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Association between the geriatric nutritional risk index and postoperative delirium in gastric surgery patients: an analysis of the MIMIC-IV database

Yan Chen^{1†}, Huangyi Chen^{2†}, Yong Zhuang³, Ying Wang^{2*} and Zhisen Dai^{1*}

Abstract

Background This study explores the correlation between nutritional status, as determined by the Geriatric Nutritional Risk Index (GNRI), and the incidence of postoperative delirium (POD) in patients undergoing gastric surgery.

Methods Data were obtained from the MIMIC-IV 2.2 database for patients aged 18 years or older who underwent gastric surgery. Patients were categorized into the malnourished group (GNRI < 98) and the non-malnourished group (GNRI ≥ 98). Multivariable logistic regression was performed to assess the association between GNRI and POD, and various potential confounders were adjusted to ensure the robustness of the results. Non-linear relationships between GNRI and POD risk were evaluated through restricted cubic spline (RCS) analysis. Subgroup analyses were conducted to examine the effect of GNRI on POD across different patient categories, and interactions were calculated. Propensity score matching (PSM) was employed to reduce confounding bias.

Results The study included a total of 4,818 patients, of whom 1,133 (23.5%) developed POD. Patients with a GNRI < 98 had a significantly higher risk of POD compared with those with a GNRI ≥ 98 (odds ratio (OR): 2.21, 95% confidence interval (CI): 1.93–2.53, $p < 0.001$). Even after adjustment for relevant confounders, GNRI remained significantly associated with POD (OR: 1.24, 95% CI: 1.04–1.48, $p < 0.001$). This association was further supported by the results from PSM (OR: 1.23, 95% CI: 1.01–1.51, $p = 0.045$). RCS analysis demonstrated a non-linear relationship between GNRI and POD risk ($p < 0.05$). Subgroup analyses revealed significant interactions within the cardiovascular disease, renal replacement therapy, benzodiazepine medication, and vasoactive drug subgroups (p for interaction < 0.05). After the patient population was adjusted to individuals aged 65 and older, this correlation remained significant (p for interaction < 0.05).

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Conclusions This study identifies a significant association between GNRI and the incidence of POD in patients undergoing gastric surgery. Improving nutritional status before surgery may lower the risk of developing POD.

Keywords MIMIC-IV database, GNRI, Postoperative delirium, Gastric surgery, Nutritional status

Introduction

Delirium, also known as acute brain dysfunction, is characterized by sudden and fluctuating disturbances in consciousness, attention, and cognition, including disorientation and impaired perception [1, 2]. The incidence of postoperative delirium (POD) is approximately 19% following elective surgery and 32% after emergency procedures, with POD being associated with higher mortality rates and increased postoperative complications, such as prolonged hospital stays and unplanned ICU admissions [3, 4]. Additionally, delirium significantly correlates with long-term cognitive decline, and delirious patients face a heightened risk of in-hospital complications and mortality, as well as delayed recovery after discharge [2, 5].

Certain studies suggest that advanced age, infection, and specific medications increase the risk of POD [6–8]. Other risk factors include pre-existing cognitive impairment, psychiatric disorders, cerebrovascular disease, end-stage renal failure, hypoalbuminemia, higher ASA scores, and intraoperative blood transfusions [9]. A study by Yamato et al. found that the risk of delirium varies by cancer type, while research on gastric cancer patients undergoing surgery reported a 4.5% incidence of POD [10]. Key risk factors included male sex, age over 75, cerebrovascular history, and the use of sleeping medications [11]. Given the unclear pathophysiology of delirium [12], identifying risk factors in surgical patients is essential for early intervention and better outcomes.

The Geriatric Nutritional Risk Index (GNRI) is an objective, easy-to-use tool for assessing nutritional status through height, weight, and serum albumin levels, and superior to subjective questionnaire-based methods [13]. GNRI has been widely applied across various patient populations [14–17], including adults, such as old patients hemodialysis patients, and those with cardiovascular diseases [18–21]. A prospective cohort study demonstrated its predictive value for prolonged hospital stays and POD in older non-cardiac surgery patients [22]. However, limited research has delved into the relationship between preoperative GNRI and POD in patients undergoing gastric surgery.

In light of this knowledge gap, our study aims to investigate and clarify the relationship between preoperative GNRI scores and the incidence of POD in patients who have undergone gastric surgery. By doing so, we seek to deepen the clinical understanding of how nutritional status may influence postoperative outcomes in this specific surgical context and inform preoperative assessments and interventions to improve patient care.

Methods

Data collection

Our data were sourced from the Medical Information Mart for Intensive Care IV version 2.2 (MIMIC-IV v2.2), a public critical care database released in January 2023 from a single medical center. This database has received institutional review board approval from Beth Israel Deaconess Medical Center (BIDMC, Boston, MA, USA) and the Massachusetts Institute of Technology (MIT, Cambridge, MA, USA), and de-identifies patient information. Therefore, this study did not require additional patient consent or ethical approval. To gain access to the database, we completed the National Institutes of Health (NIH) online course and received a certified researcher ID (12757497). Patients undergoing gastric surgery were identified in adherence to the International Classification of Diseases (ICD) ninth and tenth revisions (Supplementary Table 1). The following exclusion criteria were applied: (1) individuals aged under 18 were not selected; (2) individuals without critical data like height, weight, or albumin were not considered (Fig. 1).

Data extraction

Data were assessed by a specialized interdisciplinary team comprising researchers and clinicians to guarantee reliability. The collected data included demographics, comorbidities and medical history, laboratory parameters, and treatments. Specifically, demographic data comprised (1) Basic information: gender, age, weight, and height; (2) Comorbidities: chronic pulmonary disease, dementia, hypertension, cerebrovascular disease, myocardial infarction, congestive heart failure, diabetes; (3) Laboratory parameters: sodium, serum kalium, serum calcium, serum albumin, serum creatinine, blood urea nitrogen, glucose; (4) Treatments: sedatives (benzodiazepines, propofol, remifentanyl, dexmedetomidine), vasoactive agents (bisoprolol fumarate, epinephrine, dobutamine, dopamine, esmolol, metoprolol, nitroglycerin, norepinephrine, phenoxybenzamine), renal replacement therapy, mechanical ventilation. For variables with multiple measurements, data at the first measurement were used. In the MIMIC-IV database, missing results for laboratory indicators are common. Each continuous variable's percentage of missing values was determined to reduce sample exclusion bias. A random forest-based multiple imputation approach was employed to impute variables with missing values less than 10%; variables with missing values more than 10% were excluded [23, 24]. Variables having a variance inflation factor

