Preoperative CHO Load, Glycemic Variability & Surgical Outcomes

Robert Canelli, MD, FASA
Boston University School of Medicine

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Disclosures

- I have no disclosures to report.

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Learning Objectives

- Describe the rationale for incorporating preoperative carbohydrate loading (PCL) into Enhanced Recovery After Surgery (ERAS) protocols, including its physiological impact on insulin resistance, patient comfort, and recovery outcomes.
- Introduce the concept of glycemic variability (GV), the metrics used to assess it (e.g., GLI, CV, MAGE), and its association with surgical complications and patient outcomes.
- Evaluate the current evidence regarding the effect of PCL on GV and postoperative outcomes, including the limitations of existing studies and areas requiring further research.

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My institution prescribes a preoperative carbohydrate load (PCL) to surgical patients.

A. Yes

B. No

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My institution prescribes a preoperative carbohydrate load (PCL) to surgical patients.

A. Yes 0%

B. No 0%

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My institution prescribes a preoperative carbohydrate load (PCL) to surgical patients.

A. Yes 0%

B. No 0%

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My institution prescribes patients a PCL to drink…

A. the night before surgery only

B. the morning of surgery only

C. the night before and morning of surgery

D. No PCL

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My institution prescribes patients a PCL to drink…

A. the night before surgery only 0%

B. the morning of surgery only 0%

C. the night before and morning of surgery 0%

D. No PCL 0%

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My institution prescribes patients a PCL to drink…

the night before surgery only 0%

the morning of surgery only 0%

the night before and morning of surgery 0%

No PCL 0%

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Outline

- Brief History of ERAS and PCL
- Glycemic Variability
- PCL Science and Evidence

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The ERAS Study Group

- Survey data
  - Perioperative care across Europe was variable with minimal adoption of evidence-based practices
- 2001: ERAS Study Group gathered in London
  - Objective: Produce a protocol that would optimize outcomes based on published evidence

Table 1. Member Sites and Leads of the Original Enhanced Recovery After Surgery Study Group Formed in 2001

University and Hospital	Country	Lead(s)
University of Edinburgh	United Kingdom	Ken Fearon
Karolinska Institutet and Ersta Hospital Stockholm	Sweden	Olle Ljungqvist
University of Copenhagen and Hvidovre Hospital	Denmark	Henrik Kehlet
University of Northern Norway and Tromsö Hospital	Norway	Arthur Revhaug
University of Maastricht	The Netherlands	Martin von Meyenfeldt, Cornelius DeJong

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Preoperative Carbohydrate Load

Preoperative Gastric Emptying Effects of Anxiety and Oral Carbohydrate Administration

Nygren, Jonas M.D.[1]; Thorell, Anders M.D., Ph.D.[1]; Jacobsson, Hans M.D., Ph.D.[1]; Larsson, Stig Ph.D.[1]; Scchnell, Per-Olof M.Sc.[1]; Hylén, Lotta R.N.[1]; Ljungqvist, Olle M.D., Ph.D.[1]

Author Information

Annals of Surgery 222(6):p 728-734, December 1995

Methods

Twelve patients scheduled for elective surgery were randomly given 400 mL of either a carbohydrate-rich drink (285 mOsm/kg, 12.0% carbohydrates, n = 6) or water 4 hours before being anesthetized. Gastric emptying was measured (gamma camera, $^{99m}Tc^{(III)}$). Each patient repeated the protocol postoperatively as a control. All values were presented as the mean ± SEM by means of a nonparametric statistical evaluation.

Results

Despite the increased anxiety experienced by patients before surgery ($p < 0.005$), gastric emptying did not differ between the experimental and control situations. Initially, water emptied more rapidly than carbohydrate. However, after 90 minutes the stomach was emptied regardless of the solution administered (3.2 ± 1.1% [mean ± SEM] remaining in the stomach in the carbohydrate group *versus* 2.3 ± 1.2% remaining in the stomach in the water group).

