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MINIREVIEWS

Preoperative carbohydrate load to reduce perioperative glycemic variability and improve surgical outcomes: A scoping review

Robert Canelli, Joseph Louca, Ciana Hartman, Federico Bilotta

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Abstract

The detrimental effects of both diabetes mellitus (DM) and hyperglycemia in the perioperative period are well established and have driven extensive efforts to control blood glucose concentration (BGC) in a variety of clinical settings. It is now appreciated that acute BGC spikes, hypoglycemia, and high glycemic variability (GV) lead to more endothelial dysfunction and oxidative stress than uncomplicated, chronically elevated BGC. In the perioperative setting, fasting is the primary approach to reducing the risk for pulmonary aspiration; however, prolonged fasting drives the body into a catabolic state and therefore may increase GV. Elevated GV in the perioperative period is associated with an increased risk for postoperative complications, including morbidity and mortality. These challenges pose a conundrum for the management of patients typically instructed to fast for at least 8 h before surgery. Preliminary evidence suggests that the administration of an oral preoperative carbohydrate load (PCL) to stimulate endogenous insulin production and reduce GV in the perioperative period may attenuate BGC spikes and ultimately decrease postoperative morbidity, without significantly increasing the risk of pulmonary aspiration. The aim of this scoping review is to summarize the available evidence on the impact of PCL on perioperative GV and surgical outcomes, with an emphasis on evidence pertaining to patients with DM. The clinical relevance of GV will be summarized, the relationship between GV and postoperative course will be explored, and the impact of PCL on GV and surgical outcomes will be presented. A total of 13 articles, presented in three sections, were chosen for inclusion. This scoping review concludes that the benefits of a PCL outweigh the risks in most patients, even in those with well controlled type 2 DM. The administration of a PCL might

effectively minimize metabolic derangements such as GV and ultimately result in reduced postoperative morbidity and mortality, but this remains to be proven. Future efforts to standardize the content and timing of a PCL are needed. Ultimately, a rigorous data-driven consensus opinion regarding PCL administration that identifies optimal carbohydrate content, volume, and timing of ingestion should be established.

Key Words: Preoperative carbohydrate load; Glycemic variability; Surgical outcomes; Glucose variability; Blood glucose concentration

Core Tip: Preoperative fasting reduces the risk for aspiration perioperatively; however, it may contribute to intraoperative insulin resistance and glycemic variability (GV). High GV is associated with an increased risk for postoperative complications, including mortality. The administration of a preoperative carbohydrate load (PCL) may reduce perioperative GV and lower the risk for postoperative complications. In this scoping review, we establish the clear negative impact of GV in patients with and without diabetes mellitus in a wide range of clinical settings. However, we are unable to determine from the current body of literature whether a PCL reduces GV intraoperatively and improves surgical outcomes. Future efforts to standardize the content and timing of the carbohydrate load are needed, as well as prospective studies that are designed to evaluate the carbohydrate load effect on GV indices.

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INTRODUCTION

The detrimental effects of both diabetes mellitus (DM) and hyperglycemia in the perioperative period are well established and have driven extensive efforts to control blood glucose concentration (BGC) in a variety of clinical settings[1-3].

In critically ill patients, intensive insulin therapy titrated to maintain a BGC of 80-110 mg/dL (4.44-6.11 mmol/L) has been shown to reduce morbidity and mortality[4]. In neurosurgical patients, intensive insulin therapy resulted in reduced postoperative infection rates and shorter intensive care unit (ICU) length of stay[5]. However, efforts to maintain tight glycemic control have often resulted in a significant increase in episodes of hypoglycemia[5,6], a complication that has been associated with an increase in all-cause mortality, cardiovascular death, and death due to infectious disease[7], as well as a prolonged ICU length of stay[8].

It is now appreciated that acute BGC spikes, hypoglycemia, and high glycemic variability (GV) lead to more endothelial dysfunction and oxidative stress than uncomplicated, chronically elevated BGC. This holds true in patients with and without DM[9]. Preoperative fasting is the primary approach to reducing the risk for pulmonary aspiration in the perioperative phase; however, prolonged fasting drives the body into a catabolic state and therefore may increase GV, which can be problematic for patients that have been instructed to fast for at least 8 h before surgery. The stress response to surgery enhances gluconeogenesis and hinders glucose uptakes, further exacerbating GV, *via* the release of stress hormones and immune response suppression[10].

Elevated GV in the perioperative period is associated with an increased risk for postoperative complications, including morbidity and mortality. GV is more pronounced in patients with baseline metabolic disorders such as DM and during certain surgical procedures such as open-heart surgery. Preliminary evidence suggests that the administration of a preoperative carbohydrate load (PCL) to stimulate endogenous insulin production and reduce GV in the perioperative period may attenuate BGC spikes and ultimately decrease postoperative morbidity, however, a data-driven consensus opinion regarding this approach has not been established.

The aim of this scoping review is to summarize the available evidence on the impact of PCL on perioperative GV and surgical outcomes, with an emphasis on evidence pertaining to patients with DM. The clinical relevance of GV will be summarized, the relationship between GV and postoperative course will be explored, and the impact of PCL on GV and surgical outcomes will be presented.

A scoping review was used to map this complex, multidisciplinary topic. It was designed to capture the important facets of emerging evidence pertaining to perioperative GV, PCL, and postoperative

outcomes in patients with and without DM. The methodology of this scoping review was based on the framework of Arksey and O'Malley[11]. A scoping review was chosen to capture a wide range of literature that may have been overlooked or eliminated in a systematic review.

The first step in this scoping review was to establish the clinical implications of high GV and related surgical outcomes by performing a preliminary, non-systematic literature search. The keyword terms searched in MEDLINE/PubMed and Google Scholar search engines for this scoping review included glycemic, glucose, variability, surgery, surgical, outcomes, and postoperative.

After establishing the problem, the research question of this scoping review was developed. The effect of PCL on perioperative GV and postoperative outcomes in patients with and without DM was established as the aim of this study. The keyword search terms used to identify pertinent studies that addressed the topic included PCL, glucose variability, GV, DM, surgery, and surgical outcome.

Articles were screened for relevance based on title and abstract. Relevant articles were read and ranked by all authors individually based on quality of study, pertinence to the aim of the study, impact factor of the journal, and impact index per article score. The impact index per article score was obtained from *Reference Citation Analysis* (https://www.referencecitationanalysis.com/), an artificial intelligence technology-based open multidisciplinary citation analysis database. Authors then conferred to select the final papers to be included in each section of this scoping review. Consideration was given to include articles that were very recently published or felt to be pertinent despite low impact index per article scores.

