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Narrative Review

Preoperative carbohydrate loading in surgical patients with type 2 diabetes: Are concerns supported by data?



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A R T I C L E I N F O

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SUMMARY

Currently, there is a lack of consensus on the provision of preoperative carbohydrate loading in patients with type 2 diabetes mellitus (T2DM) due to theoretical concerns including the possibility of delayed gastric emptying, perioperative hyperglycemia, and poor surgical outcomes. This narrative review summarizes the accumulating evidence on preoperative carbohydrate loading in this population and whether these concerns are supported by preliminary evidence. In general, the available research suggests that carbohydrate loading may be implemented in those with T2DM without increased risk for intra- and postoperative hyperglycemia or surgical complications. However, there is strong justification for future research to definitively study this highly debated and timely topic. Ultimately, the inclusion of preoperative carbohydrate loading for surgical patients with DM should be guided by the surgical team's clinical judgment and individualized based on patient needs and characteristics.

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1. Introduction

During the perioperative period, surgical stress and subsequent inflammation contribute to higher glucose mobilization and reduced glucose uptake. The resulting diminished insulin sensitivity may persist for days to weeks postoperatively [1]. Perioperative hyperglycemia is common even in healthy patients, occurring in 12–30% of surgical patients without preexisting diabetes mellitus (DM) [2]. To improve postoperative insulin resistance in patients without DM, the Enhanced Recovery after Surgery (ERAS®) Society, the European Society for Clinical Nutrition and Metabolism, and the American Society for Enhanced Recovery and Perioperative Quality Initiative (ASER/POQI) recommend nutrition strategies

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such as shortened fasting periods and preoperative carbohydrate administration also known as "carbohydrate loading." [3–6].

Carbohydrate loading regimens vary across institutions but often include a 100 g oral dose of ~12% complex carbohydrate (i.e., maltodextrin) the evening before surgery and another 50 g dose provided 2–3 h prior to anesthesia. Four meta-analyses including various surgical specialties report that preoperative carbohydrate loading is associated with significantly improved postoperative insulin resistance primarily in patients without DM [7–10]. Two of these analyses revealed that those undergoing major surgeries also demonstrate a modest but statistically significant reduction in length of stay (-0.7-1.1 days) when carbohydrate loading is provided as part of an enhanced recovery protocol [8,9]. However, it remains debated whether the proposed benefits of carbohydrate loading extend to surgical patients with DM [11-14].

The prevalence of DM ranges from 20 to 40% in surgery patients with some of the highest rates reported by bariatric cohorts [15–18]. Diabetes is associated with higher risk for post-operative complications, extended length of hospital stay, and mortality [19]. Multiple mechanisms may be responsible for poor outcomes including (but not limited to) glycemic variability and hyperglycemia although causation has not yet been established [15–17]. Despite this unclear mechanism, protocols which

Abbreviations: ASER/POQI, American Society for Enhanced Recovery and Perioperative Quality Initiative; DM, Diabetes Mellitus; ERAS, Enhanced Recovery After Surgery; ESPEN, European Society for Clinical Nutrition and Metabolism; HbA1C, Hemoglobin A1c; HOMA-IR, Homeostatic Model Assessment of Insulin Resistance; ICU, Intensive Care Unit; T1DM, Type 1 Diabetes Mellitus; T2DM, Type 2 Diabetes Mellitus.

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improve postoperative recovery would seem to be especially useful in this vulnerable population, yet, enhanced recovery guidelines specifically for patients with DM are sparse.

Carbohydrate loading in patients with DM is controversial due to a handful of theoretical and practical concerns. First, patients with DM may have delayed gastric emptying, therefore, some question whether carbohydrate-containing beverages remain in the stomach longer and increase aspiration risk. Secondly, patients with DM experience a greater blood glucose response to carbohydrate than counterparts without DM, thus, some are concerned that hyperglycemia will occur throughout the surgical period. This leads to a third concern, whether preoperative carbohydrate loading may lead to poor surgical outcomes in patients with DM.

Currently, most surgical guidelines state that data are insufficient to support strong recommendations for carbohydrate loading in those with DM [3-6]. Yet, we are unaware of any publication which comprehensively reviews carbohydrate loading in surgical

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patients with DM. Therefore, this narrative review highlights accumulating evidence in this area and whether the aforementioned concerns are supported by evidence in this population.

Descriptions of the study design and results of the included, peer-reviewed studies have been summarized in Tables 1 and 2. This search also identified preliminary, non-peer-reviewed research which is not incorporated into this summary but is listed in Supplementary Table 1.

Are common concerns for carbohydrate loading surgical patients with DM supported by the available scientific literature (See Fig. 1 for summary of concerns and data)?

1. Concern #1: Does preoperative carbohydrate loading delay gastric emptying in patients with diabetes?

Age, sex, certain medications, and the severity of DM (type and degree of neuropathy) have all been associated with alterations in

Table 1

Study details of included publications which evaluate carbohydrate loading in individuals with diabetes (ordered by publication year).