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Preoperative Carbohydrate Load

Original Article

Preoperative oral carbohydrate administration reduces postoperative insulin resistance *

J. Nygren [1], M. Soop [1], A. Thorell [1], S. Efendic [*], K.S. Nair [†], O. Ljungqvist [1,‡]

Clinical Nutrition
Volume 17, Issue 2, April 1998, Pages 65-71

Method: The drink group (n = 7) received 800 ml of an isoosmolar carbohydrate rich beverage the evening before the operation (100 g carbohydrates), as well as another 400 ml (50 g carbohydrates) 2 h before the initiation of anesthesia. The fasted group (n = 7) was operated after an overnight fast.

Conclusions:

Patients given a carbohydrate drink shortly before elective colorectal surgery displayed less reduced insulin sensitivity after surgery as compared to patients who were operated after an overnight fast.

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Traditional NPO vs PCL

NPO

- Catabolic stress
- ↑ insulin resistance
- Hyperglycemia, hypoglycemia and glycemic variability
- ↑ hunger and thirst

PCL

- Improved metabolic profile
- ↑ endogenous insulin production
- ↓ endogenous glucose production
- ↓ glycemic variability
- ↓ hunger and thirst

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PCL Inclusion in ERAS

- Rationale for Inclusion
  - ↓ insulin resistance
  - Improve patient well-being and satisfaction
  - Faster recovery

Figure. Enhanced Recovery After Surgery (ERAS) Flowchart

	Preadmission	Preoperative	Intraoperative	Postoperative
Surgery	Preadmission nutritional support Cessation of smoking Control alcohol intake	Selective bowel preparation	Minimal invasive surgery Minimize drains and tubes	Early removal of drains and tubes Stop intravenous fluids
Anesthesia	Medical optimization	Preoperative carbohydrates Avoid: PONV prophylaxis	Regional analgesia Opioid-sparing anesthesia Balanced fluids Temperature control	Multimodal opioid-sparing pain control
Nursing	Preoperative information			Early mobilization Early oral intake of fluids and solids Postdischarge follow-up

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2023 American Society of Anesthesiologists Practice Guidelines for Preoperative Fasting: Carbohydrate-containing Clear Liquids with or without Protein, Chewing Gum, and Pediatric Fasting Duration—A Modular Update of the 2017 American Society of Anesthesiologists Practice Guidelines for Preoperative Fasting*

Girish P. Joshi, M.B.B.S., M.D. (Co-Chair), Basem B. Abdelmalak, M.D. (Co-Chair), Wade A. Weigel, M.D., Monica W. Harbell, M.D., Catherine I. Kue, M.D., Sulpicio G. Soriano, M.D., Paul A. Stricker, M.D., Tommie Tipton, B.S.N., R.N., C.N.O.R., Mark D. Grant, M.D., Ph.D., Anne M. Marbella, M.S., Madhulika Agarkar, M.P.H., Jaime F. Blanck, M.L.I.S., M.P.A., Karen B. Domino, M.D., M.P.H.

Anesthesiology 2023; 138:132–51

Carbohydrate-containing Clear Liquids

Recommendation

We recommend healthy adults drink carbohydrate-containing clear liquids until 2h before elective procedures requiring general anesthesia, regional anesthesia, or procedural sedation. The carbohydrates may be simple or complex.

- Strength of recommendation: Strong
- Strength of evidence: Moderate

Up to 400ml of clear liquids is considered an appropriate volume. Trial participants ingested a median of 400 ml of carbohydrate-containing clear liquids (interquartile range, 300 to 400 ml) up to 2h before anesthesia administration.

Summary of Evidence

Most patients in the studies were ASA Physical Status I or II with mean or median body mass index of 25 kg/m^2 (range, 21 to 33 kg/m^2; see Appendix). Patients drinking carbohydrate-containing clear liquids until 2h before their procedures experienced less hunger and thirst compared to fasting (table 2) and less hunger compared to drinking noncaloric clear liquids (table 3). There was no incidence of aspiration or regurgitation in any groups (tables 2 and 3

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Glycemic Variability

- The degree of fluctuations in blood glucose levels over time
  - Short-term GV (within-day or day-to-day swings)
  - Long-term GV (over weeks or months)
- This is not HYPERglycemia

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diabetes

PATHOPHYSIOLOGY | MAY 01 2008

Oscillating Glucose Is More Deleterious to Endothelial Function and Oxidative Stress Than Mean Glucose in Normal and Type 2 Diabetic Patients

