Research Article

Effect of Preoperative Oral Carbohydrates on Insulin Resistance in Older Adults Who Underwent Total Hip or Knee Arthroplasty: A Prospective Randomized Trial

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Park and B. Lee contributed equally to this work and are both corresponding authors.

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Institutional Review Board of Severance Hospital (approval no. 4-2019-1014, approved on 7 November 2019). The study is registered at ClinicalTrials.gov (no. NCT04206189, 20 December 2019). Written informed consent was obtained from all patients.

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ABSTRACT

Introduction: Preoperative carbohydrate drinks are recommended to reduce fasting time before surgery. Older adults are at risk of pulmonary aspiration and hyperglycemia after consuming carbohydrate drinks because of increased insulin resistance and delayed gastric emptying. We investigated the effects of oral carbohydrate drinks on perioperative insulin resistance, metabolic responses, and gastric volume in older adults.

Methods: Fifty-six patients (aged more than 65 years) were randomly assigned to the control or carbohydrate (CHO) group. The CHO group received 400 mL of a carbohydrate drink 2 to 3 hours before anesthesia. The control group was allowed clear fluid intake 2 hours before anesthesia. Blood glucose and insulin levels were measured before intake of the carbohydrate drink and 1 hour postoperatively. Gastric volume was measured before spinal anesthesia. Insulin resistance was calculated using the homeostasis model assessment for insulin resistance.

Results: Homeostasis model assessment for insulin resistance was not different between the control and CHO groups preoperatively (2.5 versus 3.3, $P = 0.156$) or postoperatively (2.6 versus 2.4, $P = 0.817$). Preoperative gastric volume was comparable between the control and CHO groups (35.5 versus 30.8 mL, $P = 0.696$).

Discussion: Preoperative oral consumption of carbohydrates did not affect insulin resistance or gastric volume in older adults undergoing total knee or hip arthroplasty. Preoperative carbohydrate loading is safe in older adults undergoing total knee or hip arthroplasty.

Data Availability: The data that support the findings of this study are available from the corresponding author on reasonable request.

Clinical Trial Registration: ClinicalTrials.gov (No. NCT04206189).

Because the worldwide population ages, the number of patients in older age groups who undergo surgery increases.[1] Older patients have increased insulin resistance and increased frailty.[1,2] These changes due to older age are associated with the occurrence of various postoperative complications, such as cognitive impairment and cardiovascular complications.[1,3]

Reduction in fasting time before surgery has recently been recommended for early recovery after surgery.[4,5] Many reports have shown that consuming a carbohydrate drink 2 hours before anesthesia helps early recovery after surgery.[4,6,7] If the fasting time before surgery is prolonged, insulin resistance is increased owing to the body's natural metabolic adaptation.[8] A previous study showed that intake of a carbohydrate drink before surgery lowered insulin resistance postoperatively compared with a control group.[9-11] Insulin resistance is associated with postoperative morbidity and mortality, and older patients have a higher risk of postoperative complications than younger patients do.[1,12] Thus, if preoperative carbohydrate drinks lower insulin resistance in older patients, these patients may have better recovery after surgery and a decreased risk of postoperative complications. However, because older patients already exhibit increased insulin resistance,[2,13] even those who have not been diagnosed with diabetes may be at risk of a high blood glucose level owing to carbohydrate drink consumption. Furthermore, preoperative intake of carbohydrates may increase the risk of pulmonary aspiration because of delayed gastric emptying in older patients.[14] However, there are insufficient data on preoperative carbohydrate loading in older patients.[5]

Therefore, this study aimed to investigate the effects of oral carbohydrate drinks on perioperative insulin resistance and metabolic responses in older patients without diabetes mellitus who were undergoing elective total hip or knee arthroplasty. In addition, we measured the volume of gastric contents using ultrasonography to determine the risk of pulmonary aspiration.

Methods

Study Design and Patients

This prospective randomized study was approved by the Severance Hospital Institutional Review Board (No. 4-2019-1014) and is registered at ClinicalTrials.gov (No. NCT04206189). Written informed consent was obtained from all patients. Fifty-six patients (aged more than 65 years) scheduled to undergo elective total hip or knee arthroplasty between April 2020 and January 2021 were included. Patients with the following conditions were excluded: clinical signs of diabetes mellitus, body mass index >30 kg/m^2, gastroesophageal reflux disease, gastric emptying disorder, inflammatory bowel disease, previous abdominal surgery, chronic renal failure (glomerular filtration rate <60 mL/min/1.73 m^2), and severe coronary artery disease.