GLYCEMIC VARIABILITY: CLINICAL RELEVANCE

Hyperglycemia, hypoglycemia and GV are associated with mitochondrial oxidative stress, endothelial cell apoptosis, and inflammatory cytokine release[12]. In this section, the 4 articles listed in Table 1 will identify measurable GV indices and will present the clinical relevance of high GV with respect to morbidity and mortality in patients with and without DM.

A multicenter, retrospective observational study was one of the first to investigate the relationship between GV, rather than hyperglycemia or hypoglycemia, and outcomes and had an impact index per article score of 35. This study analyzed 168837 blood glucose measurements from a cohort of 7049 critically ill patients. Patients were divided into survivors and non-survivors for comparison. Two different indices for GV were measured: The standard deviation (SD) from the mean BGC, and the coefficient of variance (CV) defined as the SD divided by the mean BGC expressed as a percentage. Both SD (1.7 ± 1.3 *vs* 2.3 ± 1.6 mmol/L, $P < 0.001$) and CV (20 ± 12 *vs* 26 ± 13%, $P < 0.001$) were significantly lower for ICU survivors when compared to non-survivors. The two GV indices were independent predictors of ICU and hospital mortality and were stronger predictors of mortality than mean BGC[13].

A single-center, retrospective cohort study of 1246 patients with sepsis aimed to investigate different measures of GV to determine which was the best predictor of in-hospital mortality risk. This article had an impact index per article score of 19.2. Three different indices for GV were measured: Glycemic lability index (GLI), mean amplitude of glycemic excursion (MAGE), and SD from the mean BGC. Although all 3 GV indices were significant predictors of mortality in patients with sepsis, GLI predicted in-hospital mortality [odds ratio (OR) 1.25, 95%CI: 1.20-1.32, $P < 0.001$] better than MAGE (OR 1.12, 95%CI: 1.07-1.18, $P < 0.001$) and SD (OR 1.16, 95%CI: 1.11-1.21, $P < 0.001$). Additionally, with each increasing GLI decile, a higher in-hospital mortality rate was observed. The association of GLI and mortality remained after adjusting for a diagnosis of DM[14].

A retrospective study of 1641 patients with an ICU stay > 2 d aimed to determine the association between GV and outcome measures, including ICU mortality and ICU-acquired infection. GV was assessed using four different indices: SD, CV, GLI, and MAGE. When compared to ICU survivors, ICU non-survivors had higher GV as determined by GLI [75.6 *vs* 50.1 $(mmol/L)^2/h/wk$, $P < 0.001$], CV (23 *vs* 21%, $P < 0.001$), SD (1.7 *vs* 1.4 mmol/L, $P < 0.001$), and MAGE (2.7 *vs* 2.4 mmol/L, $P < 0.001$). Mean BGC was not predictive of ICU mortality (7.0 *vs* 7.0 mmol/L, *P* value not reported). The predictive ability for mortality was not different between SD, CV, GLI, and MAGE; however, the risk of death increased progressively with each increase in quartile of GLI. When compared to patients without infection, patients with ICU-acquired infection had higher GV as determined by GLI [73.5 *vs* 44.6 $(mmol/L)^2/h/wk$, $P < 0.001$], CV (23 *vs* 20%, $P < 0.001$), SD (1.6 *vs* 1.4 mmol/L, $P < 0.001$), and MAGE (2.7 *vs* 2.3 mmol/L, $P < 0.001$). Mean BGC was not predictive of ICU-acquired infection (7.0 *vs* 7.0 mmol/L, *P* value not reported). GLI had a better predictive ability for ICU-acquired infections compared to MAGE, CV and SD. In patients without DM, GLI was significantly associated with ICU mortality and ICU-acquired infections, with increasing risk for each quartile increase in GLI. For patients with DM, there was no significant association between GLI and ICU mortality; however, there was an association between GLI and ICU-acquired infection[15].

A prospective observational study of 8894 patients admitted to the surgical ward aimed to investigate the association between GV and clinical outcomes including hospital length of stay, readmission rates, and mortality in patients with and without DM. GV was measured in two ways: SD and CV. Higher SD and CV were both associated with longer hospital length of stay in patients with DM (9 ± 8 *vs* 7 ± 5 d for

Table 1 Glycemic variability: Clinical relevance

Ref.	Patient population	Variability index	Reported results
Egi *et al*[13], 2006	7049 ICU patients, DM included		ICU survivors *vs* ICU non-survivors
		SD	SD: 1.7 *vs* 2.3 mmol/L, $P < 0.001$
		CV	CV: 20 *vs* 26%, $P < 0.001$
Ali *et al*[14], 2008	1246 patients with sepsis, DM included		Mortality crude odds ratio, 95%CI
		GLI	GLI: 1.25, 1.20-1.32, $P < 0.001$
		MAGE	MAGE: 1.12, 1.07-1.18, $P < 0.001$
		SD	SD: 1.16, 1.11-1.21, $P < 0.001$
Donati *et al*[15], 2014	1641 ICU patients, DM included		ICU survivors *vs* ICU non-survivors
		SD	SD: 1.4 *vs* 1.7 mmol/L, $P < 0.001$
		CV	CV: 21 *vs* 23%, $P < 0.001$
		GLI	GLI: 50.1 *vs* 75.6 (mmol/L)2/h/wk, $P < 0.001$
		MAGE	MAGE: 2.4 *vs* 2.7 mmol/L, $P < 0.001$
			No infection *vs* ICU-acquired infection
		SD	SD: 1.4 *vs* 1.6 mmol/L, $P < 0.001$
		CV	CV: 20 *vs* 23%, $P < 0.001$
		GLI	GLI: 44.6 *vs* 73.5 (mmol/L) 2/h/wk, $P < 0.001$
		MAGE	MAGE: 2.3 *vs* 2.7 mmol/L, $P < 0.001$
Akirov *et al*[16], 2019	8894 surgical patients, DM included		Hospital LOS: Low GV *vs* High GV
		SD	DM SD: 7 *vs* 9 d, $P < 0.001$
		SD	No DM SD: 7 *vs* 9 d, $P < 0.001$
		CV	DM CV: 7 *vs* 9 d, $P < 0.001$
		CV	No DM: CV 7 *vs* 9 d, $P < 0.001$
			30 d mortality: Low GV *vs* High GV
		SD	DM SD: 5% *vs* 8%, $P < 0.05$
		SD	No DM SD: 3% *vs* 9%, $P < 0.05$
		CV	DM CV: 5% *vs* 9%, $P < 0.05$
		CV	No DM CV: 3% *vs* 9%, $P < 0.05$

ICU: Intensive care unit; DM: Diabetes mellitus; CV: Coefficient of variance; GLI: Glycemic lability index; MAGE: Mean amplitude of glycemic excursion; LOS: Length of stay; GV: Glycemic variability.

both CV and SD, $P < 0.001$ for both) and without DM (9 ± 8 *vs* 7 ± 6 d for both CV and SD, $P < 0.001$ for both). There was no significant association between GV and readmission rates for both DM and non-DM patients. When compared to the low CV cohort, high CV was associated with increased 30-d mortality in patients with DM (9 *vs* 5%, OR = 1.8, 95%CI: 1.2-2.6) and without DM (9 *vs* 3%, OR = 2.7, 95%CI: 2.1-3.3). Similarly, high SD was associated with increased 30-d mortality when compared to the low SD cohort in patients with DM (8 *vs* 5%, OR = 1.6, 95%CI: 1.1-2.4) and without DM (9 *vs* 3%, OR = 2.7, 95%CI: 2.2-3.4)[16].