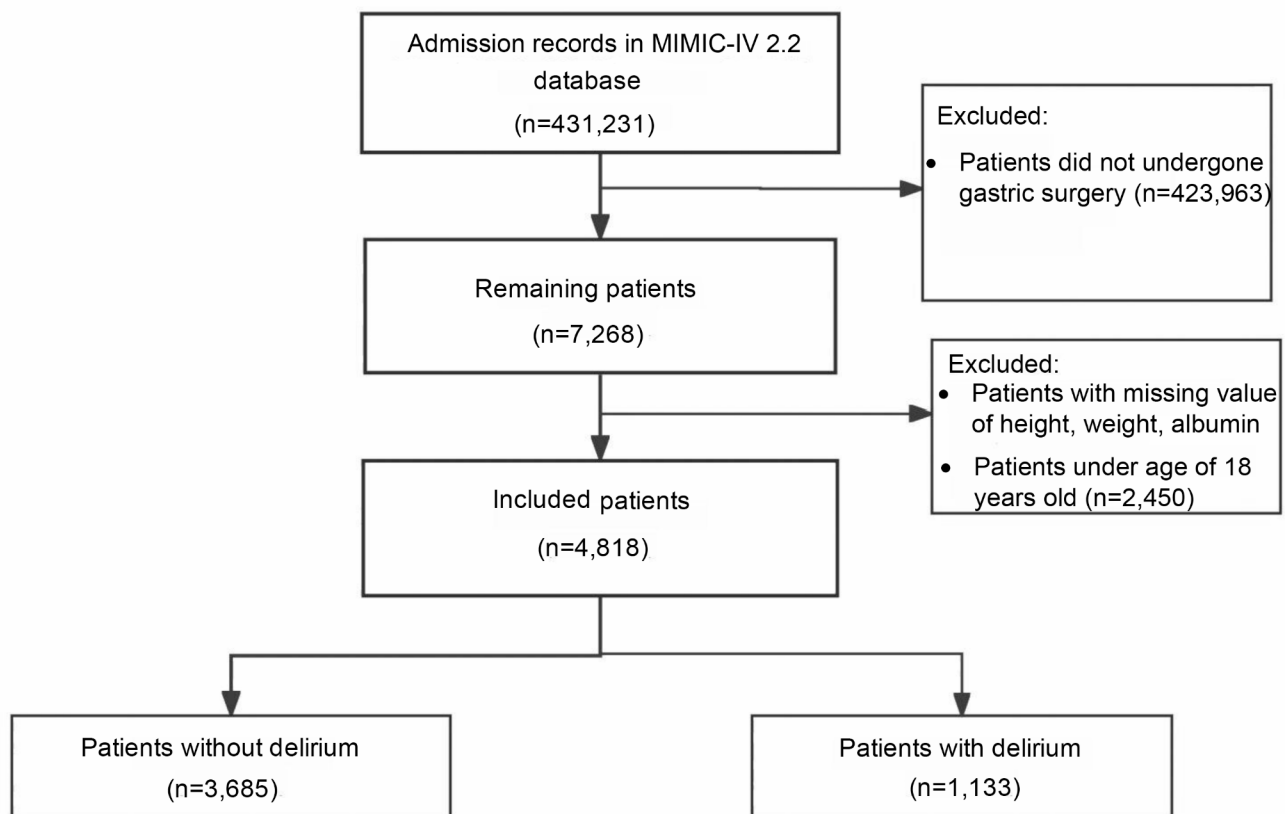


Fig. 1 Flowchart of Patient Selection. Flowchart for selecting patients from the MIMIC-IV database. Abbreviation: MIMIC-IV, Intensive Care Medical Information Market IV

larger than five were removed from the model to avoid multicollinearity.

Definition of GNRI

GNRI was applied to evaluate nutritional status upon ICU admission in patients. The formula was: $GNRI = 1.489 \times \text{serum albumin level (g/L)} + 41.7 \times (\text{actual weight (kg)} / \text{ideal weight (kg)})$. The ideal weight for males (kg) was calculated as $\text{height [cm]} - 100 - ((\text{height} - 150) / 4)$. For females, it was calculated as $\text{height [cm]} - 100 - ((\text{height} - 150) / 2.5)$. Poorer nutritional status was indicated by lower GNRI scores. Patients were classified into two groups: those without nutritional risk ($GNRI \geq 98$) and those at nutritional risk ($GNRI < 98$).

Outcomes (grouping basis)

The outcome of interest was the occurrence of delirium after gastric surgery. Delirium was defined as per ICD-9 and ICD-10 revisions (Table S1) [21].

Statistical analysis

Normally distributed quantitative data were displayed as mean \pm standard deviation (SD), non-normally distributed data as median [interquartile range (IQR)], and categorical data as counts (percentages). Variance analysis,

Kruskal-Wallis tests, and χ^2 tests assisted in comparing patient characteristics based on nutrition. Logistic regression models were employed to obtain odds ratios (ORs) and their 95% confidence intervals (95%CI), and various models included adjustment of potential confounders (Model 1: unadjusted; Model 2: adjusted for age and sex; Model 3: further adjusted for serum calcium, sodium, blood glucose, serum kalium, creatinine, urea nitrogen, renal replacement therapy, mechanical ventilation, sedatives, vasopressors, dementia, hypertension, cerebrovascular disease, diabetes, myocardial infarction, and heart failure). A restricted cubic spline (RCS) function was utilized to examine the nonlinear relation of GNRI to outcomes [21, 25, 26]. Subgroup analyses were performed for all subjects, and interaction between GNRI and other variables was investigated using likelihood ratio tests (LRT). To evaluate the robustness of primary estimates, propensity score matching (PSM) assisted in balancing baseline characteristics between patients at risk of malnutrition ($GNRI < 98$) and those not at risk ($GNRI \geq 98$) with a caliper width of 0.01, using 1:1 nearest-neighbor matching. Logistic matching based on propensity scores helped to balance baseline characteristics between patients at risk and those not at risk of delirium. According to the World Health Organization's

definition of the elderly population [27, 28], individuals under the age of 65 were excluded to further explore the relationship between GNRI and POD in individuals aged 65 and above.

Two-tailed *p*-values less than 0.05 denoted statistical significance. R (version 4.4.0) was adopted in statistical analyses.

Results

Clinical characteristics of participants

A total of 4,818 patients were included in the analysis. Among those who underwent gastric surgery, 23.5% developed POD. The cohort comprised 54.1% females; 4.8% had dementia; 59.9% had hypertension; 31.2% had

diabetes; 17.3% had cardiovascular disease; 4.9% had a history of myocardial infarction; and 22.5% had congestive heart failure. The median GNRI was 101.26 (IQR: 92.33–107.22). The incidence of POD was significantly associated with patients' age, serum calcium, blood sodium, serum potassium, creatinine, urea nitrogen, blood glucose, and GNRI values ($p < 0.05$). There were significant differences between the delirium and non-delirium groups regarding sex, presence of dementia, hypertension, diabetes, cardiovascular disease, myocardial infarction, congestive heart failure, and the use of benzodiazepines, propofol, dexmedetomidine, vasopressors, mechanical ventilation, and renal replacement therapy ($p < 0.05$) (Table 1).

