Systematic Review

Geriatric nutritional risk index predicts postoperative delirium in elderly

A meta-analysis

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ABSTRACT

الأهداف: مراجعة الأدلة الحالية لاستخدام مؤشر المخاطر الغذائية لدى كبار السن (GNRI) في التنبؤ بالهذيان بعد العملية الجراحية (POD) في المرضى المسنين.

المنهجية: أجرينا بحث في الأدبيات في قواعد البيانات الأساسية لتشمل جميع الدراسات الأترابية حول العلاقة بين GNRI وخطر POD لمزيد من التحليل التلوي.

النتائج: اشتمل هذا التحليل التلوي على مجموعة 6 دراسات و 4242مريض، والذي أظهر أن خطر الإصابة بـ GNRI كان أعلى في المرضى الذين يعانون من GNRI المعتدل والمرتفع من أولئك الذين لديهم GNRI منخفض (OR=2.04، فاصل ثقة 95% [1.58، 2.64]، p<0.001)، وGNRI المعتدل والمرتفع يزيد بشكل كبير من خطر الإصابة بـPOD لدى المرضى الذين تتراوح أعمارهم بين 60 إلى 75 عامًا أو أكثر [OR=1.98 فترة الثقة= (1.49، 2.62) p<0.001،و OR=2.79، 95%CI (1.38، 5.64)، p=0.004.

الخلاصة: لذلك، فإن GNRI المعتدل والمرتفع يزيد من خطر الإصابة بمرض POD لدى المرضى المسنين.

Objectives: To review current evidence on using the geriatric nutritional risk index (GNRI) in predicting postoperative delirium (POD) in elderly patients.

Methods: The literature search was performed in core databases to include all the cohort studies on the association between GNRI and risk of POD for further meta-analysis.

Results: A total of 6 studies with 4242 patients underwent this meta-analysis, which showed that the risk of POD was higher in patients with moderate and high GNRI than the ones with low GNRI (odds ratio [OR]=2.04, 95% confidence interval [CI] [1.58, 2.64], p<0.001), and moderate and high GNRI significantly increased the risk of POD in patients of 60 to 75 years or above [OR=1.98, 95%CI (1.49, 2.62), p<0.001; OR=2.79, 95%CI (1.38, 5.64), p=0.004, respectively].

Conclusion: Therefore, moderate and high GNRI increased the risk of POD in elderly patients.

Keywords: geriatric nutritional risk index, postoperative delirium, general anesthesia, malnutrition

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Postoperative delirium (POD) is a set of acute brain dysfunctions from impairments in consciousness and cognition to disorganized thinking in patients after surgery.[1] It has been recognized as one of the most common postoperative complications for older adults. The incidence of postoperative delirium is approximately 17-61%, but even higher in patients undergoing cardiothoracic surgery and in intensive care units.[2,3] Since POD has been associated with long-term cognitive impairment, dementia, and even death, especially in elderly patients, early identification of the risk factors of delirium could effectively change its susceptibility and prevent its occurrence.[4-6] Various risk factors are identified for POD, of which preoperative malnutrition has been associated with the development of the disease.[7-10]

Several methods have been recommended to clinically assess the nutrition status of the patients for the different settings, among which the Nutritional Risk Screening 2002 (NRS-2002) for hospitalized patients, the Malnutrition Universal Screening Tool (MUST) for ambulatory ones, and the Mini Nutritional Assessment (MNA) for the geriatric population are predominantly used in practice. However, these mentioned methods are more subjective and arbitrary. Therefore, the geriatric nutritional risk index (GNRI) proposed by Bouillanne O et al,[11] which can be readily calculated from serum albumin level and body weight, has been clinically received as a nutritional risk screening tool for evaluating the nutritional status of geriatric patients in different clinical settings to predict malnutrition-related adverse events.[11-14]

However, the consensus remains unreached on the relationship between GNRI and POD. This study will explore the relationship between GNRI and the risk of POD after general anesthesia surgery, provide a basis for clinical screening of high-risk factors for POD.

Methods. The inclusion criteria were set for this meta-analysis as follows: i) The patients of the study had general anesthesia; ii) the study adopted cohort design; iii) the full text had been published in a peer-reviewed journal; iv) the baseline GNRI level for the experimental group is graded as moderate or severe malnutrition,the baseline GNRI level for the control group is graded as mild or no malnutrition; v) the outcome index was chosen as the incidence of POD. Moreover, exclusion criteria include i) repeated publication; ii) research data that cannot be extracted or transformed; iii) non-Chinese and English literature.