Randomization and Study Protocol

Patients were assigned to the control or carbohydrate (CHO) drink group using a randomization table generated with the MedCalc Statistical Software version 18.11.3 (MedCalc Software). The CHO group received 400 mL of a carbohydrate drink (12.8% carbohydrate, 0.5 kcal/mL, 14% monosaccharides, 3% disaccharides, 83% polysaccharides, and 265 mOsm/kg) 2 to 3 h before anesthesia. In the control group, clear fluid intake was allowed up to 2 h before anesthesia. An investigator who prescribed a CHO drink and did not participate in the postoperative assessments conducted patient allocation. The remaining investigators, surgeons, attending anesthesiologists, and nurses were blinded to group assignments during the study period.

Perioperative Management

Pulse oximetry, electrocardiography, and noninvasive blood pressure measurements were done in the operating room. Patients received spinal anesthesia with hyperbaric bupivacaine and were administered 3 L of O_2 through a nasal prong. The attending anesthesiologist administered doses of 0.5% hyperbaric bupivacaine (10 to 12 mg) at their discretion. Patients who requested intraoperative sedation were administered propofol. A notable decrease in blood pressure (>20% decrease in mean blood pressure from baseline) was considered hypotension and was treated with a bolus of ephedrine (4 mg) or phenylephrine (50 μg). A continuous adductor canal block was done after total knee arthroplasty using a pump at 6 mL/hr and a 4-mL bolus (lockout time: 30 minutes) of 0.2% ropivacaine. Femoral nerve block was done after total hip arthroplasty. Celecoxib (200 mg) was routinely administered

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for pain control, and tramadol (50 mg) was intramuscularly administered if the Verbal Numerical Rating Scale score was >4. One surgeon (K.K.P.) conducted all total hip or knee arthroplasties to maintain a uniform surgical stimulus.

Outcome Assessment

Hand grip strength was measured using an electronic hand dynamometer (EH101, Camry). Blood glucose levels were measured using a finger-stick blood test (Accu-Chek Instant BGMS, Roche Diabetes Care, GmbH) at two time points: 2.5 h after intake of the carbohydrate drink (T1, before spinal anesthesia) and 1 h after the operation (T2). In addition, blood samples were obtained from an indwelling catheter in the antecubital vein at T1 and T2 to measure free fatty acid (FFA) and insulin levels. Glucagon and activated glucagon-like peptide-1 (GLP-1) were measured at T1. The homeostasis model assessment for insulin resistance (HOMA-IR) was calculated according to the following formula:

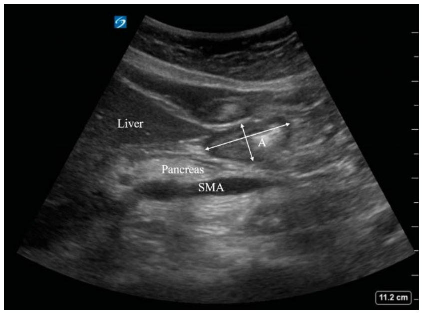
$$\text{Fasting glucose (mg/L)} \times \text{fasting insulin (mU/L)}/405^{15} \quad (1)$$

Intraoperative variables included anesthesia time, operation time, type of surgery, and fluid input and output. Postoperative variables included the length of hospitalization in days; incidence of postoperative nausea, vomiting, dizziness, and hypotension; white blood cell count; neutrophil/lymphocyte ratio; and pain scores. Pain at rest was evaluated on postoperative days 1 and 2 using an 11-point Verbal Numerical Rating Scale, with scores ranging from 0 (no pain) to 10 (worst pain imaginable).

