ORIGINAL ARTICLE

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Enhanced Recovery After Surgery (ERAS) Outcomes in Patients with Prior Diagnosis of Diabetes*

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Abstract

Objective. To determine whether a prior diagnosis of diabetes mellitus (DM) is associated with longer postoperative length of stay (LOS) and higher complication rates among patients who underwent colorectal surgery under an Enhanced Recovery After Surgery (ERAS) protocol in a single hospital setting.

Methodology. In a cross-sectional study, we grouped 157 consecutive patients who underwent elective colorectal surgery under ERAS protocol according to preoperative DM status. Patient data was abstracted from the ERAS Interactive Audit Database from January 2016 to December 2017. We compared LOS between groups. Secondary outcomes were postoperative complications, reoperations, pneumonia and wound infection. Categorical and continuous variables were analyzed with Fisher's exact test and student's t-test, respectively, using Stata/SE version 13 with a significance level of p=0.05.

Results. One hundred thirteen subjects did not have diabetes (no T2DM) while 44 patients had type 2 diabetes mellitus (T2DM). Mean postoperative length of hospital stay was 6.4±5.1 days for the no T2DM group versus 5.8±3.8 in the T2DM group (p=0.476). Complications, reoperation rate, pneumonia and wound infection did not differ between groups. Among subjects in the T2DM group, LOS did not differ between patients with preoperative HbA1c ≤7.0% and those with HbA1c >7.0% (5.7±3.7 versus 6.1±4.2 days, p=0.748).

Conclusion. Among patients who underwent colorectal surgery under ERAS protocol, a prior diagnosis of diabetes was not associated with longer LOS or more complications. A preoperative HbA1c of <7% did not affect length of stay in ERAS among patients with T2DM.

Key words: diabetes, ERAS, enhanced recovery, colorectal surgery, diabetes mellitus, length of stay

INTRODUCTION

Enhanced Recovery After Surgery is an evidence-based surgical care protocol that consists of varying interventions that reduce postoperative complications and length of stay. ERAS has been in practice internationally since 2005.[1] At the core of the ERAS philosophy is the modulation of inflammation while attenuating the hypermetabolic response to surgery, optimizing glucose control and providing nutritional support.[2] This philosophy translates into a protocol that consists of 24 preoperative, intra-operative and postoperative elements, each with the goal of early mobilization, early feeding, attenuating surgical stress and inflammation and, ultimately, early discharge (Figure 1).[2-5]

ERAS implementation reduces postoperative complications and length of stay by 50% and 30%, respectively.[4-6] However, there is a dearth of data on patients with diabetes mellitus (DM) and ERAS. The published randomized controlled trials that support ERAS interventions have excluded patients with DM or have included them only in very small numbers.[7,8] A guideline from the United Kingdom recommended the exclusion of patients with a history of diabetes from ERAS programmes, particularly because of the lack of data among patients with diabetes who have undergone ERAS surgery.[9] However, ERAS consensus statements recommend that patients with diabetes may be included provided that their conditions are optimized to international standards.[10]

Among patients who undergo colorectal surgery, 10 to 30% have diabetes mellitus.[11-13] Observational studies suggest that diabetes and hyperglycemia are independent risk factors for 30-day mortality, postoperative length of hospital stay, and complications among patients undergoing in-hospital non-cardiac surgeries, including colorectal surgery.[14,15] The Surgical Care and Outcomes

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Pre admission Elements	Preoperative Elements	Intraoperative Elements	Postoperative Elements
Cessation of smoking and excessive intake of alcohol	Structured preoperative information and engagement of patient and relatives or caretakers	Minimally invasive surgical techniques	Early mobilization
Preoperative nutritional screening, assessment and nutritional support	Preoperative carbohydrate treatment	Standardized anesthesia: (Short acting anesthetic, avoiding long acting opioids, mid thoracic/epidural anesthesia for open surgery)	Early intake of oral fluids and solids
Medical optimization of chronic disease	Preoperative prophylaxis against thrombosis	Maintaining fluid balance/avoidance of salt and water overload	Stimulation of gut motility: Use of chewing gums and laxatives and peripheral rather than central opioid blocking agents
	Preoperative prophylaxis against infection	Restrictive use of surgical site drains	Early removal of urinary catheters and IV fluids
	Preoperative prophylaxis against nausea and vomiting/ PONV prophylaxis	Removal of nasogastric tubes before anesthesia reversal	Intake of protein and energy rich nutritional supplements
	No prolonged fasting	Maintenance of normothermia (warm air flow blankets/ warmed IV fluids)	Multimodal approach to opioid sparing pain control
	No or selective bowel preparation		Prepare for early discharge
			Audit of outcomes and process in a multi professional multidisciplinary team on a regular basis