Antonio Ceriello; Katherine Esposito; Ludovica Piconi; Michael A. Ihnat; Jessica E. Thorpe; Roberto Testa; Massimo Boemi; Dario Giugliano

RESULTS—Glucose at two different levels (10 and 15 mmol/l) resulted in a concentration-dependent fasting blood glucose–independent induction of both endothelial dysfunction and oxidative stress in both normal and type 2 diabetic patients. Oscillating glucose between 5 and 15 mmol/l every 6 h for 24 h resulted in further significant increases in endothelial dysfunction and oxidative stress compared with either continuous 10 or 15 mmol/l glucose.

CONCLUSIONS—These data suggest that oscillating glucose can have more deleterious effects than constant high glucose on endothelial function and oxidative stress, two key players in favoring cardiovascular complications in diabetes. Concomitant vitamin C infusion can reverse this impairment.

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Metrics to Assess GV

- Glycemic Lability Index (GLI)
  - ↑ GLI = large glucose swings

$$GLI = \frac{\sum_{i=2}^{n}\left(\frac{(G_i - G_{i-1})^2}{\Delta t}\right)}{n-1}$$

- Coefficient of variation (CV)
  - >36% = high variability

$$CV\ (\%) = \left(\frac{\text{Standard Deviation of Glucose (SD)}}{\text{Mean Glucose}}\right) \times 100$$

- Mean amplitude of glycemic excursions (MAGE)
  - Quantifies major glucose swings over a defined period

$$MAGE = \frac{\text{Sum of amplitudes of valid excursions}}{\text{Number of excursions}}$$

SO CONFUSING! AND NOT READILY AVAILABLE!!!!

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Why does GV matter?

- Surgical Complication Rates
  - Surgical site infection
  - Delayed wound healing
  - Risk of anastomotic leak
- Impaired Immune Function
  - Neutrophil dysfunction
  - Stress response to hypoglycemia
  - Immune dysregulation
- ↑ ICU LOS
- ↑ hospital LOS
- Worse cardiovascular outcomes
  - Arrhythmias
  - Perioperative myocardial injury
- GV is a better predictor of mortality than mean glucose in ICU population

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GV: Bottom Line

- GV is a modifiable risk factor in surgical patients
- ↓ GV =
  - Improved surgical outcomes
  - ↓ infection rates
  - ↓ LOS
  - ↓ mortality

GV is an underappreciated, yet clinically actionable, component of perioperative metabolic optimization

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Prolonged Fasting

- Induction of a catabolic state
  - ↑ cortisol
  - ↑ glucagon
  - ↑ catecholamines
- Hepatic gluconeogenesis
- Lipolysis
- Insulin resistance
- Result
  - ↑ perioperative glucose excursions
  - poor glucose control

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Preoperative Carbohydrate Load

- Stabilize glucose levels
- Suppress overnight endogenous glucose production
- ↓ postoperative insulin resistance by up to 50%
- ↓ magnitude and frequency of glucose excursions

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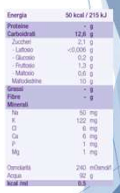
PCL and Surgical Outcomes

Outcome	Effect of PCL
Surgical site infection	↓ risk
Hospital LOS	↓ days
Readmission rates	↓ lower
Muscle strength	↑ strength
Insulin requirements	↓ units required
Patient comfort	↓ hunger, thirst, anxiety



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Contraindications to PCL

- Gastroparesis
- DM II with poor glycemic control
- DM I (patients do not make endogenous insulin)
- Risk of aspiration (ileus, bowel obstruction)
- Emergency surgery

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Cochrane Library

Preoperative carbohydrate treatment for enhancing recovery after elective surgery

Mark D Smith, John McCall, Lindsay Plank, G Peter Herbison, Mattias Soop, Jonas Nygren Authors' declarations of interest

Version published: 14 August 2014 Version history
https://doi-org.ezproxy.bu.edu/10.1002/14651858.CD009161.pub2