Gastric Ultrasonography Assessment

Preanesthesia ultrasonography assessments of gastric volume were conducted by one anesthesiologist who was instructed and supervised by an experienced radiologist; a Sonosite X-Porte (SonoSite, Bothell) with a 4-MHz convex transducer was used. Patients were scanned in both the supine and right lateral positions. The gastric antrum was identified in the sagittal or parasagittal plane between the left liver lobe and the pancreas at the level of the aorta or inferior vena cava.[16] The transducer was tilted to obtain a true cross-sectional view of the antrum. Anterior-posterior and craniocaudal diameters were measured in the supine and right lateral decubitus position as shown in Figure 1. The antral cross-sectional area and the total

Figure 1



Ultrasonography showing ultrasonographic gastric antrum measurement. A, antrum. SMA = superior mesenteric artery

volume of gastric fluid were assessed using the following standard formulas:

$$\text{Cross-sectional area} = (\text{anteroposterior diameter} \times /4 \quad (2)$$
$$\text{craniocaudal diameter} \times \Pi)$$

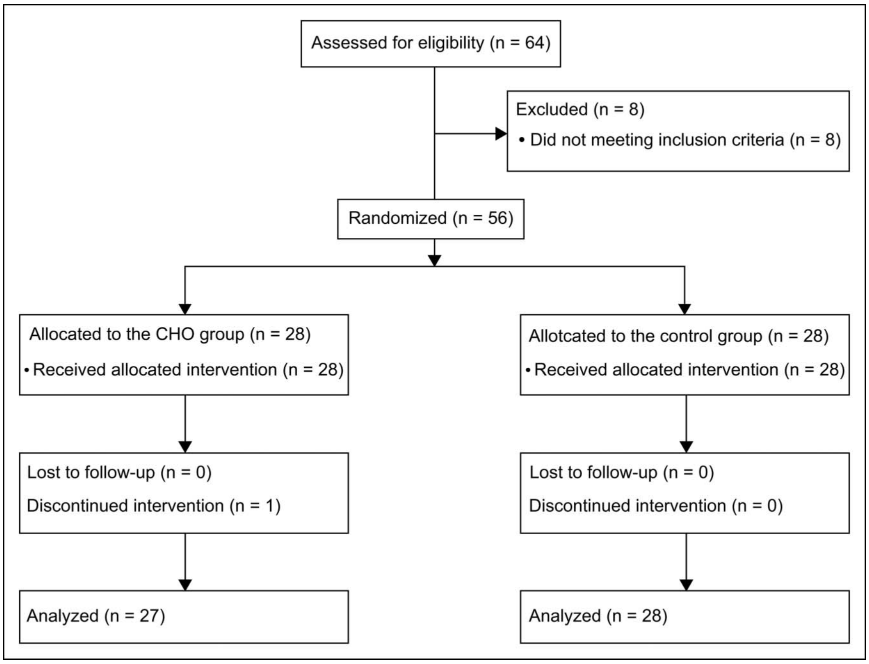
$$\text{Gastric volume (mL)} = 27.0 + 14.6 \times \text{cross-sectional area} - 1.28 \times \text{age}^{16} \quad (3)$$

A high risk of pulmonary aspiration was defined as a total gastric volume greater than 1.5 mL × the patient's body weight (kg).[16]

Statistical Analysis

The sample size was calculated to detect a difference in insulin resistance of >1.6 between the control and CHO groups.[17] Twenty-five participants were required in each group for a power of 90% at a significance level of 5%. To account for a 10% dropout rate, we enrolled 28 patients in each group. Parametricity was confirmed by the Shapiro-Wilk test and Kolmogorov-Smirnov test. Parametric continuous variables were analyzed by the independent *t*-test, and nonparametric continuous variables were analyzed by the Mann-Whitney *U* test. Intergroup comparisons of categorical variables were conducted using the Fisher exact test or $\chi 2$ test, as appropriate. Continuous variables are presented as the mean ± SD in parametric variables or median (interquartile range) in nonparametric variables, and categorical variables are presented as numbers (percentages). All statistical analyses were conducted using R version 3.5.1 (R Foundation for Statistical Computing), SPSS 23.0 (IBM), or MedCalc Statistical Software version 18.11.3. *P*-values <0.05 were considered significant.

Figure 2



Patient flowchart showing the CHO group receives 400 mL of a carbohydrate drink 2 to 3 hours before anesthesia. The control group is allowed clear fluid intake 2 h before anesthesia. CHO = carbohydrate

Results

Among 64 participants screened for eligibility, 56 were enrolled in this study and allocated to either the CHO or control group. One patient in the CHO group was excluded from the final analysis owing to missing laboratory results. Ultimately, 55 participants were included in the analysis (Figure 2).