Figure 1. Elements of ERAS protocol (adapted).[1,3]

Assessment Program (SCOAP) suggests that diabetes is associated with increased adverse outcomes in conventional colorectal surgery, with a 2-fold risk of infection and a higher risk of in-hospital mortality and reoperation. Patients with T2DM, particularly those on insulin, are more prone to postoperative morbidity: perioperative glucose levels above 180 mg/dL have been associated with greater risk of infection, reoperative interventions, longer length of stay and death.[16]

It is difficult to conclude from existing literature whether ERAS protocols should include patients with diabetes. The interventions of the ERAS protocol that raise concerns for patients with DM are preoperative carbohydrate loading and routine prophylaxis for postoperative nausea and vomiting (PONV) with steroids.[5-7,9]

In the ERAS protocol, preoperative carbohydrate loading is the administration of a 100 g carbohydrate drink on the night prior to surgery and a 50 g carbohydrate drink 2 hours prior to surgery. Among patients without diabetes, preoperative carbohydrate loading is associated with a small reduction in postoperative length of hospital stay among patients undergoing colorectal surgery. Trials have reported improved perioperative well-being, reduced hunger, reduced blood levels of insulin and insulin resistance on day 2 after surgery.[17-19]

However, among patients with diabetes, high carbohydrate drinks may compromise blood sugar control. In a study by Gustaffson et al., T2DM patients given a 50 g oral carbohydrate load had a higher mean peak glucose [242 mg/dL (13.4±0.5 mmol/L)] compared to non-DM patients [136 mg/dL (7.6±0.5 mmol/L)] despite similar gastric emptying times.[20] Some clinical practice guidelines also recommend against particular elements of ERAS, such as the use of preoperative carbohydrate loading, due to concerns in delayed gastric emptying and a lack of evidence in this area for patients with DM.[19, 21-23]

Preoperative prophylaxis against nausea and vomiting using intravenous dexamethasone is indicated in the ERAS protocol if patient has 2 or more risk factors for PONV. These risk factors include female gender, non-smoker status, history of motion sickness/PONV and opioid use.[2] Administration of systemic steroids, however, causes acute hyperglycemia due to increased hepatic gluconeogenesis, inhibition of glucose uptake in adipose tissue, and alteration of receptor and post-receptor functions.[24] Dexamethasone for PONV prophylaxis has been shown to increase blood glucose from baseline in a dose-dependent manner, to as high as 58±50 mg/dL intraoperatively and 101±71 mg/dL 24 hours postoperatively among patients with diabetes.[25,26]

Since diabetes is associated with increased adverse outcomes in conventional surgery, it is important to examine whether it will also affect surgical outcomes among patients who undergo ERAS. Published literature examining the impact of DM on surgical outcomes of patients undergoing surgery under ERAS is lacking, hence, a general reservation with the use of ERAS protocols among patients who have been diagnosed with DM. The impact of T2DM on outcomes of patients who undergo surgery under ERAS is not clear.

In this study, we aimed to determine whether a prior diagnosis of T2DM was associated with longer LOS and higher complication rates among patients who underwent colorectal surgery under ERAS protocol in a single tertiary hospital. We also aimed to compare length of stay, postoperative complications, reoperation, occurrence of pneumonia and occurrence of wound infection between patients with prior diagnosis of T2DM who achieved HbA1c of ≤7% preoperatively and those with HbA1c >7%.

METHODOLOGY

This study was approved by The Medical City (TMC) Institutional Review Board. We conducted a retrospective cohort study using data drawn from TMC ERAS Interactive Audit System (EIAS). Trained abstractors extracted data using standardized definitions as given in https://www.encare.net/healthcare-professionals/products-and-services/eras-interactive-audit-system-eias. We used data from ERAS in a single center, The Medical City-Ortigas, from January 2016 to December 2017.