Table 1 Baseline demographic characteristics

Variables	level	Overall	No delirium	Delirium	<i>p</i> value
Number of patients		4818	3685	1133	
anchor_age (years)		59.00 [46.00, 71.00]	56.00 [42.00, 68.00]	67.00 [57.00, 76.00]	< 0.001
gender	female	2605 (54.1)	2100 (57.0)	505 (44.6)	< 0.001
	male	2213 (45.9)	1585 (43.0)	628 (55.4)	
ca. (mg/dL)		9.10 [8.60, 9.50]	9.10 [8.60, 9.50]	9.00 [8.50, 9.40]	< 0.001
na (mEq/L)		139.00 [137.00, 141.00]	139.00 [137.00, 141.00]	139.00 [137.00, 141.00]	0.038
k(mEq/L)		4.20 [3.90, 4.50]	4.20 [3.90, 4.50]	4.20 [3.90, 4.60]	0.022
creatinine (mg/dL)		0.90 [0.70, 1.10]	0.80 [0.70, 1.00]	1.00 [0.80, 1.30]	< 0.001
bun (mg/dL)		16.00 [12.00, 22.00]	15.00 [11.00, 20.00]	19.00 [13.00, 27.00]	< 0.001
glu (mg/dL)		105.00 [90.00, 134.00]	102.00 [89.00, 129.00]	113.00 [95.00, 151.00]	< 0.001
Presence of hypertension	No	1933 (40.1)	1609 (43.7)	324 (28.6)	< 0.001
	Yes	2885 (59.9)	2076 (56.3)	809 (71.4)	
Presence of diabetes	No	3313 (68.8)	2655 (72.0)	658 (58.1)	< 0.001
	Yes	1505 (31.2)	1030 (28.0)	475 (41.9)	
Presence of MI	No	4101 (85.1)	3291 (89.3)	810 (71.5)	< 0.001
	Yes	717 (14.9)	394 (10.7)	323 (28.5)	
Presence of CHF	No	3734 (77.5)	3093 (83.9)	641 (56.6)	< 0.001
Presence of dementia	No	4586 (95.2)	3622 (98.3)	964 (85.1)	< 0.001
	Yes	232 (4.8)	63 (1.7)	169 (14.9)	
Presence of cerebrovascular disease	No	3986 (82.7)	3254 (88.3)	732 (64.6)	< 0.001
	Yes	832 (17.3)	431 (11.7)	401 (35.4)	
	Yes	1084 (22.5)	592 (16.1)	492 (43.4)	
Ventilation_status	No	3287 (68.2)	2830 (76.8)	457 (40.3)	< 0.001
	Yes	1531 (31.8)	855 (23.2)	676 (59.7)	
Use of renal replacement therapy	No	4539 (94.2)	3555 (96.5)	984 (86.8)	< 0.001
	Yes	279 (5.8)	130 (3.5)	149 (13.2)	
Use of vas	No	2098 (43.5)	1914 (51.9)	184 (16.2)	< 0.001
	Yes	2720 (56.5)	1771 (48.1)	949 (83.8)	
Use of dex	No	4250 (88.2)	3429 (93.1)	821 (72.5)	< 0.001
	Yes	568 (11.8)	256 (6.9)	312 (27.5)	
Use of bzds	No	1673 (34.7)	1483 (40.2)	190 (16.8)	< 0.001
	Yes	3145 (65.3)	2202 (59.8)	943 (83.2)	
Use of prox	No	3353 (69.6)	2866 (77.8)	487 (43.0)	< 0.001
	Yes	1465 (30.4)	819 (22.2)	646 (57.0)	
GNRI		101.26 [92.33, 107.22]	102.75 [93.82, 107.22]	96.79 [87.86, 104.24]	< 0.001

Notes: Ca: Serum calcium; Na: Serum sodium; K: Serum kalium; Creatinine: Serum Creatinine; BUN: Blood Urea Nitrogen; Glu: Glucose; MI: Myocardial Infarction; CHF: Congestive Heart Failure; Ventilation_status: Mechanical Ventilation; Dialysis type: Renal Replacement Therapy; Vas: Vasoactive Drugs; Dex: Dexmedetomidine; BZDs: Benzodiazepines; Prop: Propofol. Non-normally distributed continuous variables were presented as median (IQR). Categorical variables were presented as number (percentage)

Table 2 Association between GNRI and postoperative delirium in patients undergoing gastric surgery

Characteristic	Modle 1	Modle 2		Modle 3					
	OR ¹	95% CI ¹	p-value	OR ¹	95% CI ¹	p-value	OR ¹	95% CI ¹	p-value
GNRI1									
≥98									
<98	2.21	1.93, 2.53	<0.001	1.66	1.44, 1.91	<0.001	1.24	1.04, 1.48	0.014

¹ OR=Odds Ratio, CI=Confidence Interval

Modle 1: unadjusted

Modle 2: adjusted for age and sex

Notes: Ca: Serum calcium; Na: Serum sodium; K: Serum kalium; Creatinine: Serum Creatinine; BUN: Blood Urea Nitrogen; Glu: Glucose; MI: Myocardial Infarction; CHF: Congestive Heart Failure; Ventilation_status: Mechanical Ventilation; Dialysis type: Renal Replacement Therapy; Vas: Vasoactive Drugs; Dex: Dexmedetomidine; BZDs: Benzodiazepines; Prop: Propofol

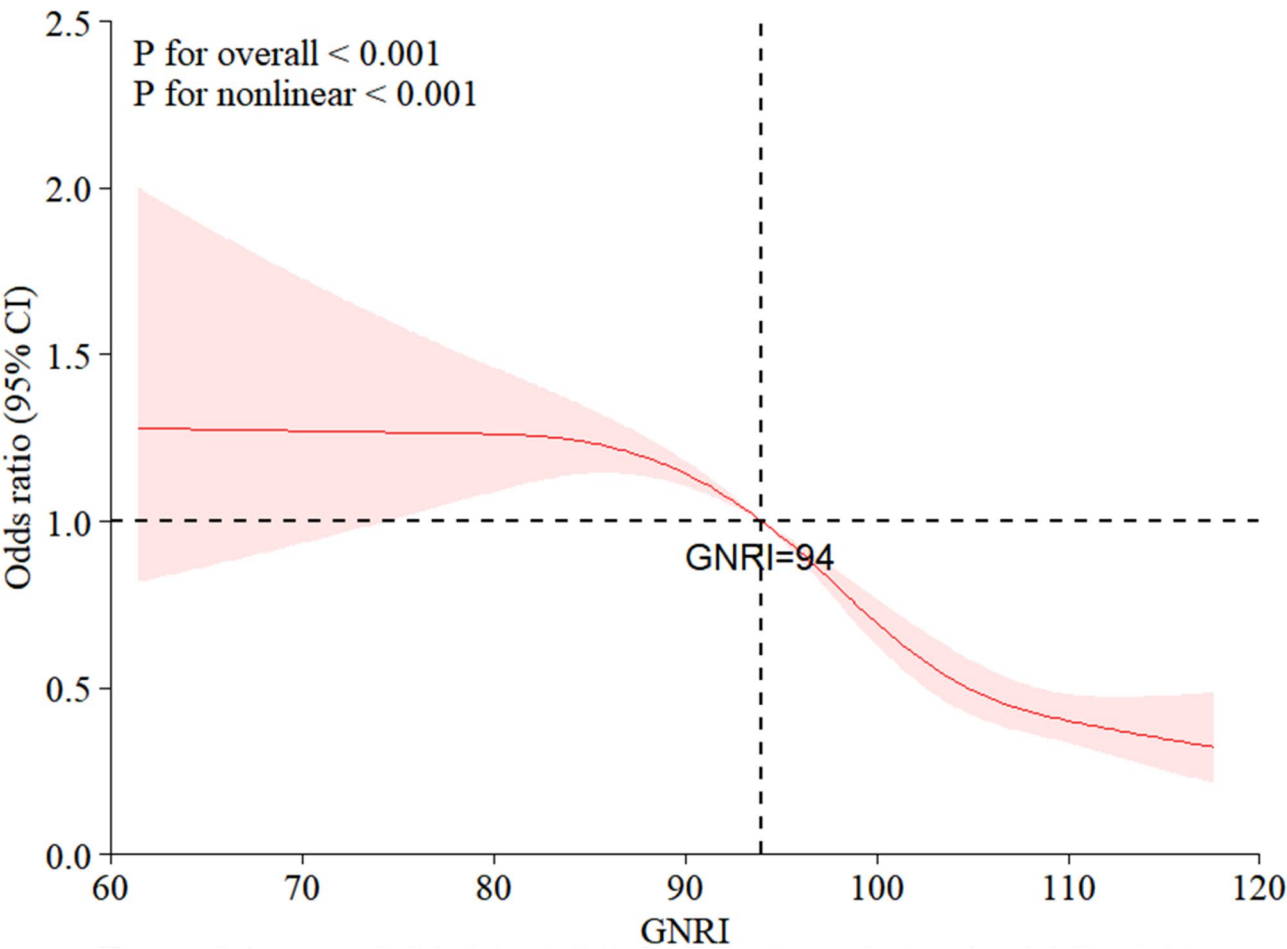


Fig. 2 Restricted cubic spline plot between GNRI and delirium, with the red bold line indicating the odds ratio and the shaded area representing the 95% confidence interval

