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RESEARCH

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Effect of preoperative oral carbohydrate on postoperative delirium in elderly patients undergoing lower extremity orthopedic surgery: a prospective randomized trial

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Abstract

Background Postoperative metabolic disorders and inflammatory responses are closely associated with postoperative delirium (POD). Preoperative oral carbohydrate intake can alleviate postoperative insulin resistance and the inflammatory response. This study aimed to evaluate the effects of preoperative oral carbohydrate intake on the incidence of POD in older patients undergoing lower limb orthopedic surgery.

Methods Eighty patients were randomly assigned to oral intake of 200 mL carbohydrate solution (Group CHO) 2 h before surgery or fasting for 8 h before surgery (Group C). The primary outcome was the incidence of POD. Fasting plasma glucose, interleukin (IL)-6, and C-reactive protein (CRP) levels were assessed before surgery and 1, 3, and 5 days after surgery (D1, D3, and D5).

Results The incidence of POD in Group CHO was lower than that in Group C ($P = 0.005$). Blood glucose, IL-6 and CRP levels of Group CHO were significantly lower than those of Group C on D1 and D3 ($P < 0.05$).

Conclusions Preoperative oral carbohydrate intake can reduce the incidence of POD in older patients by ameliorating postoperative metabolic disorders and reducing inflammatory responses.

Trial registration ChiCTR2300070154, Date of registration: 03/04/2023.

Keywords Older patients, Postoperative delirium, Carbohydrate, Orthopedic surgery

Background

Postoperative delirium (POD) is a major challenge in geriatric medicine and surgery. The acute and transient nature of POD, characterized by inattention, altered consciousness, and cognitive dysfunction, emphasizes the complexity of its management and the urgency for effective prevention and treatment strategies. Fluctuating symptoms, typically resolving within a week, pose diagnostic and therapeutic challenges, underscoring the necessity for a multifaceted approach to care. The incidence of POD in older patients undergoing orthopedic surgery ranges from 13 to 41% [1–4], indicating significant variability that is potentially attributable to differences in patient populations, surgical procedures, anesthesia types, and perioperative management practices.

Studies have demonstrated that energy metabolism disorders and inflammatory responses are significant

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mechanisms underlying POD [5–9]. Metabolic disorders, particularly fluctuations in blood glucose levels, have been implicated in POD incidence. The relationship between blood glucose level and POD is complex and involves various physiological and biochemical pathways. Studies have highlighted that blood glucose levels significantly influence POD development.The maintenance of stable glucose levels may mitigate this risk. Perioperative glucose management is emphasized as a potential strategy for preventing POD, underscoring the need for careful monitoring and regulation of blood glucose levels during surgery [10–12].

Inflammatory biomarkers such as interleukin-6 (IL-6) and C-reactive protein (CRP) are strongly associated with POD [13–15]. Elevated levels of these biomarkers suggest an inflammatory state that may worsen postoperative cognitive dysfunction. These studies confirm the correlation between inflammatory markers and the incidence of POD, emphasizing the crucial role of inflammation management in reducing the risk of delirium.

Preoperative oral carbohydrate administration improves postoperative metabolic disorders and reduces inflammatory responses [16, 17], indicating that preoperative oral carbohydrates may also prevent POD. However, there are few reports on the effects of preoperative carbohydrate intake on POD. This study aimed to evaluate the effect of preoperative oral carbohydrate administration on the incidence of POD, investigate its underlying mechanisms, and propose novel strategies for POD prevention.

Methods

Study design

This study was a single-center, single-blinded, prospective, randomized, controlled trial which was approved by the Ethics Committee of the Affiliated Hospital of North Sichuan Medical College (No.2023ER001-1). All patients or their legal representatives signed a written informed consent. This trial was conducted according to the guiding principles of the Helsinki Declaration and was registered at Chinese Clinical Trial Registry on 03/04/2023 with registration number ChiCTR2300070154.

Randomization

A random number table was used to determine patient allocation. Patients were randomised (1:1) to be selected for the conventional fasting group (Group C) and the preoperative carbohydrate group (Group CHO).

According to inclusion and exclusion criteria. A researcher conducted preoperative visits and interviewed candidates who met the inclusion criteria and signed the informed consent. The other investigator assigned carbohydrate drinks to patients in the CHO group based on the time of the previous surgery.

Inclusion and exclusion criteria

The inclusion criteria were as follows: Patients aged 65–79 years of either sex, American Society of Anesthesiologists (ASA) physical status I–III, and patients who had undergone hip or knee replacement surgery under spinal anesthesia.

