Effect of preoperative carbohydrate intake on inflammatory factors and clinical outcomes in elderly patients undergoing radical prostatectomy: a single-center, double-blind randomized controlled trial

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Abstract

BACKGROUND: To investigate the advantages of Carbohydrate (CHO) in inflammatory markers, comfort and clinical outcomes in elderly patients undergoing open radical prostatectomy.

METHODS: Patients of ≥65 years old with radical prostatectomy who underwent open radical prostatectomy were randomized to the CHO group, water group, and fasted group. Patients in the CHO group and water group received oral CHO, 800 ml of placebo water before surgery, and oral CHO and placebo water 400 ml 2 to 3 hours before surgery; the fasted group did not drink any liquid. The main outcomes are inflammatory markers. The secondary outcomes are cellular immunity, comfort, the index of grip strength of body mass and clinical outcomes.

RESULTS: A total of 90 patients were included in current study (i.e., CHO group, n=28; water group, n=30; fasted group, n=32). The three groups matched well in age, body mass index, the grade of (American Society of Anesthesiologists) ASA, operation time, blood loss, and fluid volume. CHO reduces IL-6 of Day1 and Day7 (P = 0.009, 0.005, respectively), IL-8 (P=0.005) of Day1, Day1, Day 3, and Day 7 TNF (P = 0.001, 0.006, 0.003 respectively) compared with the fasted group ; placebo water reduced Day 1 and Day 7 TNF (P = 0.005, 0.038, respectively), Day 1of IL-8 (P = 0.045). CHO reduced Day3 of TNF (P=0.026) compared to placebo water. In the CHO group and the water group, the morning thirst scores (0.68, 1.26, respectively) and starvation (0.24, 0.47, respectively) were decreased. The first time to leave bed in the fasted group (39.21 (15-93) h) was much later than in the CHO group (28.57 (10-100) h) and the water group (28.71 (12-70) h).

Conclusion: Compared with routine water ban, preoperative CHO and placebo water can reduce the levels of IL-6, IL-8 and TNF in elderly patients undergoing radical prostatectomy, which can improve the patient's preoperative comfort and shorten the patient's first time to leave bed. Compared with placebo water, CHO has no significant advantage in improving inflammatory markers and clinical outcomes.

Background:

Patients who undergo radical prostatectomy are generally old with more comorbidities. Surgical trauma generally cause a longer recovery times therefore a need for accelerated rehabilitation is required. . With the popularity of enhanced recovery after surgery(ERAS) [1-2], preoperative oral carbohydrate (Carbohydrate, CHO) has become a common clinical practice [3-4]. Drinking CHO before operation can reduce insulin resistance, reduce protein loss, and significantly reduce hunger and anxiety of patients before operation without affecting gastric emptying. CHO can make the intestinal function recover early and shorten the hospitalization time [6]. At present, the most common studies are the effects of CHO on insulin resistance and comfort, and the effects of minimally invasive surgery [9] and unconventional fasting [10] on postoperative immune function. There are few studies on the improvement of postoperative immune function by CHO.

Major open abdominal or pelvic surgery has a higher incidence of postoperative adverse events, like cardiopulmonary insufficiency, pain, thromboembolic complications and infection. The main reason is the stress response caused by surgical trauma, followed by a relatively high-level demand of patient's immunity and energy reserve. The relatively high-level demand for patient's organ function is thought to be mediated by endocrine and metabolic changes caused by trauma.

The levels of cytokines C-reactive protein and cytokines are closely related to the immune reaction, the inflammatory response and the extent of the inflamed tissue. The level of IL-6 is related to the incidence of postoperative complications, and it is one of the predictors of the incidence of adverse events after surgical intervention.

Methods:

Patients who underwent open radical resection of prostate cancer in the Shanghai Tenth People's Hospital were selected for this study. The inclusion criteria were as follows: elective radical resection of prostate cancer, age range from 65 to 85 years old, body mass index (BMI): 17.0-32.0 kg/m^2, American Society of Anesthesiologists (ASA) grade: Ⅰ~Ⅲ, and normal heart, lung, liver, kidney, and blood coagulation function. Oral anticoagulants were stopped for 5-7 days before operation. The exclusion criteria were as follows: below 65 years of age, inability to drink transparent liquid or allergy, gastrointestinal emptying disorder or obstruction, diabetes, liver cirrhosis, severe cardiac and renal insufficiency, corticosteroids for more than 5 mg/ days and (ASA) IV and above of the American Association of Anesthesiologists. The trial was approved by the Ethics Committee of the Shanghai Tenth People's Hospital, and all patients signed a written informed consent form before randomization.