Relationship between GNRI and POD in gastric surgery patients

Logistic regression analysis indicated that patients in the nutritional risk group (GNRI<98) had a higher risk of developing POD than those in the non-nutritional risk group (GNRI≥98). Specifically, the unadjusted model (Model 1) showed an OR of 2.21 (95% CI: 1.93–2.53), the population-adjusted model (Model 2) exhibited an OR of 1.66 (95% CI: 1.44–1.91), and the fully adjusted model (Model 3) reported an OR of 1.24 (95% CI: 1.04–1.48). In

all models, a GNRI<98 was significantly associated with an increased risk of POD ($p<0.05$) (Table 2). RCS analysis further demonstrated a nonlinear correlation between GNRI and POD risk (p for nonlinearity<0.0001), with a critical point of 94. The risk of delirium decreased progressively when GNRI was ≥94. (Fig. 2).

Subgroup analysis

Subgroup analyses revealed significant interactions between GNRI and various patient characteristics,

including cardiovascular disease (with cardiovascular disease: OR, 0.91; 95% CI, 0.66–1.25 vs. without cardiovascular disease: OR, 1.42; 95% CI, 1.16–1.75), renal replacement therapy (with renal replacement therapy: OR, 0.51; 95% CI, 0.27–0.97 vs. without renal replacement therapy: OR, 1.38; 95% CI, 1.15–1.66), benzodiazepine use (with benzodiazepine use: OR, 1.13; 95% CI, 0.93–1.37 vs. without benzodiazepine use: OR, 1.93; 95% CI, 1.30–2.89), and vasoactive drug use (with vasoactive drug use: OR, 1.14; 95% CI, 0.94–1.39 vs. without vasoactive drug use: OR, 1.66; 95% CI, 1.14–2.40) (p for interaction < 0.05). The association between nutritional risk (GNRI < 98) and POD was stronger in patients without cardiovascular disease, those not undergoing renal replacement therapy, those not using benzodiazepines, and those not receiving vasoactive drugs. Specifically, in comparison to patients with a GNRI ≥ 98 (no nutritional risk), the elevated risk of POD associated with a GNRI < 98 was significant among female patients (OR: 1.39, 95% CI: 1.07–1.79), patients aged ≥ 65 years (OR: 1.30, 95% CI: 1.03–1.63), and those without myocardial infarction (OR: 1.33, 95% CI: 1.09–1.62), hypertension (OR: 1.58, 95% CI: 1.15–2.17), heart failure (OR: 1.25, 95% CI: 1.01–1.56), or dementia (OR: 1.30, 95% CI: 1.09–1.56). The association was also significant among diabetic patients (OR: 1.47, 95% CI: 1.10–1.96), patients not receiving mechanical ventilation (OR: 1.43, 95% CI: 1.12–1.83), renal replacement therapy (OR: 1.38, 95% CI: 1.15–1.66), benzodiazepines (OR: 1.93, 95% CI: 1.30–2.89), propofol (OR: 1.29, 95% CI: 1.01–1.65), dexmedetomidine (OR: 1.29, 95% CI: 1.09–1.59), or vasoactive drugs (OR: 1.66, 95% CI: 1.14–2.40), indicating a consistent pattern of increased delirium risk with lower GNRI across multiple clinical contexts. The results of the subgroup analysis are presented in the form of a forest plot, as shown in Fig. 3 and Supplementary Fig. 1.

Sensitivity analysis

To confirm the robustness of the findings and lower the impact of potential confounders, adjustments were made for various confounders in the original unmatched cohort. The adjusted results were consistent with the primary estimates, as shown in the adjusted baseline information (Table S2). After full adjustment, the OR for POD in the GNRI < 98 group relative to the GNRI ≥ 98 group was 1.23 (OR: 1.23, 95% CI: 1.01–1.51, $p = 0.045$). Furthermore, individuals under the age of 65 were removed, and the results indicated that among elderly patients undergoing gastric surgery, those with a GNRI < 98 had a significantly higher risk of POD compared to those with a GNRI ≥ 98 (OR: 1.28, 95% CI: 1.02–1.61, $p = 0.032$).

Discussion

This investigation has demonstrated that patients experiencing malnutrition following gastric surgery are at an elevated risk of POD. Our findings indicate a non-linear relationship between GNRI and the incidence of POD, with a marked reduction in POD risk as GNRI values exceed 94. Notably, subgroup analyses have uncovered significant interactions between GNRI and POD across various patient groups, including those with and without a history of cardiovascular disease, as well as those who have received or not received renal replacement therapy, benzodiazepines, and vasopressors. These insights underscore the complex interplay between nutritional status and the risk of delirium in the postoperative period.

Previous studies have demonstrated a significant relationship between GNRI and POD. A previous study demonstrated an inverse correlation between preoperative GNRI and POD in older cardiac surgery patients, suggesting that incorporating GNRI into prediction models could improve accuracy [29]. Similarly, Zhao Yan et al. used GNRI to predict both length of stay and POD progression in older non-cardiac surgery patients [29]. However, a prospective cohort study on malnourished elderly non-cardiac surgery patients reported contradictory results [30]. A retrospective study demonstrated that GNRI is a useful predictor of POD in elderly patients undergoing spinal surgery [31]. Another study further proved GNRI as an independent predictor of delirium in older ICU patients, enhancing prediction model accuracy [32]. A retrospective study identified GNRI as a significant predictor of complications and overall survival in elderly gastric cancer patients and recommended routine GNRI assessment [33]. Our study adds to this body of evidence by confirming a significant negative association between GNRI values and delirium in patients undergoing gastrointestinal surgery.