The exclusion criteria were as follows: patients who refused to participate; those with diabetes, abnormal glucose tolerance, or on medications affecting insulin sensitivity; patients experiencing nausea, vomiting, gastroesophageal reflux, gastric emptying disorders, or pyloric obstruction; individuals with severe cardiac, pulmonary, hepatic, renal, or cerebral conditions; patients with a suspected or confirmed history of alcohol or drug abuse or preoperative mini-mental state examination (MMSE) score <23 points (evaluated 1 day before surgery); individuals with a history of Alzheimer's disease, Parkinson's disease, or delirium; patients receiving any corticosteroid therapy;contraindications to spinal anesthesia and patients unable to communicate effectively due to severe sensory impairments (such as vision and hearing loss) or other reasons affecting evaluation.

Treatment protocol

In Group C, patients started fasting at midnight before surgery. The patients in Group CHO also started fasting from midnight before surgery, except for receiving 200 mL carbohydrate drink (Fuan [12.6% carbohydrate]; 214.2 kJ/100 mL, 280 mOsm/kg and 200 mL per bottle) 2 h before surgery.

The anesthesia protocol for both groups was standardized and involved spinal anesthesia. Upon patient arrival in the operating room, peripheral venous access was routinely established and oxygen was administered via a nasal cannula at a rate of 3 L/min. Continuous monitoring of invasive blood pressure, measurement of SpO2, and an electrocardiogram were performed. The patient was placed in the lateral decubitus position, and spinal anesthesia was performed at the L3-4 or L2-3 levels. Upon unobstructed cerebrospinal fluid flow, a mixture of 0.75% bupivacaine (1–1.3 mL) and cerebrospinal fluid (0.5 mL) was injected, resulting in a total volume of 1.5–1.8 L to maintain the anesthesia level at T8 during the procedure. Ephedrine (6 mg intravenously) was administered if the systolic blood pressure fell below 90 mm Hg, and atropine (0.5 mg) was administered if the heart rate dropped below 50 beats per minute. Heart rate and mean arterial pressure fluctuations during the operation were maintained within 20% of the baseline values.

All the surgeries were performed by the same group of surgeons. Intravenous analgesia was administered by pump to both groups after surgery. The standardized medication regime was sufentanil 150 g + butorphanol 8 mg + tolansetron 5 mg, added to saline and diluted to 150 mL, background dose: 2.5 mL/h; single dose: 1 mL; locking time: 15 min.

Observation indicators

Baseline clinical characteristics, including age, sex, height, weight, ASA classification, and type of surgery, were recorded preoperatively, as was the preoperative MMSE score. Operative time, fluid volume, and intraoperative blood loss were also recorded. The mean arterial pressure (MAP) and heart rate (HR) were measured at four specific time points: 5 min after admission to the operating room (T0), 5 min after anesthesia (T1), 30 min after commencement of surgery (T2), and immediately after surgery (T3). At the four research time points, the patients were monitored for symptoms such as thirst, nausea, and vomiting.

POD was assessed on postoperative days 1–5, conducted daily between 08:00–10:00 a.m. and 16:00–20:00 p.m. by trained observers who were unaware of specific group assignments. The 3-Minute Diagnostic Confusion Assessment Method (3D-CAM) scale [18] was used for the detection of POD, and the specific diagnostic criteria were: (1) acute change of mental state with volatility; (2) attention disorder; (3) confusion of thinking; (4) change of consciousness level. (1) and (2) existing at the same time, plus any one of (3) or (4), which requires the patient to have an acute onset of change or fluctuating mental status, inattention, and either disorganized thinking or an altered level of consciousness. Patients were considered delirious if delirium was present in the 3D-CAM on any postoperative day; otherwise, patients were considered non-delirious.

Venous blood samples were collected before the intervention on the morning of the day of surgery and postoperatively on days 1, 3, and 5. Serum levels of blood glucose, IL-6, and CRP were determined using enzyme-linked immunosorbent assay (ELISA).

Statistical analysis

Based on a preliminary trial, the incidence of lower-extremity orthopedic POD in older patients was approximately 30%. Following oral carbohydrate administration, the incidence of POD decreased to approximately 5%. Therefore, using a power analysis with a 95% confidence interval and power of 80%, accounting for a dropout rate of 10%, the final sample size required was calculated to be 40 cases per group, resulting in a total of 80 cases.

Statistical software (SPSS 27.0) was used for the analysis. Continuous data are expressed as mean ± standard deviation or median (quartile 1 (Q1), quartile 3 (Q3)). All continuous data with normal distribution were compared using an independent sample t-test, whereas the Mann–Whitney U nonparametric test was used for non-normally distributed data. Numerical data were analyzed using the chi-square test. $P < 0.05$ was considered as statistical significance.