Data specification

The EIAS (https://www.encare.net/healthcare-professionals/products-and-services/eras-interactive-audit-system-eias) is an online web-based central database designed for interactive audit and research for collecting registry data.

The database was opened in 2007 and is tailored to the ERAS Society guidelines. This was adopted by The Medical City-Ortigas in July 2015. Each patient's data field contains 140 different variables, including patient demographics [preoperative body mass index (BMI), pre-morbid health status] surgical procedures and postoperative outcomes (time to achieve targeted mobility, total length of hospital stay, complications, 30-day mortality). For security purposes in our study, data were de-identified on submission and the database was held on a password and firewall-protected secure internet server. All patients who fulfilled the inclusion and exclusion criteria were referred by their attending surgeons. Data were gathered and encoded consecutively into the EIAS by the ERAS Coordinator.

Subjects

Patients who underwent elective colorectal surgery under the TMC ERAS protocol from January 2016 to December 2017 with data entered into the EIAS were eligible for inclusion. Exclusion criteria were emergency surgery, type 1 diabetes mellitus, intake of steroids prior to admission and procedure, and non-major abdominal surgery. Entries with incomplete data and no known diabetes status were excluded from the analysis.

Clinical risk factors

The EIAS records were used to obtain patient demographic data pertaining to age, gender, BMI, smoking status, alcohol usage, T2DM status, American Society of Anesthesiologists (ASA) physical classification, PONV prophylaxis, preoperative carbohydrate loading, antibiotic prophylaxis before incision and length of operation. Preoperative health status was assessed using the ASA classification.

Subjects were grouped according to their DM status as classified by the EIAS registry: patients who had a diagnosis of diabetes were classified into the T2DM group and those without were classified into the no T2DM group. Under EIAS, patients were classified to have DM based on either a medical history of diabetes elicited from the patient, assessment of the attending physician or the presence of an HbA1c >6.5% on chart review. To attenuate recall and misclassification bias, authors performed chart review for preoperative HbA1c and/or preoperative blood sugar.

Outcomes

The primary outcome was postoperative length of hospital stay, defined as the number of nights in the hospital after primary operation until declared cleared for discharge by the ERAS surgical attending physician. The secondary outcomes were discharge within 30 postoperative days, postoperative complications, reoperation, occurrence of pneumonia and occurrence of wound infection.

Sample size

The sample size was computed using Stata/SE version 13 (StataCorp LP, College Station, TX, USA). This was based on the 45% complication rate of ERAS patients with HbA1c >6% versus the 25% complication rate of patients with HbA1c <6% from the study of Gustaffson et al, using an alpha level of 0.05 and a power of 0.80.[27]

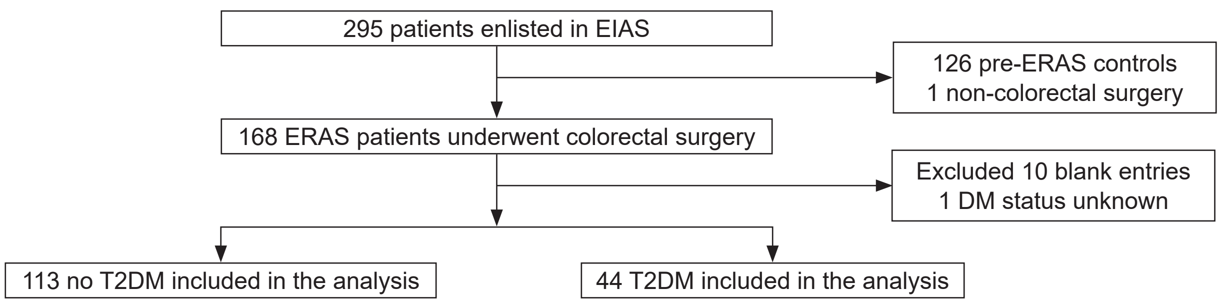
Statistical analysis

Statistical analysis was performed using Stata/SE version 13. We used the independent t-test to compare continuous variables (age, BMI, length of operation, length of stay) and Fisher's exact test for categorical variables (gender, smoking, alcohol use, ASA Physical Classification status, PONV prophylaxis, preoperative carbohydrate loading, antibiotic prophylaxis, reoperation, complications, pneumonia, wound dehiscence, inadequate postoperative glycemic control). A p value of 0.05 was considered significant. A subgroup analysis of the T2DM group was done to compare outcomes between patients with T2DM who had preoperative HbA1c <7.0% and those with higher HbA1c.

