The Effect of Preoperative Oral Carbohydrate Administration on Postoperative Glucometabolic Response, Subjective Well Being and Quality of Life in Patients Undergoing Colorectal Surgery: A Randomized Controlled Double-Blind Study

Trial registration: NCT05402592

Date of the document: 06.03.2025

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INTRODUCTION

Preoperative fasting has traditionally been a standard practice for patients undergoing elective surgery, primarily aimed at reducing the risk of pulmonary aspiration (1). However, prolonged fasting periods have been associated with increased preoperative anxiety, delayed surgical recovery, and heightened perioperative insulin resistance (PIR) (2,3). Surgical trauma, combined with prolonged fasting, exacerbates catabolic processes and triggers a metabolic stress response, leading to increased patient discomfort and complications (4,5). In response to these challenges, recent research and evidence-based guidelines have shifted focus toward minimizing the duration of preoperative fasting. Notably, the administration of oral carbohydrates in the preoperative period has been recommended to mitigate these adverse effects (6,7).

The Enhanced Recovery After Surgery (ERAS) protocols advocate for preoperative oral carbohydrate loading, particularly in patients undergoing elective colorectal surgery (6). Preoperative carbohydrate intake has been shown to modulate perioperative metabolism, reduce the stress response to surgical trauma, prevent complications, improve surgical outcomes, shorten hospital stays, and decrease postoperative morbidity and mortality (8–11). The International Society of Anaesthesia has confirmed the safety of oral carbohydrate intake, stating that it does not increase the risk of anesthesia-related complications. Furthermore, reducing the fasting period and administering carbohydrate-containing liquids have been shown to alleviate perioperative thirst, hunger, weakness, fatigue, anxiety, postoperative nausea and vomiting, and to promote intestinal peristalsis and shorter hospital stays (12–15).

Despite these advancements, there remains a gap in the literature regarding the comprehensive impact of preoperative carbohydrate loading on postoperative quality of life and subjective well-being, particularly in the context of colorectal surgery. While previous studies have primarily focused on metabolic outcomes and clinical recovery parameters, the effects on

patient-reported outcomes such as quality of life and subjective well-being have not been thoroughly investigated. This study aims to address this gap by examining the effects of preoperative oral carbohydrate ingestion on postoperative glucometabolic response, subjective well-being, quality of life, and surgical clinical outcomes in patients undergoing colorectal surgery.

The originality of this study lies in its holistic approach to evaluating both clinical and patient-centered outcomes. By integrating traditional clinical metrics with patient-reported outcomes, this research provides a more comprehensive understanding of the benefits of preoperative carbohydrate loading. Furthermore, the study employs a double-blind, randomized controlled design, ensuring robust and unbiased results. The findings of this study have the potential to inform clinical practice by highlighting the multifaceted benefits of preoperative carbohydrate administration, thereby contributing to the optimization of perioperative care protocols.

Research Hypotheses

H1-1: Preoperative oral carbohydrate intake reduces postoperative insulin resistance in patients undergoing colorectal surgery.

H1-2: Preoperative oral carbohydrate intake improves subjective well-being in patients undergoing colorectal surgery.

H1-3: Preoperative oral carbohydrate intake enhances the quality of life in patients undergoing colorectal surgery.

METHODS

Participants and sampling

This prospective, randomized controlled double-blind study was conducted at the General Surgery Clinic of A University Hospital between January 2022 and April 2023. The sample size was determined based on an effect size calculation derived from a previous study by Yagci et al. (3), which reported a mean glucose level difference of 12.18 mg/dL between the

experimental and control groups. Using this data, the effect size (d) was calculated as 0.72. With a 95% confidence level (1-α) and 80% statistical power (1-β), the G*Power software (version 3.1) was used to determine that a minimum of 25 participants per group (50 participants in total) would be required to detect significant differences between the groups.

The study population consisted of patients aged 18 years or older who were scheduled for elective colorectal surgery and had the capacity to provide informed consent. Participants were classified as American Society of Anesthesiologists (ASA) physical status I, II, or III. Exclusion criteria included patients diagnosed with diabetes, gastroesophageal reflux disease (GERD), severe liver or kidney failure, hiatal hernia, or those with oral nutrition difficulties. Additionally, emergency cases and patients classified as ASA IV or higher were excluded from the study.