Author	Study design	Surgery subtype	Participant details and sample size	Carbohydrate dose and timing
Breuer et al., 2006 [39]	Sub analysis of patients with DM within a prospective, randomized, double- blind, controlled study	Cardiac	Comparison of 10 patients with T2DM which received carbohydrate load, 14 patients with T2DM received flavored water and 7 patients with T2DM fasted after midnight	800 mL carbohydrate-beverage ("iso-osmolar, 12.5% carbohydrates, 50 kcal/100 mL, 290 mOsm/kg, pH 5.0") on evening before surgery and 400 mL 2 h before surgery
Gustafsson et al., 2008 [30]	Observational	Non-surgical participants	All participants received carbohydrate loading. Compared 25 participants with T2DM (HbA1c <7%; controlled by diet, oral anti-diabetic drugs or insulin) and 10 healthy controls	One "400 mL carbohydrate-rich beverage (12.5 g 100/mL carbohydrates, 12% monosaccharides, 12% disaccharides, 76% polysaccharides, 285 mOsm/kg)"
Can et al., 2009 [31]	Prospective controlled study	Cholecystectomy or thyroidectomy	All patients received carbohydrate loading. Eight patients with insulin resistance (homeostatic model assessment of insulin resistance (HOMA-IR score >2.5) were compared to 26 health controls (HOMA-IR score <2.5)	800 mL carbohydrate-beverage ("12.5 g/100 mL of carbohydrate, 12% monosaccharide, 12% disaccharide, 76% polysaccharide, 285 mOsm/ kg") on evening before surgery and 400 mL 2 -3 h before surgery
Azugary et al., 2015 [43]	Sub analysis of patients with DM within a randomized trial	Bariatric	101 in the control group and 97 in the intervention group (22 patients with T2DM in control and 16 in the intervention group)	800 mL carbohydrate beverage ("12.5 g of carbohydrate per 100 mL, 12% monosaccharide, 12% disaccharide, 76% polysaccharide, 250 mOsm/kg and 50 kcal") 12 h pre-anesthesia and 400 mL 2 h before surgery
Laffin et al., 2018 [38]	Prospective observational non- inferiority cohort study	Cardiac, Neurology, Urology, General and Other	106 patients with self-reported diagnosis of T1DM or T2DM were asked to consume preoperative carbohydrate load. Authors compared those that adhered (consuming either one or two carbohydrate load drink(s) before surgery) to those that did not adhere	500 mL of commercially available cranberry cocktail or apple juice, first drink consumed 1 h prior to sleeping night before operation, second drink consumed 3 h preoperatively
Brethauer et al., 2019 [44]	Sub analysis of patients with DM within a multicenter, quality improvement program	Bariatric	Included 2436 patients with insulin-dependent and noninsulin-dependent T2DM. Compared those who adhered to carbohydrate loading recommendations to those who did not adhere. Adherence was 72% the night prior to surgery and 69% the day of surgery	Sports drink or fruit juice the evening before and the morning of surgery (volume not specified in manuscript)
Festejo- Villamiel et al., 2019 [45]	Cross-sectional study	Colorectal	Comparison of 113 healthy controls (95.5% consumed preoperative carbohydrate drink) and 44 patients with documented diagnosis of T2DM (88.6% consumed preoperative carbohydrate drink)	Details not provided
Talutis et al., 2020 [41]	Retrospective chart review	Bariatric, Colorectal, Surgical Oncology	Comparison of 80 patients with T2DM who received carbohydrate loading and 89 patients with T2DM who did not receive carbohydrate loading	32-ounce (946 mL) bottle of sports drink "containing 55 g carbohydrate." Patients were asked to drink half the bottle the night before surgery and the other half the morning of surgery
Cua et al., 2021 [40]	Retrospective chart review	Partial or total colectomy	Compared 41 pre-ERAS patients with T2DM to 58 post-ERAS patients with T2DM	"Two bottles of commercially prepared, maltodextrin-based drink with 50 g of carbohydrate per bottle." One was consumed the evening before surgery and one 2 h before surgery
Suh et al., 2021 [42]	Sub analysis of patients with DM within a randomized, controlled trial	Bariatric	Compared 20 patients with DM who were randomized to carbohydrate drink to 15 patients with DM who fasted prior to surgery	Two 296 mL carbohydrate drinks each containing 50 g of complex carbohydrate (maltodextrin). One drink was consumed at 8pm the night before surgery and the second was consumed 3 h prior to surgery start time.