All patients were randomly divided into three groups: carbohydrate group (CHO)、 placebo group (Water group) and routine water abstinence group (Fasted group, Fasted). The patients were randomly divided into three groups by the method of random number table and the method of random number remainder grouping. The specific operation method is as follows: according to the required sample size of 120 cases, 120 two-digit random number series are generated by the method of random number table. The order of the remainder obtained by dividing the two-digit random number series by 3 is the order in which the patients are randomly divided into three groups. Finally, the grouping scheme is written in a sealed envelope. The patients in the group were assigned to the grouping scheme marked in the sealed envelope in turn: carbohydrate group or placebo group or routine water abstinence group. Patients and researchers are unaware of the patient's fluid distribution. Fluid was given to patients by a person who knew the distribution of CHO and placebo water and was not involved in the study.

Patients who met the criteria were selected and randomly assigned to the CHO group (CHO) or water group (placebo) or routine water deprivation group (fasted group) according to the envelope clue. CHO (Su Qian, commonly known as maltodextrin fructose drink) and placebo products are produced by

Jiangsu Zhengda Fenghai Pharmaceutical Co., Ltd., and both products have the same outer packaging. After completing data entry and database locking, the company released the product code to the researchers. The study design is shown in Figure 1 and Flow chart is shown in Figure 2.

All three groups of patients were fasted with solid food for at least 6 hours before surgery. From 19:00 to 24:00 on the evening before the operation, patients in the CHO group were given 800 ml of a CHO drink (Su Qian contains 12.6% CHO, 50 kcal/100 ml, 290 mOsm/kg, pH 5.0, 200 ml per bottle). On the day of the operation, the patients in the CHO group consumed about 400 ml of Su Qian 2 to 3 h before the scheduled induction of anesthesia, with an interval of more than 20 minutes. Patients in the water group were given the same amount of seasoning water at the same time (sucralose 0 kcal/100 ml, citric acid 0 kcal/100 ml, 107 mOsm/kg, pH 5.0), which had the same taste and appearance as the CHO drink. In the routine fasted group, no fluid was given before operation. To ensure the smooth implementation of the experiment, these patients were usually scheduled for the first operation on the surgery day. All operations were performed by the same group of experienced urological surgeon.

All patients received the same general anesthesia regimen, sufentanil 0.25 ~ 0.5 μg / kg, propofol 1.5~2mg/kg, cis atracurium benzenesulfonate 0.2mg/kg general anesthesia induction. After endotracheal intubation, sevoflurane inhalation maintained anesthesia to maintain the end-expiratory sevoflurane volume fraction at 0.9-1.2 minimum alveolar effective concentration, remifentanil 2-5 μg / kg/h for analgesia, and cis-atracurium besylate for 4-10 mg/h to maintain muscle relaxation. During the operation, fluid infusion was guided according to blood pressure, heart rate, bleeding and urine volume. Sodium lactate Ringer's solution was mainly used, hydroxyethyl starch was used as a supplement, crystal: glue = 3 / 1, and appropriate adjuvant vasoactive drugs.

After the operation, the patients were encouraged to sit by the bedside or get out of bed as soon as their health conditions permit. If there was no nausea and vomiting, the patients were asked to drink water and eat as soon as possible. Infection is defined as the presence of sepsis, which can be diagnosed as sepsis: body temperature > 38 °C or < 36 °C; heart rate > 90 beats / min; systolic blood pressure ≤ 100mmHg; respiratory rate > 22 beats / min or $PaCO_2$ < 32 mmHg (< 4.3 kPa); white blood cell count > 12 × 109xL or < 4 × 109xL or immature cells > 10%); change of consciousness.

At approximately 7 AM before the operation, the venous blood of the patients was collected to the measure the levels of interleukin (IL), tumor necrosis factor (TNF), C-reactive protein (CRP), and cellular immunity. Venous blood samples were obtained repeatedly at the same time on days 1, 3, and 7 after the operation. In addition, the comfort and grip strength of the patients were measured at the same time before the operation and on days 1, 3, and 7 after the operation. Comfort was measured by a 100-mm visual analogue scale (VAS) [11] on the following parameters: anxiety, hunger, thirst, nausea, and fatigue. The grip strength was measured using a grip force device, and all measurements were performed using the same dominant hand. The first exhaust time, the independent standing time after surgery, the time to intake of water, and the time to intake of oral diet were recorded, and the results related to postoperative infection were assessed.