Main results

In 19 trials including 1351 participants, preoperative carbohydrate treatment was associated with shortened length of hospital stay compared with placebo or fasting (by 0.30 days; 95% confidence interval (CI) 0.56 to 0.04; very low-quality evidence). No significant effect on length of stay was noted when preoperative carbohydrate treatment was compared with placebo (14 trials including 867 participants; mean difference -0.13 days; 95% CI -0.38 to 0.12). Based on two trials including 86 participants, preoperative carbohydrate treatment was also associated with shortened time to passage of flatus when compared with placebo or fasting (by 0.39 days; 95% CI 0.70 to 0.07), as well as increased postoperative peripheral insulin sensitivity (three trials including 41 participants; mean increase in glucose infusion rate measured by hyperinsulinaemic-euglycaemic clamp of 0.76 mg/kg/min; 95% CI 0.24 to 1.29; high-quality evidence).

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JPEN Journal of Parenteral and Enteral Nutrition | aspen

Trends in preoperative carbohydrate load practice: A systematic review

Robert J. Canelli MD, FASA Joseph Louca MD, Rafael M. Gonzalez MD, Luis F. Rendon MD, Ciana R. Hartman MPH, Federico Bilotta MD

First published: 27 April 2024 | https://doi-org.ezproxy.bu.edu/10.1002/jpen.2633

- Aim:
  - Catalog PCL characteristics with respect to timing of ingestion, percentage of carbohydrate concentration, and PCL volume to guide the standardization and optimization of PCL prescription practices.
- Design:
  - Systemic review – 67 RCTs, 6551 patients

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Journal of Parenteral and Enteral Nutrition

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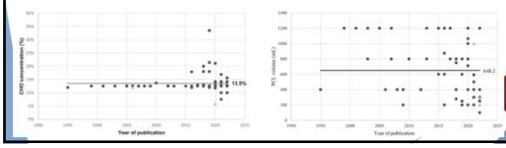
- Results:

  Timing: night before + morning of 49.3% vs. morning of only 47.8%



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- Conclusion:

  Variation in PCL practices prevent meaningful data pooling and outcome analysis.

  Efforts dedicated to the establishment of a **gold standard** PCL prescription are needed.

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Journal of Clinical Medicine

Preoperative Carbohydrate Load Does Not Alter Glycemic Variability in Diabetic and Non-Diabetic Patients Undergoing Major Gynecological Surgery: A Retrospective Study

Robert Canelli [1], Joseph Louca [2], Mauricio Gonzalez [2], Michelle Sia [2], Maxwell B. Baker [1,3,*], Shama Varghese [3,4], Erin Dienes [1] and Federico Bilotta [1]

J Clin Med. 2024 Aug 10;13(16):4704.

- Aim

  To determine the effect of a PCL on postoperative GV in both diabetic and non-diabetic patients having major gynecological surgery
- Design

  Retrospective analysis after institutional ERAS protocol vs historical controls
- Outcomes

  GV (CV and GLI), pain scores, incentive spirometry

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J Clin Med. 2024 Aug 10;13(16):4704.

- Results

Variable	No PCL ($n = 45$)	PCL ($n = 63$)	p-Value
Mean BGC (mg/dL)	158.4	152.6	0.48
Standard Deviation	29.6	29.3	0.91
CV (%)	18.6	19.3	0.65
GLI	0.54	0.58	0.86
PACU Pain Score	5.2	4.5	0.23
PACU IS (mL)	1245	1262	0.87

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My takeaways: PCL…

- Is safe, even in DM II
  - Zero aspiration events noted in any studies
    - ASA Clinical Practice Guidelines
- Enhances patient comfort
  - ↓ thirst ↓ hunger
- Improves metabolic profile of the surgical patient
- Has no proven consistent impact on GV or recovery **YET…**

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My Questions…

- How do we study 1 element of a care bundle while correcting for other care bundle variables, especially when the care bundle is now standard of care?
- What is the best way to measure GV?
- Which PCL prescription practice should be the gold standard?
- Should diabetic patients be included?

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Goals

- Standardize PCL protocol
  - Timing (night before + morning of)
  - CHO content (12.5% CHO)
  - Volume (800 ml in pm + 400 ml in am)
- Conduct large-scale prospective trial
- Include DMII and diverse populations
- Standardize GV metrics and outcomes

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Thank you!

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