Results

We conducted an eligibility review of 90 patients who were scheduled to undergo lower limb orthopedic surgery under spinal anesthesia between April 2023 to April 2024.

Based on the inclusion and exclusion criteria, four patients with concomitant diabetes or impaired glucose tolerance, two patients with cognitive impairments, and four patients who did not consent to participate in the study were excluded. Ultimately, 80 patients were included in the study (Fig. 1). The control group (Group C) and the carbohydrate group (Group CHO) comprised 40 patients each.

Comparison of baseline characteristics between the two groups

There were no statistically significant differences between the two groups in terms of age, sex, body mass index (BMI), ASA classification, type of surgery, preoperative MMSE score, operation time, bleeding volume, or fluid infusion (Table 1).

Comparison of MAP and HR

There were no statistically significant differences in the MAP or HR between the two groups at any time points (all $P > 0.05$) (Table 2).

Incidence of POD

POD occurred in 13 patients in Group C (32.5%) and three patients in the Group CHO (7.5%). The incidence of POD in Group CHO was lower than that in Group C ($X^2 = 7.813$, $P = 0.005$). Additionally, the incidence of POD was significantly higher on D1 in both groups (Table 3).

Comparison of blood glucose levels between the two groups

Blood glucose levels in both groups increased significantly at D1 ($P < 0.001$). No significant differences were observed between the two groups preoperatively or on D3 or D5. Blood glucose levels in Group CHO were significantly lower than those in the Group C on D1and D3 ($P < 0.05$) (Table 4).