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Summary of Outcomes reported in included	publications	(ordered by publication ye	ar)
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Author	Reported outcome(s)	Results
Breuer et al., 2006	Intraoperative and postoperative insulin requirement	No significant differences in insulin infusion rates were reported between groups (complete data not shown in manuscript).
[39]	Intraoperative and postoperative blood glucose levels	No significant differences in glucose levels were reported between groups (complete data not shown in manuscript).
Gustafsson et al., 2008	Blood glucose response to carbohydrate consumption	Participants with T2DM had significantly higher peak blood glucose following consumption of carbohydrate load than healthy controls (241 vs. 137 mg/dL, $P < 0.01$). In participants with T2DM, blood glucose returned to baseline after 180 min, whereas in healthy controls, blood glucose returned to baseline after 120 min.
[30] Can et al., 2009 [31]	Gastric emptying rate Preoperative glucose (measured at baseline, 40 min and 90 min post- consumption, and at anesthesia induction)	Gastric emptying rate was significantly higher in participants with T2DM. No significant differences in glucose were reported at any timepoint between groups.
	Preoperative insulin Intraoperative gastric volume and acidity Adverse events	Insulin was significantly elevated in patients with insulin resistance at baseline, 40 min post consumption and 90 min post consumption, but not significantly different at anesthesia induction. No significant differences in gastric volume or acidity were reported between groups.
Azugary et al., 2015 [43]	Negative outcomes	No negative outcomes were reported in patients with DM who received carbohydrate load (complete data not shown in manuscript).
Laffin et al., 2018 [38]	Preoperative blood glucose, incidence of preoperative hyperglycemia, use of preoperative insulin infusion, length of stay, postoperative pneumonia	No outcome was found to be significantly different between groups. No operations were cancelled for hyperglycemia.
Brethauer et al., 2019	30-day wound occurrence	No significant differences in 30-day wound occurrence were reported between groups with evening carbohydrate beverage. No significant differences in 30-day wound occurrence were reported between groups with day of surgery carbohydrate beverage.
Festejo- Villamiel et al., 2019 [45]	Length of stay, discharge within 30 days, postoperative complications, reoperation, pneumonia and wound infection occurrence	P < 0.01). No significant difference was reported if carbohydrate load was consumed the morning of surgery. No outcome was found to be significantly different between participants with DM who consumed carbohydrate load as part of an ERAS protocol and participants without DM who consumed carbohydrate load as part of an ERAS protocol and participants without DM who consumed carbohydrate load as part of an ERAS protocol.
Talutis et al., 2020 [41]	Perioperative glucose levels Perioperative insulin requirements	Preoperative median glucose was significantly higher in the group receiving carbohydrate load (142 vs 129.5 mg/dL, $P = 0.017$). No difference in median glucose was reported in the operating room, postoperatively or on postop day 0 or days 2–5. Postop day 1 median glucose was higher in the group receiving carbohydrate load (152 vs. 137.5, $P = 0.004$). No significant difference was reported in median insulin units used in the operating room or on postop day 0–5 between groups.
Cua et al., 2021 [40]	Postoperative complications Perioperative glucose levels->	No significant difference was reported in complications between groups. No patient in the group receiving carbohydrate experienced aspiration or pulmonary complication. Preoperative mean peak glucose was significantly higher in the group receiving carbohydrate load (192 vs. 140 mg/dL, P < 0.000). No significant difference in mean peak glucose intraoperatively, postoperatively, on postop day 1 or days 4 -7. Mean peak glucose on postop day 2 was lower in the ERAS group receiving carbohydrate load (164 vs. 186, P = 0.034).
	Rates of hyperglycemia (serum glucose \geq 180 mg/dL) Length of stay	"A linear regression model indicated that T2DM patients on an enhanced recovery protocol experienced reduced rates of hyperglycemia compared with T2DM control patients ($P = 0.017$)." The post-ERAS group that received carbohydrate load had a significantly reduced length of stay compared to the pre-ERAS group (4.9 vs. 7.4, $P = 0.001$).
Suh et al., 2021 [42]	Postoperative blood glucose (measured on postoperative day 0,1 and 2)	No statistically significant differences in glucose were reported at any timepoint between groups
	Postoperative complications	One participant in the intervention and one in the control group experienced a postoperative complication. No significant difference between groups.

gastric emptying and gastrointestinal motility. Thus, some question whether surgical patients with DM will experience delayed emptying of gastric contents and an increased risk for aspiration following administration of a preoperative carbohydrate load [20]. This assumption may be based on reports which found that elevated blood glucose was associated with reduced gastric emptying in healthy controls and patients with T1DM [21–23]. Yet, the association between hyperglycemia and gastric emptying rate is less clear in patients with T2DM. In a recent study, gastric emptying rate of a solid meal was significantly faster in non-surgical participants with well-controlled T2DM (HbA1c \geq 6% and \leq 7.9%; controlled by diet or metformin), when compared to age-

and BMI-matched non-surgical participants without T2DM [24]. Additionally, gastric emptying was significantly faster in younger rather than older subjects and in participants with T2DM who were treated with metformin when compared to those with T2DM controlled by the diet.

Previous studies of patients with T2DM remain inconclusive regarding the relationship between glucose concentrations and gastric emptying. For example, blood glucose has been associated with either increased, decreased or no changes in gastric emptying rate. This led to the hypothesis that rapid gastric emptying may be more common early in T2DM development whereas delayed gastric emptying may be a long-term complication of T2DM

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Fig. 1. Describes three common concerns for providing preoperative carbohydrate loading to patients with Diabetes Mellitus (DM). The available evidence is summarized for each of the concerns and the key references for these summarizes are listed. Remaining questions and opportunities for future research are also highlighted.

[25–27]. However, repeat assessment of gastric emptying over a period of 14 years demonstrated that gastric emptying of liquid and solid meals did not become more delayed over time in a small cohort of individuals with T2DM [28].

Although the relationship between DM and gastric emptying rate remains unclear, reviews estimate that 30–50% of those with DM have demonstrated delayed gastric emptying which may place them at risk for aspiration during surgery [29]. Therefore, studies on the impact of carbohydrate loading on gastric emptying in patients with DM are important to ensure that there is no increased risk of aspiration and to optimize timing and dose of preoperative carbohydrates for this patient population.

Two published studies evaluated gastric emptying rates following carbohydrate drink administration in individuals with T2DM or insulin resistance. Gustafsson et al., evaluated glycemic response and gastric emptying rate following a 50 g, 400 mL carbohydratecontaining beverage in non-surgical participants with wellcontrolled T2DM (n = 25; mean HbA1c: 6.2 \pm 0.2%) in comparison to controls without DM (n = 10). While gastric emptying was slightly faster in participants with DM, the authors concluded participants with T2DM did not show signs of delayed gastric emptying [30]. In a smaller study of 8 patients with insulin resistance (defined as a HOMA-IR > 2.5) and 26 patients without insulin resistance (HOMA-IR < 2.5), no difference in gastric content volume was reported between groups following a 100 g carbohydrate load on the evening before and 50 g carbohydrate the morning of surgery [31]. Finally, a recent abstract reported that gastric emptying was not consistently different between non-surgical participants without DM (n = 27), those with pre-DM (n = 28; mean HbA1c: 5.8 \pm 0.1%), and those with T2DM (n = 25; mean HbA1c: 7.2 \pm 0.1%) following a 50 g dose of carbohydrate [32]. These three studies suggest that gastric emptying is not drastically different between patients with DM and those without DM, however, additional research is warranted in larger samples of surgical patients and in those with a history of uncontrolled T2DM, T1DM and gastroparesis.

