Effects of Preoperative Oral Electrolyte-Carbohydrate Nutrition Supplement on Postoperative Outcomes in Elderly Patients Receiving Total Knee Arthroplasty: A Prospective Randomized Controlled Trial

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Objective: Patients undergoing total knee arthroplasty (TKA) were primarily geriatric, with high risk of postoperative electrolyte disorders and malnutrition. Randomized controlled trials regarding oral nutrition supplement (ONS) strategies in TKA was sparse. This study aimed to evaluate the efficacy of preoperative oral electrolyte-carbohydrate nutrition supplement (OECNS) on patients (aged >65 years) undergoing TKA.

Methods: From April 2019 to January 2020, 94 patients undergoing primary elective unilateral TKA in our hospital were considered in this prospective randomized controlled study. This study included patients aged over 65 years with ASA I-III, and excluded patients with electrolyte disorders, malnutrition, and comorbidities. The control group (control group) received meal nutrition supplements (preoperative 6 h [Pre 6h]) and water (Pre 2h), while OECNS group (intervention group) received meal nutrition supplements (Pre 6h) and OECNS (Pre 2). The Student’s t test and χ² test was used. The primary outcomes were the patient-reported comfort indicators (PRCIs) including hunger, thirst, nausea, vomiting, weakness, pain, anxiety, and general comfort. The secondary outcomes included indicators of electrolyte, nutrition, functional scores, clinical results, and complications.

Results: The scores of preoperative hunger (0.43 ± 0.10), pain (2.30 ± 0.34), and anxiety (9.04 ± 2.71) were significantly lower in OECNS group compared with control group (hunger, 1.19 ± 0.21; pain, 3.79 ± 0.26; anxiety, 11.21 ± 3.02) (Pre 1h) (all p < 0.05) as well as the weakness score on the first postoperative day (POD1) (OECNS group 3.57 ± 0.24; control group 5.15 ± 0.29; p < 0.001). A higher level of Na⁺ (OECNS group 140.54 ± 3.39; control group 138.07 ± 5.21; p = 0.008) and a reduced rate of hyponatremia (OECNS group 6.4%; control group 21.3%; p = 0.036) on POD1 were found. Moreover, the higher level of blood glucose (Post 2h) and reduced rates of abnormal blood glucose (Pre 2h, Post 6h) were verified in control group (all p < 0.05). There was no significant difference regarding the other outcomes.

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**Background**

Total knee arthroplasty (TKA) is a standard procedure for patients with end-stage knee joint diseases, effectively relieving pain, correcting deformity, and improving function. In the past 10 years, the number of TKA in China has increased from 53,880 (2011) to 374,833 (2019), indicating a six-fold increase. It is worth noting that patients undergoing TKA were primarily geriatric. An investigation showed that more than 80% of patients were 65 years or older. Along with the accelerated aging population, the prevalence of TKA in the elderly is expected to increase. However, elderly patients who received TKA were exposed to high risks of postoperative electrolyte disorders and malnutrition. Studies found that malnutrition caused discomfort and anxiety, prolonged length of hospital stay, and affected clinical recovery. In addition, electrolyte disorders had increased risks of delirium, myocardial infarction, and surgical site infection after orthopaedic surgeries. It was crucial to apply nutrition management to prevent malnutrition or electrolyte disorders after surgery.

The oral nutrition supplement (ONS) contains either macronutrient (proteins, fat, carbohydrates), micronutrients (vitamins, minerals), or mixtures of these supplements. The European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines recommend patients to take standard ONS (i.e. carbohydrates, protein, vitamins, and other immune nutrients) during the preoperative period unrelated to their nutritional status. Three randomized controlled trials (RCTs) reported the efficacy of ONS on general surgical patients, but their results were controversial. Smedley et al. found a significant reduction in minor complications, while the other two studies showed no significant impact on the outcome. There were no standard ONS strategies since patients and procedures varied in previous studies.