RESULTS

Subjects

From July 2015 to December 2017, a total of 295 patients were enlisted in the EIAS. One hundred fifty eight underwent elective colorectal surgery under TMC ERAS protocol. One patient had unknown T2DM status and was excluded from the analysis. Of the 157 patients included, 113 were in the no T2DM group and 44 in the T2DM group (Figure 2).



ERAS, Enhanced Recovery After Surgery; EIAS, ERAS Interactive Audit System; DM, diabetes mellitus; T2DM, type 2 diabetes mellitus.

Figure 2. Flow diagram of subjects enlisted from the EIAS database.

Patients were mostly female, at their sixth to seventh decade of life and were overweight by Asia-Pacific International Obesity Task Force classification. There was no significant difference in smoking and alcohol use, length of operation, administration of preoperative PONV prophylaxis and preoperative carbohydrate loading. Patients in the T2DM group were older, had a greater percentage of use of laparoscopic surgical technique, and had more systemic disease by ASA Classification. In the T2DM group, 34% had a preoperative HbA1c exceeding 7.0% (Table 1).

Outcomes

There were no significant differences in postoperative length of hospital stay, complication rate during primary stay, reoperation, pneumonia and wound infection between the no T2DM and T2DM groups (Table 2).

Table 3 shows the preoperative HbA1c values of the patients in the T2DM group. Among the patients in the T2DM group who underwent colorectal surgery under ERAS, 34% did not have HbA1c <7% within target prior to surgery. The mean HbA1c in this subgroup was 9.0%. The outcomes pertaining to postoperative LOS, complications during primary stay, reoperation and pneumonia were not significantly different in these patients compared to those with preoperative HbA1c ≤7%. None of the patients in our sample had wound or surgical site infection (Table 4).

DISCUSSION

In this study, we compared the postoperative length of stay among patients with and without prior diagnosis of T2DM among patients who underwent major colorectal surgery in an ERAS protocol.

Studies on non-cardiac surgery have demonstrated the association of perioperative hyperglycemia and increased LOS, hospital complications and mortality.[28] The data presented in SCOAP demonstrated that patients with diabetes were more likely to have inadequate perioperative glycemic control, with a 7% increase in infectious complications, and significantly longer length of hospital stay compared to patients without diabetes who underwent colorectal surgery (6.0±8.5 versus 5.3±7.4 days).[16]

Perioperative hyperglycemia may have an indirect effect on length of stay because of its effect on complications.[14] Hyperglycemia is a predictor of nosocomial infection in general surgery.[14, 29-31] Short-term hyperglycemia, with a capillary blood glucose reading >252 mg/dL, is associated with impairment of the immune system seen as abnormalities in neutrophil and monocyte immune cell activity, increased expression of adhesion molecules and E-selectins, increased activation of the cytokine cascade via interleukin-6 and TNF-alpha, and altered microvasculature in response to nitric oxide.[11]

Table 1. Clinical characteristics of patients who underwent colorectal surgery under ERAS[a] protocol