Outcome indicators:

1. Main outcome indicators: level of inflammatory markers (IL-1, IL-2, IL-6, IL-8, IL-10, TNF, and CRP).
2. Secondary outcomes: cellular immunity level (CD3, CD4, CD8, CD4/CD8, CD19, CD16/CD56), comfort (anxiety, hunger, thirst, nausea, fatigue), the index of grip strength of body mass (grip strength (kg)/body weight (kg) × 100%), clinical outcomes (first exhaust time, independent standing time after surgery, time to intake of water, time to intake of oral diet, and incidence of postoperative infection).

Statistical analysis: SPSS 19.0 statistical software was used for analysis. The measurement data of normal distribution were expressed as mean ± standard deviation ( ), and t-test was used to compare two independent samples. For the repeated measurement data, repeated measures analysis of variance was used to compare different time points in the group, and multivariate analysis of variance was used to compare the groups at the same time point. The measurement data of non-normal distribution were expressed as median, and the counting data were compared by the chi-square test. Multivariate logistic regression was performed using the pre- and intra-operative factors, including age, BMI, operation time, group, blood loss, fluid intake to determine the factors associated with elevated IL-6 level after operation. Differences with $P < 0.05$ were statistically significant.

Results:

It has been shown in Table 1 that three groups matched well in age, body mass index, preoperative blood glucose, ASA, operation time, bleeding volume and fluid replacement volume. The patient characteristics, operation time, and fluid replacement volume is shown in (Table 1). One patient in Placebo Group with intraoperative bleeding of 900ml was infused with 1U of red cell suspension.

It has been shown in Figure 3 and Table 2 that compared with conventional water deprivation, CHO decreased the IL-8 of Day1 and Day1, IL-6 of Day1 and TNF of Day 7; placebo decreased the TNF of Day1 of Day7 and IL-8 of Day1. Compared with the placebo group, CHO decreased the TNF of Day3. There was no statistical difference in IL1, IL2, IL10, CRP among the three groups. There was no statistical difference in the indexes of cellular immunity.

It has been shown in Table 3 that compared with the routine fasted group, the CHO and water groups showed a significant decrease in the thirst score (0.68 and 1.26, respectively, $P < 0.001$) and hunger score (0.24 and 0.47, respectively, $P< 0.05$) in the morning of the operation day, but no difference was observed in the weight grip strength index among the groups.

It has been shown in Table 4 that the independent standing time after surgery of the routine fasted group was 39.21 h (15-93 h), which was much later than those of the other two groups (CHO, 28.57 (10-100) h; water group, 28.71 (12-70) h). There was no difference in the first exhaust time, the time to intake of

water, and the time to intake of oral diet among the three groups. Moreover, no significant difference in postoperative infection incidence was noted among the three groups within 7 days after the operation.

Furthermore, in order to determine whether group was an independent variable among various pre- and intra-operative factors for post-operative inflammatory reaction, taking elevated IL-6 level 7 days post operation as representative, we performed multivariate analysis. The results showed that older age, higher BMI, longer operation time and group were all independent factors associated with higher IL-6 level (all $p < 0.05$). (Table 5)

Discussion:

The indexes of clinical evaluation of immune function are inflammatory markers (IL such as IL-2, IL-6, IL-8, and IL-10; TNF; and CRP) and cellular immunity (T cells, T helper cells, NK cells, and human leukocyte antigen DR (HLA-DR)). Usually, the decrease in inflammatory markers and the increase in the level of cellular immunity indicate a better immune function of the individual [13-14]. To reduce the incidence of postoperative complications, some studies have suggested that accelerating rehabilitation surgery, especially minimally invasive surgery [15], and unconventional fasting before operation can improve the immune function after operation, reduce the level of inflammatory response, and increase cell-mediated specific immunity. In 2006, the GERDIEN [16] team studied the effects of preoperative oral CHO-rich liquid diet on postoperative immune function. Compared with the routine water deprivation group before operation, the oral CHO floating diet group did not a decrease in HLA-DR, and the body's fluid balance in this group was not significantly disturbed. This shows that preoperative oral administration of CHOs can avoid the subsequent immune response and reduce the occurrence of infectious complications. However, another study by Mathur showed that CRP and IL-6 levels had no effect on systemic inflammation in patients undergoing major abdominal surgery [17]. Therefore, the authors consider that there is no evidence that the CHO load is essential to reduce surgical stress response. Tran [18] found that the levels of IL-6 and CRP were not affected by the preoperative use of CHO during coronary artery bypass grafting and spinal surgery.