In summary, for patients in high acuity settings, elevated GV is associated with worse outcomes including hospital length of stay, readmission rates, and overall morbidity and mortality in patients with and without DM. This holds true for a variety of measured GV indices, including SD, CV, GLI, and MAGE. All GV indices appear to be better predictors of morbidity and mortality than mean BGC.

PERIOPERATIVE GLYCEMIC VARIABILITY AND POSTOPERATIVE COURSE

Due to current preoperative fasting guidelines, stress-induced metabolic changes from surgery, and

coexisting endocrine disorders in a subset of surgical patients, the perioperative period is frequently associated with insulin resistance and high GV[17]. In this section, the 3 articles listed in Table 2 will present the impact of perioperative GV on postoperative morbidity and mortality.

The relationship between GV and surgical outcomes has been studied in cardiac surgery. Abnormal GV may be more pronounced in this surgical population as a result of the elevated stress response associated with cardiopulmonary bypass and increased insulin resistance due to iatrogenic intraoperative hypothermia. A prospective, single center observational study aimed to establish whether GV was associated with major adverse events (MAEs) after cardiac surgery in DM and non-DM patients, and had an impact index per article score of 7.2. A total of 1461 patients undergoing coronary artery bypass grafting with or without valvular surgery were enrolled. All enrolled patients had glycated hemoglobin (HbA1c) measured within 30 d of surgery. Patients were grouped into HbA1c > 6.5% and < 6.5% for comparison, and GV was measured by CV. Major adverse event was a composite primary endpoint that included in-hospital death, myocardial infarction, re-operation, deep sternal wound infection, cardiac tamponade, pneumonia, stroke, or renal failure. Patients that experienced an MAE had higher CV when compared to those that did not have an MAE (24 ± 0.07 *vs* 21 ± 0.08%, $P = 0.001$). Patients with an HbA1c > 6.5% had a higher CV (26 ± 9 *vs* 20 ± 7%, $P < 0.001$) than patients with an HbA1c < 6.5%[18].

A retrospective study of 5058 patients aimed to investigate the relationship between GV and adverse outcomes following total hip and knee arthroplasty and had an impact index per article score of 6. Patients were grouped into tertiles defined by CV for comparison of low variability (first tertile, CV ≤ 11.23%), medium variability (second tertile, CV 11.24%-18.54%), and high variability (third tertile, CV ≥ 18.55%). Adverse outcomes included hospital length of stay (LOS), 90-d mortality, re-operations, periprosthetic joint infections and surgical site infections. Average LOS increased as tertile increased (first 4.6 ± 2.5 d, second 5.6 ± 3.9 d, third 6.5 ± 5.5 d, $P < 0.001$). When compared to patients in the first tertile of CV, patients in the third tertile had an increase in the mortality rate at 90 d (0.4 *vs* 0.1%, OR 3.25, 95%CI: 0.93-11.35, $P = 0.06$), periprosthetic joint infections (0.9 *vs* 0.5%, OR 1.86, 95%CI: 1.10-3.13, $P = 0.02$), surgical site infections (1.4 *vs* 1%, OR 1.49, 95%CI: 1.01-2.21, $P = 0.03$). There was no difference in the re-operation rate between these two groups[19].

A retrospective cohort study of 264 patients investigated the relationship between GV and postoperative outcomes for patients having posterior cervical decompression and fusion. This was a relatively new study in the literature and had a low impact index per article score but was included because of its pertinence to the topic. Patients were grouped into tertiles based on postoperative CV (low < 12.3%, moderate 12.4%-20.7% and high 20.8%-57.9%). Of note, patients with types 1 and 2 DM were included. Measured outcomes included inpatient complications, hospital LOS, 90-d readmission, revision, and surgical site infection rates. There was no significant difference in the overall rate of inpatient complications between the low (12.5%), moderate (17.0%), and high (20.4%) CV tertiles ($P = 0.37$). The average hospital LOS was significantly increased for higher CV tertile (low 3.90 *vs* moderate 5.73 *vs* high 6.06 d, $P = 0.01$). When compared to the low CV tertile, the high CV tertile was associated with significantly increased odds of hospital readmission (OR 4.77, 95%CI: 1.10-6.05, $P = 0.03$) and development of surgical site infection (OR 4.35, 95%CI: 1.09-15.05, $P = 0.04$), but not rates of revision surgery (OR 1.76, 95%CI: 0.70-6.50, $P = 0.19$)[20].

In summary, elevated perioperative GV is associated with increased hospital length of stay and an increased risk for postoperative morbidity and mortality for patients with and without DM. The risk of reoperation does not appear to be associated with elevated GV.

PREOPERATIVE CARBOHYDRATE LOAD: IMPACT ON GLYCEMIC VARIABILITY AND SURGICAL OUTCOMES IN PATIENTS WITH AND WITHOUT DM

Reducing the magnitude of GV has been shown to reduce oxidative stress and systemic inflammatory markers in nonsurgical, diabetic patients[21]. In surgical patients, the administration of a PCL increases endogenous insulin production, reduces the risk of the body entering a catabolic state, and may reduce GV. In this section, the 6 studies listed in Table 3 will present the impact of PCL on GV and surgical outcomes. Notably, early PCL studies, including the first three in Table 3, excluded patients with DM, citing concerns for delayed gastric emptying, increased risk for aspiration, and/or exaggerated BGC response to the PCL. The subsequent three studies were included in this review because they established the safety of PCL administration to patients with type 2 DM.