Randomization and blinding

Randomization was performed by a researcher who were not directly involved in the clinical aspects of the study, with a sequence generated by a computer program (https://www.random.org) to assign 50 patients randomly to 2 groups in an unbiased manner. The list was kept secret from the patients and the researchers who registered and evaluated the patients until the final of the study. To maintain blinding, the study beverages were prepared in bottles of the same form by a nutrition company employee who was not actively engaged in the research process. Additionaly, the statistical analysis was performed independently by an experienced statistician, who was not directly involved in the study.

Data collection

The data were compiled via a personal interview with the participants, who were asked to complete a four-part evaluation form. This form was designed by the research team and based on the findings of relevant literature.

Observation indicators

Primary outcomes: Reducing insulin resistance (below 2.5 mg/dl), shortening hospital stay, ensuring subjective well-being.

Secondary outcomes: The early return of bowel movements, shorter passing-gas time, and higher quality of life on the 30th day after surgery were observed in patients who received carbohydrate-rich drinks.

Interventions

The study interventions were designed to evaluate the effects of preoperative carbohydrate intake on postoperative outcomes. Participants were divided into two groups: the intervention group (carbohydrate drink) and the control group (water). Both groups followed a standardized protocol, as outlined below:

Intervention Group: Patients in the intervention group were administered 800 mL of a carbohydrate-rich drink (12.5 g carbohydrate per 100 mL, containing 12% monosaccharides, 12% disaccharides, and 76% polysaccharides, with an osmolality of 285 mOsm/kg) until midnight on the day before surgery. Additionally, 400 mL of the same carbohydrate drink was given 2-3 hours before the surgical procedure (Figure 1).

Control Group: Patients in the control group received 800 mL of water until midnight on the day before surgery and 400 mL of water 2-3 hours before the procedure (Figure 1).

Data Collection:

Data were collected in four main categories:

Descriptive Characteristics: Age, gender, education level, marital status, occupation, body mass index (BMI), smoking and alcohol use, presence of chronic diseases, ASA score, and clinical outcomes (time to first flatulence, first defecation, first oral feeding, first mobilization, and hospital stay).

Laboratory Findings: Gastric pH, gastric volume, and blood markers (glucose, insulin, cortisol, albumin, potassium, sodium, magnesium, and urea) were measured at specific time points (preoperatively and 24 hours postoperatively).

Subjective Well-Being: Postoperative comfort indicators (pain, thirst, hunger, dry mouth, nausea, vomiting, weakness, and anxiety) were assessed using a Visual Analog Scale (VAS). The VAS is a 10 cm horizontal or vertical line, with endpoints labeled "No Pain" (0) and "Unbearable Pain" (10). Patients mark their level of discomfort on the line, and the score is measured in centimeters. A score of 0 indicates no discomfort, 1-4 indicates mild discomfort, 5-6 indicates moderate discomfort, and 7-10 indicates severe discomfort (16). The VAS was administered at specific postoperative time points (e.g., 8, 12, and 24 hours) to evaluate changes in subjective well-being.

Quality of Life: The SF-36 Quality of Life Scale was used to evaluate eight health domains 30 days after surgery. The SF-36 is a self-reported questionnaire consisting of 36 items that assess physical functionality, social functionality, role limitations due to physical and emotional problems, mental health, vitality, pain, and general health perception. Each domain is scored from 0 to 100, with higher scores indicating better health-related quality of life (17). The SF-36 was administered 30 days postoperatively to assess the long-term impact of preoperative carbohydrate intake on patients' quality of life.

Application of the Intervention

- Patients were informed about the study during their preoperative assessment and provided both verbal and written consent.
- Participants were instructed to maintain regular eating and sleeping patterns for three days prior to hospitalization.
- Blood samples were collected at four time points: before the morning dose, 40 minutes and 90 minutes after drink ingestion, and during anesthesia induction.

- Gastric residue was measured intraoperatively using a nasogastric or orogastric tube, and pH values were recorded using a urine pH meter.

