthesiologists.
[a] Significance applies to comparison across 3 groups using ANOVA.

days for all three groups (p = 0.38). Notably, no patient in either ERAS group suffered an aspiration or pulmonary complications despite consumption of a beverage.

Binary logistic regression was used to investigate the associations of various factors with morbidity of patients in both groups with DMII, adjusting for cofounders related to perioperative glucose control (Table 5). Complications were not influenced by the preoperative Hgb A1C (OR 0.642, CI [0.372, 1.109], p = 0.11), number of DMII medications (OR 1.316, CI [0.489, 3.537], p = 0.59), home insulin dosage (OR 0.983, CI [0.958, 1.009], p = 0.19), or preoperative glucose level (OR 1.008 CI [0.993, 1.204], p = 0.31).

Discussion

This study provides evidence supporting the usage of preoperative CHO beverages in patients with DMII. Perioperative glucose measurements and insulin requirements among ERAS patients with DMII were essentially similar to those of pre-ERAS patients with DMII, despite the introduction of preoperative CHO-loading. Consistent with ERAS literature, in our study sample, patients with and without DMII experienced lower rates of postoperative complications versus historical patients with DMII, although these findings were not significant.[3,4]

Initial studies of preoperative CHO administration focused upon dextrose infusions[9,10] and later examined oral consumption.[3] Investigations of preoperative oral CHO-loading have primarily examined benefits among patients without diabetes. Preoperative CHO-rich beverages in general populations have resulted in reductions of insulin-resistance, protein loss, metabolic derangements, and immune dysfunction.[3] In fact, insulin-resistance has been reduced by 50% among patients without diabetes who consume preoperative CHO beverages. Proponents of the preoperative CHO-loading argue that, in addition to the physiologic benefits of CHO-loading, patient satisfaction is also improved.[6]

Diabetes is present in 7.2–11.4% of the populace worldwide, and those with diabetes are more likely to require operations. In fact, 10–15% of patients undergoing operations have DMII, and that figure rises to 40% among those undergoing bariatric operations.[11] Patients with diabetes have higher rates of complications, utilize more medical resources, and experience longer lengths of hospital stay than do patients without diabetes[6,11].

The slow adoption of CHO-loading among patients with DMII arises from concerns that hazards such as hyperglycemia outweigh potential benefits of this component of ERAS pathways.[6,11] The association of hyperglycemia with immune suppression (e.g., impaired neutrophil activity, attenuated inflammatory cytokine cascade, and diminished reactive oxygen species production) has been well documented and may promote an environment favorable

Table 2
Preoperative variables among patients with DMII.

	ERAS Patients with DMII (n = 80)	Historical Patients with DMII (n = 89)	p value
Median Hemoglobin A1C, % (range)	7 (5–12.5)	7.4 (5.5–12.6)	0.43
Home Diabetes Medications, % (n)			0.41
Oral Agent	90 (72)	92.1 (82)	
Insulin	28.8 (23)	23.6 (21)	
Number of Agents			0.70
1	58.8 (47)	66.3 (59)	
2	25.0 (20)	22.5 (20)	
3	7.5 (6)	9.0 (8)	
4	3.8 (3)	2.2 (2)	
Median Home Insulin Dosing, Units (range)	36 (6–178)	39 (6–200)	0.76

Number of agents includes the sum of subcutaneous insulin, non-insulin subcutaneous hypoglycemic injections, and oral hypoglycemic medications.

Table 3
Perioperative glucose control among patients with DMII.

	ERAS Patients with DMII (n = 80)	Historical Patients with DMII (n = 89)	p value
Median Glucose, mg/dL (range)			
Preoperative (Holding Area)	142 (66–392)	129.5 (82–316)	**0.017***
Operating Room	158 (95–286)	174.8 (100–279.5)	0.91
1st Postoperative	159 (102–309)	173 (96–295)	0.23
Daily Median			
Postoperative Day 0	184.5 (106–320)	175 (86–350)	0.15
Postoperative Day 1	152 (84–323)	137.5 (86–279)	**0.004***
Postoperative Day 2	135.3 (82–223)	131 (82–240)	0.45
Postoperative Day 3	134 (67–207)	134.8 (78–220.5)	0.63
Postoperative Day 4	135.5 (81–232)	138.3 (89.5–201.5)	0.79
Postoperative Day 5	135 (85–171.5)	146 (79–220)	0.44
Intraoperative Insulin Infusion, % (n)	11.3% (9/80)	14.6% (13/89)	0.65
Insulin, Median Units (range)			
OR	0 (0–16.5)	0 (0–19.2)	0.63
Postoperative Day 0	2 (0–62)	2 (0–75.83)	0.67
Postoperative Day 1	4 (0–75)	0 (0–79)	0.09
Postoperative Day 2	0 (0–53)	0 (0–41)	0.19
Postoperative Day 3	4 (0–47)	0 (0–50)	1.00
Postoperative Day 4	4 (0–54)	2 (0–45)	0.77
Postoperative Day 5	2 (0–37)	0 (0–55)	0.77
Hypoglycemia (glucose $\leq$ 70), % (n)	7.5 (6)	5.6 (5)	0.76
Inpatient Endocrine Consultation, % (n)	41.3 (33)	37.1 (33)	0.64

to adverse outcomes such as postoperative wound infections, cardiac events, and other complications.[2,6,11] Conversely, strict postoperative glucose control reduces the incidence of infection, neuropathy, and renal failure among patients with DMII.[6]