The analysis of the present study showed that, in terms of the overall trend, compared with the routine fasted water group, the levels of inflammatory markers of the oral water placebo and CHO groups were lower, with an apparent decrease in the CHO group. Compared with the routine fasted water group, the CHO group showed a decrease in TNF on the first, third, and seventh day after the operation, a decrease in IL-6 on the first and sixth day after the operation, and a decrease in IL-8 on the first day after the operation. The reduction in TNF and IL-8 levels on the first and seventh day after the operation indicated that the CHO and water groups had a significant advantage in terms of reduction in postoperative inflammatory markers. CHO administration decreased TNF only on the third day after the operation when compared with the oral water group; thus, it may not have much advantage in terms of reduction in the levels of inflammatory markers. In other words, taking a certain amount of liquid before operation,

regardless of whether it is CHO or sweet water or other clear liquid, has a similar effect on postoperative inflammatory markers. Su Qian is an energy-rich carbohydrate drink, while placebo water is an energy-free clear liquid; the difference between these two drinks is that their sugar and energy content is 1 and 0, respectively. Sugar and energy may not play an important role in regulating the levels of inflammatory markers, and the intake of a certain amount of liquid before operation may play a decisive role in postoperative outcome. Compared with routine water deprivation, the intake of a certain amount of liquid before operation can significantly reduce the level of inflammatory markers in the body. Although the IL-6, IL-8, and TNF levels showed significant differences among the three groups, no difference was noted in the indices of cellular immunity and the incidence of postoperative infection among the three groups; thus, no clinical significance of CHO administration could be established. Because several factors affect the incidence of postoperative infection, the present study suggests that preoperative use of liquid may not be a key factor for reducing postoperative infection incidence.

After multivariate analysis, it was found that age, BMI, operation time and grouping were the independent risk factors for the increase of postoperative IL-6 of Day7 , that means that the older the age leads the higher BMI and the longer operation time, and the grouping were the independent risk factors for the increase of IL-6 7 days after operation. The IL-6 of CHO, Placebo and Fasted increased in turn at 7 days after operation, which were 7.9 ±6.27 pg/ml,18.29 ±19.95 pg/ml,27.49 ±33.83 pg/ml, respectively. It is suggested that preoperative administration of CHO or placebo can inhibit the increase of IL-6 to some extent, and the effect of CHO is better than that of placebo.

Several studies [19-20] have shown that preoperative administration of CHO can significantly reduce preoperative hunger and anxiety, and does not affect gastric volume. The present study found that the preoperative administration of fluid, either CHO or clear liquid, can significantly improve thirst and hunger scores in the early morning (usually 90 to 120 min after drinking the liquid in the morning) when compared with conventional water deprivation. A similar effect was observed for the comfort parameters on the operation day. Furthermore, perhaps drinking liquid, not necessarily CHO, can significantly improve patient comfort.

The time of getting out of bed is affected by many factors such as medical staff education, renewal of medical cognition, patients' fear of getting out of bed, and postoperative pain. The independent standing time after surgery for the CHO and water groups for patients who got out of bed after the operation was shorter than that for the routine water deprivation group; this was a surprising result in this study. This finding shows that the intake of liquid before operation can actually lead to better clinical outcome of patients. CHO, however, had no real advantage over the oral placebo water.

Some studies [21] have identified that the preoperative CHO load is associated only with a small reduction in the time of hospital stay, and has no effect on the incidence of complications. In China, the length of hospital stay is affected by many factors; therefore, the postoperative time of hospital stay was not included as a clinical outcome of this study. Compared with the Veenhof [15] team study, this study added a group of placebo water control; compared with the Mathur [17] team study, this study added a

group of blank controls. The present study showed that CHO and placebo water had the same advantage in reducing the levels of inflammatory markers, but there was no significant difference in postoperative infection incidence among the three groups. The present study has some limitations. The sample size was small, and the level of inflammatory markers was not necessarily positively correlated with the infection incidence. The effects of CHO or clear liquid on inflammatory markers and clinical outcomes in elderly patients who undergo major surgery thus need to be further studied.

Conclusions:

Compared with conventional water deprivation, the intake of CHO and oral water before operation can reduce the levels of IL-6, IL-8, and TNF in elderly patients with open radical resection of prostate cancer; improve the comfort of patients before operation; and shorten the independent standing time after surgery. Compared with placebo, CHO had no significant advantage in regulating the levels of inflammatory markers and improving clinical outcomes.