Malnutrition has been demonstrated to be closely related to POD and other postoperative complications, such as infections, wound healing issues, and delayed recovery [34–36]. Perioperative nutritional support, as emphasized in Enhanced Recovery After Surgery (ERAS) protocols, has proven to be a key factor in ameliorating surgical outcomes [37]. Future research should focus on interventions for nutritionally at-risk populations to enhance recovery [38]. Malnutrition is particularly prevalent among gastrointestinal cancer patients, especially older and diabetic individuals, who are more vulnerable to POD [39, 40]. It is also a predictor of complications after gastric and rectal cancer surgeries [41, 42]. These findings underscore the significance of monitoring and optimizing the state of nutrition before and after surgery [43]. GNRI offers a simple, rapid, and non-invasive assessment especially suited for physically impaired patients [44]. Originally designed to assess malnutrition

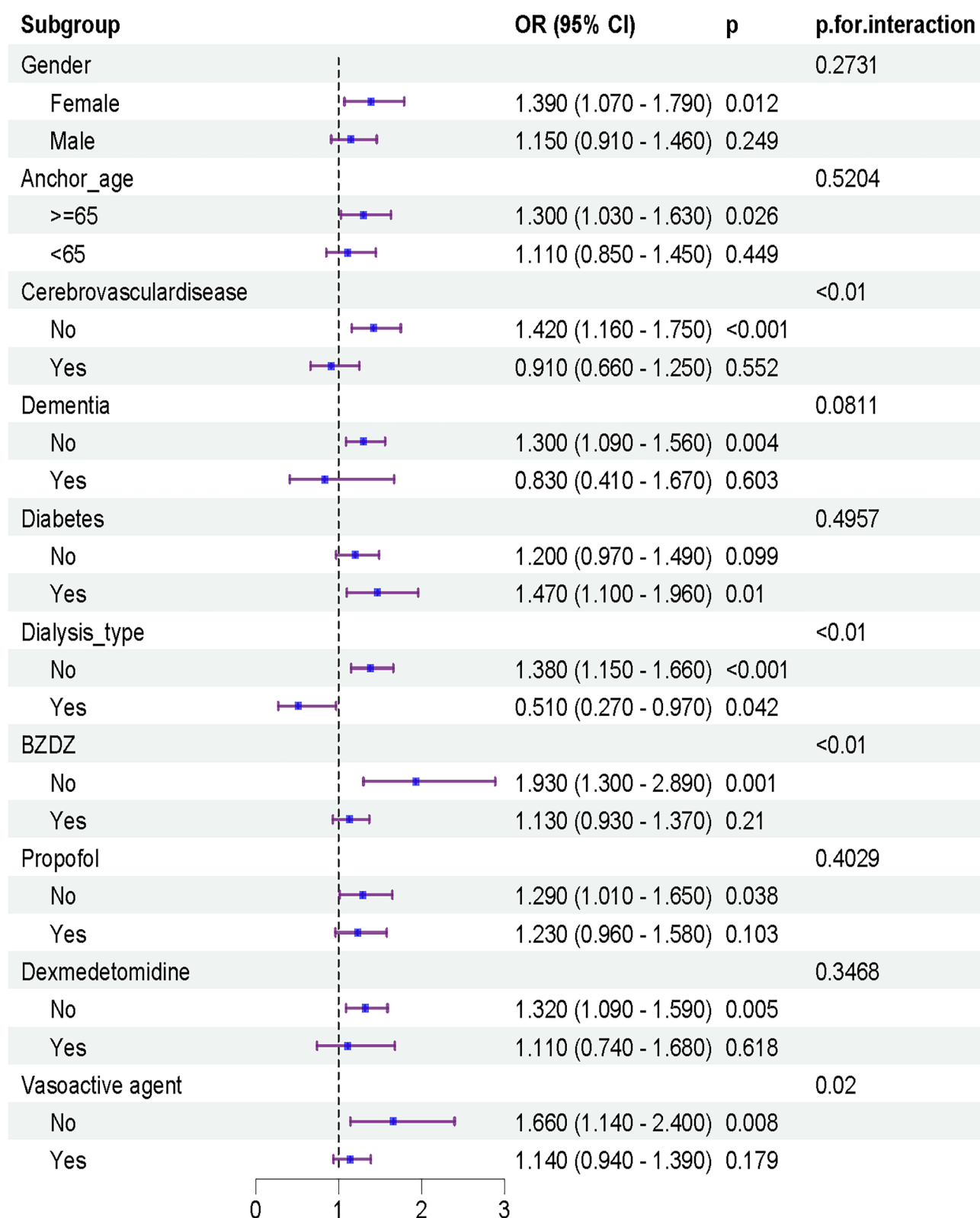


Fig. 3 Forest plot of subgroup analysis. Notes: Binary logistic regression is applied to evaluate the connection between POD and nutritional status in various subgroups. The results are shown as OR with 95%CI. Interaction p-values are computed through binary logistic regression to assess interactions between subgroups and nutritional status. Ca: Serum calcium; Na: Serum sodium; K: Serum kalium; Creatinine: Serum Creatinine; BUN: Blood Urea Nitrogen; Glu: Glucose; MI: Myocardial Infarction; CHF: Congestive Heart Failure; Ventilation status: Mechanical Ventilation; Dialysis type: Renal Replacement Therapy; Vas: Vasoactive Drugs; Dex: Dexmedetomidine; BZDs: Benzodiazepines; Prop: Propofol

in elderly patients, GNRI has also been widely utilized for evaluating malnutrition in adult patients [14–17] and is considered to be associated with various health risks across different adult populations. Low GNRI scores are associated with increased risks of POD and other complications [29, 45, 46]. As a practical tool, GNRI aids clinicians in identifying high-risk patients and guiding perioperative management [47]. This study, based on previous research, validates the significant association between malnutrition and POD in gastrointestinal surgery patients and offers fresh perspectives and evidence for perioperative risk assessment.

The incidence of POD varies among different patient populations, with specific subgroups such as diabetic patients exhibiting a notably higher risk [48]. Diabetic patients are more susceptible to severe brain and hippocampal atrophy, as well as microvascular damage, compared to their non-diabetic counterparts [48]. This susceptibility is further exacerbated by the potential for nutritional deficiencies in diabetics due to abnormal glucose metabolism, which may predispose them to acute cerebral metabolic disturbances during surgery [49]. Within a short follow-up period of 3 to 12 months, hyperglycemia in diabetic patients has been shown to exacerbate negative effects on brain function due to surgical stress [50]. A review article suggests that the abnormal glucose metabolism in diabetic patients may play a crucial role in cognitive dysfunction by affecting glucose transport and metabolism, alongside other factors such as oxidative stress, inflammation, and mitochondrial dysfunction, ultimately leading to synaptic transmission and neuroplasticity impairments, and neuronal and cognitive function damage [51]. This indirectly elucidates the association between diabetes, nutritional deficiencies, and POD after gastrointestinal surgery.

The impact of benzodiazepines on the risk of POD is significant yet contentious [52, 53]. Benzodiazepines are frequently administered due to their sedative, anxiolytic, and amnesic properties, which are beneficial during anesthesia and surgery. However, the correlation between benzodiazepines and POD is debated, with a prevailing view suggesting an elevated risk of delirium [44]. Wang et al.'s systematic review and meta-analysis on the safety and efficacy of perioperative benzodiazepine administration concluded that its use does not increase POD incidence, although this conclusion is based on low-quality evidence [53]. Our study suggests that malnourished patients not receiving benzodiazepines are more prone to POD, possibly due to the heightened need for care in such patients, who are more affected by noisy environments and sleep disturbances. Benzodiazepines may mitigate anxiety and thus reduce POD risk [54, 55]. In malnourished patients, drug metabolism is generally slower. However, in certain circumstances, the slowed metabolism of

benzodiazepines may lead to lower but stable concentrations in the body, thereby improving sleep quality. This sustained sedative effect could help lower the incidence of POD without causing excessive sedation [56]. Moreover, the nervous systems of malnourished patients are often more vulnerable, and benzodiazepines may reduce the risk of postoperative cognitive dysfunction by suppressing neuronal excitability and mitigating oxidative stress and inflammatory responses in the brain. These pharmacological effects may contribute to the recovery of postoperative cognitive function [57].