Our previous study evidenced that oral nutrition powder enriched with fat, protein, and carbohydrate could reduce albumin transfusion rate and electrolyte disorders. However, patients had to take four bags of nutrition power, which increased the digestive system burden of the elderly patients and increased the costs during the hospital stay. Recently, a clinical trial had found that 1000 mL of carbohydrate ONS administered the night before surgery did not improve any clinical outcomes but affected the patients’ sleep quality, which resulted in shorter sleep time and more nighttime urination. Therefore, we designed a novel and convenient ONS strategy that included a meal ONS given 6 h before surgery and an electrolyte-carbohydrate nutrition supplement (OECNS) given 2 h before surgery with the cooperation of the departments of anesthesiology and nutrition. Considering the electrolyte loss in TKA patients, we added sodium, potassium, and calcium into the OECNS with a total volume of 200 mL to decrease the burden on patients.

The purpose of this study was (i) to investigate the effects of preoperative OECNS on patient-reported comfort indicators (PRCIs) (including hunger, thirst, nausea, vomiting, weakness, pain, anxiety, and general comfort); (ii) to determine whether preoperative OECNS are beneficial for postoperative metabolism by comparing the indicators of nutrition, electrolyte, and blood glucose; (iii) to confirm the safety of OECNS in elderly (>65 years) TKA patients.

**Materials and Methods**

This study is a prospective single-center randomized controlled trial. Approval was obtained from our institution’s Clinical Trials and Biomedical Ethics Committee (2019-845) and registered with the Chinese Clinical Trial Registry (Chi-CTR-2200056660). The study was conducted between April 2019 and January 2020 at our hospital according to the CONSORT (Consolidated Standards of Reporting Trials) Statement.

**Patients and Inclusion Criteria**

Eligible criteria were (i) patients who underwent primary elective unilateral TKA; (ii) the American Society of Anesthesiologists (ASA) scales were between I and III; (iii) aged over 65 years; (iv) volunteered to participate in this study, fully cooperated with the medical researchers, and signed the informed consent form. Exclusion criteria included (i) hemoglobin (Hb) < 120 g/L, albumin (ALB) < 35 g/L, sodium (Na+) < 135 mmol/L, potassium (K+) < 3.5 mmol/L, calcium (Ca+) < 2.10 mmol/L; (ii) patients had comorbidities included diabetes, cirrhosis, infection, ischemic heart disease, severe cardiac diseases, and renal insufficiency; (iii) malnutrition patients (NRS2002 scores >5 points); (iv) patients who were unable to complete the study or withdrew. The drop out criteria were patients who refused to continue this trial.

**Randomizations**

Eligible patients were randomized into two groups (control group and OECNS group) using a computer-generated list of random numbers by investigator A who did not participate in the surgery, outcomes assessment, data collection, and statistical analysis. The random numbers were sealed in opaque envelopes, and the patients were required to select an envelope randomly to determine the group. The surgeons,
anesthetists, data collectors, outcome assessors, and statistical analysts did blind interventions and group allocations.

**Procedures of Interventions**

Before surgery: the general information of the patients was collected by investigator B in the outpatient ward. On the day of surgery: patients in control group were given one bag of meal nutrition powder mixed with 250 ml water 6 h before surgery and drank 200 ml water 2 h before surgery; meanwhile, patients in OECNS group were given one bag of meal nutrition powder mixed with 250 ml water 6 h before surgery and one bag of electrolyte-carbohydrate powder mixed with 200 ml water 2 h before the surgery. The composition and usage of nutrition powder are represented in Appendix S1. A professional nurse collected data without knowing the interventions. A dietitian was responsible for nutrition powder preparation and patient instructions.

**Surgical Procedure**

All TKA procedures used the standard medial parapatellar approach without a tourniquet. Measured resection and gap balancing techniques were utilized. Intravenous tranexamic acid was administrated to reduce blood loss during surgery (1 g) and 8 hours after surgery (1 g). The cemented, fixed-bearing, and posterior stabilized implants from Depuy Attune (DePuy, IN, USA) knee systems were implanted. All the surgeries were done by one senior orthopaedic surgeon in our center.

**Perioperative Management**

All subjects underwent standard perioperative multimodal pain management regimens in our center. Preoperatively, alprazolam (oral, 0.4 mg, the night before surgery) was used to help sleep. Postoperatively, dexamethasone (intravenous, 10 mg) and ondansetron (intravenous, 8 mg) were used as postoperative nausea and vomiting (PONV) prophylaxis. Moreover, celecoxib (oral, 200 mg, twice daily) was administered for pain management after surgery till discharge. The cold packs were used on the surgical site to alleviate pain for 1 day postoperatively. Oxycodone hydrochloride tablet (oral, 10 mg) and morphine hydrochloride (subcutaneously, 5 mg) were reserved as rescue analgesia when patients had outbreak pain (VAS >6). Half-dose enoxaparin (subcutaneously, 2000 I.U.) was routinely scheduled 12 h postoperatively, and a total dose (subcutaneously, 4000 I.U.) was given every 24 h until discharge. After discharge, rivaroxaban (oral, 10 mg) was used for 14 days.