Patient characteristics, American Society of Anesthesiologists physical status classification, hand grip strength, and gastric volume were comparable between the two groups (Table 1). Intraoperative variables, such

Table 1. Patient Characteristics

	Control Group (N = 28)	CHO Group (N = 27)	*P*-Value
Age (yr)	71.3 ± 4.1	71.9 ± 4.8	0.639
Female sex	22 (79%)	24 (88.9%)	0.469
Height (cm)	156.5 ± 7.4	153.3 ± 7.6	0.115
Weight (kg)	64.5 ± 8.6	60.6 ± 8.9	0.104
Body mass index (kg/m^2)	26.3 ± 2.7	25.7 ± 2.3	0.374
ASA class (I/II/III)	4/18/6	6/15/6	0.755
Hypertension	16 (57%)	15 (56%)	>0.999
Hand grip strength (kg)	19.6 (17.2-22.0)	17.3 (15.6-19.4)	0.068
CSV in supine (cm^2)	5.6 ± 1.6	4.9 ± 1.5	0.164
CSV in RLD (cm^2)	6.9 (6.0-8.0)	7.1 (4.9-8.3)	0.718
Gastric volume (mL) in RLD	35.5 (16.9-53.7)	30.8 (6.4-62.4)	0.696
Gastric volume/kg (mL/kg)	0.6 (0.3-1.0)	0.6 (0.1-1.0)	0.850
Patients with >1.5 mL/kg	2 (7%)	3 (11%)	0.669

ASA = American Society of Anesthesiologists, CSA = cross-sectional area, RLD = right lateral decubitus
Values are presented as median (interquartile range), mean ± SD, or number of patients (%).

Table 2. **Intraoperative Variables**

	Control Group (N = 28)	CHO Group (N = 27)	*P*-Value
Anesthesia time (min)	133 (105-170)	125 (100-173)	0.787
Operation time (min)	86 (73-125)	85 (62-132)	0.556
The kind of operation	—	—	>0.999
Total knee arthroplasty	19 (68%)	18 (67%)	—
Total hip arthroplasty	9 (32%)	9 (33%)	—
Fluid input (mL)	500 (350-625)	500 (400-650)	0.761
Urine output (mL)	150 (100-250)	200 (100-300)	0.423
Intraoperative bleeding (mL)	80 (50-100)	50 (50-100)	0.313
The lowest mean blood pressure (mmHg)	65 ± 10	67 ± 10	0.628
Vasopressor use	18 (64%)	19 (70%)	0.847

CHO = carbohydrate
Values are presented as median (interquartile range), mean ± SD, or number of patients (%).

as anesthesia time, operation time, fluid input and output, blood pressure, and use of a vasopressor, did not differ between the two groups (Table 2).

The measured time intervals between carbohydrate intake and T1 and T1 and T2 were all approximately 3 h. Glucose levels at the two time points did not differ between the two groups (Table 3). Insulin levels were higher in the CHO group than in the control group, but this difference was not significant (13.0 versus 10.1 μU/mL, $P = 0.050$). HOMA-IR, active GLP-1 levels, and glucagon levels were comparable between the two groups. FFA was lower in the CHO group than in the control group, but this difference was not significant (461 versus 682 μEq/L, $P = 0.057$). No statistical difference was observed in the postoperative metabolic variables between the two groups after stratifying the kind of surgery (Supplemental Table 1, http://links.lww.com/JAAOS/A792).