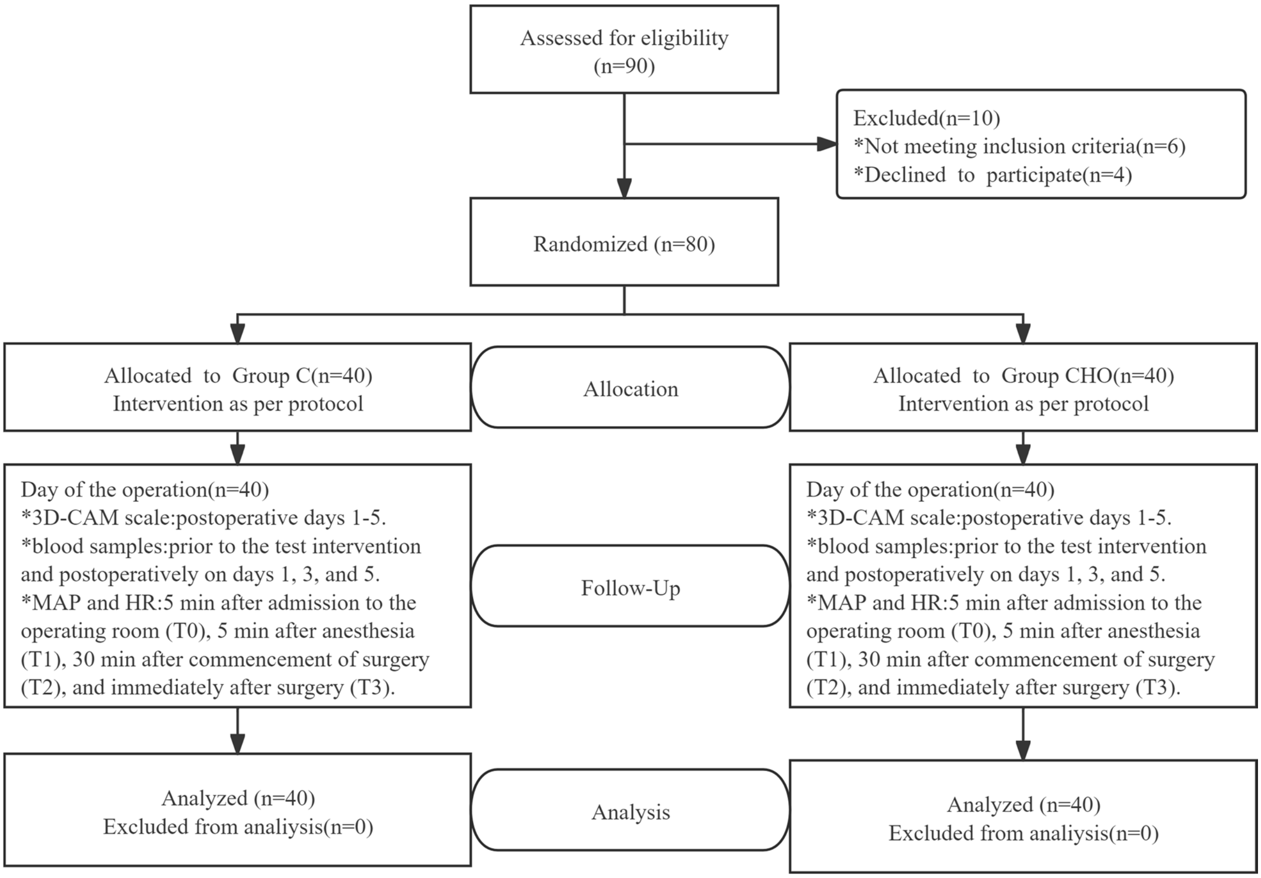

Fig. 1 Consolidated Standards of Reporting Trials (CONSORT) flowchart

Table 1 Comparison of baseline clinical characteristics between the two groups

Clinical characteristics	Group C (n = 40)	Group CHO (n = 40)	*P*
Age (yr)	73.62 ± 4.07	72.55 ± 3.56	0.212
Sex, male/female	14/26	19/21	0.256
BMI (kg/m^2)	23.31 ± 2.93	23.59 ± 1.79	0.603
ASA grade			
II [n (%)]	23 (57.5)	19 (47.5)	0.37
III [n (%)]	17 (42.5)	21 (52.5)	
Type of surgery			
Hip surgery [n (%)]	23 (57.5)	21(52.5)	0.653
Knee surgery [n (%)]	17 (42.5)	19(47.5)	
MMSE score	25 (24, 25)	25 (24, 26)	0.423
Operation time (min)	121.38 ± 15.65	120.40 ± 18.79	0.802
Bleeding volume (mL)	175 (100, 200)	150 (100, 200)	0.605
Fluid infusion (mL)	1435.00 ± 180.53	1437.50 ± 195.71	0.953

Normally distributed continuous data are represented by mean ± SD and non-normally distributed data are represented by median (Q1, Q3); BMI, Body mass index; ASA, American Society of Anesthesiologists; Group C, preoperative fasting group; Group CHO, preoperative carbohydrate-loading group

Table 2 Comparison of MAP and HR between the two groups

Indicators	Timing	Group C (n = 40)	Group CHO (n = 40)	*P*
MAP (mm Hg)	T0	101.95 ± 10.76	102.75 ± 9.65	0.528
	T1	98.42 ± 9.12	98.70 ± 7.96	0.069
	T2	94.70 ± 9.58	94.43 ± 7.73	0.923
	T3	96.02 ± 7.75	92.40 ± 7.64	0.992
HR (bpm)	T0	79.12 ± 8.06	78.35 ± 10.37	0.488
	T1	79.77 ± 8.33	77.92 ± 9.11	0.857
	T2	76.37 ± 5.54	75.45 ± 9.89	0.23
	T3	75.82 ± 5.86	73.85 ± 8.48	0.384

MAP, Mean arterial pressure; HR, Heart rate; T0, 5 min after admission to the operating room; T1, 5 min after anesthesia; T2, 30 min after commencement of surgery; T3, immediately after surgery

Comparison of IL-6 and CRP levels between the two groups

Compared to preoperative levels, the levels of IL-6 and CRP in serum in the two groups significantly increased on D1, D3 and D5 ($P < 0.001$). The serum levels of IL-6 and CRP in Group CHO were significantly lower than for Group C on D1 and D3 ($P < 0.05$). No significant

Table 3 Comparison of the incidence of POD between the two groups

	D1	D2	D3	D4	D5	Incidence
Group C (n = 40 [n (%)])	10 (25.0)	3 (7.5)	0	0	0	13 (32.5)
Group CHO (n = 40 [n (%)])	3 (7.5)	0 (0)	0	0	0	3 (7.5)
X^2						7.813
P						0.005

D1, 1 d after surgery; D2, 2 d after surgery; D3, 3 d after surgery; D4, 4 d after surgery; D5, 5 d after surgery

Table 4 Comparison of blood glucose levels between the two groups

		Group C (n = 40)	Group CHO (n = 40)	P
Blood Glucose (mmol/L)	Preoperatively	4.93 (4.18, 6.03)	5.00(4.70, 5.70)	0.668
	D1	6.16 (5.74, 7.24)[a]	5.65 (5.20, 5.90)[a,b]	< 0.05
	D3	5.20 (4.93, 6.05)	5.10 (4.90, 5.48)[b]	< 0.05
	D5	4.97 (4.57, 5.32)	4.90 (4.55, 5.35)	0.504