![Flow diagram of patients’ selection and exclusion](image-url)
**Outcome Measurements**

The primary outcomes were the PRCIs, including hunger, thirst, nausea, vomiting, weakness, pain, anxiety, and general comfort. Secondary outcomes included electrolyte (sodium, potassium, calcium), hemoglobin, albumin, Interleukin 6 (IL-6), C-reactive protein (CRP), blood glucose, vital signs (body temperature, heart rate, respiratory rate, blood pressure), nutrition score, functional score, infusion volume, length of hospital stay, satisfaction, and complications (aspiration, infection, wound disease, thrombosis).

Visual analog scale (VAS) was used to measure six PRCIs (hunger, thirst, nausea, vomiting, pain, and weakness) at preoperative 1 h (Pre 1h) and on the first postoperative day (POD1). We propose using the VAS device to increase the efficiency and precision in assessing subjective and unpleasant sensations where 0 indicates no symptom and 10 indicates severe symptom. Anxiety scores were measured by the Amsterdam Preoperative Anxiety and Information Scale (APAIS) questionnaire and at Pre 1d, the general comfort scores were measured by the General Comfort Questionnaire (GCQ) on POD1. Blood samples were collected and assayed for electrolyte, hemoglobin, albumin, IL-6, and CRP on POD1; blood glucose was measured at Pre 2h, Post 2h, and Post 6h; vital signs were measured at Pre 4h, Pre 2h, in the post-anesthesia care unit (PACU), Post 2h, and Post 4h. The nutrition scores were measured by the Nutrition Risk Screening 2002 (NRS-2002) at Pre 1d, on POD1, while the functional scores were measured by Hospital for Special Surgery Knee-Rating Scale (HSS) at Pre 1d, Post 1m, and Post 3m after surgery. The length of hospital stay, surgical duration, infusion volume, satisfaction, and the rates of complications were recorded after surgery. Special personnel were scheduled to investigate the unplanned readmission rate (30, 60 days after surgery) and mortality (30 days, 1 year after surgery) in the form of telephone follow-up.

**Statistical Analysis**

The sample size was calculated concerning the primary outcome: VAS score of hunger. Our preliminary trial included 10 patients received Pre-2h OECNS, and another 10 patients received Pre-2h water. Their preoperative mean VAS scores of hunger were 0.45/0.10 and 1.85/0.22, respectively. The difference of VAS scores >1.0 was significant clinically (considered standard deviation). Power analysis applied by PASS 11.0 software suggested that the samples for each group were at least 40 patients with a two-sided alpha level of 0.05 and a power of 90%. Furthermore, the sample size was increased by 20%, and the minimum sample was 12 for each group (Appendix S2). Normally distributed continuous data are expressed as means/standard deviation and were analyzed using the Student’s t test. If the numerical variable