Other concerns regarding CHO-loading among patients with DMII have focused on delayed gastric emptying and the associated risk of aspiration upon anesthesia induction. However, it is difficult to confidently correlate the impact of ERAS protocols upon gastroparesis due the low incidence of this condition that affects just 1% of patients with DMII versus 0.2% of patients without DMII.[12] In addition, delayed gastric emptying in patients with DMII seems to affect solid rather than liquid intake and is more pronounced among those who have longstanding DMII. While some might argue that screening for gastroparesis would allow safe CHO-loading in selected patients with DMII, there are no reliable ways to predict delayed gastric emptying, as it has not been related to autonomic neuropathy or other sequelae of diabetes.[6] Two small studies evaluated the effects of preoperative CHO-consumption upon gastric emptying in patients with DMII. In one series, 10.9% ± 0.7 (standard deviation) of a CHO-rich beverage with a paracetamol marker remained in the stomachs of patients with DMII versus 13.3% ± 1.2 among patients without diabetes, 2-h post-consumption. These data suggest slightly faster, or at least comparable, gastric emptying among patients with DMII. Both studies demonstrated complete gastric emptying by 180 min.[6,13] In our

Table 5
Logistic regression - odds of any complication among patients with DMII.

	Odds Ratio	95% Confidence Interval		p Value
		Lower	Upper	
Hemoglobin A1C	0.642	0.372	1.109	0.11
Number of Hypoglycemic Medications	1.316	0.489	3.537	0.59
Preoperative Insulin Dosing	0.983	0.958	1.009	0.19
Preoperative Glucose Measurement	1.008	0.993	1.024	0.31

Table 4
Outcomes of patients with and without DMII.

	ERAS Patients without DMII (n = 275)	ERAS Patients with DMII (n = 80)	Historical Patients with DMII (n = 89)	p value
Clavien-Dindo Classification[a], % (n)[a]				0.65
No Complication	78.9 (217)	80 (64)	73.0 (65)	
Grade I	7.6 (21)	12.5 (10)	14.6 (13)	
Grade II	8.7 (24)	5 (4)	7.9 (7)	
Grade IIIa	2.5 (7)	2.5 (2)	2.2 (2)	
Grade IIIb	2.2 (6)	0 (0)	2.2 (2)	
Anti-Emetic Doses, median (range)	0 (0–9)	0 (0–5)	1 (0–13)	<0.99
Length of Stay, median (range)	2 (0–37)	2 (2–33)	2 (1–14)	0.38

[a] **Clavien-Dindo Classification definition:** Grade I include any deviation from the normal postoperative course which requires additional monitoring without the need for administration of medication (i.e. ileus). Grade II encompasses a postoperative occurrence requiring pharmacologic treatment or infusion (i.e. blood transfusion). Grade III includes interventional radiologic intervention (IIIa) or surgical intervention (IIIb).

series, we did not specifically evaluate the duration of the DMII diagnosis or investigate the presence of gastroparesis. Administration of anti-emetic agents in this cohort did not differ between ERAS patients with and without DMII. While this measure was collected as a surrogate for postoperative ileus, it might also identify patients with gastroparesis.

To date there have been no randomized, controlled trials to evaluate preoperative CHO-loading in patients with diabetes.[11] While small studies evaluating the biochemical and physiological effects of preoperative CHO-rich beverages have provided some justification for their consumption by patients with DMII, ERAS literature in general does not provide specific guidance about the quantity of CHO or type of beverage for these patients. In our institution, we provide all ERAS patients with Gatorade® to consume before operations, regardless of the diagnosis of DMII, although some ERAS protocols simply allow the preoperative consumption of any clear liquid, without further recommendations. Future studies may investigate specific CHO composition for patients with and without DMII to assess any impact upon perioperative glucose levels, insulin requirements, and other outcomes.

There are limitations to this study. This is an investigative study regarding outcomes of patients with DMII during the first year of ERAS implementation in a single institution. Although the sample sizes of both DMII groups are comparable, a multi-institutional trial would likely be necessary to provide adequate power to definitively assess changes in absolute glucose measurements or insulin dosing related to CHO-loading. Moreover, the retrospective design relies upon accurate documentation of study variables. For example, while we included only patients with confirmed preoperative consumption of the CHO-rich beverage, we also allowed patients to drink other clear liquids until 2 h prior to operations. The preoperative holding area nurses do not routinely inquire about the nature of those additional liquids that could conceivably affect glucose measurements. In addition, recent recommendations from the Surgical Infection Society have proposed target blood glucose levels of 110–150 mg/dL for all patients during the perioperative period, regardless of the diagnosis of diabetes.[14] At our institution, patients without diabetes and even patients with diet-controlled diabetes do not ordinarily have bedside point-of-care glucose measurements, and so we cannot accurately assess whether perioperative glucose values truly differ among ERAS patients with and without DMII. We were reluctant to compare serum glucose values on POD 1 due to variable timing of meals. In our analysis Hgb A1C was not found to have a significant association with postoperative complications. This relationship may have not been observed due to our sample size with only a small number of patients having high Hgb A1C levels. Another limitation is that this series includes a high number of patients who underwent laparoscopic gastric bypass, an operation known to improve glucose control. However, this effect is variable in timing and may not influence perioperative glucose levels. Bariatric operations are admittedly associated with few complications and short lengths of hospital stay, which might reconcile the lack of differences among the groups. Nevertheless, we included these patients in the series because a substantial number of them have DMII. Finally, the great majority of operations were laparoscopic, which might have attenuated some the stress response associated with open abdominal operations.

In conclusion, this experience indicates that a preoperative CHO-loading is safely tolerated by patients with DMII, without increasing glucose levels, insulin requirements, the incidence of complications, or lengths of hospital stay. Patients with DMII may benefit from the physiologic benefits of this beverage, just as do patients without DMII in ERAS protocols. Further randomized studies are needed to confirm our findings and to explore protocols for carbohydrate loading in patients with type 1 diabetes.

Declaration of competing interest

The authors have no conflicts of interest.

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