D1, 1 d after surgery; D3, 3 d after surgery; D5: 5 d after surgery

[a] $P < 0.001$, compared with the preoperative values in the same group

[b] $P < 0.05$, compared with Group C

Table 5 Comparison of IL-6 and CRP Levels between the two groups

		Group C (n = 40)	Group CHO (n = 40)	P
IL-6 (pg/L)	Preoperatively	5.89 (3.19, 11.66)	4.47 (2.83, 7.64)	0.143
	D1	44.91 (23.56, 74.43)[a]	29.38 (18.73, 39.13)[a,b]	< 0.05
	D3	37.99 (23.9, 57.36)[a]	28.73 (17.48, 42.07)[a,b]	< 0.05
	D5	17.24 (11.20, 29.25)[a]	21.57 (12.44, 28.81)[a]	0.648
CRP (mg/mL)	Preoperatively	4.61 (2.44, 18.82)	3.14 (1.90, 15.80)	0.390
	D1	55.63 (39.70, 73.52)[a]	17.05 (11.80, 42.96)[a,b]	< 0.05
	D3	69.02 (47.28, 84.25)[a]	56.37 (27.92, 71.36)[a,b]	< 0.05
	D5	42.81 (23.84, 65.51)[a]	43.88 (20.14, 64.40)[a]	0.528

D1, 1 d after surgery; D3, 3 d after surgery; D5: 5 d after surgery

[a] $P < 0.001$, compared with the preoperative values in the same group

[b] $P < 0.05$, compared with Group C

differences were observed between the two groups preoperatively or on D5 (Table 5).

Comparison of postoperative complications between two groups

The incidence of thirst in Group CHO was significantly lower than in Group C (42.5% vs 12.5%, $X^2 = 9.028$, $P = 0.003$). However, there was no significant difference in nausea (20.0% vs 7.5%, $X^2 = 1.686$, $P = 0.194$) or vomiting (10.0% vs 2.5%, $X^2 = 0.853$, $P = 0.356$) between two groups.

Discussion

Amid the rapid evolution of the socioeconomic landscape and the growing older population, the postoperative outcomes of geriatric patients have garnered significant clinical attention. POD, a common complication in older patients, continues to present substantial challenges in clinical settings. Although the pathogenesis of POD remains unclear, it is hypothesized to result from the interaction of multiple mechanisms, including neuroinflammatory responses, neurotransmitter imbalances, and oxidative stress [19–21]. Recently, the adoption of the Enhanced Recovery After Surgery (ERAS) concept has led to domestic guidelines recommending modifications to the traditional preoperative fasting and fluid restriction protocols [22–24]. These modifications aim to shorten the duration of fasting and fluid restriction, alleviate preoperative and postoperative discomfort, improve perioperative stress responses, reduce related complications, accelerate patient recovery, and ultimately shorten hospital stay.

Preoperative carbohydrate consumption can reduce glycogen depletion, enhance insulin secretion, and improve glucose utilization, thereby augmenting postoperative insulin sensitivity and mitigating insulin resistance [25, 26]. This metabolic modulation aids in maintaining the energy balance during the perioperative period and may consequently reduce the risk of POD [27]. Moreover, preoperative carbohydrate intake can attenuate stress responses during the perioperative period [28], which often result in increased metabolic activity and fluctuations in insulin and glucocorticoid levels, subsequently affecting blood glucose regulation. Persistent postoperative hyperglycemia increases the risk of infection, impairs wound healing, and prolongs hospital stay [29].Therefore, preoperative oral intake of carbohydrates may intricately linked to the mechanisms and prevention strategies for POD through the mitigation of postoperative stress responses and the regulation of blood glucose levels.

Research conducted by Liu et al. and Chen et al. [10, 30] identified perioperative stress responses and blood glucose levels as significant risk factors for POD development. In this study, the group that received preoperative oral carbohydrates exhibited lower blood glucose concentrations on day 1 after surgery than Group C ($P < 0.05$). Additionally, the incidence of delirium on the first day after surgery was significantly lower in Group CHO compared to Group C ($P < 0.05$), corroborating the previous findings.

Previous research has shown that severe trauma and postsurgical conditions frequently induce systemic inflammatory responses that can precipitate delirium [31]. Inflammatory mediators compromise the blood–brain barrier and disrupt neuronal activity, contributing to the onset of delirium. Previous investigations have established that the body's inflammatory response is integral to the development and progression of POD, with peripheral blood levels of inflammatory factors serving as predictive markers [14, 32, 33]. Key inflammatory factors include IL-6 and CRP. The current study demonstrated that Group CHO exhibited significantly lower levels of IL-6 and CRP on days 1 and 3 after surgery than Group C (both $P < 0.05$). Additionally, the incidence of POD on the first day after surgery was significantly lower in Group CHO group than in Group C. This suggests that preoperative oral carbohydrate administration attenuates the postoperative systemic inflammatory response, thereby reducing the incidence of POD in older patients and aiding recovery. These results are largely congruent with those of Hu et al. [34].