Abbreviations

CHO
Carbohydrate
ASA
American Society of Anesthesiologists
ERAS
recovery after surgery
IR
insulin resistance
LOS
length of stay
BMI
body mass index
IL
levels of interleukin
TNF
tumor necrosis factor
CRP
C-reactive protein
VAS
visual analogue scale
HLA-DR
leukocyte antigen DR

Declarations

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Tables

	CHO	Placebo	Fasted	p value
Number of patients	28	30	32	
Age at surgery(years) Mean(min-max)	71.79(65-81)	70.25(65-81)	72.44(58-83)	0.286
BMI (kg/m^2)	23.82(17.30-31.91)	23.97(18.51-29.76)	24.16(19.00-30.76)	0.92
Mean(min-max)		4.9(4.1-7.8)		
Preoperative fasting blood glucose (mmol/L)	4.8(3.9-6.9)		5.1(4.0-9.1)	0.748
Mean(min-max)				
ASA grade(n/%)				
Ⅰ	5(18)	6(20)	6(19)	
Ⅱ	17(61)	18(60)	19(59)	
Ⅲ	6(21)	6(20)	7(22)	
OR Time(min)	178.8(105-330)	158.5(100-330)	169.5(90-285)	0.416
Mean(min-max)				
Blood loss(ml)	189.29(50-500)	225(100-900)	201.56(50-500)	0.628
Mean(min-max)				
Intraoperative Fluid(ml) Mean(min-max)	2078.57(1500-3500)	1925(1250-2750)	2007.81(1500-2750)	0.136

Table 1: Patient demographics and surgical characteristics

Note:CHO，Carbohydrate，BMI，body mass index, ASA，American Society of Anesthesiologists, OR Time，Operative Time

Table 2

	CHO Mean(SD)	Placebo Mean(SD)	Fasted Mean(SD)	CHO vs Placebo Mean difference(95% CI);p value	CHO vs Fasted Mean difference(95% CI);p value	Placebo vs Fasted Mean difference(95% CI);p value
IL-6(pg/ml)						
Day 0	9.6(18.29)	9.09(14.58)	17.1(33.58)	0.51(-14.32 to 15.35);0.945	-7.5(-21.1 to 6.09);0.275	-8.01(-22.14 to 6.11);0.262
Day 1	72.98(58.67)	109.09(116.58)	134.6(81.28)	-36.1(-86.48 to 14.27);0.157	-61.62(-107.62 to -15.61);0.009	-25.51(-74.37 to 23.34);0.301
Day 3	27.03(39.55)	33.88(38.61)	33(58.92)	-6.86(-33.75 to 20.03);0.613	-5.98(-31.79 to 19.83);0.646	0.88(-25.77 to 27.54);0.948
Day 7	7.9(6.27)	18.29(19.95)	27.49(33.83)	-10.39(-24.53 to 3.75);0.147	-19.59(-32.98 to -6.2);0.005	-9.2(-22.59 to 4.19);0.175
IL-8(pg/ml)						
Day 0	179.23(305.38)	181.03(376.86)	197.96(233.26)	-1.81(-181.65 to 178.03);0.984	-18.73(-183.56 to 146.1);0.821	-16.92(-188.17 to 154.32);0.844
Day 1	253.29(444.17)	406.38(665.09)	851.78(1014.13)	-153.08(-601.84 to 295.67);0.499	-598.49(-1008.32 to -188.66);0.005	-445.4(-880.59 to -10.22);0.045
Day 3	344.74(618.95)	466.31(714.82)	428.44(808.19)	-121.56(-532.1 to 288.97);0.557	-83.7(-477.77 to 310.36);0.673	37.86(-369.08 to 444.81);0.853
Day 7	325.83(604.03)	265.24(340.08)	654.45(1027.1)	60.59(-378.15 to 499.34);0.784	-328.62(-744.05 to 86.81);0.119	-389.21(-804.65 to 26.22);0.066
TNF(pg/ml)						
Day0	14(25.01)	13.83(15.14)	20.47(12.86)	0.17(-10.65 to 10.99);0.975	-6.46(-16.38 to 3.45);0.198	-6.63(-16.94 to 3.67);0.204
Day1	11.74(11.57)	13.06(8.15)	24.06(17.07)	-1.32(-9.11 to 6.46);0.736	-12.32(-19.43 to -5.21);0.001	-11(-18.55 to -3.45);0.005
Day3	9.64(8.88)	19.57(21.36)	21.39(13.7)	-9.93(-18.61 to -1.25);0.026	-11.75(-20.08 to -3.42);0.006	-1.82(-10.42 to 6.78);0.674
Day7	9.59(8.58)	12.88(10.97)	19.77(13.88)	-3.3(-10.19 to 3.59);0.343	-10.18(-16.76 to -3.6);0.003	-6.88(-13.39 to -0.38);0.038

| | CHO Mean(SD) | Placebo Mean(SD) | Fasted Mean(SD) | CHO vs Placebo Mean difference(95% | CHO vs Fasted Mean difference(95% | Placebo vs Fasted Mean difference(95% |