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### TABLE 1 Baseline data

| Characteristics | Control group | ONCES group | $\chi^2/t$ | p-value |
|-----------------|---------------|-------------|-----------|---------|
| Demographic characteristics | | | | |
| Age (years)† | 67.11 (8.76) | 67.55 (7.68) | 0.196 | 0.659 |
| Gender (male/female) | 9/38 | 14/33 | 1.439 | 0.337 |
| Height (cm) † | 155.83 (6.34) | 157.60 (7.33) | 0.451 | 0.503 |
| Weight (kg) † | 65.33 (9.74) | 64.83 (11.63) | 0.538 | 0.465 |
| BMI (kg/m²) | 26.90 (3.60) | 26.05 (3.98) | 0.098 | 0.755 |
| ASA (I/II/III) | 0/27/20 | 0/34/13 | 2.288 | 0.194 |
| History of osteoarthritis (years) † | 15.72 (5.98) | 15.02 (5.64) | 0.018 | 0.895 |
| Smoking (use/non-use) | 7/40 | 8/39 | 0.079 | 0.778 |
| Alcohol (use/non-use) | 7/40 | 8/39 | 0.079 | 0.778 |
| Comorbidities | | | | |
| Hypertension | 7 (14.89%) | 15 (31.91%) | 3.886 | 0.143 |
| Cardiovascular | 10 (21.27%) | 9 (19.14%) | | |
| Others | 30 (63.82%) | 23 (48.93%) | | |
| Preoperative laboratory examination † | | | | |
| Hemoglobin (g/L) | 119.97 (17.74) | 126.68 (17.93) | 0.005 | 0.946 |
| Albumin (g/L) | 40.24 (3.99) | 40.26 (4.03) | 0.126 | 0.723 |
| Na⁺ (mmol/L) | 141.60 (3.17) | 141.48 (3.78) | 0.440 | 0.509 |
| K⁺ (mmol/L) | 4.44 (0.59) | 4.45 (0.59) | 0.779 | 0.380 |
| Ca²⁺ (mmol/L) | 2.36 (0.22) | 2.41 (0.16) | 1.187 | 0.279 |
| CRP (mg/L) | 3.52 (2.04) | 3.50 (1.90) | 0.166 | 0.684 |
| IL-6 (ng/L) | 3.46 (1.69) | 3.40 (2.43) | 0.787 | 0.377 |
| Side (Left/Right) | 27/20 | 25/22 | 0.172 | 0.678 |
| Length of stay (day) | 3.40 (0.68) | 3.34 (0.70) | 0.143 | 0.707 |
| Blood loss (ml) | 132.98 (7.58) | 134.81 (9.07) | -0.154 | 0.108 |
| Surgical duration (min) | 88.7 (5.2) | 88.2 (7.1) | 0.161 | 0.695 |
| VAS pain score | 5.4 (1.4) | 5.8 (1.5) | -0.184 | 0.101 |

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index.; † The values are presented as the mean and the standard deviation.; ‡ The values are presented as the number and the percentage.
### TABLE 2 Subjective comfort parameters

| Characteristics                  | Control group | ONCES group | \( \chi^2 \)/\( t \) | \( p \)-Value |
|----------------------------------|---------------|-------------|----------------------|----------------|
| **Patient-reported comfort indicators** |               |             |                      |                |
| Nausea†                          |               |             |                      |                |
| Pre 1h                           | 0.21 (0.09)   | 0.17 (0.08) | 0.347                | 0.729          |
| No. of patients had nausea†‡     | 5 (10.6%)     | 4 (8.5%)    | 0.0001               | 1              |
| Post 1 day                       | 0.38 (0.14)   | 0.34 (0.14) | 0.211                | 0.833          |
| No. of patients had nausea       | 7 (14.9%)     | 6 (12.8%)   | 0.089                | 0.765          |
| Vomiting†                        |               |             |                      |                |
| Pre 1h                           | 0             | 0           | N/A                  | N/A            |
| No. of patients had vomiting     | 0             | 0           | N/A                  | N/A            |
| Post 1 day                       | 0.43 (0.16)   | 0.38 (0.17) | 0.177                | 0.860          |
| No. of patients had vomiting     | 7 (14.9%)     | 5 (10.6%)   | 0.382                | 0.536          |
| Hungry†                          |               |             |                      |                |
| Pre 1h                           | 1.91 (0.21)   | 0.43 (0.10) | 6.141                | <0.001*        |
| Post 1 day                       | 0.43 (0.16)   | 0.43 (0.14) | 0                    | 1              |
| Thirsty†                         |               |             |                      |                |
| Pre 1h                           | 0.68 (0.17)   | 1.83 (0.21) | 0.360                | 0.550          |
| Post 1 day                       | 0.68 (0.21)   | 0.66 (0.19) | 0.073                | 0.942          |
| Weakness†                        |               |             |                      |                |
| Pre 1h                           | 0.26 (0.09)   | 0.26 (0.09) | 0                    | 1.00           |
| Post 1 day                       | 5.15 (0.29)   | 3.57 (0.24) | 4.162                | <0.001*        |
| Pain†                            |               |             |                      |                |
| Pre 1h                           | 3.79 (0.26)   | 2.30 (0.34) | 3.447                | 0.010*         |
| Post 1 day                       | 4.64 (0.18)   | 4.55 (0.19) | 0.325                | 0.746          |
| APAIS scores†                    |               |             |                      |                |
| Overall score                    | 17.34 (4.08)  | 13.74 (3.30) | 12.519               | 0.001*         |
| Anxiety                          | 11.21 (3.02)  | 9.04 (2.71) | 5.549                | 0.021*         |
| Need-for-information             | 6.13 (1.75)   | 4.70 (1.60) | 0.361                | 0.549          |
| GCQ score†                       | 85.85 (7.30)  | 90 (6.57)   | 3.015                | 0.086          |