This study found that the administration of preoperative oral carbohydrates significantly reduced perioperative thirst ($P < 0.05$), thereby enhancing patient comfort. These findings align with those of previous research [34–37], which demonstrated that the ingestion of carbohydrate-rich beverages 2 h before surgery alleviated postoperative thirst and hunger.

Preoperative oral carbohydrate administration reduced the incidence of postoperative nausea and vomiting (PONV) in patients undergoing laparoscopic surgery [38, 39]. The findings of this study suggest that consuming carbohydrates orally 2 h prior to surgery may decrease the incidence of PONV, although this reduction was not statistically significant. This outcome could have been influenced by the type of surgery included in the study, as the incidence of PONV is lower in patients undergoing lower limb surgery than in those undergoing laparoscopic procedures [40, 41]. Furthermore, these results underscore the relative safety of preoperative oral carbohydrate intake as it does not increase the incidence of PONV.

There are some limitations to this study. First, the stress indicators assessed were limited to blood glucose levels, and did not include the insulin resistance index, which may constrain a comprehensive evaluation of the postoperative stress response. Furthermore, this study only investigated the effect of oral administration of 200ml carbohydrate 2 h before surgery on the incidence of POD, and the specific dosage of CHO needs further study. Thus, future studies can explore the effect of different CHO doses on the incidence of POD according to the ERAS protocol. Additionally, the small sample size raises concerns regarding the generalizability of the findings to a broader population, indicating the need for further validation. Consequently, future studies should aim to increase the sample size and include a broader spectrum of stress indicators to thoroughly investigate the effects of preoperative oral carbohydrate intake on the postoperative recovery of older patients.

Conclusion

The administration of carbohydrates 2 h prior to lower limb orthopedic surgery in older patients can attenuate postoperative stress responses and lower inflammatory marker levels, thereby decreasing the incidence of POD. This intervention presents a novel approach for preventing POD in older patients, thereby promoting favorable postoperative recovery.

Abbreviations

POD	Postoperative delirium
ASA	American Society of Anesthesiologists
MMSE	Mini-mental State Examination
MAP	Mean arterial blood pressure
HR	Heart rate
3D-CAM	3-Minute Diagnostic Confusion Assessment Method
BMI	Body mass index
PONV	Postoperative nausea and vomiting

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None

Author contributions

LTL, XHW, and YBZ designed the study. LTL, XHW, YHH, JL, and YH collected the data and performed the analyses. LTL, XHW, YHH, and JL wrote the manuscript. YBZ and HXC critically revised the manuscript. The authors have read and approved the final manuscript.

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Data availability

The datasets used in this study are available from the corresponding author upon request.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Affiliated Hospital of North Sichuan Medical College (No. 2023ER001-1), Sichuan Province. All procedures involving human participants performed in this study were in accordance with the Ethical Standards of the Institutional Ethics Committee and the 1964 Helsinki Declaration. Informed consent was obtained from all patients or their close relatives before their participation.

Consent for publication
Informed consent for the collection of research information was obtained from all participants, and the hospital review board provided informed consent for publication.

Competing interests
The authors declare that they have no competing interests.