Postoperative length of hospital stay, postoperative nausea and vomiting, hypotension, white blood cell

Table 3. **Intraoperative Glucose and Hormone Levels**

	Control Group (N = 28)	CHO Group (N = 27)	*P*-Value
Glucose (mg/dL)			
Preoperative	103 (99-112)	101 (92-116)	0.448
Postoperative	112 (104-119)	117 (103-126)	0.668
Insulin (μU/mL)			
Preoperative	10.1 (6.2-13.3)	13.0 (7.8-21.4)	0.050
Postoperative	9.5 (4.9-13.4)	9.3 (5.2-15.8)	0.883
HOMA-IR			
Preoperative	2.5 (1.5-3.6)	3.3 (1.9-4.8)	0.156
Postoperative	2.6 (1.3-3.8)	2.4 (1.4-4.0)	0.817
Active GLP-1 (pM)	2.0 (2.0-2.0)	2.0 (2.0-3.0)	0.069
Glucagon (pg/mL)	106.0 (76.0-147.5)	128.5 (101.0-192.0)	0.148
FFA (μ Eq/L)			
Preoperative	681.5 (537.5-868.5)	461.0 (274.0-799.5)	0.057
Postoperative	801.5 ± 178.0	819.4 ± 321.8	0.804

FFA = Free fatty acid, GLP = glucagon-like peptide, HOMA-IR = Homeostasis Model Assessment for Insulin Resistance as fasting glucose (mg/dL) × fasting insulin (μU/mL)/405
Values are presented as median (interquartile range), mean ± SD, or number of patients (%).

Table 4. Postoperative Outcome

	Control Group (N = 28)	CHO Group (N = 27)	*P*-Value
Postoperative hospital day	3 (3-3)	3 (3-3)	0.673
PONV	14 (50%)	16 (62%)	0.563
Dizziness	7 (25%)	5 (19%)	0.856
Hypotension	4 (14%)	3 (11%)	>0.999
White blood cell (cells/μL)			
Postoperative	10236 ± 2,697	10413 ± 3,760	0.841
Postoperative 1 d	9,757 ± 2,633	8,508 ± 2,576	0.081
Neutrophil/lymphocyte ratio			
Postoperative	5.7 (3.7-8.5)	5.1 (4.0-7.0)	0.835
Postoperative 1 d	7.8 (6.2-9.3)	7.1 (4.8-9.5)	0.398
Pain scores at rest			
Postoperative 6 hr	3 (0-5)	2 (0-5)	0.462
Postoperative 24 hr	3 (1-5)	3 (0-5)	0.362
Postoperative 48 hr	2 (0-3)	0 (0-2)	0.249

CHO = control or carbohydrate, PONV = postoperative nausea and vomiting
Values are presented as median (interquartile range), mean ± standard deviation, or number of patients (%).

count, and pain score were comparable between the two groups (Table 4).

Discussion

To the best of our knowledge, this is the first randomized trial to investigate the effect of preoperative carbohydrate therapy on insulin resistance and gastric volume in older patients without diabetes who were undergoing lower limb arthroplasty. Our results showed that preoperative administration of an oral carbohydrate drink did not affect insulin resistance and gastric volume in older patients undergoing elective total hip or knee arthroplasty.

Postoperative insulin resistance is a feature of the catabolic response to surgical injury; the extent of insulin resistance is related to the amount of surgical trauma.[18] Perioperative insulin resistance is associated with a higher risk of postoperative complications.[19] Previous studies have recommended preoperative carbohydrate loading for early recovery after surgery.[4,6,7] Preoperative carbohydrate loading has been associated with reduced postoperative insulin resistance, enhanced return of bowel function, and shorter hospital stays.[7,20] Furthermore, oral carbohydrates markedly improved the clinical outcome of patients undergoing major colorectal surgery.[21,22] With the exception of major abdominal surgery, preoperative carbohydrate drink consumption has not been shown to accelerate the achievement of discharge criteria or reduce postoperative complications.[20] Studies on carbohydrate drink intake before orthopaedic surgery revealed a reduction in nausea and hunger and attenuation of postoperative glucose release; however, no notable benefit was observed about insulin sensitivity and clinical outcome.[23-25] Therefore, protocols for early recovery after some surgical procedures do not currently recommend the routine use of carbohydrate loading.[5,26] However, the benefits of carbohydrate loading in older patients have not been sufficiently researched.