Statistical analysis

The statistical analysis was conducted via the IBM SPSS Statistics 26 software (IBM Corp., Armonk, NY, USA). The distribution of scores obtained from each continuous variable was investigated using a combination of descriptive, graphical and statistical methods. The Shapiro-Wilk test was employed to ascertain the normality of the scores obtained from a continuous variable utilising a statistical methodology. Categorical variable data are presented as frequencies (n, %), while continuous variable data are presented as means±standard deviations. In order to make comparisons between two groups in relation to normally distributed quantitative variables, an independent sample t-test was employed. Conversely, when the variables in question were not normally distributed, a Mann-Whitney U test was used. To compare qualitative data between groups, chi-square tests (including the Yates correction and Fisher's exact test) were employed. The results were evaluated for statistical significance within the 95% confidence interval, with $p<0.05$ deemed significant.

RESULTS

Patient descriptive characteristics

The mean age of the patients included in the study was 66.64±10.26 years, 52% were male, the average BMI level was 25.44±3.37, 84% were married, and 74% were primary education. It was determined that 30% of the participants smoked, 20% consumed alcohol and 72% had a chronic disease. No statistically significant differences were observed in the distribution of the descriptive characteristics of the patients according to the research groups (Table 1).

Postoperative features

In the preoperative period, a comparison was made among the patients in the experimental group and those in the control group in the postoperative period; gas, stool passage, transition

to oral feeding, mobility, and length of stay were statistically significantly shorter ($p<0.001$) (Table 2).

Laboratory findings

The plasma glucose level in the patients in the experimental group was found to be statistically significantly lower in the preoperative period ($p=0.002$). However, plasma glucose ($p<0.001$) and insulin ($p = 0.029$) levels were determined to be higher in the measurement made during anaesthesia induction. Preoperative CRP ($p=0.013$) and both preoperative and postoperative 24th hour urea ($p=0.034$ and $p=0.040$) levels were significantly lower in the patients in the experimental group; It was determined that preoperative magnesium ($p=0.025$), postoperative 24th hour potassium ($p=0.035$) and both preoperative and postoperative 24th hour albumin ($p=0.003$ and $p<0.001$) levels were significantly higher (Table 2).

Life quality

When the SF-36 quality of life scale scores of the patients were examined, except for the vitality and emotional role difficulty sub-dimensions ($p>0.05$), all other sub-dimensions were different between the research groups ($p<0.01$ and $p<0.001$). It was demonstrated that the quality of life, as measured by physical functionality, physical role difficulties, general health, pain, social function and mental health, was significantly superior in the patients in the experimental group. (Table 2).

Patients' subjective well-being-related characteristics

Thirst at the 8th postoperative hour ($p=0.018$); The level of hunger ($p=0.005$) at the 12th hour and pain ($p=0.007$) at the 24th hour in the patients in the experimental group; It was established that the level of fatigue at the 12th and 24th postoperative hours ($p<0.001$) was significantly better only in the in the control group patients (Table 3).

Ethics approval and consent to participate

The single-center, randomized controlled double-blind study was registered in the ClinicalTrials database (https://clinicaltrials.gov, NCT05402592). Prior to the commencement of the research, approval was sought and obtained from the Mugla Sitki Kocman University Clinical Research Ethics Committee (22.12.2021-27/II) and the chief physician of the hospital where the research would be conducted. In conducting the research, the authors adhered to the principles set forth in the Declaration of Helsinki. Written and verbal informed consent was obtained from all patients participating in the study. It was explained to the patients that all data would be confidential and that they had the right to withdraw from the study at any time. This research was conducted in accordance with Consolidated Standards of Reporting Trials (CONSORT) 2010 guidelines.

Table 1: Patient descriptive characteristics

Characteristics	Total (n=50)	Experiment (n=25)	Control (n=25)	Test value	*P*-value
Age, mean±SD	66.64±10.26	67.04±7.63	66.24±12.51	0.273[a]	0.786
BMI, mean±SD	25.44±3.37	25.86±3.81	25.02±2.89	0.886[a]	0.380
Gender, n (%)				0.721[b]	0.396
Female	24(48.0)	14(56.0)	10(40.0)		
Male	26(52.0)	11(44.0)	15(60.0)		
Marital status, n (%)				-[c]	0.999
Married	42(84.0)	21(84.0)	21(84.0)		
Single	8(16.0)	4(16.0)	4(16.0)		
Education, n (%)				0.884[c]	0.804
Primary education	37(74.0)	18(72.0)	19(76.0)		
High school	6(12.0)	4(16.0)	2(8.0)		
University	7(14.0)	3(12.0)	4(16.0)		
Smoking, n (%)				0.000[b]	0.999
Yes	15(30.0)	7(28.0)	8(32.0)		
No	35(70.0)	18(72.0)	17(68.0)		
Alcohol, n (%)				-[c]	0.289
Yes	10(20.0)	7(28.0)	3(12.0)		
No	40(80.0)	18(72.0)	22(88.0)		
Chronic disease, n (%)				2.480[b]	0.115
Yes	36(72.0)	15(60.0)	21(84.0)		