Among patients without cardiovascular diseases, a low GNRI is more significantly correlated with POD following gastric surgery. This could be because cardiovascular diseases often lead to chronic hypoxia, reduced cerebral blood flow, and higher risks of postoperative complications, such as hypotension and cardiac dysfunction [57]. Moreover, patients with cardiovascular diseases often have compromised immune function [58], which may result in poorer postoperative recovery and greater susceptibility to stress, infections, and inflammation. These factors themselves could raise the incidence of POD, rendering the independent impact of a low GNRI on POD relatively smaller. Vasoactive drugs, which improve tissue perfusion and oxygenation, exert their effects by altering vascular tone, heart rate, and myocardial contractility, thereby enhancing tissue perfusion and oxygenation [59]. This process may reduce cerebral hypoxia and metabolic disturbances. Additionally, vasoactive drugs can lower levels of inflammatory markers such as tumor necrosis factor- α (TNF- α) [60]. This may be an important reason for the interaction observed in subgroup analyses between the absence of vasoactive drug use and the occurrence of POD in gastric surgery patients.

Patients requiring renal replacement therapy often exhibit varying degrees of cognitive impairment. Dialysis itself is associated with at least three distinct central nervous system disorders: dialysis disequilibrium syndrome, dialysis dementia, and progressive intellectual dysfunction [61, 62]. In contrast, patients not requiring renal replacement therapy are more susceptible to nerve injury and inflammatory responses induced by malnutrition. Patients undergoing renal replacement therapy often present with complex medical conditions, including chronic kidney disease and cardiovascular disease, which may independently increase the risk of postoperative complications [63, 64]. Dialysis or mechanical ventilation can affect nutritional status, with nutrient loss during dialysis and reduced appetite and absorption in mechanically ventilated patients [65]. However, these patients typically receive more rigorous preoperative evaluation and management, including nutritional support and temperature regulation, potentially mitigating the impact of malnutrition on POD [66]. Mechanically ventilated

patients may face delays in postoperative evaluation due to intubation and continuous sedation, potentially affecting the accuracy of POD conclusions [67].

This study has several limitations. First, its retrospective design may lead to selection bias. Second, although sensitivity analyses were conducted to verify the consistency of the results, the study was unable to include other potential risk factors for POD due to limitations of public databases, such as education level, smoking history, ward environment, preoperative cognitive function assessment, detailed comorbid conditions, serum C-reactive protein (CRP) levels, ASA classification, and the duration of surgery and anesthesia [68], which could provide a more comprehensive strategy for prevention and treatment. Furthermore, this study did not account for whether patients received perioperative nutritional support, which could confound the relationship between GNRI and POD [54, 66].

In future research, more observational indicators, such as education level, smoking history, detailed cognitive function status, and nutritional interventions, should be included to better control the effects of confounding factors on outcomes. Additionally, the predictive value of GNRI in different populations and surgical types needs to be validated, and further exploration is required on how to optimize the nutritional status of perioperative patients to lower the incidence rate of POD.

Conclusion

Our study firmly establishes a correlation between malnutrition and POD risk in patients undergoing gastrointestinal surgery. The data highlight the importance of nutritional support during the perioperative period. We recommend mandatory preoperative nutritional assessments for all patients, followed by targeted interventions such as dietary modifications or supplements to reduce POD risk. Clinicians should incorporate nutritional status into their preoperative risk assessments to develop personalized treatment plans. This proactive strategy can improve recovery quality, lower healthcare costs, and increase patient satisfaction. Our findings offer actionable insights for optimizing perioperative care in gastrointestinal surgery by addressing nutritional deficiencies.

Abbreviations

OR	Odds ratio
CI	Confidence interval
GNRI	Geriatric Nutritional Risk Index
LRT	Likelihood ratio tests
IQR	Interquartile range
POD	Postoperative delirium
RCS	Restricted cubic spline
PSM	Propensity score matching
BIDMC	Beth Israel Deaconess Medical Center
MIT	Massachusetts Institute of Technology
MIMIC-IV v2.2	Medical Information Mart for Intensive Care IV version 2.2
NIH	National Institutes of Health

ICD
ERAS

International Classification of Diseases
Enhanced Recovery After Surgery

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

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Not applicable.

Author contributions

All authors contributed to the study conception and design. Writing - original draft preparation: Yan Chen, Huangyi Chen, Yong Zhuang, Ying Wang, Zhisen Dai; Writing - review and editing: Yan Chen, Huangyi Chen; Conceptualization: Yan Chen, Huangyi Chen; Methodology: Yan Chen, Yong Zhuang; Formal analysis and investigation: Yong Zhuang; Funding acquisition: Ying Wang; Resources: Huangyi Chen; Supervision: Ying Wang, Zhisen Dai, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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References

1. Inouye SK, Westendorp RGJ, Saczynski JS. Delirium in elderly people. *Lancet*. 2014;383(9920):911–22.
2. Marcantonio ER. Delirium in hospitalized older adults. *N Engl J Med*. 2017;377(15):1456–66.
3. Yan E, Veitch M, Saripella A, Alhmdah Y, Butris N, Tang-Wai DF, Tartaglia MC, Nagappa M, Englesakis M, He D, et al. Association between postoperative delirium and adverse outcomes in older surgical patients: a systematic review and meta-analysis. *J Clin Anesth*. 2023;90:111221.
4. Aldecoa C, Bettelli G, Bilotta F, Sanders RD, Aceto P, Audisio R, Cherubini A, Cunningham C, Dabrowski W, Forokhi A et al. Update of the European Society of Anaesthesiology and Intensive Care Medicine evidence-based and