	CHO	Placebo	Fasted	p value（CHO vs Fasted）	p value（Placebo vs Fasted）
anxiety					
Day 0	1.20(0-8)	1.76(0-5)	1.56(0-4)	0.141	0.338
Day of surgery	0.95(0-4)	1.68(0-5)	1.22(0-8)	0.838	0.119
Day 1	0.86(0-7)	0.63(0-5)	0.66(0-4)	0.603	0.999
Day 3	0.27(0-2)	0.16(0-2)	0.5(0-5)	0.339	0.365
thirst					
Day 0	1.70(0-6.5)	1.42(0-5)	2.38(0-5)	0.451	0.52
Day of surgery	0.68(0-4)	1.26(0-4)	3.03(1-8.5)	<0.001	0.001
Day 1	2.16(0-8)	1.82(0-8)	2.22(0-7)	0.7	0.335
Day 3	1.23(0-7)	0.37(0-2)	0.78(0-5)	0.692	0.306
hunger					
Day 0	0.93(0-3)	0.39(0-4.5)	0.95(0-4)	0.934	0.78
Day of surgery	0.24(0-3)	0.47(0-3)	1.39(0-7)	0.004	0.01
Day 1	1.86(0-8)	1.18(0-5)	1.50(0-6)	0.474	0.886
Day 3	0.83(0-5.5)	0.42(0-5)	0.89(0-5)	0.889	0.439
nausea					
Day 0	0(0-0)	0.21(0-3)	0(0-0)	0.999	0.07
Day of surgery	1.24(0-3)	1.53(0-6)	2(0-6)	0.666	0.916
Day 1	0.54(0-5)	1.84(0-6)	1.33(0-3)	0.828	0.758
Day 3	0.57(0-5)	0.05(0-1)	0.06(0-3)	0.138	0.585
fatigue					
Day 0	1.09(1-2)	1.04(1-2)	1(0-2)	0.125	0.563
Day of surgery	2.18(0-6)	2.47(1-6)	2.41(0-6)	0.553	0.979

Day 1	1.63(0-7.5)	0.89(0-3)	1.02(0-4)	0.128	0.786
Day 3	0.91(0-5)	0.42(0-3)	0.71(0-2)	0.791	0.172
Grip Strength Index（%）					
Day 0	44.67(29.04-67.74)	46.86(33.38-67.69)	44.07(30.71-62.27)	0.211	0.588
Day of surgery	38.38(26.22-68.06)	41.45(32.77-57.50)	41.29(25.88-57.88)	0.57	0.475
Day 1	39.15(27.57-65.97)	42.14(24.80-63.23)	43.00(30.88-61.21)	0.968	0.567
Day 3	42.41(29.73-66.13)	44.11(25.13-63.13)	44.08(28.86-64.85)	0.496	0.691

Table 3

	CHO Mean(min-max)	Placebo Mean(min-max)	Fasted Mean(min-max)	CHO vs Placebo Mean difference(95% CI);p value	CHO vs Fasted Mean difference(95% CI);p value	Placebo vs Fasted Mean difference(95% CI);p value
	24.70(5.5-101)	26.46(7.5-64)	25.02(1.5-93)	-1.76(-11.19 to 7.66);0.711	-0.32(-9.30 to 8.65);0.943	1.44(-7.91 to 10.79);0.76
Time to first anal exhaust(h)						
Independent standing time after surgery (h)	28.57(10-100)	28.71(12-70)	39.21(15-93)	-1.37(-10.15 to 9.88);0.978	-10.64(-20.03 to -1.25);**0.027**	-10.50(-20.29 to -0.712);**0.036**
Time to intake of water(h)	24.70(5.5-101)	26.46(7.5-64)	25.02(1.5-93)	-3.93(-4.56 to 3.78);0.851	-1.97(-5.87 to 1.92);0.316	-1.58(-5.69 to 2.53);0.446
Time to intake of oral diet(h)	27.94(12-73)	34.82(8-72)	34.60(2.5-80)	-6.88(-16.50 to 2.73);0.158	-6.65(-15.72 to 2.40);0.147	0.22(-9.68 to 9.24);0.963
number of infection patient						
Day 1	4	4	3	0.916	0.554	0.623
Day 3	2	2	3	0.943	0.755	0.696
Day 7	0	0	0			