Abbreviations: APAIS, Amsterdam Preoperative Anxiety, and Information Scale; GCQ, The General Community Quarantine; HSS, Hospital for Special Surgery; NRS-2002, The Nutrition Risk Screening 2002.* \( p \)-Values <0.05 indicating a significant difference between the two groups are bold.; † The values are presented as the mean and the standard deviation.; ‡ The values are presented as the number and the percentage.

### TABLE 3 Laboratory indices and clinical outcomes

| Characteristics                  | Control group | ONCES group | \( \chi^2 \)/\( t \) | \( p \)-Value |
|----------------------------------|---------------|-------------|----------------------|----------------|
| **Postoperative laboratory examination** |               |             |                      |                |
| Hemoglobin† (g/L)                | 116.79 (16.58) | 117.66 (19.99) | 0.818                | 0.23           |
| Blood infusion‡                  | 0             | 0           | N/A                  | N/A            |
| Albumin† (g/L)                   | 39.34 (4.56)  | 38.41 (4.18) | 1.03                 | 0.306          |
| Albumin infusion                 | 8 (17.02%)    | 7 (14.89%)  | 0.079                | 0.778          |
| Na⁺ (mmol/L)                     | 138.07 (5.21) | 140.54 (3.39) | -2.718               | 0.008*         |
| Hyponatremia†                    | 10 (21.3%)    | 3 (6.4%)    | 4.374                | 0.036*         |
| K⁺ (mmol/L)                      | 3.95 (0.37)   | 3.94 (0.43) | -0.088               | 0.93           |
| Hyperkalemia†                    | 3 (6.4%)      | 3 (6.4%)    | 0.0001               | 1              |
| Ca²⁺ (mmol/L)                    | 2.15 (0.10)   | 2.14 (0.13) | -0.241               | 0.81           |
| Hypocalcemia†                    | 2 (4.3%)      | 1 (2.1%)    | 1.0001               | 1              |
| CRP (mg/L)                       | 3.91 (1.79)   | 4.10 (1.67) | 0.514                | 0.608          |
| IL-6 (ng/L)                      | 22.96 (33.00) | 22.14 (20.90) | -0.144               | 0.886          |
| No. of patients had electrolyte disorder | 0             | 0           | N/A                  | N/A            |
| **NRS-2002 score†**              |               |             |                      |                |
| Pre 1 day                        | 1.26 (0.71)   | 1.36 (0.53) | 1.13                 | 0.291          |
| Post 1 day                       | 1.57 (0.927)  | 1.36 (0.529) | 1.367               | 0.176          |
| No. of patients had malnutrition | 0             | 0           | N/A                  | N/A            |
| **HSS score†**                   |               |             |                      |                |
| Preoperative                     | 46.34 (4.89)  | 47.83 (5.20) | 1.434                | 0.394          |
| 1 month                          | 69.74 (5.19)  | 69.72 (5.89) | 0.399                | 0.529          |
| 3 months                         | 84.04 (5.493) | 84.77 (4.502) | 0.019               | 0.985          |
| Infusion Volume† (ml)            | 1257.23 (129.88) | 1205.11 (111.41) | 2.088               | 0.040*         |
| Satisfaction†                    | 93.08 (6.50)  | 93.34 (6.45) | 0.004                | 0.95           |

Abbreviations: BP, blood pressure; BT, body temperature; DBP, diastolic blood pressure; HR, heart rate; Post, post-surgery; Pre, pre-surgery; RR, respiratory rate; SBP, systolic blood pressure.; * \( p \)-values <0.05 indicating a significant difference between the two groups are bold.; † The values are presented as the mean and the standard deviation.; ‡ The values are presented as the number and the percentage.
had non-normal distribution or unequal variance, the Wilcoxon Mann–Whitney U-test was used. Categorical variables are presented as frequencies and were analyzed using the χ²-test or Fisher’s exact test, as appropriate. All statistical analyses were performed using IBM SPSS 23.0 (IBM, Armonk, NY). Differences with a p-value < 0.05 indicated statistically significant.