- consensus-based guideline on postoperative delirium in adult patients. *Eur J Anaesthesiol* 2024, 41(2).
5. Goldberg TE, Chen C, Wang Y, Jung E, Swanson A, Ing C, Garcia PS, Whittington RA, Moitra V. Association of Delirium with Long-Term Cognitive decline: a Meta-analysis. *JAMA Neurol*. 2020;77(11):1373–81.
 6. Chin YC, Koh GC, Tay YK, Tan CH, Merchant RA. Underdiagnosis of delirium on admission and prediction of patients who will develop delirium during their inpatient stay: a pilot study. *Singap Med J*. 2016;57(1):18–21.
 7. Krinitski D, Kasina R, Klöppel S, Lenouvel E. Associations of delirium with urinary tract infections and asymptomatic bacteriuria in adults aged 65 and older: a systematic review and meta-analysis. *J Am Geriatr Soc*. 2021;69(11):3312–23.
 8. He ZJ, Kangjie KJ, Huang ZX, Fang J. [Effect of reducing-opioids consumption on postoperative delirium incidence in elderly patients after gastric cancer surgery]. *Zhonghua Yi Xue Za Zhi*. 2022;102(5):326–31.
 9. Bramley P, McArthur K, Blayney A, McCullagh I. Risk factors for postoperative delirium: an umbrella review of systematic reviews. *Int J Surg*. 2021;93:106063.
 10. Yamato M, Ikeda A, Endo M, Filomeno R, Kiyohara K, Inada K, Nishimura K, Tanigawa T. An association between cancer type and delirium incidence in Japanese elderly patients: a retrospective longitudinal study. *Cancer Med*. 2023;12(3):2407–16.
 11. Honda S, Furukawa K, Nishiwaki N, Fujiya K, Omori H, Kaji S, Makuuchi R, Irino T, Tanizawa Y, Bando E, et al. Risk factors for postoperative Delirium after Gastrectomy in Gastric Cancer patients. *World J Surg*. 2018;42(11):3669–75.
 12. Mattison MLP. Delirium. *Ann Intern Med*. 2020;173(7):Itc49–64.
 13. Cereda E, Pedrolli C. The geriatric nutritional risk index. *Curr Opin Clin Nutr Metabolic Care*. 2009;12(1):1–7.
 14. Li Y, Wang Z, Sun T, Zhang B, Liang X. Geriatric nutritional risk index was associated with in-hospital mortality among cardiac intensive care unit patients. *Front Nutr*. 2023;10:1218738.
 15. Miyasato K, Kobayashi Y, Ichijo K, Yamaguchi R, Takashima H, Maruyama T, Abe M. Oral Frailty as a risk factor for Malnutrition and Sarcopenia in patients on Hemodialysis: a prospective cohort study. *Nutrients* 2024, 16(20).
 16. Czinege MG, Nyulas V, Halaşiu VB, Tolescu C, Cojocariu LO, Popa T, Nyulas T, Benedek T. Interrelationship between altered left ventricular ejection Fraction and Nutritional Status in the Post-acute Myocardial Infarction patient. *Nutrients* 2024, 16(13).
 17. Jia H, Yin K, Zhao J, Che F. Association of inflammation/nutrition-based indicators with Parkinson's disease and mortality. *Front Nutr*. 2024;11:1439803.
 18. Nakagawa N, Maruyama K, Hasebe N. Utility of geriatric nutritional risk index in patients with chronic kidney disease: a mini-review. *Nutrients*. 2021;13(11):3688.
 19. Li H, Cen K, Sun W, Feng B. Prognostic value of geriatric nutritional risk index in elderly patients with heart failure: a meta-analysis. *Aging Clin Exp Res*. 2021;33:1477–86.
 20. Cereda E, Pedrolli C, Zagami A, Vanotti A, Piffer S, Opizzi A, Rondanelli M, Caccialanza R. Nutritional screening and mortality in newly institutionalised elderly: a comparison between the geriatric nutritional risk index and the mini nutritional assessment. *Clin Nutr*. 2011;30(6):793–8.
 21. Chen Z, Hao Q, Sun R, Zhang Y, Fu H, Liu S, Luo C, Chen H, Zhang Y. Predictive value of the geriatric nutrition risk index for postoperative delirium in elderly patients undergoing cardiac surgery. *CNS Neurosci Ther*. 2024;30(2):e14343.
 22. Zhao Y, Xia X, Xie D, Liao Y, Wang Y, Chen L, Ge N, Yue J. Geriatric nutritional risk index can predict postoperative delirium and hospital length of stay in elderly patients undergoing non-cardiac surgery. *Geriatr Gerontol Int*. 2020;20(8):759–64.
 23. Ibrahim JG, Chu H, Chen MH. Missing data in clinical studies: issues and methods. *J Clin Oncol*. 2012;30(26):3297–303.
 24. You J, Ellis JL, Adams S, Sahar M, Jacobs M, Tulpan D. Comparison of imputation methods for missing production data of dairy cattle. *Animal*. 2023;17:100921.
 25. Chen Y, Li S, Yang K, Wu B, Xie D, Peng C, Lai W. Triglyceride-glucose index and prognosis in individuals afflicted with heart failure and chronic kidney disease. *ESC Heart Fail*. 2024;11(5):3120–32.
 26. Wei F, Cheng H, He R, Yang X, Hu Z, Liu J, Wang Y. Geriatric nutritional risk index independently predicts delirium in older patients in intensive care units: a multicenter cohort study. *Arch Gerontol Geriatr*. 2024;118:105288.
 27. Beard JR, Officer A, de Carvalho IA, Sadana R, Pot AM, Michel JP, Lloyd-Sherlock P, Epping-Jordan JE, Peeters G, Mahanani WR, et al. The World report on ageing and health: a policy framework for healthy ageing. *Lancet*. 2016;387(10033):2145–54.
 28. Zuo W, Jiang S, Guo Z, Feldman MW, Tuljapurkar S. Advancing front of old-age human survival. *Proc Natl Acad Sci U S A*. 2018;115(44):11209–14.
 29. Chen Y, Sun Y, Wang L, Xu K, Wang DW. Genetic insights into associations of multisite chronic pain with common diseases and biomarkers using data from the UK Biobank. *Br J Anaesth*. 2024;132(2):372–82.
 30. Zhang F, He S-T, Zhang Y, Mu D-L, Wang D-X. Malnutrition is not related with emergence delirium in older patients after noncardiac surgery. *BMC Geriatr*. 2021;21(1):319.
 31. Chen Q, Zhu C, Ai Y, Wang J, Ding H, Luo D, Li Z, Song Y, Feng G, Liu L. Preoperative geriatric nutritional risk index is useful factor for predicting postoperative delirium among elderly patients with degenerative lumbar diseases. *Eur Spine J*. 2024;33(3):1055–60.
 32. Chen Y, Xie Y, Ci H, Cheng Z, Kuang Y, Li S, Wang G, Qi Y, Tang J, Liu D, et al. Plasma metabolites and risk of seven cancers: a two-sample mendelian randomization study among European descendants. *BMC Med*. 2024;22(1):90.
 33. Hirahara N, Tajima Y, Fujii Y, Kaji S, Kawabata Y, Hyakudomi R, Yamamoto T, Taniura T. Prediction of postoperative complications and survival after laparoscopic gastrectomy using preoperative Geriatric Nutritional Risk Index in elderly gastric cancer patients. *Surg Endosc*. 2021;35(3):1202–9.
 34. Li ZE, Lu SB, Kong C, Sun WZ, Wang P, Zhang ST. A prospective comparative study of the MNA-SF and GNRI nutritional screening tools in predicting infectious complications among elderly patients over 70 years undergoing posterior lumbar arthrodesis. *Aging Clin Exp Res*. 2021;33(7):1947–53.
 35. Weimann A, Braga M, Carli F, Higashiguchi T, Hübner M, Klek S, Laviano A, Ljungqvist O, Lobo DN, Martindale RG, et al. ESPEN practical guideline: clinical nutrition in surgery. *Clin Nutr*. 2021;40(7):4745–61.
 36. Matsui R, Sagawa M, Sano A, Sakai M, Hiraoka S-I, Tabei I, Imai T, Matsumoto H, Onogawa S, Sonoi N, et al. Impact of Perioperative Immunonutrition on post-operative outcomes for patients undergoing Head and Neck or Gastrointestinal Cancer surgeries: a systematic review and Meta-analysis of Randomized controlled trials. *Ann Surg*. 2024;279(3):419–28.
 37. Martínez-Ortega AJ, Piñar-Gutiérrez A, Serrano-Aguayo P, González-Navarro I, Remón-Ruiz PJ, Pereira-Cunill JL, García-Luna PP. Perioperative Nutritional support: a review of current literature. *Nutrients* 2022, 14(8).
 38. Mart MF, Girard TD, Thompson JL, Whitten-Vile H, Raman R, Pandharipande PP, Heyland DK, Ely EW, Brummel NE. Nutritional risk at intensive care unit admission and outcomes in survivors of critical illness. *Clin Nutr*. 2021;40(6):3868–74.
 39. Durán Poveda M, Suárez-de-la-Rica A, Cancer Minchot E, Ocón Bretón J, Sánchez Pernaute A, Rodríguez Caravaca G. The prevalence and impact of Nutritional Risk and Malnutrition in Gastrointestinal Surgical Oncology patients: a prospective, observational, Multicenter, and exploratory study. *Nutrients* 2023, 15(14).
 40. Tamura Y, Omura T, Toyoshima K, Araki A. Nutrition Management in older adults with diabetes: a review on the importance of shifting Prevention strategies from metabolic syndrome to Frailty. *Nutrients* 2020, 12(11).
 41. McIsaac DI, MacDonald DB, Aucoin SD. Frailty for Perioperative clinicians: a narrative review. *Anesth Analg*. 2020;130(6):1450–60.
 42. Liao C-K, Chern Y-J, Hsu Y-J, Lin Y-C, Yu Y-L, Chiang J-M, Yeh C-Y, You J-F. The Clinical Utility of the Geriatric Nutritional Risk Index in Predicting Postoperative Complications and Long-Term Survival in Elderly Patients with Colorectal Cancer after Curative Surgery. *Cancers (Basel)* 2021, 13(22).
 43. Wang X, Yu D, Du Y, Geng J. Risk factors of delirium after gastrointestinal surgery: a meta-analysis. *J Clin Nurs*. 2023;32(13–14):3266–76.
 44. Zhang X, Wang Y, Xu M, Zhang Y, Liu Q. The malnutrition in AECOPD and its association with unfavorable outcomes by comparing PNI, GNRI with the GLIM criteria: a retrospective cohort study. *Front Nutr*. 2024;11:1365462.
 45. Chen Y, Yang X, Zhu Y, Zhang X, Ni J, Li Y. Malnutrition defined by Geriatric Nutritional Risk Index predicts outcomes in severe stroke patients: a propensity score-matched analysis. *Nutrients* 2022, 14(22).
 46. Li S, Zhang L, Hou Y, Yang T, Li C, Wei Q, Ou R, Chen X, Shang H. Prevalence and prognostic significance of malnutrition in early-stage multiple system atrophy. *Front Nutr*. 2023;10:1248349.
 47. Fan H, Huang Y, Zhang H, Feng X, Yuan Z, Zhou J. Association of Four Nutritional scores with all-cause and Cardiovascular Mortality in the General Population. *Front Nutr*. 2022;9:846659.
 48. Hayashi K, Kurioka S, Yamaguchi T, Morita M, Kanazawa I, Takase H, Wada A, Kitagaki H, Nagai A, Bokura H, et al. Association of cognitive dysfunction with hippocampal atrophy in elderly Japanese people with type 2 diabetes. *Diabetes Res Clin Pract*. 2011;94(2):180–5.
 49. Scherer T, Sakamoto K, Buettner C. Brain insulin signalling in metabolic homeostasis and disease. *Nat Rev Endocrinol*. 2021;17(8):468–83.