A single center, randomized controlled trial aimed to determine the effectiveness of a PCL on postoperative nausea and vomiting and postoperative pain in same-day surgery patients. This article had an impact index per article score of 5.0. Patients with DM were excluded. A total of 120 patients scheduled for laparoscopic cholecystectomy were randomized into three groups: 40 patients in the intervention group were instructed to consume one PCL drink [400 mL, 12.5% carbohydrates (CHO), 500 kcal/L] the night before surgery and a half PCL drink (200 mL, 12.5% CHO, 500 kcal/L) 2 h prior to surgery, 40 patients in the placebo group were instructed to drink 400 mL of flavored (0 kcal/L) water before midnight and 200 mL of flavored water 2 h prior to surgery, and 40 patients in the control group

Table 2 Perioperative glycemic variability and postoperative course

Ref.	Patient population	Variability index	Reported results
Subramaniam *et al*[18], 2014	1461 cardiac surgery patients, DM included	CV	No MAE *vs* MAE
			CV: 21% *vs* 24%, $P = 0.001$
			HbA1c < 6.5% *vs* > 6.5%
			CV: 20% *vs* 26%, $P < 0.001$
Shohat *et al*[19], 2018	5058 patients for total joint arthroplasty	CV	1st tertile of CV *vs* 3rd tertile of CV
			Mortality: 0.1% *vs* 0.4%, $P = 0.06$
			PPJI: 0.5% *vs* 0.9%, $P = 0.02$
			SSI: 1% *vs* 1.4%, $P = 0.03$
			Reop: 1.6% *vs* 1.5%, $P = 0.83$
Patel *et al*[20], 2021	264 patients for cervical spine surgery	CV	1st tertile of CV *vs* 3rd tertile of CV
			Complication: 12.5% *vs* 20.4%, $P = 0.37$
			Hospital LOS: 3.9 *vs* 6.06 d, $P = 0.01$
			Readmission: 3.4% *vs* 7.8%, $P = 0.03$
			SSI: 1.1% *vs* 9.5%, $P = 0.04$
			Reop: 0.4% *vs* 3.8%, $P = 0.19$

DM: Diabetes mellitus; CV: Coefficient of variance; MAE: Major adverse event; MI: Myocardial infarction; Reop: Reoperation; DSWI: Deep sternal wound infection; CVA: Cerebrovascular accident; PNA: Pneumonia; PPJI: Periprosthetic joint infection; SSI: Surgical site infection.

adhered to traditional fasting after midnight guidelines. The intervention group reported lower nausea scores 0-4 h postoperatively when compared to the placebo group (0.65 ± 0.70 *vs* 1.30 ± 0.85, $P < 0.001$) and the control group (0.65 ± 0.70 *vs* 1.23 ± 1.10, $P = 0.009$) but no significant difference in nausea between 4-12 h and 12-24 h. The incidence of vomiting at 0-4 h was 17.5% for the intervention group, 42.5% for the placebo group, and 47.5% for the control group which was significantly lower for the intervention group when compared to the placebo group and control group ($P < 0.001$ and $P = 0.004$ respectively). Pain scores were significantly lower in the intervention group when compared to the placebo and control groups at 0-4 h ($P = 0.001$) and 4-12 h ($P = 0.005$)[22].

A large multi-center, randomized, placebo-controlled phase III trial aimed to evaluate the effectiveness of PCL *vs* placebo in preventing postoperative infections after major elective abdominal surgery. This article had an impact index per article score of 13.5. There was no traditional fasting group in this study. Patients with DM and patients with fasting BGC > 125 mg/dL (7 mmol/L) were excluded. A total of 662 patients were enrolled and randomized into two groups: 331 patients in the intervention group were instructed to consume one PCL drink (800 mL, 12.6% CHO, 500 kcal/L) from the night before surgery to 2 h prior to surgery, and 331 patients in the placebo group received 800 mL of water with the same consumption directions. The primary outcome was the occurrence of at least one postoperative infection including superficial or deep wound infection, organ/space infection, urinary tract infection, pneumonia, sepsis, and septic shock. The primary outcome occurred in 16.3% of the intervention group and 16.0% of the placebo group [relative risk (RR) 1.019, 95%CI: 0.720-1.442, $P = 1.00$] which was not significantly different. Secondary outcomes included insulin requirements, antibiotic therapy, total complications, reoperation, ICU LOS, and hospital LOS. BGC was recorded from the first hour after surgery to postoperative day 3 and insulin was administered for BGC > 180 mg/dL (10 mmol/L). Insulin was required in 2.4% of patients in the intervention group and 16.0% of patients in the placebo group (RR 0.15, 95%CI: 0.07-0.31, $P < 0.001$), with a number needed to treat of 7. No other secondary outcomes were significantly different. Notably, no aspiration episodes were observed in either group[23].

A single-center, randomized controlled study aimed to evaluate the effect of PCL *vs* fasting on outcomes in patients undergoing elective craniotomy. This article had an impact index per article score of 3.0. Patients with DM and patients with fasting BGC > 125 mg/dL (7 mmol/L) were excluded. A total of 120 patients were enrolled into two groups: 58 patients in the intervention group were instructed to consume one PCL drink (400 mL, 12.5% CHO, 500 kcal/L) 2 h before surgery and 62 patients in the control group fasted for at least 8 h prior to surgery. The primary outcome was glucose homeostasis defined by BGC measurements from blood samples drawn perioperatively. The BGC was significantly higher in the intervention group upon entering the operating room (6.3 ± 1.6 *vs* 5.6 ± 1.0 mmol/L, $P =$

Table 3 Preoperative carbohydrate load: Impact on glycemic variability and surgical outcomes