2. Concern #2: Does preoperative carbohydrate loading increase risk of hyperglycemia in patients with diabetes?

Patients with T2DM have exaggerated blood glucose responses following carbohydrate ingestion compared to those without DM. In surgical patients, hyperglycemia has been associated with an increased risk for negative outcomes including pneumonia, infectious complications, increased length of hospital and ICU stay, and mortality [15,16,33–37]. Notably, the association between hyperglycemia and poor outcomes has been found to be more pronounced in those without DM than those with DM, and may differ depending on glucose concentration cut-offs used to define hyperglycemia or the specific timing of hyperglycemia measurement within the perioperative period [15,34,36,37].

The concern for perioperative hyperglycemia following carbohydrate loading in patients with DM is important and is the most reported outcome of the publications included in this review. Initial work in non-surgical participants, reported that carbohydrate loading led to a significantly higher blood glucose peak in individuals with well-controlled T2DM as compared to healthy controls without DM (241 vs. 137 mg/dL, P < 0.01) [30]. However, both groups were able to return to baseline glucose values around 120 min following consumption in healthy controls and 180 min following consumption in those with DM. This work was recently replicated in a non-peer reviewed abstract (cited previously) [32]. Briefly, a carbohydrate drink containing 50 g maltodextrin was provided to participants without DM, participants with pre-DM and participants with well-controlled T2DM. Those with T2DM had significantly higher glucose following consumption but after adjustment for covariates, there was no difference in peak plasma glucose between groups. Similar to Gustafsson et al., this abstract reported that blood glucose returned to baseline values at 150 min following consumption in the non-DM and pre-DM group and 210 min following consumption in the group with DM. Importantly, both of these works enrolled healthy participants rather than surgical patients. In contrast, six studies have enrolled surgical patients with DM or insulin resistance and evaluated blood glucose response to carbohydrate loading at different time points during the perioperative period [31,38–42].

Laffin and colleagues included surgical patients with selfreported T1DM or T2DM (n = 106). Patients (28.5% were taking insulin preoperatively) were instructed to consume carbohydrates the evening prior to surgery and 3 h preoperatively [38]. Patients who were compliant with carbohydrate loading recommendations as determined by self-reported consumption on the day of surgery (n = 54) were compared to those who were non-compliant (n = 52). No statistical differences were reported in mean preoperative blood glucose or prevalence of preoperative hyperglycemia between groups. Preoperative insulin infusion use was reported to be 19.2% in those who complied with carbohydrate loading on the day of surgery versus 7.4% in those who were non-compliant, however, this difference was not statistically significant (P = 0.07). The authors concluded that carbohydrate loading was not inferior to fasting in this cohort. Two additional studies lend limited support that carbohydrate loading may not have deleterious effects on blood glucose in patients with T2DM or insulin resistance. Breuer et al. conducted a sub analysis of 31 patients with non-insulin dependent T2DM within a three-arm randomized trial comparing a carbohydrate drink to flavored water or fasting. Breuer et al. concluded, "Almost all patients required exogenous insulin. There was no significant difference in glucose levels or insulin requirements. This was also independent of preexisting T2DM (data not shown)." [39] Additionally, the study by Can et al., which was described previously and included patients with insulin resistance also reported no difference in preoperative blood glucose [31].

Recently, the effect of an enhanced recovery protocol that included preoperative carbohydrate loading was examined in a retrospective study in patients with T2DM undergoing colorectal surgery [40]. Patients with T2DM that received carbohydrate loading as part of an enhanced recovery protocol (n = 58) were compared to patients with T2DM that received care prior to implementation of the enhanced recovery protocol (control group; n = 41). Average HbA1c of the control group and the enhanced recovery group was 7.28% and 6.91%, respectively (P = 0.373) Patients with T2DM in the enhanced recovery program had elevated mean peak preoperative glucose compared with patients with T2DM in the control group (192.2 vs. 139.8 mg/dL, P < 0.000). However, mean peak intraoperative and postoperative glucose were not statistically different in patients with T2DM in the enhanced recovery.

A pre-post comparison of GI surgery patients found that 89 historical controls with T2DM (who did not receive preoperative carbohydrate loading) had similar insulin requirements as 80 patients with T2DM who received 55 g of carbohydrate preoperatively as part of an enhanced recovery protocol [41]. The HbA1c of these patients ranged from 5 to 12.6% and did not differ between pre- and post-groups. The authors also reported median daily blood glucose at nine timepoints (seven of which were not statistically significantly different between groups). Notably, preoperative and postoperative day one blood glucose levels were significantly higher in the group receiving carbohydrate loading. However, the authors conclude that this finding was not clinically significant (the difference between median glucose at these timepoints ranged from 12.5 to 14.5 mg/dL) and that measurements on postoperative day one may have been influenced by meal timing which was not controlled for in the study. An alternative explanation is that the sample size of this study may have limited their ability to draw strong conclusions.

Suh et al. reported on blood glucose response in the postoperative period. Bariatric patients were randomized to a control group (fasting from midnight prior to surgery) or carbohydrate loading the evening prior to surgery and 3 h before surgery [42]. Fifteen patients with DM were included in the control group, and 20 patients with DM were in the carbohydrate loading group. Subanalysis of patients with DM reported no difference in blood glucose between the carbohydrate loading group and fasted group on postoperative day 0 (168.3 vs. 147.5 mg/dL, P = 0.07), postoperative day 1 (143.6 vs. 139 mg/dL, P = 0.75) or postoperative day 2 (140.1 vs. 130.7 mg/dL, P = 0.53). The authors concluded that, "Bariatric ERAS protocols can safely include carb drinks for patients with diabetes." The generalizability of this conclusion is unknown due to small sample size and omitted details such as the type of DM and HbA1C range of these patients with DM.