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References

1. Urits I, Orhurhu V, Jones M, Hoyt D, Seats A, Viswanath O. Current perspectives on postoperative cognitive dysfunction in the ageing population. Turk J Anaesthesiol Reanim. 2019;47(6):439–47.
2. Rizk P, Morris W, Oladeji P, Huo M. Review of postoperative delirium in geriatric patients undergoing hip surgery. Geriatr Orthop Surg & Rehabil. 2016;7(2):100–5.
3. Wang CG, Qin YF, Wan X, Song LC, Li ZJ, Li H. Incidence and risk factors of postoperative delirium in the elderly patients with hip fracture. J Orthop Surg Res. 2018;13(1):186.
4. Maffulli N, Aicale R. Proximal femoral fractures in the elderly: a few things to know, and some to forget. Medicina (Kaunas). 2022;58(10):1314.
5. Wilson JE, Mart MF, Cunningham C, Shehabi Y, Girard TD, MacLullich AMJ, et al. Delirium. Nat Rev Dis Prim. 2020;6(1):90.
6. Kneussel M, Friese MA. SnapShot: Neuronal dysfunction in inflammation. Neuron. 2021;109(10):1754-e1.
7. Yan X, Huang J, Chen X, Lin M. Association between increased systemic immune-inflammation index and postoperative delirium in older intertrochanteric fracture patients. J Orthop Surg Res. 2024;19(1):219.
8. Huang JW, Yang YF, Gao XS, Xu ZH. A single preoperative low-dose dexamethasone may reduce the incidence and severity of postoperative delirium in the geriatric intertrochanteric fracture patients with internal fixation surgery: an exploratory analysis of a randomized, placebo-controlled trial. J Orthop Surg Res. 2023;18(1):441.
9. Rong X, Ding ZC, Yu HD, Yao SY, Zhou ZK. Risk factors of postoperative delirium in the knee and hip replacement patients: a systematic review and meta-analysis. J Orthop Surg Res. 2021;16(1):76.
10. Liu S, Xv L, Wu X, Wang F, Wang J, Tang X, et al. Potential value of preoperative fasting blood glucose levels in the identification of postoperative delirium in non-diabetic older patients undergoing total hip replacement: the perioperative neurocognitive disorder and biomarker lifestyle study. Front Psych. 2022;13: 941048.
11. Wang W, Zhang Y, Yao W, Tang W, Li Y, Sun H, et al. Association between preoperative persistent hyperglycemia and postoperative delirium in geriatric hip fracture patients. BMC Geriatr. 2024;24(1):585.
12. Park SJ, Oh AR, Lee JH, Yang K, Park J. Association of preoperative blood glucose level with delirium after non-cardiac surgery in diabetic patients. Korean J Anesthesiol. 2024;77(2):226–35.
13. Tarazona-Santabalbina FJ, Llabata-Broseta J, Belenguer-Varea Á, Álvarez-Martínez D, Cuesta-Peredo D, Avellana-Zaragoza JA. A daily multidisciplinary assessment of older adults undergoing elective colorectal cancer surgery is associated with reduced delirium and geriatric syndromes. J Geriatr Oncol. 2019;10(2):298–303.
14. Zhang Y, Hu J, Zuo W, He P, Xue Q, Feng X, et al. Longitudinal profiling of plasma cytokines and its association with postoperative delirium in elderly patients undergoing major lower limb surgery: a prospective observational study. Anesth Analg. 2023;136(1):34–42.
15. Wang S, Greene R, Song Y, Chan C, Lindroth H, Khan S, et al. Postoperative delirium and its relationship with biomarkers for dementia: a meta-analysis. Int Psychogeriatr. 2022;34:377–90.
16. Nygren J, Soop M, Thorell A, Sree Nair K, Ljungqvist O. Preoperative oral carbohydrates and postoperative insulin resistance. Clin Nutr (Edinburgh, Scotland). 1999;18(2):117–20.
17. Choi YS, Cho BW, Kim HJ, Lee YS, Park KK, Lee B. Effect of preoperative oral carbohydrates on insulin resistance in older adults who underwent total hip or knee arthroplasty: a prospective randomized trial. J Am Acad Orthop Surg. 2022;30(20):971–8.
18. Rieck KM, Pagali S, Miller DM. Delirium in hospitalized older adults. Hosp Pract. 2020;48(1):3–16.
19. Gamberale R, D'Orlando C, Brunelli S, Meneveri R, Mazzola P, Foti G, et al. Study protocol: understanding the pathophysiologic mechanisms underlying delirium in older people undergoing hip fracture surgery. BMC Geriatr. 2021;21(1):633.
20. Pappa M, Theodosiadis N, Tsounis A, Sarafis P. Pathogenesis and treatment of post-operative cognitive dysfunction. Electron Phys. 2017;9(2):3768–75.
21. Xu Y, Ma Q, Du H, Yang C, Lin G. Postoperative delirium in neurosurgical patients: recent insights into the pathogenesis. Brain Sci. 2022;12(10):1371.