No	14(28.0)	10(40.0)	4(16.0)

p>0.05, a: Independent samples t test, b: Chi-square test with Yates correction, c: Fisher's exact testi, SD:Standard deviation

Table 2: Some laboratory, quality of life and other postoperative findings of the patients

	Total (n=50)	Experiment (n=25)	Control (n=25)		
Variables	**Mean±SD**	**Mean±SD**	**Mean±SD**	**Test value**	***P*-value**
Gas output	43.30±5.12	40.60±4.52	46.00±4.22	**-4.010[a]**	**<0.001***
Stool output	75.24±10.71	68.64±7.94	81.84±8.97	**-4.721[a]**	**<0.001***
Oral nutrition	46.12±4.93	43.80±4.84	48.44±3.87	**-3.675[a]**	**<0.001***
Mobilisation	12.58±1.64	12.16±1.77	13.00±1.41	1.853[b]	0.070
Duration of postoperative hospitalisation	12.48±3.36	10.64±1.52	14.32±3.69	**-4.494[a]**	**<0.001***
HOMA-IR score	1.83±0.52	1.70±0.41	1.97±0.59	-1.951[a]	0.051
Gastric pH	4.76±5.72	5.59±8.04	3.94±0.92	-0.223[a]	0.823
Gastric volume	0.37±0.06	0.37±0.05	0.37±0.07	0.211[b]	0.834
Plasma-glucose					
Preoperative	87.50±16.30	80.24±7.66	94.75±19.35	**-3.150[a]**	**0.002***
40.min	95.86±17.70	91.04±10.67	100.67±21.84	-1.400[a]	0.162
90.min	103.04±20.83	105.04±21.02	101.04±20.87	-1.399[a]	0.162
Anaesthesia induction	115.63±22.26	123.80±18.96	107.47±22.66	**-3.611[a]**	**<0.001***
Plasma-insulin					
Preoperative	8.54±1.69	8.68±2.10	8.40±1.19	-0.160[a]	0.873
40.min	9.18±2.40	9.98±2.91	8.37±1.40	-1.792[a]	0.073
90.min	10.64±4.79	12.13±6.33	9.16±1.47	-1.679[a]	0.093
Anaesthesia induction	10.72±3.27	11.91±4.16	9.68±1.71	**-2.184[a]**	**0.029***
Plasma-cortisol					
Preoperative	12.35±1.77	12.08±2.17	12.60±1.29	1.024[b]	0.311
40.min	14.27±4.95	15.25±6.85	13.32±1.46	-0.071[a]	0.943
90.min	14.94±4.91	15.67±6.78	14.24±1.79	-0.789[a]	0.430
Anaesthesia induction	15.13±2.56	15.32±3.51	14.96±1.23	-1.008[a]	0.313
CRP					