Ref.	Patient population	PCL composition and timing	Reported conclusion
Singh *et al*[22], 2015	120 same-day surgery patients, DM excluded	12.5% CHO, 500 kcal/L; 400 mL before MN + 200 mL 2 h before surgery	Intervention *vs* placebo *vs* control Nausea score 0-4 h: 0.65 *vs* 1.30 *vs* 1.23, $P = 0.001$ 4-12 h: 0.70 *vs* 0.83 *vs* 1.05, $P = 0.066$ 12-24 h: 0.25 *vs* 0.43 *vs* 0.35, $P = 0.257$ Vomit incidence 0-4 h: 17.5% *vs* 42.5% *vs* 47.5%, P (I-P) ≤ 0.001, P (I-C) = 0.004 4-12 h: 7.5% *vs* 12.5% *vs* 32.5%, P (I-P) = 0.459, P (I-C) = 0.005 12-24 h: 0% *vs* 2.5% *vs* 2.5%, P (I-P) = 0.314, P (I-C) = 0.314 Pain score 0-4 h: 5.75 *vs* 7.13 *vs* 6.95, $P = 0.001$ 4-12 h: 3.53 *vs* 4.08 *vs* 4.65, $P = 0.005$ 12-24 h: 1.95 *vs* 2.08 *vs* 2.25, $P = 0.223$
Gianotti *et al*[23], 2018	662 patients undergoing elective major abdominal surgery, DM excluded	12.6% CHO, 500 kcal/L; 800 mL between 8 pm and 2 h before surgery	Intervention *vs* placebo Composite infection: 16.3% *vs* 16.0%, $P = 1.00$ Insulin requirement: 2.4% *vs* 16%, $P < 0.001$ Antibiotic therapy: 30.8% *vs* 29.9%, $P = 0.87$ Total complications: 28.1% *vs* 28.4%, $P = 1.00$ Hospital LOS: 11 *vs* 11 d, $P = 0.44$ Aspiration events: 0 *vs* 0, $P = 1.00$
Liu *et al*[24], 2019	120 patients undergoing elective craniotomy, DM excluded	12.5% CHO, 500 kcal/L; 400 mL 2 h before surgery	Intervention *vs* control Preop BGC: 6.3 *vs* 5.6 mmol/L, $P = 0.020$ POD3 BGC: 5.6 *vs* 6.3 mmol/L, $P = 0.001$ POD3 handgrip: 25.3 *vs* 19.9 kg, $P < 0.0001$ POD3 PEFR: 315.8 *vs* 270.0 L/min, $P = 0.036$ Postop LOS: 4 *vs* 7 d, $P < 0.0001$
Talutis *et al*[25], 2020	169 patients with DM2 undergoing elective major abdominal surgery	55 g CHO in 32 oz (946.35 mL), 5.8% CHO; 16 oz (473 mL) before MN + 16 oz 2 h before surgery	Intervention *vs* control Preop BGC: 142 *vs* 129.5 mg/dL, $P = 0.017$ 1st postop BGC: 159 *vs* 173 mg/dL, $P = 0.23$ POD1 BGC: 152 *vs* 137.5 mg/dL, $P = 0.004$ Intraop insulin: 0-16 *vs* 0-19 units, $P =$

			0.63 POD1 insulin: 0-75 *vs* 0-79 units, P = 0.09 Complication rate: 20% *vs* 27%, P = 0.65 Hospital LOS: 2 *vs* 2 d, P = 0.38 Aspiration events: 0 *vs* 0, P = 1.00
Suh *et al*[26], 2021	134 patients undergoing bariatric surgery, DM2 included	50 g CHO in 296 mL, 16.9% CHO, 682 kcal/L; 296 mL before MN + 296 mL 3 h before surgery	Intervention *vs* control Hospital LOS: 2.0 *vs* 2.1 d, P = 0.65 PONV score: 13.8 *vs* 15.4, P = 0.77 BGC: 140.7 *vs* 135.3 mg/dL, P = 0.34 Antiemetics: 5.3 *vs* 6 doses, P = 0.43 Readmission: 4.7% *vs* 5.7%, P = 0.79 Complication: 3.1% *vs* 4.3%, P = 0.72 Aspiration events: 0 *vs* 0, P = 1.00
Lee *et al*[27], 2022	46 patients with DM2 undergoing elective total joint arthroplasty	12.8% CHO, 500 kcal/mL; 400 mL 2-3 h before anesthesia	Intervention *vs* control CV: 16.5% *vs* 10.1%, P = 0.008 J index: 25.3 *vs* 18.9, P = 0.046 HOMA-IR: 8.5 *vs* 2.7, P < 0.001 Hospital LOS: 3 *vs* 3 d, P = 0.516 Nausea: 46% *vs* 29%, P = 0.402 Vomiting: 32% *vs* 8%, P = 0.066 Hypotension: 5% *vs* 13%, P = 0.609 Delirium: 18% *vs* 0%, P = 0.045 Wound dehiscence: 9% *vs* 8%, P = 0.999 Pain score at 6 h: 2 *vs* 2, P = 0.725

PCL: Preoperative carbohydrate load; DM: Diabetes mellitus; CHO: Carbohydrate; MN: Midnight; LOS: Length of stay; BGC: Blood glucose concentration; Preop: Preoperative; POD: Postoperative day; PEFR: Peak expiratory flow rate; postop: Postoperative; DM2: Type 2 diabetes mellitus; ERAS: Enhanced recovery after surgery; intraop: Intraoperative; PONV: Postoperative nausea and vomiting; CV: Coefficient of variance; HOMA-IR: Homeostasis Model Assessment Insulin Resistance.

0.020); was similar on postoperative days 1 and 2; and was significantly lower on postoperative day 3 in the intervention group (5.6 ± 1.0 *vs* 6.3 ± 1.2 mmol/, P = 0.001). Secondary outcomes included handgrip strength, pulmonary function as measured by peak expiratory flow rate, postoperative surgical and nonsurgical complications, and length of stay. Hand grip strength (25.3 ± 7.1 kg *vs* 19.9 ± 7.5 kg, P < 0.0001) and peak expiratory flow rate (315.8 ± 91.5 L/min *vs* 270.0 ± 102.7 L/min, P = 0.036) were significantly better in the intervention group on postoperative day 3. Postoperative length of stay was significantly reduced in the intervention group (4 *vs* 7 d, P < 0.0001)[24].

A retrospective chart review aimed to determine the effects of a PCL as part of an enhanced recovery after surgery (ERAS) pathway on patients with DM. This article had an impact index per article score of 4.0. The intervention group included a total of 80 ERAS patients with DM undergoing bariatric, gastric, pancreatic, and colorectal surgery, and was compared to the control group of 89 non-ERAS patients with DM undergoing similar surgeries from 1 year prior to inception of the ERAS pathway. Patients with a history of type 1 DM were excluded. The patients in the ERAS group were instructed to consume one PCL drink (473 mL, 5.8% CHO) on the night before surgery and another PCL drink on the morning of surgery. The non-ERAS patients adhered to traditional fasting after midnight guidelines. Primary outcomes included perioperative BGC measurements and insulin requirements. Secondary outcomes included development of postoperative complications. The ERAS patients with DM had elevated BGC measurements in the preoperative holding area (142, range 66-392 *vs* 129.5, range 82-316 mg/dL, P =

0.017) and on postoperative day 1 (152, range 84-323 *vs* 137.5, range 86-279 mg/dL, $P = 0.004$) when compared to non-ERAS patients with DM. Intraoperative BGC and postoperative BGC on days 2-5 were not different. Intraoperative and postoperative insulin administration did not differ between the two groups. The complication rates and hospital length of stay were not significantly different. None of the patients experienced an aspiration event[25].