Glucose tolerance declines with advancing age; declining glucose tolerance is associated with insulin resistance and decreased insulin secretion.[27] After adjustment for confounding factors, insulin sensitivity has been shown to decrease markedly with advancing age.[13] A previous study assessed the relationship between insulin resistance and verbal fluency in an adult population over the course of 11 years.[15] Their results found that insulin resistance predicts a steeper decline in verbal fluency.[15] Numerous studies have analyzed the relationship between insulin resistance and poor cognitive function.[15,17] Preoperative insulin resistance is associated with the occurrence of postoperative cognitive dysfunction.[17] Prevention and treatment of insulin resistance may help reduce future cognitive decline in older patients. We predicted that preoperative carbohydrate drink consumption would reduce insulin resistance in older patients, as observed in previous studies.[9,10] However, in our study, carbohydrate loading before surgery did not have a notable effect on insulin resistance in older patients.

Several studies have used HOMA-IR to reveal a decrease in postoperative insulin resistance between a CHO and control group; the decreased insulin resistance was attributed to decreasing inflammatory responses and modified insulin metabolism.[9,10,17,28] The participants in these studies underwent abdominal surgeries such as cholecystectomy or colectomy. However, similar studies analyzing other types of surgeries have found no difference in insulin resistance between CHO and control groups.[29,30] Another study found no difference in insulin resistance in patients undergoing abdominal surgery in the CHO and control groups.[31]

In our study, the CHO group had lower preoperative FFA levels than the control group, but this was not notable. Preoperative GLP-1 and glucagon, and postoperative FFA levels were comparable between the two groups. A fasting state activates catabolic pathways, thereby inducing glycogenolysis, reducing muscle uptake of glucose, and increasing lipolysis and FFA levels.[8] Preoperative carbohydrate drink consumption did not seem to affect postoperative FFA metabolism according to our results. Both glucagon and GLP-1 are essential hormones. Glucagon helps control blood glucose and insulin levels,[32] whereas GLP-1 is crucial for normal glucose tolerance and gastric motility.[33] Preoperative carbohydrate loading had no effect on either hormone.

As age increases, insulin resistance increases,[2] leading to hyperglycemia. Hyperglycemia can also be induced by the ingestion of carbohydrate beverages, even in older patients without diabetes.[8] Furthermore, increased insulin resistance was associated with gastroesophageal reflux disease.[34] Oral carbohydrates may increase the risk of aspiration in patients with delayed gastric emptying or gastrointestinal motility disorders.[35] Gastric dysmotility is also related to old age.[14,36] Therefore, it is necessary to determine whether it is safe for older patients to consume carbohydrate beverages before surgery. The results of our study showed that preoperative carbohydrate drink consumption did not increase gastric volume, blood glucose level, or insulin resistance before anesthesia in older patients. Thus, it seems to be safe for older patients to consume carbohydrate drinks. Considering previous studies have reported that preoperative carbohydrate drink intake reduces patient discomfort,[11,37] we believe carbohydrate drink consumption will be useful for increasing patient satisfaction without increasing the risk of complications.

Muscle strength decreases during normal aging owing to hormonal changes, the onset of anabolic resistance, and decreased physical activity.[38] Hand grip strength is strongly associated with overall muscle strength and is a valuable indicator of well-being, functional status, and frailty and can be a predictor of falls and postsurgical complications in older adults.[38,39] The pathophysiology of frailty is related to insulin resistance.[40] Therefore, the frailty of participants in the two groups was compared using hand grip strength but no difference was observed.

This study had a few limitations. First, this study included patients undergoing elective surgery conducted in the morning to compare the two groups under the same conditions. Thus, different outcomes may be observed in patients undergoing a longer fasting duration or emergency surgery. Second, the time interval between intake of the carbohydrate drink and the start of the operation was not uniform because it is a real perioperative condition. However, the results of our study reflect actual clinical practice. Third, relatively healthy patients who underwent total knee or hip arthroplasty at a single center were enrolled. Thus, the results of this study cannot be extended to other subsets of patients undergoing more invasive surgeries that may lead to a strong inflammatory response or intraoperative bleeding. Additional studies focusing on frail older patients, in whom this intervention may have a meaningful effect on the postoperative outcomes, are needed. Finally, this study was not powered to detect secondary outcomes.

In conclusion, preoperative oral carbohydrate loading did not markedly affect insulin resistance and gastric volume in older patients undergoing total knee or hip arthroplasty. Preoperative carbohydrate therapy did not increase the glucose level or gastric volume, but it did not show any metabolic benefit. Therefore, preoperative carbohydrate therapy can be used safely in older patients undergoing total knee or hip arthroplasty.

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