Preoperative	29.76±72.18	4.61±11.61	54.91±95.83	**-2.484[a]**	**0.013***
Postoperative 24th hour	95.96±81.83	73.33±48.74	118.58±101.14	-1.106[a]	0.269
Albumin					
Preoperative	40.61±7.16	43.64±3.28	37.57±8.64	**-2.935[a]**	**0.003***
Postoperative 24th hour	36.89±7.54	40.72±4.13	33.07±8.28	**4.135[b]**	**<0.001***
Potassium					
Preoperative	4.30±0.48	4.32±0.47	4.29±0.49	0.262[b]	0.795
Postoperative 24th hour	4.19±0.46	4.35±0.36	4.04±0.51	**-2.110[a]**	**0.035***
Sodium					
Preoperative	139.73±2.49	139.80±2.33	139.65±2.68	0.211[b]	0.834
Postoperative 24th hour	140.34±2.26	140.20±1.44	140.48±2.89	0.434[b]	0.667
Magnesium					
Preoperative	2.26±0.54	2.47±0.62	2.05±0.36	**-2.244[a]**	**0.025***
Postoperative 24th hour	2.20±0.53	2.34±0.58	2.05±0.44	-1.569[a]	0.117
Urea					
Preoperative	26.33±12.17	23.01±5.65	29.65±15.74	**-2.125[a]**	**0.034***
Postoperative 24th hour	26.74±25.68	20.84±4.72	32.64±35.38	**-2.057[a]**	**0.040***
SF-36					
Physical functioning	71.70±17.46	82.00±11.81	61.40±16.17	-4.357[a]	**<0.001***
Role limitations due to physical health	50.00±33.12	63.00±30.72	37.00±30.72	-2.770[a]	**0.006***
Pain	67.75±13.18	73.20±13.95	62.30±9.92	-3.467[a]	**0.001***
General health	61.40±14.81	68.80±15.09	54.00±10.31	-4.171[a]	**<0.001***
Vitality	69.40±12.23	72.20±13.77	66.60±9.97	-1.637[a]	0.102
Social functioning	60.25±21.23	71.00±22.16	49.50±13.73	-3.791[a]	**<0.001***
Role limitations due to emotional health	80.00±29.35	81.33±27.35	78.67±31.74	-0.133[a]	0.894
Mental health	78.48±10.28	83.36±7.36	73.60±10.58	-3.336[a]	**0.001***

*p<0.05, a=Mann-Whitney U Test, b=Independent Samples Test, SD=Standard deviation

Table 3: Subjective well-being-related characteristics of patients

Variables	Grup	At 06.00 a.m.	Preop	Postop 8th hour	Postop 12th hour	Postop 24th hour
		Mean±SD	**Mean±SD**	**Mean±SD**	**Mean±SD**	**Mean±SD**
Pain	Experiment	0.16±0.55	0.12±0.44	1.80±1.41	3.24±0.72	3.12±0.97
	Control	0.00±0.00	0.00±0.00	1.44±1.42	3.24±0.97	3.88±0.93
	Test value[a]	-1.429	-1.429	-0.915	-0.023	**-2.675**
	***P*-value**	0.153	0.153	0.360	0.982	**0.007***
Dehydration	Experiment	0.24±0.66	0.12±0.44	1.00±1.91	2.92±1.50	4.76±1.05
	Control	0.00±0.00	0.16±0.37	1.52±1.23	2.80±1.12	4.32±1.52
	Test value[a]	**-2.063**	-0.792	**-2.360**	-0.627	-0.529
	***P*-value**	**0.039***	0.428	**0.018***	0.531	0.597
Hunger	Experiment	0.24±1.20	0.28±1.21	0.48±1.64	1.36±1.66	4.00±1.55
	Control	0.08±0.40	0.52±0.71	0.88±1.42	2.52±1.76	4.08±1.38
	Test value[a]	-0.029	**-2.509**	-1.830	**-2.802**	-0.409
	***P*-value**	0.977	**0.012***	0.067	**0.005***	0.683
Dry Mouth	Experiment	0.20±0.50	0.16±0.62	1.92±1.50	3.44±1.19	5.08±1.08
	Control	0.00±0.00	0.12±0.33	2.24±1.09	3.60±1.04	4.88±1.67
	Test value[a]	**-2.063**	-0.410	-1.779	-1.322	-0.454
	***P*-value**	**0.039***	0.682	0.075	0.186	0.650
Nausea	Experiment	0.04±0.20	0.08±0.28	0.68±0.80	1.44±0.96	1.96±1.27
	Control	0.04±0.20	0.56±0.92	1.08±1.08	1.88±1.17	2.16±1.37
	Test value[a]	0.000	**-2.225**	-1.276	-1.552	-0.627
	***P*-value**	1.000	**0.026***	0.202	0.121	0.531
Fatigue	Experiment	0.00±0.00	0.00±0.00	1.56±1.19	2.76±0.97	3.84±1.25
	Control	0.00±0.00	0.00±0.00	1.12±1.09	1.32±1.31	1.72±1.54
	Test value[a]	0.000	0.000	-1.298	**-3.805**	**-4.699**
	***P*-value**	1.000	1.000	0.194	**<0.001***	**<0.001***
Anxiety	Experiment	2.36±2.12	3.64±2.18	2.68±1.49	2.76±1.59	3.32±1.55
	Control	1.28±2.64	1.52±2.57	1.44±1.78	1.08±1.32	1.04±1.59
	Test value[a]	**-2.425**	**-3.153**	**-2.560**	**-3.569**	**-4.278**
	***P*-value**	**0.015***	**0.002***	**0.010***	**<0.001***	**<0.001***