Results

A total of 120 patients were assessed for eligibility, as shown in the flowchart (Figure. 1). Sixteen patients were excluded for not meeting the included criteria: eight patients refused to participate in the study, and two patients had difficulties in communicating. The remaining 94 eligible patients went through a randomization process. Finally, we allocated 47 patients into each group. The demographic data, including age, gender, BMI, ASA status, comorbidities, preoperative laboratory indexes, and the other clinical confounding factors, were similar and balanced between the two groups (Table 1).

Primary Outcome

The VAS scores of hunger (0.43 ± 0.10) and pain (2.30 ± 0.34) were significantly lower in the OECNS group compared with the control group (hunger 1.91 ± 0.21; pain 3.79 ± 0.26) preoperatively (p < 0.001, p = 0.01, respectively). The preoperative APAIS anxiety score in the OECNS group (9.04 ± 2.71) was significantly lower than that in the control group (11.21 ± 3.02; p = 0.021). The weakness score measured on POD1 was significantly lower in the OECNS group (3.57 ± 0.24) compared with the control group (5.15 ± 0.29; p < 0.001). There was no significant difference in the VAS scores of nausea, vomiting, or the rates of patients who had nausea or vomiting perioperatively. Furthermore, the general comfort scores did not differ between the two groups (Table 2).

Secondary Outcomes

In our study, patients in the intervention group had significantly higher levels of sodium (140.54 ± 3.39 mmol/L) than those in the control group (138.07 ± 5.21 mmol/L) after surgery (p = 0.008). The rate of hyponatremia was reduced in the OECNS group (3, 6.4%) compared with the control group (10, 21.3%) postoperatively (p = 0.036). There were no significant differences in hemoglobin, albumin, potassium, calcium, IL-6, CRP, or the rates of hypocalcemia, hypokalemia, or electrolyte disorder between the two groups after surgery. Patients in the intervention group (1205.11 ± 111.41 mL) had significantly lower infusion volumes than that in the control group (1257.23 ± 129.88 mL) (p = 0.040). The results of secondary outcomes are shown in Table 3.

Moreover, patients in the intervention group (5.56 ± 0.79 mmol/L) had significantly higher levels of blood glucose (at Post 2h) compared with the control group (5.09 ± 1.04 mmol/L) (p = 0.010). However, there was no significant difference in blood glucose levels at the other two time points (Pre 2h, Post 6h). The rates of abnormal blood glucose (>6.1 or <3.9) were significantly reduced in the OECNS group (Pre 2h: 17, 36.2% vs. 30, 63.8%, p = 0.007; Post 6h: 27, 57.4% vs. 37, 78.7%, p = 0.027), while the mean level of blood pressure did not differ between the two groups (Table 4, Figure 2).

No significant difference was found in vital signs, including body temperature, pulse, and respiratory rate peroperatively (Figure 3). There was no significant difference between the two groups in nutrition scores (NRS-2002), functional scores (HSS), length of hospital stay, volume of blood loss, surgical duration, or patient satisfaction (Table 3).

![Fig. 2 The levels of blood glucose between the two groups](image)

### TABLE 4 The level of blood glucose

| Characteristics        | Control group | ONCES group | χ²/t   | p-value |
|------------------------|---------------|-------------|--------|---------|
| Blood glucose* (mmol/L)|               |             |        |         |
| Pre 2h                 | 5.58 (0.95)   | 5.45 (0.90) | 0.705  | 0.483   |
| >6.1 or <3.9 mmol/L    | 30 (63.8%)    | 17 (36.2%)  | 7.191  | 0.007*  |
| Post 2h                | 5.99 (1.04)   | 5.56 (0.79) | 2.445  | 0.010*  |
| >6.1 or <3.9 mmol/L    | 17 (36.2%)    | 13 (27.7)   | 0.783  | 0.376   |
| Post 6h                | 6.27 (1.34)   | 5.49 (1.27) | 2.897  | 0.735   |
| >6.1 or <3.9 mmol/L    | 37 (78.7%)    | 27 (57.4%)  | 4.896  | 0.027*  |

* p Values <0.05 indicating a significant difference between the two groups are bold.; † The values are presented as the mean and the standard deviation.
Predefined complications did not occur in two groups (aspiration, regurgitation, infection, wound disease, thrombosis, dizziness, or fall). No patients had unplanned readmission rates (30 and 90 days) and mortality (30 days and 1 year) in both groups.