50. Lachmann G, Feinkohl I, Borchers F, Ottens TH, Nathoe HM, Sauer AM, Dieleman JM, Radtke FM, van Dijk D, Spies C, et al. Diabetes, but not hypertension and obesity, is Associated with postoperative cognitive dysfunction. *Dement Geriatr Cogn Disord*. 2018;46(3–4):193–206.
51. Zhang S, Zhang Y, Wen Z, Yang Y, Bu T, Bu X, Ni Q. Cognitive dysfunction in diabetes: abnormal glucose metabolic regulation in the brain. *Front Endocrinol (Lausanne)*. 2023;14:1192602.
52. Wang E, Belley-Côté EP, Young J, He H, Saud H, D'Aragon F, Um K, Alhazzani W, Piticar J, Hedden M, et al. Effect of perioperative benzodiazepine use on intraoperative awareness and postoperative delirium: a systematic review and meta-analysis of randomised controlled trials and observational studies. *Br J Anaesth*. 2023;131(2):302–13.
53. Pandharipande P, Shintani A, Peterson J, Pun BT, Wilkinson GR, Dittus RS, Bernard GR, Ely EW. Lorazepam is an independent risk factor for transitioning to delirium in intensive care unit patients. *Anesthesiology*. 2006;104(1):21–6.
54. Chen J, Ji X, Xing H. Risk factors and a nomogram model for postoperative delirium in elderly gastric cancer patients after laparoscopic gastrectomy. *World J Surg Oncol*. 2022;20(1):319.
55. Fong TG, Tulebaev SR, Inouye SK. Delirium in elderly adults: diagnosis, prevention and treatment. *Nat Rev Neurol*. 2009;5(4):210–20.
56. Piccirillo A, Perri F, Vittori A, Ionna F, Sabbatino F, Ottaiano A, Cascella M. Evaluating nutritional risk factors for Delirium in intensive-care-unit patients: present insights and prospects for Future Research. *Clin Pract*. 2023;13(6):1577–92.
57. Inouye SK, Westendorp RG, Saczynski JS. Delirium in elderly people. *Lancet*. 2014;383(9920):911–22.
58. Sugita Y, Miyazaki T, Shimada K, Shimizu M, Kunimoto M, Ouchi S, Aikawa T, Kadoguchi T, Kawaguchi Y, Shiozawa T et al. Correlation of Nutritional Indices on Admission to the Coronary Intensive Care Unit with the Development of Delirium. *Nutrients* 2018, 10(11).
59. Boerma EC, Ince C. The role of vasoactive agents in the resuscitation of microvascular perfusion and tissue oxygenation in critically ill patients. *Intensive Care Med*. 2010;36(12):2004–18.
60. Ma XJ, Guo CY, Yin HJ, Liu Y, Shi DZ. [Effect of activating blood circulation or activating blood circulation and detoxication on platelet activation, inflammation, and coagulation status in acute myocardial infarction rats]. *Zhongguo Zhong Xi Yi Jie He Za Zhi*. 2014;34(11):1329–34.
61. Fraser CL, Arief AL. Nervous system complications in uremia. *Ann Intern Med*. 1988;109(2):143–53.
62. Liu H, Chen Y, Feng T, Liu X, Han Y, Wu X, Shi A, Zhou S, Lin Y, Yu P. The association between physical activity and cardiovascular events, tumors and all-cause mortality in patients with maintenance hemodialysis with different nutritional status. *Sci Rep*. 2024;14(1):16924.
63. Gaudry S, Palevsky PM, Dreyfuss D. Extracorporeal kidney-replacement therapy for acute kidney Injury. *N Engl J Med*. 2022;386(10):964–75.
64. Bellomo R, Baldwin I, Ronco C, Kellum JA. ICU-Based renal replacement therapy. *Crit Care Med*. 2021;49(3):406–18.
65. Lo S-C, Ma KS-K, Li Y-R, Li Z-Y, Lin C-H, Lin H-C, Yang S-F. Nutritional support for successful weaning in patients undergoing prolonged mechanical ventilation. *Sci Rep*. 2022;12(1):12044.
66. Ju JW, Nam K, Sohn JY, Joo S, Lee J, Lee S, Cho YJ, Jeon Y. Association between intraoperative body temperature and postoperative delirium: a retrospective observational study. *J Clin Anesth*. 2023;87:111107.
67. Chen T-J, Chung Y-W, Chang H-CR, Chen P-Y, Wu C-R, Hsieh S-H, Chiu H-Y. Diagnostic accuracy of the CAM-ICU and ICDSC in detecting intensive care unit delirium: a bivariate meta-analysis. *Int J Nurs Stud*. 2021;113:103782.
68. Igwe EO, Ding P, Charlton KE, Nealon J, Traynor V. Association between Malnutrition and Delirium in older chronic kidney Disease patients admitted to Intensive Care Units: A Data linkage study. *J Nutr Health Aging*. 2023;27(7):571–7.

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