In summary, preoperative blood glucose was reported to be 12.5–52.4 mg/dL higher in patients with T2DM who consume carbohydrate load than those who do not [40,41]. Data from non-surgical patients with T2DM suggests that blood glucose returns to baseline at approximately 3 h after consumption [30,32]. During and following surgery, blood glucose was not significantly different between patients with T2DM who consume carbohydrate load and those who do not [38,40–42].

3. Concern #3: Does preoperative carbohydrate loading increase risk of perioperative complications in individuals with diabetes?

The final and perhaps most important concern in the debate on carbohydrate loading in patients with DM is whether it will cause harm to patients or result in less favorable surgical outcomes (i.e., complications, pneumonia, wound infections, length of stay, and adverse events). In general, complications including aspiration and adverse events were not reported to be more common in patients with DM or insulin resistance who received preoperative carbohydrates when compared to respective controls [31,40,41]. In the previously described study by Laffin et al., it was also reported that no operations were cancelled due to hyperglycemia [38]. Patients with DM who receive carbohydrate loading are not reported to have an increased risk of pneumonia, 30-day wound occurrence or wound infections [38,44,45].

Length of stay was reported in three studies. Laffin et al. reported no difference in the length of stay [38]. Festejo-Villamiel et al., conducted a retrospective chart review of colorectal surgery patients to determine if patients with T2DM have worse outcomes with ERAS protocols (including carbohydrate loading the night before and day of surgery) than healthy controls [45]. This study included 157 patients with T2DM with HbA1c ranging from less than 5.5% to greater than 10%. The authors reported that there was no increased risk of extended length of stay, reoperations, or complications between groups. Recent data from Cua et al., show that implementation of an enhanced recovery protocol including a maltodextrin-based carbohydrate load led to significantly decreased length of stay in both colorectal surgery patients with T2DM (- 2.6 days) and those without T2DM (- 3.4 days) as compared to respective controls [40].

Finally, results from the ENERGY trial, a national quality improvement project including 36 institutions, suggest that

bariatric patients with T2DM who received carbohydrate the evening before surgery as part of an enhanced recovery protocol had a significantly lower incidence of 30-day morbidity versus those who were non-adherent [44]. Timing may be an important consideration as this difference was not statistically significant when the cohort was split by adherence to carbohydrate intake on the day of surgery. Notably, this protocol allowed sports drinks or juice for carbohydrate loading rather than a complex carbohydrate drink, which may have influenced study outcomes.

Overall, the available research suggests that patients with T2DM who receive carbohydrates prior to surgery do not experience increased risk of adverse events or extended length of stay and may even have a lower incidence of morbidity.

2. Discussion

The practice of preoperative carbohydrate loading varies across institutions and across the globe. A recent survey of U.S. colorectal ERAS programs found that of 78 participating hospitals, 98.5% administered some type of carbohydrate-containing beverage to patients without DM prior to surgery, 80.9% reported providing carbohydrate-containing beverages to patients with DM not taking insulin and 60.3% provided carbohydrate loading to those taking insulin [46]. This survey also revealed that the type of carbohydrate provided (simple versus complex) did not appear to differ by DM status. Given the heterogeneity of carbohydrate loading practices in patients with DM, we sought to summarize the accumulating evidence in this surgical population.

Previous reviews on carbohydrate loading are available, however, most do not specifically focus on patients with DM [47,48]. Recently, Ge et al. conducted a systematic review which summarized five randomized controlled trials and concluded that carbohydrate loading was "probably beneficial" in surgical patients with DM [48]. Notably, due to differences in inclusion criteria and a rapid increase of recent publications in this area, only three of the ten publications reviewed in this current narrative review were included in the systematic review by Ge et al.

Our review revealed several key research gaps for future investigation. First, within the existing literature there is variability in the type, dose and timing of carbohydrate load used preoperatively (see Table 1). Importantly, the ASER/POQI joint consensus statement suggests a lower-osmolality, preoperative beverage containing ~12% complex carbohydrate, in a 50 g dose for surgical patients without DM [3]. It may seem intuitive that those with DM would most benefit from complex carbohydrates rather than simple carbohydrates, however, whether dose and type of carbohydrate makes an impact on the response of patients with DM remains to be elucidated. Preliminary evidence in a cohort of bariatric patients suggests that glycemic variability was improved when patients with well-controlled DM (mean HbA1C <7%) received three servings of a maltodextrin-based carbohydrate beverage (n = 36) rather than three 12 oz servings of grape juice (n = 45) [49]. However, in this study, it is not clear whether the two groups were matched for dose of carbohydrate.

Secondly, previous research has suggested that carbohydrate loading may improve patient reported outcomes including lowered thirst, reduced anxiety, and lower or no difference in postoperative nausea and vomiting, however, these studies rarely include patients with DM with the exception of a recent study from Shin et al. [50–54] Shin et al., compared oral carbohydrate versus IV dextrose in orthopedic surgical patients with T2DM (n = 82) [54]. Oral carbohydrate loading was associated with a small, but statistically significant increase in postoperative nausea and vomiting when compared to IV dextrose. The authors concluded that the

"preoperative carbohydrate drink did not increase hyperglycemia, which suggests that it may be a safe component of perioperative care in diabetic patients." However, this study did not include a control group, therefore, it was not able to address the common concerns discussed in this review because it is unclear whether similar results would be observed in patients not receiving any preoperative carbohydrate load. In addition to patient reported outcomes, more investigation is needed into the impact of carbohydrate loading on emerging outcome measures such as discharge status, functional outcomes, and days at home within 30 days of surgery [55,56].