Table 4

Variable	HR	95% CI range	p value
Age	1.275	1.064-1.527	0.008
BMI	1.303	1.012-1.677	0.040
Operation Time	1.017	1.002-1.033	0.031
Group	3.018	1.166-7.809	0.023
Blood Loss	0.996	0.989-1.003	0.217
Intraoperative Fluid	1	0.998-1.002	0.896

Table 5 :Multivariate analysis of risk factors for elevated IL-6 7 days post-operation
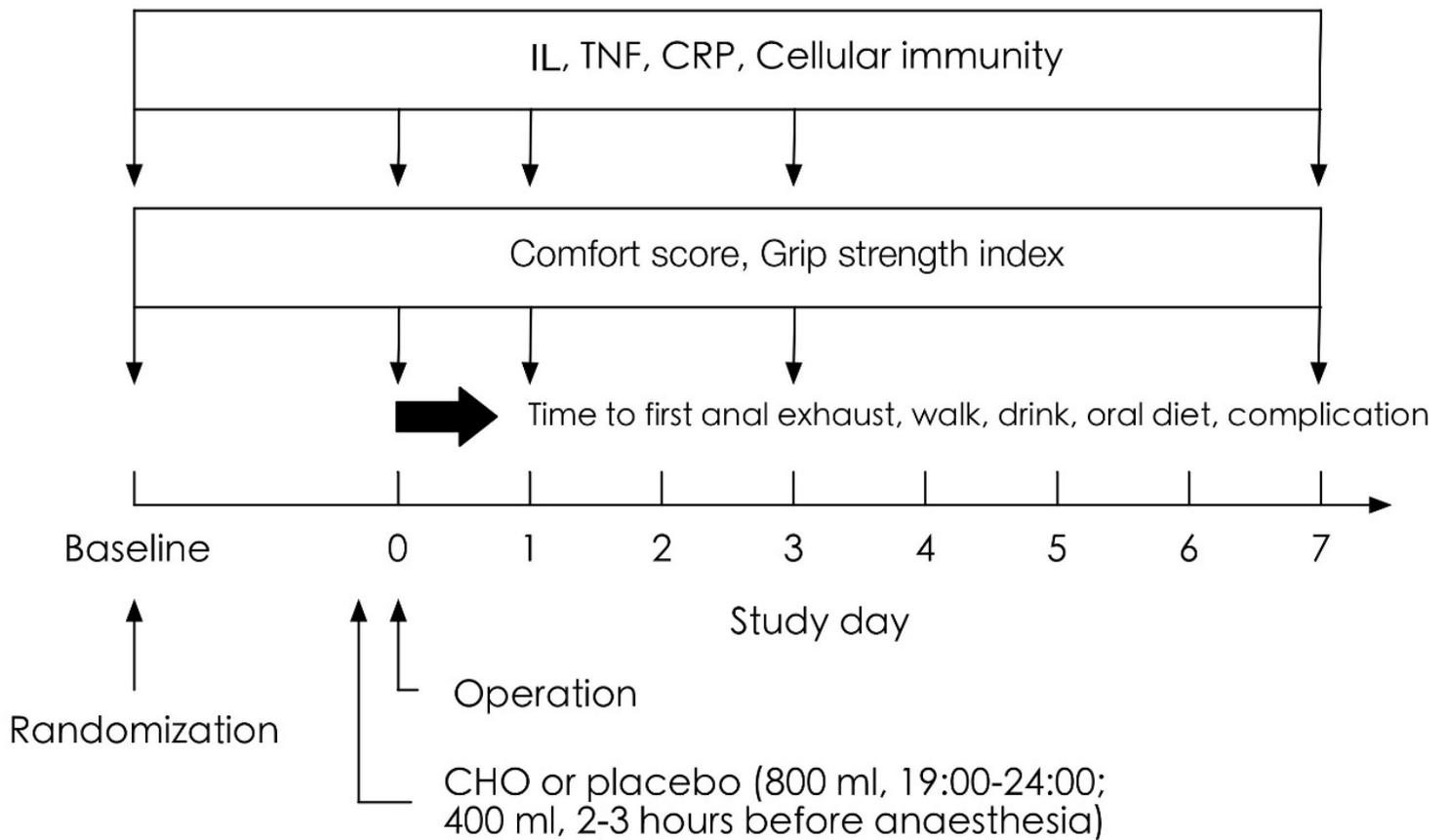
HR: hazard ratio; CI: confidence interval