A single center, randomized controlled trial aimed to characterize the impact of PCL administration on postoperative outcomes in bariatric surgery. This article had an impact index per article score of 2.0 but was felt to contribute significantly to the body of literature in this scoping review. Patients with DM were included in this study. A total of 134 patients were enrolled and randomized into 2 groups: 64 patients in the intervention group were instructed to consume one PCL drink (296 mL, 16.9% CHO, 682 kcal/L) on the night before surgery and another PCL drink 3 h before surgery and 70 patients in the control group adhered to traditional "nothing by mouth" after midnight prior to surgery fasting guidelines. The primary outcome was a clinically significant reduction in hospital length of stay. Secondary outcomes included postoperative nausea and vomiting (PONV), postoperative BGC, antiemetics received, hospital readmission rates, and overall complications amongst other outcomes. There was no significant difference noted in hospital length of stay between the intervention and control groups (2.0 ± 1.2 *vs* 2.1 ± 0.9 d, $P = 0.65$). Additionally, there was no significant difference between the two groups with regards to PONV scores, postoperative BGC measurements, antiemetics received, hospital readmission rates, or postoperative complication rates. Notably, none of the patients experienced aspiration during induction of anesthesia[26].

A single center, randomized control trial investigated the effects of PCL on perioperative GV, gastric volume, and postoperative outcomes in patients with DM undergoing elective total knee and hip arthroplasty. This article was recently published and so has not had a significant amount of time to be included as a citation in other works. A total of 46 patients were included in the final cohort of this study. Patients were randomized into 2 groups: 22 patients in the intervention group were instructed to consume one PCL drink (400 mL, 12.8% CHO, 500 kcal/L) 2-3 h before anesthesia and 24 patients in the control group adhered to traditional fasting after midnight guidelines. The primary outcome was GV measured by CV and J index ($0.001 \times [\text{mean} + \text{SD}]^2$), calculated from capillary BGC measurements taken at 5 intraoperative time points. Patients in the intervention group experienced higher CV (16.5% *vs* 10.1%, $P = 0.008$) and J index scores (25.3, range 17.9-39.7 *vs* 18.9, range 16.0-25.3, $P = 0.046$) than the control group. Insulin resistance was calculated using the homeostasis model assessment insulin resistance value (HOMA-IR) = [fasting glucose (mg/dL) × fasting insulin (μU/mL)]/405. Patients in the intervention group experienced higher HOMA-IR scores than the control group (8.5, range 5.6-19.2 *vs* 2.7, range 2.2-4.8, $P < 0.001$). Secondary outcomes included gastric volume, and postoperative complications including nausea, vomiting, dizziness, hypotension, delirium, wound dehiscence, and pain scores. There was no difference between the two groups with respect to gastric volume or any of the reported postoperative complications, except for delirium which was higher in the intervention group (4 *vs* 0, $P = 0.045$)[27].

In summary, several early studies that examined patients without DM demonstrated that PCL significantly improved patient experience (nausea, vomiting, pain) and postoperative muscle function (hand grip strength, peak expiratory flow rate). Administration of a PCL in this patient population also reduced postoperative insulin requirements and improved postoperative BGC. Later studies that did not exclude patients with DM showed that administration of a PCL does not increase the risk for postoperative morbidity in most respects, in particular with regards to aspiration of gastric contents.

DISCUSSION

In this original scoping review, the clinical relevance of GV and the clinically significant relationship between GV and surgical outcomes were described. The available evidence on the impact of PCL on GV and surgical outcomes in patients with and without DM was presented. High GV has clear negative implications in both patients with and without DM in a wide range of inpatient clinical settings; however, it remains uncertain whether PCL reduces GV perioperatively and improves surgical outcomes in this patient population.

The clinical impact of GV has been studied extensively, in particular as a predictor of morbidity and mortality in patients with and without DM in a variety of inpatient clinical settings, including surgical and non-surgical. Several different indices of GV, including SD, CV, GLI, and MAGE, show a correlation with morbidity and mortality, and so practitioners that use this data point may reasonably select whichever index is most accessible for their practice setting. At the same time, the lack of a gold standard GV index may reduce standardization across study designs and produce clinical data that is more challenging to compare. Two studies presented in this scoping review suggest that GLI may be the most accurate predictor[14,15]; however, one study recommends CV as the most practically accessible [20].

There is a lack of consensus on both the carbohydrate composition and the volume of an optimal PCL [28]. The type of dextrose-containing solutions used in the reviewed PCL studies varied. Additionally,

the timing of PCL administration varied throughout the examined literature. Future research to elucidate the optimal type and timing of PCL administration would allow subsequent clinical trials to follow more standardized protocols and therefore more definitively determine the risks and benefits of the PCL.

Of the studies analyzed for this scoping review, there is a paucity of evidence investigating the impact of a PCL on perioperative GV. The one such study included in this review did find an increase in GV after PCL administration in 46 patients with DM; however, the investigators analyzed BGC obtained from capillary blood, which may not be as accurate as whole blood[29]. In a retrospective analysis of 83 non-diabetic patients undergoing colorectal surgery, investigators found that a PCL with complex carbohydrates had a beneficial impact on GV when compared to a PCL with simple carbohydrates[30]. More studies looking directly at the effect of a PCL on GV indices are needed before a consensus determination can be reached. Similarly, there is insufficient evidence to determine that PCL improves surgical outcomes for patients with and without DM, though it does not appear to be associated with worse outcomes.

Despite the widespread exclusion of patients with DM in early PCL studies, there is a significant body of evidence suggesting that PCL is safe in patients with well controlled type 2 DM. A narrative review of emerging evidence on PCL safety and effectiveness in patients with type 2 DM suggested that consuming a PCL raises preoperative BGC; however, the PCL did not significantly impact intraoperative or postoperative BGC[30]. Additionally, the PCL improved patient satisfaction measures postoperatively without increasing the risk for complications such as aspiration of gastric contents, pneumonia, and postoperative surgical site infection[31-34]. Of note, because the PCL reduces GV by stimulating endogenous insulin secretion, it is not recommended for those with insulin deficiency such as type 1 DM and should be used with caution in patients with poorly controlled type 2 DM or severe insulin resistance[35]. Large randomized placebo controlled trials investigating the PCL could ultimately determine whether it improves a variety of clinical outcomes or is solely a non-inferior intervention that improves patients' perioperative comfort and satisfaction.

This scoping review was intended to link clinical concepts together with a historical perspective to identify knowledge gaps and research opportunities pertaining to present day practice. It was designed to summarize emerging evidence pertaining to perioperative GV, PCL, and postoperative outcomes in patients with and without DM. By specifying an aim early on, all relevant literature was collected and gaps in knowledge were identified. This process allowed for recommendations for future research to be made based on where current research is lacking or non-existent.