Limitations of this summary include that this was a narrative review of the literature rather than a systematic review. Due to the small number of studies available, results were combined from multiple surgical subsets (primarily elective rather than emergency procedures) and from studies using a variety of carbohydrate loading drinks and regimens. Therefore, the generalizability of these findings is unknown. Within enhanced recovery protocols, it is unclear whether certain aspects are more impactful than others. Although the focus of this review was carbohydrate loading, enhanced recovery protocols may include additional nutrition interventions such as prehabilitation, diminished fasting times, early postoperative intake of solids and/or immunonutrition supplementation for 5-7 days before and after surgery which have also been shown to improve outcomes. Preoperative dose adjustments of oral hypoglycemic medications, injectables, and/or insulin could also help decrease the expected rise in postprandial hyperglycemia and consequently a decision to proceed with or delay time of surgery. The independent contribution of these aspects is not completely understood or summarized in this review.

3. Future directions

To conclusively answer whether carbohydrate loading is beneficial for surgical patients with diabetes, adequately powered studies which include surgical patients and consider outcomes such as perioperative glycemia and insulin response, surgical complications and safety outcomes are needed. Future studies should: 1) strive to include patients from multiple surgical specialties, 2) follow evidence-based guidelines for selection of carbohydrate dose and type, 3) report on compliance to carbohydrate loading protocol, and 4) report characteristics of those with DM such as HbA1c, concurrent medication use and duration of diabetes. Most research to date includes patients with well-controlled DM (typically defined by an HbA1c <7%). Because carbohydrate loading aims to increase insulin secretion, the use of carbohydrate loading is not recommended for those with T1DM [3]. Additionally, a recent case study suggests carb loading should be approached with caution in patients with T2DM, gastroparesis and poor glucose control [57]. In situations of insulin deficiency or severe insulin resistance, the efficacy and safety of carbohydrate loading remains unknown.

4. Conclusion

This narrative review summarized clinical studies which investigated the use of preoperative carbohydrate loading in patients with DM. In general, the available research suggests that carbohydrate loading may be implemented in those with wellcontrolled T2DM without increased risk for intra- and postoperative hyperglycemia or surgical complications. Ultimately, the inclusion of preoperative carbohydrate loading for surgical patients with DM should be guided by the surgical team's clinical judgment and individualized based on patient needs and characteristics. This critically-needed review describes the state of the evidence for carbohydrate loading in patients with DM. Considered along with the growing incorporation of ERAS into the standard of care worldwide, there is strong justification for future research to definitively study this highly debated and timely topic.

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Author contributions

Robinson: This author helped with study conception and design, acquisition of data, analysis and interpretation of data, drafting of manuscript, critical revision and final approval of the manuscript. Cassady: This author helped with acquisition of data, analysis and interpretation of data, drafting of manuscript, critical revision and final approval of the manuscript. Hegazi: This author helped with study conception and design, analysis and interpretation of data, drafting of manuscript, critical revision and final approval of the manuscript. Wischmeyer: This author helped with study conception and design, analysis and interpretation of data, drafting of manuscript, critical revision and final approval of the manuscript.

Declaration of competing interest

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.clnesp.2021.08.023.

References

- Ljungqvist O, Jonathan E. Rhoads lecture 2011: insulin resistance and enhanced recovery after surgery. JPEN - J Parenter Enter Nutr 2012;36(4): 389–98.
- [2] Duggan EW, Carlson K, Umpierrez GE. Perioperative hyperglycemia management: an update. Anesthesiology 2017;126(3):547–60.
- [3] Wischmeyer PE, Carli F, Evans DC, Guilbert S, Kozar R, Pryor A S, et al. American society for enhanced recovery and perioperative quality initiative joint consensus statement on nutrition screening and therapy within a surgical enhanced recovery pathway. Anesth Analg 2018;126:1883–95.
- [4] Ljungqvist O. ERAS—enhanced recovery after surgery: moving evidencebased perioperative care to practice. JPEN - J Parenter Enter Nutr 2014;38(5): 559–66.
- [5] Ljungqvist O, Scott M, Fearon KC. Enhanced recovery after surgery: a review. JAMA Surg 2017;152(3):292–8.