**Discussions**

**Key Findings**

This prospective study has confirmed that the patients (>65 years) who underwent TKA receiving OECNS had better outcomes than patients who received water regarding preoperative subjective comfort indicators (lower scores of hunger, pain, anxiety, and weakness), postoperative electrolyte (higher levels of sodium, and lower rate of hyponatremia), perioperative blood glucose (higher levels of blood glucose at Post 2h, and lower rate of abnormal blood glucose), and infusion volume (lower volume of infusions). No anesthesia-related complications occurred in one case.

**Overview**

Patients who underwent TKA were at a high risk of electrolyte disorder due to electrolyte loss (up to 83%)\(^{21,22}\). Furthermore, the metabolic stress evoked by surgeries will decompose body nutrients and cause patients to more easily develop acute malnutrition (up to 49%)\(^{23}\). Studies suggested that malnutrition and electrolyte disorder were associated with poor clinical outcomes (i.e. decreased patient comfort, prolonged length of hospital stay, increased complications, etc.)\(^{24,25}\). Preoperative fasting duration was relevant to the level of electrolyte loss and stress response, with the recommended protocol being 2 h for water and 6 h for food\(^{22,26}\). Even with the appropriate fasting, malnutrition and electrolyte disorder were high in the elderly patients due to the degraded organ functions. In 2021, the newest ESPEN guidelines recommended using preoperative ONS to improve surgical patients’ nutrition status despite nutrition risks, while the choice of components was controversial\(^{7,26}\). The positive clinical benefits of preoperative oral carbohydrates were confirmed in many trials, such as reduced length of hospital stay, improved nutrition status, and decreased rates of mortality in abdominal surgery patients\(^{27,28}\). However, most of the studies only investigated the efficacy of carbohydrates in different volumes, doses, or concentrations—the supplementation of electrolytes to carbohydrate ONS has not been investigated\(^{22}\). Though the Enhanced Recovery After Surgery (ERAS) has been successfully applied in many surgical specialties, the literature on orthopaedic surgery is limited, with limited prospective data\(^{29–33}\). Our study was the first prospective randomized trial to assess the efficacy of a 200 ml preoperative electrolyte carbohydrate oral nutrient supplement on TKA patients. The creation of our nutritional formula was based on the principles that meet the needs of a 60-kilogram adult receiving a selective total joint surgery.

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Fig. 3 The vital signs between the two groups. (A) Body temperature. (B) Pulse. (C) Systolic blood pressure. (D) Diastolic blood pressure.
without increasing anesthetic risks. Our protocol was approved by the anesthesia and nutrition departments in our center.

**Patient-Reported Comfort Indicators**

The experience of the patient was crucial in improving surgery quality. The discomfort indicators reported in our trial included hunger, thirst, nausea, vomiting, weakness, pain, and anxiety. The results showed that administration of OECNS 2 hours before TKA significantly improved patients’ feelings regarding hunger (1.48), pain (1.49), and anxiety (2.17). The results were in line with previous studies. The improved preoperative hunger experiences may be related to energy intake. Moreover, anxiety was another vital indicator, and the causes of anxiety in elderly patients varied, such as concerns about surgery, anesthesia, complications, and treatment costs. We used the APAIS questionnaire, and it was an effective screening instrument to assess preoperative anxiety and need-for-information in clinical practice, mainly due to its brevity. The decreased anxiety scores were possibly associated with the secretion of serotonin after carbohydrates intake. Similar results were evidenced in previous studies. Furthermore, many factors affect pain in patients with knee diseases. Our study found an improved preoperative pain experience in the intervention group. However, the result should be cautiously interpreted since they did not reach the minimal clinically important differences (MCID). We assumed that the relieved stress response might help relieve the preoperative pain. However, there appears to be insufficient evidence to draw a definitive conclusion. Moreover, the VAS scores for nausea and vomiting did not differ between the two groups perioperatively, and our results were consistent with others. Possible reasons were the medicine we used to prevent nausea and vomiting. The other postoperative subjective comfort scores were similar between the two groups.