Characteristic	no T2DM[b] (n=113)	T2DM[b] (n=44)	*p* value
Male gender (%)	40 (35.4)	23 (52.3)	0.070
Mean age, year (SD[c])	59.1 (14.2)	65.5 (9.7)	0.007
Mean BMI[d], kg/m^2 (SD[c])	25.0(4.0)	26.3 (5.4)	0.100
Smoker (%)	9 (7.9)	3 (6.8)	0.511
Alcohol usage (%)	2 (1.8)	1 (2.3)	0.630
ASA class[e] (%)			0.000
ASA I: healthy	2 (1.8)	0 (0.0)	
ASA II: mild systemic disease	54 (48.2)	3 (6.8)	
ASA III: severe systemic disease	55 (49.1)	40 (90.9)	
ASA IV: severe, life-threatening systemic disease	1 (0.9)	1 (2.3)	
Preoperative carbohydrate drink (%)	107 (95.5)	39 (88.6)	0.160
PONV[f] prophylaxis (%)	96 (85.7)	35 (79.6)	0.426
Antibiotic prophylaxis (%)	111 (98.2)	44 (100)	1.000
Surgical approach (%)			0.028
Open surgery	73 (65.2)	18 (40.9)	
Standard laparoscopic surgery	25 (22.3)	35 (79.6)	
Hand-assisted laparoscopic surgery	5 (4.5)	5 (11.4)	
Converted to open surgery	9 (8.0)	7 (15.9)	
Mean length of operation, hours (SD)	5.3 (2.5)	5.0 (2.4)	0.498
Preoperative HbA1c >7.0% (%)	N/A	15 (34)	0.000

[a] ERAS, Enhanced Recovery After Surgery
[b] T2DM, type 2 diabetes mellitus
[c] SD, standard deviation
[d] BMI, body mass index
[e] ASA, American Society of Anesthesiologists classification[37]
[f] PONV, postoperative nausea and vomiting

Table 2. Outcomes of patients who underwent colorectal surgery under ERAS[a] protocol

Outcome	no T2DM[b] (n=113)	T2DM[b] (n=44)	*p* value
Mean post-operative LOS[c], day (SD[d])	6.4 (5.1)	5.8 (3.8)	0.476
Discharged within 30 postoperative days (%)	112 (0.99)	43 (97.7)	0.282
Complications during primary stay (%)	37 (33.0)	14 (31.8)	0.521
Reoperation (%)	9 (8.0)	4 (9.1)	0.628
Pneumonia (%)	4 (3.6)	3 (6.8)	0.403

[a] ERAS, Enhanced Recovery After Surgery
[b] T2DM, type 2 diabetes mellitus
[c] LOS, length of hospital stay
[d] SD, standard deviation

Table 3. Preoperative HbA1c values of patients in T2DM group

HbA1c, %	Frequency (%) (n=44)
<5.5	3 (6.8)
5.5 to 5.9	4 (9.1)
6.0 to 6.49	12 (27.3)
6.5 to 7.0	10 (22.7)
7.1 to 7.9	6 (13.6)
8.0 to 8.9	4 (9.1)
9.0 to 9.9	2 (4.5)
>10	3 (6.8)

In a population-based Taiwanese cohort, diabetes conferred a higher risk prolonged LOS [odds ratio (OR) 2.3, 95% confidence interval (CI) 2.16-2.44] and 30-day postoperative mortality (OR 1.84, 95% CI 1.46-2.32).[15]

The impact of glycemic control on surgical outcomes among patients without diabetes who underwent colorectal surgery under a standardized ERAS protocol was demonstrated in a study in Sweden. Patients with preoperative HbA1c >6.0% had longer duration of surgery and greater perioperative blood loss. While a preoperative HbA1c >6.0% was found to confer a 2.9-fold increased risk of postoperative complications (95% CI 1.1-7.9), there was no significant difference in length of hospital stay between the two groups (8.5±5.4 versus 7.3±5.6 days).[27] An exploratory study compared consecutive patients who underwent elective major colorectal procedures under ERAS over the span of one year. Patients with DM had longer median LOS of 7 days with an interquartile range (IQR) of 5 to 15.5 days (n=18, p=0.041) compared to than those without diabetes (5 days, IQR 4 to 7.5 days, n=125). The study suggested that a diagnosis of diabetes had a significant impact on LOS even with ERAS interventions. However, the study did not analyze the impact of glycemic control of the patients included in the study.[32]

In our study, in spite of the effects of carbohydrate loading and dexamethasone PONV prophylaxis on short-term hyperglycemia, we observed no difference in LOS or complication rates between the no T2DM and T2DM groups.