- [6] Lobo DN, Gianotti L, Adiamah A, Barazzoni R, Deutz NE, Dhatariya K, et al. Perioperative nutrition: recommendations from the ESPEN expert group. Clin Nutr 2020;39(11):3211–27.
- [7] Li L, Wang Z, Ying X, Tian J, Sun T, Yi K, et al. Preoperative carbohydrate loading for elective surgery: a systematic review and meta-analysis. Surg Today 2012;42(7):613–24.
- [8] Awad S, Varadhan KK, Ljungqvist O, Lobo DN. A meta-analysis of randomised controlled trials on preoperative oral carbohydrate treatment in elective surgery. Clin Nutr 2013;32(1):34–44.
- [9] Amer MA, Smith MD, Herbison GP, Plank LD, McCall JL. Network meta-analysis of the effect of preoperative carbohydrate loading on recovery after elective surgery. Br J Surg 2017;104(3):187–97.
- [10] Koffis K, Jamiol-Milc D, Skonieczna-Żydecka K, Folwarski M, Stachowska E. The effect of preoperative carbohydrate loading on clinical and biochemical outcomes after cardiac surgery: a systematic review and meta-analysis of randomized trials. Nutrients 2020;12(10):3105.
- [11] Rushakoff RJ, Wick EC, McDonnell ME. Enhanced recovery in patients with diabetes: is it time for a moratorium on use of preoperative carbohydrate beverages? Ann Surg 2019;269(3):411–2.
- [12] Morin NP. Comment on "enhanced recovery in patients with diabetes: is it time for a moratorium on use of preoperative carbohydrate beverages?" I agree with your perspective. Ann Surg 2019;270(6):e120–1.
- [13] Soop M, Nygren J, Thorell A. Response to comment on "Rushakoff et al, Annals of Surgery 2018". Ann Surg 2019;270(6):e83-4.
- [14] Rushakoff RJ, Wick EC, McDonnell ME. Response to comment on "Letter in response to Soop et al". Ann Surg 2019;270(6):e84–5.
- [15] Frisch A, Chandra P, Smiley D, Peng L, Rizzo M, Gatcliffe C, et al. Prevalence and clinical outcome of hyperglycemia in the perioperative period in noncardiac surgery. Diabetes Care 2010;33(8):1783–8.
- [16] Akirov A, Shochat T, Dotan I, Diker-Cohen T, Gorshtein A, Shimon I. Glycemic variability and mortality in patients hospitalized in general surgery wards. Surgery 2019;166(2):184–92.
- [17] Shah NJ, Leis A, Kheterpal S, Englesbe MJ, Kumar SS. Association of intraoperative hyperglycemia and postoperative outcomes in patients undergoing non-cardiac surgery: a multicenter retrospective study. BMC Anesthesiol 2020;20(1):1–9.
- [18] Moghadamyeghaneh Z, Stamos MJ, Stewart L. Patient co-morbidity and functional status influence the occurrence of hospital acquired conditions more strongly than hospital factors. J Gastrointest Surg 2019;23(1):163–72.
- [19] Levy N, Dhatariya K. Pre-operative optimisation of the surgical patient with diagnosed and undiagnosed diabetes: a practical review. Anaesthesia 2019;74(Suppl 1):58–66.
- [20] Robinson M, Davidson A. Aspiration under anaesthesia: risk assessment and decision-making. Cont Ed Anaestesia Crit Care Pain 2014;14(4):171–5.
- [21] Schvarcz ER, Palmer MA, Aman J, Horowitz MI, Stridsberg MA, Berne C. Physiological hyperglycemia slows gastric emptying in normal subjects and patients with insulin-dependent diabetes mellitus. Gastroenterology 1997;113(1):60–6.
- [22] Bharucha AE, Batey-Schaefer B, Cleary PA, Murray JA, Cowie C, Lorenzi G, et al. Delayed gastric emptying is associated with early and long-term hyperglycemia in type 1 diabetes mellitus. Gastroenterology 2015;149(2):330–9.
- [23] Halland M, Bharucha AE. Relationship between control of glycemia and gastric emptying disturbances in diabetes mellitus. Clin Gastroenterol Hepatol 2016;14(7):929–36.
- [24] Watson LE, Xie C, Wang X, Li Z, Phillips LK, Sun Z, et al. Gastric emptying in patients with well-controlled type 2 diabetes compared with young and older control subjects without diabetes. J Clin Endocrinol Metab 2019;104(8): 3311–9.
- [25] Horowitz M, Harding PE, Maddox AF, Wishart JM, Akkermans LM, Chatterton BE, et al. Gastric and oesophageal emptying in patients with type 2 (non-insulin-dependent) diabetes mellitus. Diabetologia 1989;32(2): 151–9.
- [26] Phillips WT, Schwartz JG, McMahan CA. Rapid gastric emptying of an oral glucose solution in type 2 diabetic patients. J Nucl Med 1992;33(8):1496–500.
- [27] Marathe CS, Horowitz M, Trahair LG, Wishart JM, Bound M, Lange K, et al. Relationships of early and late glycemic responses with gastric emptying during an oral glucose tolerance test. J Clin Endocrinol Metab 2015;100(9): 3565-71.
- [28] Watson LE, Phillips LK, Wu T, Bound MJ, Jones KL, Horowitz M, et al. Longitudinal evaluation of gastric emptying in type 2 diabetes. Diabetes Res Clin Pract 2019;154:27–34.
- [29] Horowitz M, Wishart JM, Jones KL, Hebbard GS. Gastric emptying in diabetes: an overview. Diabet Med 1996;13(9 Suppl 5):S16–22.
- [30] Gustafsson UO, Nygren J, Thorell A, Soop M, Hellström PM, Ljungqvist O, et al. Pre-operative carbohydrate loading may be used in type 2 diabetes patients. Acta Anaesthesiol Scand 2008;52(7):946–51.
- [31] Can MF, Yagci G, Dag B, Ozturk E, Gorgulu S, Simsek A, et al. Preoperative administration of oral carbohydrate-rich solutions: comparison of glucometabolic responses and tolerability between patients with and without insulin resistance. Nutrition 2009;25(1):72–7.
- [32] Cassady BA, McDonald JD, Maki KC. The impact of a carbohydrate loading drink on postprandial glycemic responses and gastric emptying in adults with

prediabetes and type 2 diabetes mellitus. JPEN - J Parenter Enter Nutr 2021;45(S1):S173-4.