**Postoperative Metabolism Indicators**

Dehydration usually occurs in surgical patients due to fasting and fluid loss. The dehydrated states usually result in electrolyte disorders, such as hyponatremia, hypotension, etc. Our trial found a higher sodium level and reduced hyponatremia in the intervention group, and the results were similar to the previous studies. The potassium and calcium levels were similar in the two groups, and the rates of hypokalemia and hypocalcemia did not differ between the two groups. The electrolyte disorders did not occur in any patient, while this benefit should be considered cautiously since all patients are appropriately optimized. The other laboratory indexes, such as hemoglobin, albumin, IL-6, and CRP, were similar between the two groups. These benefits may come from the comprehensive care of ERAS implemented in our center and multidisciplinary team cooperation. One of the main concerns of using carbohydrate supplements is the uncertainty of how blood glucose levels will react. Our study found a difference in blood glucose at 2 h post-surgery, but the difference was little and lacked clinical significance. Our results were similar to previous studies. Of note, the events of abnormal blood glucose were significantly reduced in the intervention group. No study reported this indicator before, and we believe our findings would give the clinical staff more information in deciding the components of ONS. However, we did not include patients who had diabetes, and the results should be considered cautiously in these patients. Moreover, we found a significant difference (200 mL) in the total infusion volume though the reasons are unclear now. Optimizing fluid management was one of the essential goals in ERAS of TKA. Reduced infusion could increase the heart burden and prevent related complications.

**Safety**

The study showed no difference in perioperative vital signs, postoperative nutrition scores, functional recovery, patient satisfaction, and the other clinical outcomes. In our study, no difference was observed in the complications (including aspiration, regurgitation, superficial or deep infections, wound diseases, thrombosis, dizziness, or fall). And no patients reported unplanned readmission and mortality when followed up at 30, 60 days, and 1 year postoperatively.

**Strengths and Limitations**

Our study was the first RCT to investigate the efficacy of ONCES administered 2 h before surgery in elderly patients (over 65 years) undergoing TKA. And we provided a number of novel outcome indicators that could comprehensively reflect the efficacy of ONCES in both subjective and objective views. There are several limitations in our study. Firstly, many participants were women, which may influence the results since women had higher levels of pain and anxiety in other studies. However, the proportion of women was balanced between the two groups, thus would not influence the results. Secondly, the population was relatively small and reflected our center experience though power analysis showed that the number of patients would be enough to detect the difference. Thirdly, the difference between statistical and clinical significance has been a concern by surgeons, but most of the outcomes alluded to earlier in the paper (such as APAIS scores) lacked relevant data.

**Conclusions**

Our study has confirmed that 200 mL of ONCES administered 2 h before surgery can significantly improve subjective comfort, electrolytes, and blood glucose with reduced infusions in elderly patients (over 65 years) undergoing total knee arthroplasty, without increasing the complication rates. The addition of electrolytes to carbohydrate ONS was recommended based on our findings. Future studies could compare the economic expenses and the burdens of clinical staff when applying ONCES into practice.
AUTHOR CONTRIBUTIONS

Hye Yuce: Designing the study, collecting and analyzing the data, writing the manuscript. Tang Xiumei: Designing the study, collecting and analyzing the data, writing the manuscript. Ning Ning: Designing the study, collecting and analyzing the data, writing the manuscript. Chen Jiali: Designing the study, collecting and analyzing the data, writing the manuscript. Li Peifang: Collecting and analyzing the data. Kang Pengde: Collecting and analyzing the data, help revising the manuscript.

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ETHICAL APPROVAL

This study has been approved by the Clinical Trials and Biomedical Ethics Committee of West China Hospital, Sichuan University, and registered with the Chinese Clinical Trial Registry (ID: ChiCTR200056660). Written informed consent was obtained from all participants before surgery. All experiments were performed following relevant guidelines and regulations. This study was conducted following the Declaration of Helsinki.

CONSENT TO PARTICIPATE

Written informed consent was obtained from all participants.

CONSENT FOR PUBLICATION

All authors have stated consent for publication.

DATA AVAILABILITY STATEMENT

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Supporting Information

Additional Supporting Information may be found in the online version of this article on the publisher’s web-site: Appendix S1

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