ERAS protocols recommend that patients with chronic disease such as diabetes be optimized to international standards.[16] While there is currently no recommended preoperative HbA1c target, this recommendation implies that good glycemic control is a prerequisite to enrolling patients with diabetes to ERAS.[33] In our study, majority of the patients with DM had well-controlled diabetes. This may explain why our results showed that having prior diagnosis of DM was not associated with longer LOS or more complications. Although no difference in outcomes were noted among DM patients who did not achieve an HbA1c <7% prior to surgery, it is important to note that only a small percentage of our sample had poor perioperative glycemic control. Only eleven percent had HbA1c >9%.

Surgical site infections (SSI) can be as high as 15% in patients undergoing colorectal surgery with hyperglycemia in the perioperative period.[16] The use of surgical drains is one such reported risk factor. In our sample, there were no reported wound infections. The limited use of drains, as advocated by the ERAS protocol, could have contributed to fewer surgical site infections.

One factor that has been shown to significantly contribute to length of stay and recovery is the use of laparoscopic surgery.[34] Among the T2DM group, there was a greater proportion of patients who underwent laparoscopic surgery. Our results suggest that the preference for a laparoscopic approach in ERAS may be a contributory factor.

Limitations of the study and recommendations

The varied elements of the ERAS protocol may attenuate the known risk factors for SSI among patients with T2DM. These include the limited use of surgical drains, preference for laparoscopic approach and preoperative optimization of chronic diseases such as diabetes. One important outcome that was not measured in this study was postoperative blood sugar. Under the current study protocol, we were unable to document whether ERAS interventions, such as preoperative carbohydrate loading and PONV prophylaxis with dexamethasone, produced clinically significant hyperglycemia. Documentation of postoperative hyperglycemia in patients with and without diabetes who undergo ERAS should be done for future prospective studies, particularly those that examine the individual elements of the ERAS protocol.

Subjects were classified into T2DM and no T2DM groups based on medical history and assessment of attending physicians. Since data on preoperative HbA1c was not available for patients without prior diagnosis of diabetes, this is inadvertently subject to recall bias.

In our study, one patient with T2DM died within 30 postoperative days and one patient had prolonged hospital stay. The differences in secondary outcomes were still not significant between groups. The effect of ERAS on 30-day postoperative mortality, length of stay, complications or outcomes among patients with T2DM cannot be answered by our study design. This important outcome can be determined by comparing data before and after implementation of the ERAS protocol for DM patients.[35,36]

Table 4. Outcomes of T2DM[a] patients grouped by preoperative HbA1c

Outcome	HbA1c ≤7.0 (n=29)	HbA1c >7.0 (n=15)	*p* value
Mean HbA1c, % (SD[b])	6.2 (0.5)	9.0 (2.0)	<0.00001
Mean post-operative LOS[c], day (SD[b])	5.7 (3.7)	6.1 (4.2)	0.748
Complications during primary stay (%)	10 (34.5)	4 (26.7)	0.738
Reoperation (%)	3 (10.3)	1 (6.6)	1.000
Pneumonia (%)	2 (6.9)	1 (6.7)	1.000

[a] T2DM, type 2 diabetes mellitus
[b] SD, standard deviation
[c] LOS, length of hospital stay

There is a need for evidence-based support for the implementation of the ERAS protocol for patients with T2DM undergoing colorectal surgery. The best evidence that will support the use of ERAS protocols among patients with diabetes is a well-powered randomized controlled trial (RCT). Currently, there are no published RCTs that have examined individuals with diabetes randomized to ERAS versus conventional care. A systematic review of MEDLINE, the Cochrane Central Register of Controlled Trials, EMBASE, conference proceedings and ongoing clinical trials yielded no such high-quality articles that included patients with diabetes undergoing ERAS surgery.[8]

In spite of differences in age and premorbid status, our findings showed that there is no difference in outcomes between patients with prior diagnosis of DM and those without under ERAS. The ERAS protocol has multiple interventions that may contribute to reducing length of stay. While individual ERAS interventions have yet to be examined and deemed appropriate for patients with diabetes, our results show that, for patients with good preoperative glycemic control, the ERAS protocol as a whole does not pose additional harm to the patient with diabetes.

CONCLUSION

A prior diagnosis of T2DM was not associated with longer length of stay or more complications among patients who underwent colorectal surgery under the TMC ERAS protocol. A preoperative HbA1c less than 7% did not affect length of stay in ERAS.

Statement of Authorship
All authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure
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