Figures

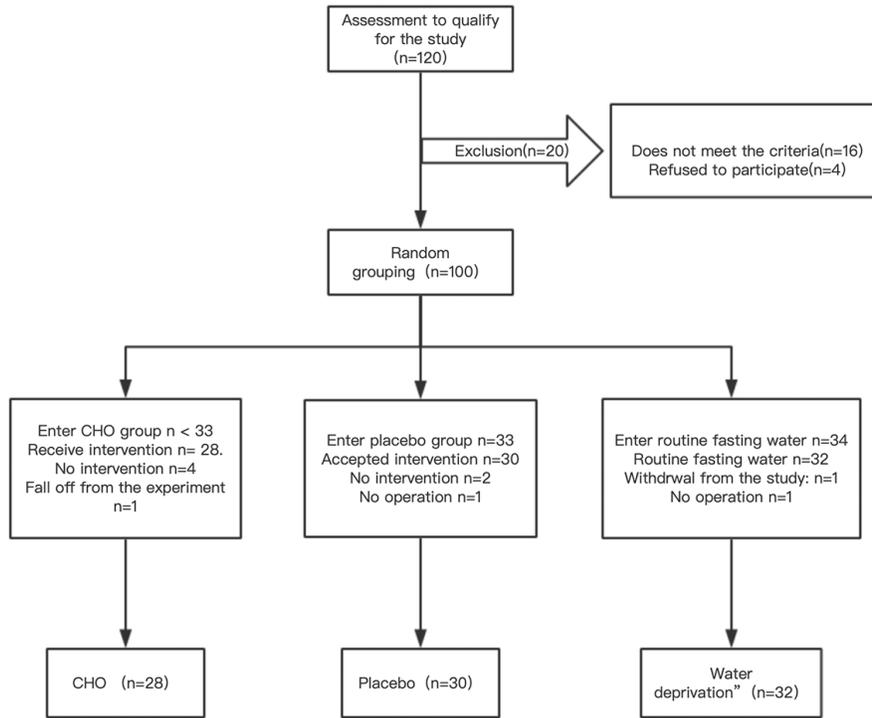## Figure 1

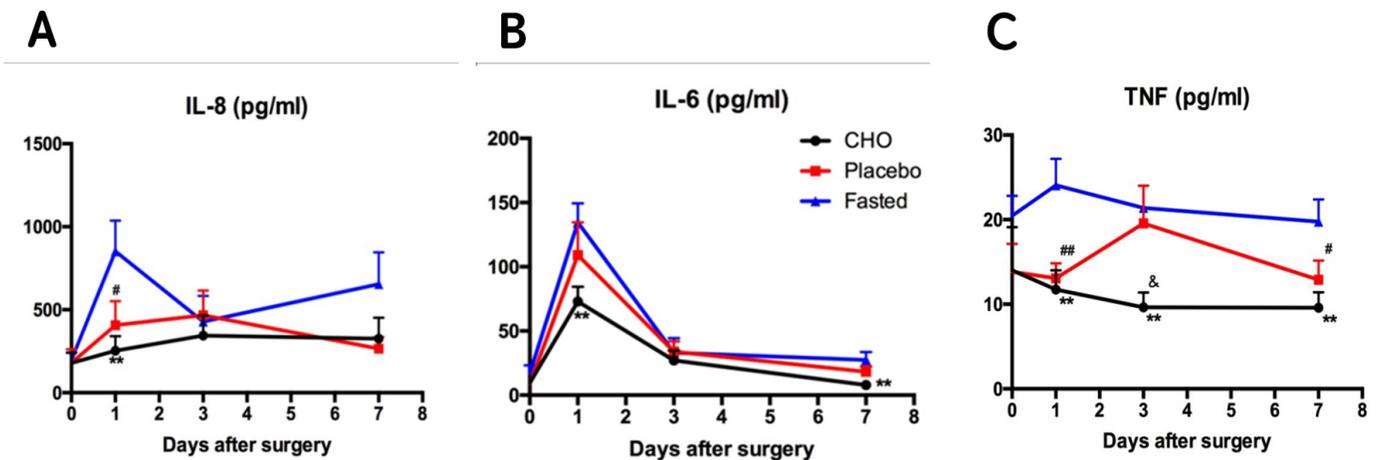Illustration of the experimental design

Figure 2

Experimental flow chart

Figure 3

Changes of postoperative inflammatory factors（including IL-8、IL-6、TNF） in different groups