*p<0.05, a=Mann-Whitney U Test, SD=Standard deviation

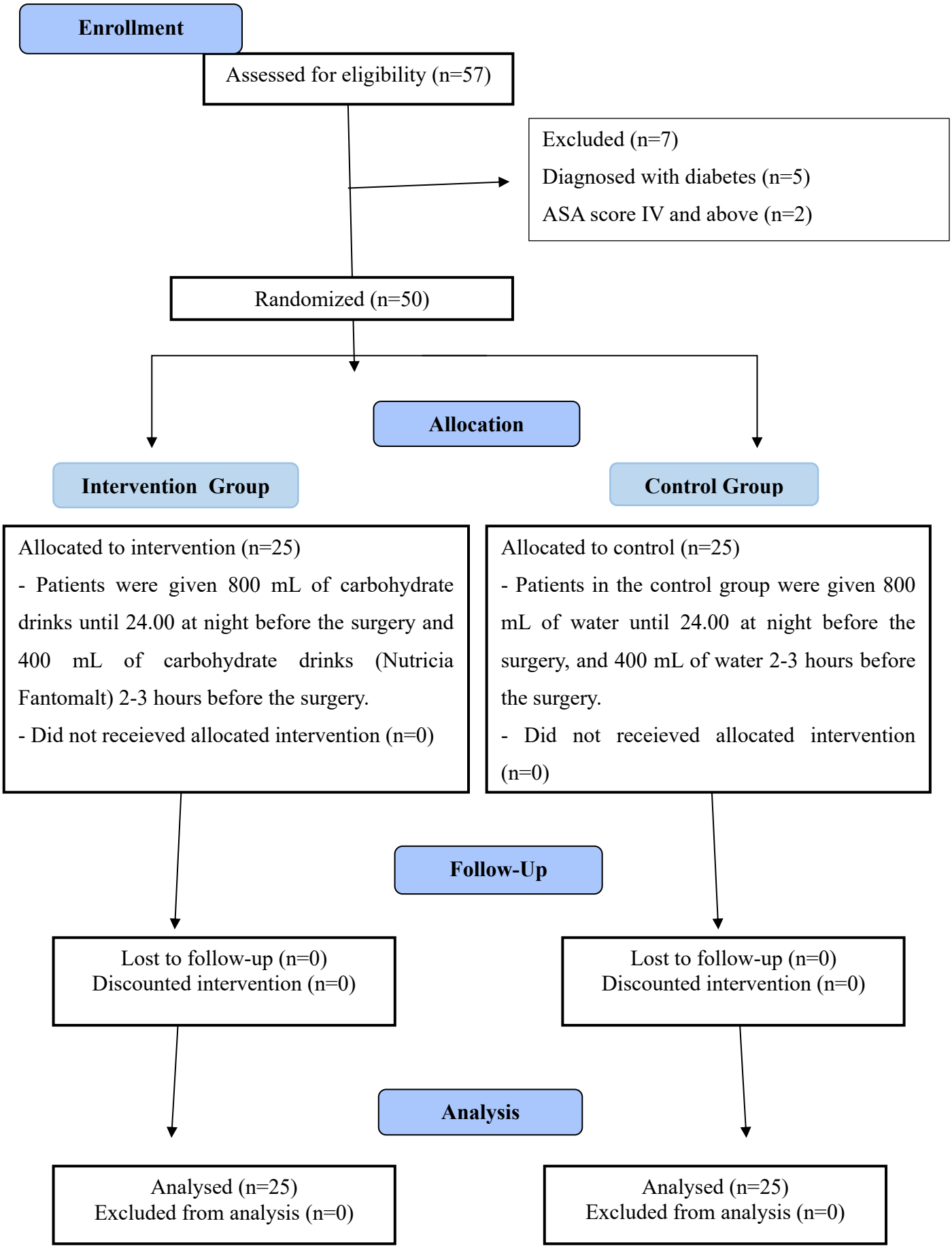

Figure 1: CONSORT Flow Diagram

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