22. Engelman DT, Ben Ali W, Williams JB, Perrault LP, Reddy VS, Arora RC, et al. Guidelines for perioperative care in cardiac surgery: enhanced recovery after surgery society recommendations. JAMA Surg. 2019;154(8):755–66.
23. Ljungqvist O, Scott M, Fearon KC. Enhanced recovery after surgery: a review. JAMA Surg. 2017;152(3):292–8.
24. Wainwright TW, Gill M, McDonald DA, Middleton RG, Reed M, Sahota O, et al. Consensus statement for perioperative care in total hip replacement and total knee replacement surgery: Enhanced Recovery After Surgery (ERAS(®)) Society recommendations. Acta Orthop. 2020;91(1):3–19.
25. Rajan S, Rahman AA, Kumar L. Preoperative oral carbohydrate loading: effects on intraoperative blood glucose levels, post-operative nausea and vomiting, and intensive care unit stay. J Anaesthesiol Clin Pharmacol. 2021;37(4):622–7.
26. Gjessing PF, Constantin-Teodosiu D, Hagve M, Lobo DN, Revhaug A, Irtun Ø. Preoperative carbohydrate supplementation attenuates post-surgery insulin resistance via reduced inflammatory inhibition of the insulin-mediated restraint on muscle pyruvate dehydrogenase kinase 4 expression. Clin Nutr (Edinburgh, Scotland). 2015;34(6):1177–83.
27. Mi Y, Wen O, Lei Z, Ge L, Xing L, Xi H. Insulin resistance and osteocalcin associate with the incidence and severity of postoperative delirium in elderly patients undergoing joint replacement. Geriatr Gerontol Int. 2024;24(4):421–9.
28. Gümüs K, Pirhan Y, Aydın G, Keloglan S, Tasova V, Kahveci M. The effect of preoperative oral intake of liquid carbohydrate on postoperative stress parameters in patients undergoing laparoscopic cholecystectomy: an experimental study. J Perianesthesia Nurs: Off J Am Soc Perianesthesia Nurses. 2021;36(5):526–31.
29. Choi YS, Kim TW, Chang MJ, Kang SB, Chang CB. Enhanced recovery after surgery for major orthopedic surgery: a narrative review. Knee Surg & Related Res. 2022;34(1):8.
30. Chen Y, Liang S, Wu H, Deng S, Wang F, Lunzhu C, et al. Postoperative delirium in geriatric patients with hip fractures. Front Aging Neurosci. 2022;14:1068278.
31. Schenning KJ, Deiner SG. Postoperative delirium in the geriatric patient. Anesthesiol Clin. 2015;33(3):505–16.
32. Vasunilashorn SM, Ngo L, Inouye SK, Libermann TA, Jones RN, Alsop DC, et al. Cytokines and postoperative delirium in older patients undergoing major elective surgery. J Gerontol A Biol Sci Med Sci. 2015;70(10):1289–95.
33. Alam A, Hana Z, Jin Z, Suen KC, Ma D. Surgery, neuroinflammation and cognitive impairment. EBioMedicine. 2018;37:547–56.
34. Hu Z, Liu J, Wang F. Effects of preoperative carbohydrate intake on inflammatory markers and clinical outcomes in elderly patients undergoing radical prostatectomy: a single-centre, double-blind randomised controlled trial. Front Surg. 2021;8: 744091.
35. Wang Y, Zhu Z, Li H, Sun Y, Xie G, Cheng B, et al. Effects of preoperative oral carbohydrates on patients undergoing ESD surgery under general anesthesia: a randomized control study. Medicine. 2019;98(20): e15669.
36. Cheng PL, Loh EW, Chen JT, Tam KW. Effects of preoperative oral carbohydrate on postoperative discomfort in patients undergoing elective surgery: a meta-analysis of randomized controlled trials. Langenbecks Arch Surg. 2021;406(4):993–1005.
37. Wang X, Zhuang J, Cheng J, Wang Z, Sheng J, Guo S, et al. Effect of preoperative oral carbohydrates on insulin resistance in patients undergoing laparoscopic cholecystectomy: a randomized controlled trial. Langenbecks Arch Surg. 2024;409(1):77.

38. Bisgaard T, Kehlet H. Randomized clinical trial of the effects of oral preoperative carbohydrates on postoperative nausea and vomiting after laparoscopic cholecystectomy (Br J Surg 2005; 92: 415–421). British J Surg. 2006;93(1):120.
39. Hausel J, Nygren J, Thorell A, Lagerkranser M, Ljungqvist O. Randomized clinical trial of the effects of oral preoperative carbohydrates on postoperative nausea and vomiting after laparoscopic cholecystectomy. Br J Surg. 2005;92(4):415–21.
40. Kadado A, Shaw JH, Ayoola AS, Akioyamen NO, North WT, Charters MA. Effects of preoperative carbohydrate-rich drinks on immediate postoperative outcomes in total knee arthroplasty: a randomized controlled trial. J Am Acad Orthop Surg. 2022;30(11):e833–41.
41. Shin S, Choi YS, Shin H, Yang IH, Park KK, Kwon HM, et al. Preoperative carbohydrate drinks do not decrease postoperative nausea and vomiting in type 2 diabetic patients undergoing total knee arthroplasty-a randomized controlled trial. J Am Acad Orthop Surg. 2021;29(1):35–43.