- [33] Long CA, Fang ZB, Hu FY, Arya S, Brewster LP, Duggan E, et al. Poor glycemic control is a strong predictor of postoperative morbidity and mortality in patients undergoing vascular surgery. J Vasc Surg 2019;69(4):1219–26.
- [34] Nair BG, Neradilek MB, Newman SF, Horibe M. Association between acute phase perioperative glucose parameters and postoperative outcomes in diabetic and non-diabetic patients undergoing non-cardiac surgery. Am J Surg 2019;218(2):302–10.
- [35] Kwon S, Thompson R, Dellinger P, Yanez D, Farrohki E, Flum D. Importance of perioperative glycemic control in general surgery: a report from the Surgical Care and Outcomes Assessment Program. Ann Surg 2013;257(1):8–14.
- [36] Kotagal M, Symons RG, Hirsch IB, Umpierrez GE, Dellinger EP, Farrokhi ET, et al. Perioperative hyperglycemia and risk of adverse events among patients with and without diabetes. Ann Surg 2015;261(1):97–103.
- [37] Abdelmalak BB, Knittel J, Abdelmalak JB, Dalton JE, Christiansen E, Foss J, et al. Preoperative blood glucose concentrations and postoperative outcomes after elective non-cardiac surgery: an observational study. Br J Anaesth 2014;112(1):79–88.
- [38] Laffin MR, Li S, Brisebois R, Senior PA, Wang H. The use of a pre-operative carbohydrate drink in patients with diabetes mellitus: a prospective, noninferiority, cohort study. World J Surg 2018;42(7):1965-70.
- [39] Breuer JP, von Dossow V, von Heymann C, Griesbach M, von Schickfus M, Mackh E, et al. Preoperative oral carbohydrate administration to ASA III-IV patients undergoing elective cardiac surgery. Anesth Analg 2006;103(5): 1099–108.
- [40] Cua S, Humeidan M, Beal EW, Brethauer S, Pervo V, Papio J, et al. The effect of an enhanced recovery protocol on colorectal surgery patients with diabetes. J Surg Res 2021;257:153–60.
- [41] Talutis SD, Lee SY, Cheng D, Rosenkranz P, Alexanian SM, McAneny D. The impact of preoperative carbohydrate loading on patients with type II diabetes in an enhanced recovery after surgery protocol. Am J Surg 2020;220(4): 999–1003.
- [42] Suh S, Hetzel E, Alter-Troilo K, Lak K, Gould JC, Kindel TL, et al. The influence of preoperative carbohydrate loading on postoperative outcomes in bariatric surgery patients: a randomized, controlled trial. Surg Obes Relat Dis 2021;12(8):1480–8.
- [43] Azagury DE, Ris F, Pichard C, Volonté F, Karsegard L, Huber O. Does perioperative nutrition and oral carbohydrate load sustainably preserve muscle mass after bariatric surgery? A randomized control trial. Surg Obes Relat Dis 2015;11(4):920–6.
- [44] Brethauer SA, Petrick A, Grieco A, Fraker TR, Evans-Labok K, Smith AN, et al. Employing new enhanced recovery goals for bariatric surgery (ENERGY): a metabolic and bariatric surgery accreditation and quality improvement

(MBSAQIP) National Quality Improvement Project. Surg Obes Relat Dis 2019;15(11):1977–89.

- [45] Festejo-Villamiel KM, Yao C, Sioson M. Enhanced recovery after surgery (ERAS®) outcomes in patients with prior diagnosis of diabetes. J ASEAN Fed Endocr Soc 2019;34:73–9.
- [46] Singh SM, Liverpool A, Romeiser JL, Miller JD, Thacker J, Gan TJ, et al. A US survey of pre-operative carbohydrate-containing beverage use in colorectal enhanced recovery after surgery (ERAS) programs. Perioperat Med 2021;10(1):1–5.
- [47] Ackerman RS, Tufts CW, DePinto DG, Chen J, Altshuler JR, Serdiuk A, et al. How sweet is this? A review and evaluation of preoperative carbohydrate loading in the enhanced recovery after surgery model. Nutr Clin Pract 2020;35(2):246–53.
- [48] Ge LN, Wang L, Wang F. Effectiveness and safety of preoperative oral carbohydrates in enhanced recovery after surgery protocols for patients with diabetes mellitus: a systematic review. BioMed Res Int 2020;2020:1–6.
- [49] Knight P, Chou J, Dusseljee M, Verseman S, Elian A. Effective reduction in stress induced postoperative hyperglycemia in bariatric surgery by better carb loading. Am J Surg 2020;219(3):396–8.
- [50] Canbay Ö, Adar S, Karagöz Ah Çeleb C, Bilen CY. Effect of preoperative consumption of high carbohydrate drink (Pre-Op®) on postoperative metabolic stress reaction in patients undergoing radical prostatectomy. Int Urol Nephrol 2014;46(7):1329–33.
- [51] Singh BN, Dahiya D, Bagaria D, Saini V, Kaman L, Kaje V, et al. Effects of preoperative carbohydrates drinks on immediate postoperative outcome after day care laparoscopic cholecystectomy. Surg Endosc 2015;29:3267–72.
- [52] Cheng PL, Loh EW, Chen JT, Tam KW. Effects of preoperative oral carbohydrate on postoperative discomfort in patients undergoing elective surgery: a metaanalysis of randomized controlled trials. Langenbeck's Arch Surg 2021;406(4): 1–3.
- [53] Hausel J, Nygren J, Thorell A, Lagerkranser M, Ljungqvist O. Randomized clinical trial of the effects of oral preoperative carbohydrates on postoperative nausea and vomiting after laparoscopic cholecystectomy. Br J Surg 2005;92(4):415–21.
- [54] Shin S, Choi YS, Shin H, Yan IH, Park KK, Kwon HM, et al. Preoperative carbohydrate drinks do not decrease postoperative nausea and vomiting in type 2 diabetic patients undergoing total knee arthroplasty-a randomized controlled trial. J Am Acad Orthop Surg 2021;29(1):35–43.
- [55] Hyder JA, Hirschberg RE, Nguyen LL. Home discharge as a performance metric for surgery. JAMA Surg 2015;150(2):96–7.
- [56] Bell M, Eriksson LI, Svensson T, Hallqvist L, Granath F, Reilly J, et al. Days at home after surgery: an integrated and efficient outcome measure for clinical trials and quality assurance. EClinicalMedicine 2019;11:18–26.
- [57] How JA, Siedel JH, Shafer A. Post-operative gastroparesis following carbohydrate loading in a diabetic patient. Gynecol Oncol Rep 2021 May 1;36:100714.