This scoping review does not incorporate all of the available literature pertaining to this broad topic that may otherwise have been included in a systematic review. Instead, this scoping review encompassed some aspects of glycemic control that are interconnected clinically but may be conceptually separated in literature searches. Each of the three broad topics discussed could be presented as an individual systematic review. A literature search that included all of these elements systematically would be cumbersome.

Given the limitations of a scoping review, there is the possibility that some available evidence has not been mentioned or cited. This is not because the authors have an underlying conflict of interest. None of the authors have any personal interest or conflict of interest with regards to this topic.

CONCLUSION

In conclusion, the benefits of a PCL outweigh the risks in most patients, even those with type 2 DM. The administration of a PCL might effectively minimize metabolic derangements such as GV and ultimately result in reduced postoperative morbidity and mortality, but this remains to be proven. Future efforts to standardize the content and timing of a PCL are needed. Prospective studies should be appropriately designed to evaluate the PCL effect on GV indices in the immediate postoperative period, and on long term postoperative complications in patients with and without DM.

FOOTNOTES

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REFERENCES

1 **Wukich DK**. Diabetes and its negative impact on outcomes in orthopaedic surgery. *World J Orthop* 2015; **6**: 331-339 [PMID: 25893176 DOI: 10.5312/wjo.v6.i3.331]
2 **MacIntosh BJ**, Cohen E, Colby-Milley J, Fang J, Zhou L, Ouk M, Wu CY, Shah BR, Lanctôt K, Herrmann N, Linkewich E, Law M, Black SE, Swartz RH, Kapral MK, Edwards JD, Swardfager W. Diabetes Mellitus Is Associated With Poor In-Hospital and Long-Term Outcomes in Young and Midlife Stroke Survivors. *J Am Heart Assoc* 2021; **10**: e019991 [PMID: 34219470 DOI: 10.1161/JAHA.120.019991]
3 **Frisch A**, Chandra P, Smiley D, Peng L, Rizzo M, Gatcliffe C, Hudson M, Mendoza J, Johnson R, Lin E, Umpierrez GE. Prevalence and clinical outcome of hyperglycemia in the perioperative period in noncardiac surgery. *Diabetes Care* 2010; **33**: 1783-1788 [PMID: 20435798 DOI: 10.2337/dc10-0304]
4 **van den Berghe G**, Wouters P, Weekers F, Verwaest C, Bruyninckx F, Schetz M, Vlasselaers D, Ferdinande P, Lauwers P, Bouillon R. Intensive insulin therapy in critically ill patients. *N Engl J Med* 2001; **345**: 1359-1367 [PMID: 11794168 DOI: 10.1056/NEJMoa011300]
5 **Bilotta F**, Caramia R, Paoloni FP, Delfini R, Rosa G. Safety and efficacy of intensive insulin therapy in critical neurosurgical patients. *Anesthesiology* 2009; **110**: 611-619 [PMID: 19237874 DOI: 10.1097/ALN.0b013e318198004b]
6 **Bilotta F**, Caramia R, Cernak I, Paoloni FP, Doronzio A, Cuzzone V, Santoro A, Rosa G. Intensive insulin therapy after severe traumatic brain injury: a randomized clinical trial. *Neurocrit Care* 2008; **9**: 159-166 [PMID: 18373223 DOI: 10.1007/s12028-008-9084-9]
7 **Egi M**, Bellomo R, Stachowski E, French CJ, Hart GK, Taori G, Hegarty C, Bailey M. Hypoglycemia and outcome in critically ill patients. *Mayo Clin Proc* 2010; **85**: 217-224 [PMID: 20176928 DOI: 10.4065/mcp.2009.0394]
8 **Krinsley J**, Schultz MJ, Spronk PE, van Braam Houckgeest F, van der Sluijs JP, Mélot C, Preiser JC. Mild hypoglycemia is strongly associated with increased intensive care unit length of stay. *Ann Intensive Care* 2011; **1**: 49 [PMID: 22115519 DOI: 10.1186/2110-5820-1-49]
9 **Ceriello A**, Esposito K, Piconi L, Ihnat MA, Thorpe JE, Testa R, Boemi M, Giugliano D. Oscillating glucose is more deleterious to endothelial function and oxidative stress than mean glucose in normal and type 2 diabetic patients. *Diabetes* 2008; **57**: 1349-1354 [PMID: 18299315 DOI: 10.2337/db08-0063]
10 **Kratzing C**. Pre-operative nutrition and carbohydrate loading. *Proc Nutr Soc* 2011; **70**: 311-315 [PMID: 21781358 DOI: 10.1017/S0029665111000450]
11 **Arksey H**, O'Malley L. Scoping studies: Towards a methodological framework. *Int J Social Research Methodology* 2005; **8**: 19-32 [DOI: 10.1080/1364557032000119616]
12 **Piconi L**, Quagliaro L, Assaloni R, Da Ros R, Maier A, Zuodar G, Ceriello A. Constant and intermittent high glucose enhances endothelial cell apoptosis through mitochondrial superoxide overproduction. *Diabetes Metab Res Rev* 2006; **22**: 198-203 [PMID: 16453381 DOI: 10.1002/dmrr.613]
13 **Egi M**, Bellomo R, Stachowski E, French CJ, Hart G. Variability of blood glucose concentration and short-term mortality in critically ill patients. *Anesthesiology* 2006; **105**: 244-252 [PMID: 16871057 DOI: 10.1097/00000542-200608000-00006]
14 **Ali NA**, O'Brien JM Jr, Dungan K, Phillips G, Marsh CB, Lemeshow S, Connors AF Jr, Preiser JC. Glucose variability and mortality in patients with sepsis. *Crit Care Med* 2008; **36**: 2316-2321 [PMID: 18596625 DOI: 10.1097/CCM.0b013e3181810378]
15 **Donati A**, Damiani E, Domizi R, Botticelli L, Castagnani R, Gabbanelli V, Nataloni S, Carsetti A, Scorcella C, Adrario E, Pelaia P, Preiser JC. Glycaemic variability, infections and mortality in a medical-surgical intensive care unit. *Crit Care Resusc* 2014; **16**: 13-23 [PMID: 24588431]
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**: 184-192 [PMID: 30979427 DOI: 10.1016/j.surg.2019.02.022]
17 **Thorell A**, Efendic S, Gutniak M, Häggmark T, Ljungqvist O. Insulin resistance after abdominal surgery. *Br J Surg* 1994; **81**: 59-63 [PMID: 8313123 DOI: 10.1002/bjs.1800810120]
18 **Subramaniam B**, Lerner A, Novack V, Khabbaz K, Paryente-Wiesmann M, Hess P, Talmor D. Increased glycemic variability in patients with elevated preoperative HbA1C predicts adverse outcomes following coronary artery bypass grafting surgery. *Anesth Analg* 2014; **118**: 277-287 [PMID: 24445629 DOI: 10.1213/ANE.0000000000000100]
19 **Shohat N**, Restrepo C, Allierezaie A, Tarabichi M, Goel R, Parvizi J. Increased Postoperative Glucose Variability Is Associated with Adverse Outcomes Following Total Joint Arthroplasty. *J Bone Joint Surg Am* 2018; **100**: 1110-1117 [PMID: 29975266 DOI: 10.2106/JBJS.17.00798]
20 **Patel PD**, Canseco JA, Wilt Z, Okroj KT, Chang M, Reyes AA, Bowles DR, Kurd MF, Rihn JA, Anderson DG, Hilibrand AS, Kepler CK, Vaccaro AR, Schroeder GD. Postoperative Glycemic Variability and Adverse Outcomes After Posterior

Cervical Fusion. *J Am Acad Orthop Surg* 2021; **29**: 580-588 [PMID: 34135295 DOI: 10.5435/JAAOS-D-20-00126]

21 **Rizzo MR**, Barbieri M, Marfella R, Paolisso G. Reduction of oxidative stress and inflammation by blunting daily acute glucose fluctuations in patients with type 2 diabetes: role of dipeptidyl peptidase-IV inhibition. *Diabetes Care* 2012; **35**: 2076-2082 [PMID: 22688551 DOI: 10.2337/dc12-0199]

22 **Singh BN**, Dahiya D, Bagaria D, Saini V, Kaman L, Kaje V, Vagadiya A, Sarin S, Edwards R, Attri V, Jain K. Effects of preoperative carbohydrates drinks on immediate postoperative outcome after day care laparoscopic cholecystectomy. *Surg Endosc* 2015; **29**: 3267-3272 [PMID: 25609319 DOI: 10.1007/s00464-015-4071-7]

23 **Gianotti L**, Biffi R, Sandini M, Marrelli D, Vignali A, Caccialanza R, Viganò J, Sabbatini A, Di Mare G, Alessiani M, Antomarchi F, Valsecchi MG, Bernasconi DP. Preoperative Oral Carbohydrate Load Versus Placebo in Major Elective Abdominal Surgery (PROCY): A Randomized, Placebo-controlled, Multicenter, Phase III Trial. *Ann Surg* 2018; **267**: 623-630 [PMID: 28582271 DOI: 10.1097/SLA.0000000000002325]

24 **Liu B**, Wang Y, Liu S, Zhao T, Zhao B, Jiang X, Ye L, Zhao L, Lv W, Zhang Y, Zheng T, Xue Y, Chen L, Wu Y, Li Z, Yan J, Wang S, Sun X, Gao G, Qu Y, He S. A randomized controlled study of preoperative oral carbohydrate loading *vs* fasting in patients undergoing elective craniotomy. *Clin Nutr* 2019; **38**: 2106-2112 [PMID: 30497695 DOI: 10.1016/j.clnu.2018.11.008]

25 **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**: 999-1003 [PMID: 32252984 DOI: 10.1016/j.amjsurg.2020.03.032]

26 **Suh S**, Hetzel E, Alter-Troilo K, Lak K, Gould JC, Kindel TL, Higgins RM. The influence of preoperative carbohydrate loading on postoperative outcomes in bariatric surgery patients: a randomized, controlled trial. *Surg Obes Relat Dis* 2021; **17**: 1480-1488 [PMID: 34016554 DOI: 10.1016/j.soard.2021.04.014]

27 **Lee B**, Kim SY, Cho BW, Suh S, Park KK, Choi YS. Preoperative Carbohydrate Drink Intake Increases Glycemic Variability in Patients with Type 2 Diabetes Mellitus in Total Joint Arthroplasty: A Prospective Randomized Trial. *World J Surg* 2022; **46**: 791-799 [PMID: 35006328 DOI: 10.1007/s00268-021-06437-1]

28 **Ricci C**, Ingaldi C, Alberici L, Serbassi F, Pagano N, De Raffele E, Minni F, Pironi L, Sasdelli AS, Casadei R. Preoperative carbohydrate loading before elective abdominal surgery: A systematic review and network meta-analysis of phase II/III randomized controlled trials. *Clin Nutr* 2022; **41**: 313-320 [PMID: 34999325 DOI: 10.1016/j.clnu.2021.12.016]

29 **Rice MJ**, Pitkin AD, Gravenstein N. All glucose measurements are not equal. *Anesthesiology* 2009; **111**: 1160; author reply 1160-1160; author reply 1161 [PMID: 19858882 DOI: 10.1097/ALN.0b013e3181ba3a35]

30 **Kielhorn BA**, Senagore AJ, Asgeirsson T. The benefits of a low dose complex carbohydrate/citrulline electrolyte solution for preoperative carbohydrate loading: Focus on glycemic variability. *Am J Surg* 2018; **215**: 373-376 [PMID: 29128103 DOI: 10.1016/j.amjsurg.2017.10.029]

31 **Robinson KN**, Cassady BA, Hegazi RA, Wischmeyer PE. Preoperative carbohydrate loading in surgical patients with type 2 diabetes: Are concerns supported by data? *Clin Nutr ESPEN* 2021; **45**: 1-8 [PMID: 34620304 DOI: 10.1016/j.clnesp.2021.08.023]

32 **Bilku DK**, Dennison AR, Hall TC, Metcalfe MS, Garcea G. Role of preoperative carbohydrate loading: a systematic review. *Ann R Coll Surg Engl* 2014; **96**: 15-22 [PMID: 24417824 DOI: 10.1308/003588414X13824511650614]

33 **Noba L**, Wakefield A. Are carbohydrate drinks more effective than preoperative fasting: A systematic review of randomised controlled trials. *J Clin Nurs* 2019; **28**: 3096-3116 [PMID: 31112338 DOI: 10.1111/jocn.14919]

34 **Cheng PL**, Loh EW, Chen JT, Tam KW. Effects of preoperative oral carbohydrate on postoperative discomfort in patients undergoing elective surgery: a meta-analysis of randomized controlled trials. *Langenbecks Arch Surg* 2021; **406**: 993-1005 [PMID: 33629128 DOI: 10.1007/s00423-021-02110-2]

35 American Society for Enhanced Recovery and Perioperative Quality Initiative Joint Consensus Statement on Nutrition Screening and Therapy Within a Surgical Enhanced Recovery Pathway: Erratum. *Anesth Analg* 2018; **127**: e95 [PMID: 30335662 DOI: 10.1213/ANE.0000000000003784]

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