Literature search strategy. Chinese and English databases such as Web of Science, PubMed, Embase, Cochrane Library, CINAHL, CNKI, China Biomedical Literature Database, Wanfang Database, and VIP Database were searched by computer. The search time limit is from inception to March 2023, using a combination of subject words and free words, and the English search terms are "geriatric nutritional risk index/GNRI" "delirium/postoperative delirium/delirium, postoperative/delirium, postoperative / delusion/deliri*/acute brain syndrome/acute organic brain syndrome/intensive care unit (ICU) syndrome/cognitive disorder/cognitive impairment/POD/cognit*/awakening delirium/emergence delirium", the Chinese search term is "senile nutrition risk index/nutrition risk index/nutrition risk/nutritional risk assessment/nutritional assessment" "delirium/postoperative delirium/delirious/postoperative cognition/cognitive impairment/acute encephalopathy syndrome/ICU syndrome/emergence delirium/anesthesia emergence delirium". Taking the PubMed database as an example, the simplified search formula is ("geriatric nutritional risk index" OR "GNRI") AND ("delirium" OR "postoperative delirium" OR "delirium, postoperative" OR "delirium, postoperative" OR "delusion" OR "deliri*" OR "acute brain syndrome" OR "acute organic brain syndrome" OR "ICU syndrome" OR "cognitive disorder" OR "cognitive impairment" OR "POD" OR "cognit*" OR "awakening delirium" OR "emergence delirium"). Taking CNKI as an example, the retrieval formula is SU=(nutrition risk index for the elderly + nutrition risk index + nutrition risk + nutrition risk assessment + nutrition assessment) AND (SU=delirium + postoperative delirium + delirium + postoperative cognition + cognition cognitive impairment + acute encephalopathy syndrome + ICU syndrome + emergence delirium + anesthesia emergence delirium).

Literature screening and data extraction. EndNote X9 software was used to manage all the retrieved literature. Two researchers independently screened the literature and extracted data according to the inclusion and exclusion criteria. When the 2 researchers disagreed on the selection of any study, a third person was sought to judge whether the selection was included. The extracted data included the first author, publication time, country, age, sample size, operation type, and outcome indicators.

Quality evaluation. Two reviewers independently scored the quality of the included literature according to the Newcastle-Ottawa Quality Scale (NOS), which covers eight items and was detailed as the representativeness of the exposed group, representativeness of the non-exposed group, determination of exposure factors, lack of outcome indicators for observation during the study, comparability between groups, independent evaluation of blinding, sufficient follow-up time and thoroughness of follow-up.[15] The total score for the NOS was 9 points, which was further designated as 0-5

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points for low-quality research and 6-9 points for high-quality research.

Statistical methods. The results of data analyses were based on the odd ratio of the combined effect of POD occurrence. The random or fixed effect model was applied in the statistical analyses based on the heterogeneity among the included studies. The χ^2 test and I^2 value were determined to demonstrate the heterogeneity among the studies from the literature, and $p\leq0.1$ and $I^2\geq50\%$ suggested the existence of heterogeneity among the studies. Furthermore, subgroup analysis was performed according to the essential characteristics of the included studies, and sensitivity analysis was carried out to assess the stability of the results. Statistical analyses were conducted using RevMan 5.4 software, and a *p*-value less than 0.05 was considered statistically significant.

Results.

Literature search results. A total of 1,998 articles were initially retrieved and 1,714 articles were obtained after deleting duplicate articles. As a result, 6 studies with 4,242 patients were included for meta-analysis (Table 1).[16-21] The literature screening flowchart and results are shown in Figure 1.

Evaluation of literature quality. The quality of the included studies was evaluated by the NOS scale, which gave a total score of 8-9 points for the included studies (Table 2).

Results from meta-analysis. The meta-analysis included 6 studies on the relationship between GNRI and the risk of POD after general anesthesia.[16-21] Since heterogeneity was not found among these studies (p=0.63, I^2=0%), the fixed effect model was used for the analysis. The results from the analysis showed that the risk of POD in the group with moderate or high GNRI group significantly increased compared with that in the low or normal GNRI group, (OR=2.04, 95%CI [1.58, 2.64], p<0.001) (Figure 2).

Subgroup analyses were performed according to age. Three studies involving patients aged between 60 and 75 years showed no heterogeneity (p=0.32, I^2=13%), promoting the use of the fixed effect model for the analysis.[16,17,19] The results indicated that malnutrition at medium and high risk was associated with an increased risk of POD (OR=1.98, 95%CI [1.49, 2.62], p<0.001). Similarly, 2 studies on patients over 75 years of age also demonstrated no heterogeneity (p=0.78, I^2=0%), also recommending the use of the fixed effect model for analysis.[18,21] The meta-analysis revealed that GNRI had a predictive effect on POD in patients over 75 (OR=2.79, 95% CI [1.38, 5.64], p=0.004) (Appendix 1).

Surgical procedures can be categorized into 2 main types: cardiovascular surgery and non-cardiovascular surgery. One included study was for cardiovascular surgery, and 5 other studies were for non-cardiovascular surgery.[16-21] Meta-analysis showed that GNRI could increase the risk of POD in patients with non-cardiovascular surgery (OR=2.07, 95%CI [1.59, 2.69], p<0.001), but the predictive effect on cardiovascular surgery was not statistically significant (Appendix 2).

Sensitivity analysis and publication bias. Individual studies were excluded one by one for sensitivity analysis, and the meta-analysis results were stable. A funnel plot against the OR values (Appendix 3) shows that the

Table 1 - Basic characteristics of included studies (n=6).

Included study	Year	Country	Age (Year-old)		Sample		Surgery	POD case and percentage	
			Study arm	Control arm	Study arm	Control arm		Study arm	Control arm
Geng et al [16]	2022	China	72.6±5.8	71.3±5.0	239	676	Non-cardiac surgery	38 (15.9)	66 (9.8)
Takahashi et al [17]	2021	Japan	70 (64-75)		205	270	NSCLC surgery	8 (3.9)	9 (3.3)
Zhao et al [28]	2020	China	75 (73-79)	Low risk 75 (72-78), no risk 74 (71-77)	45	243	Non-cardiac surgery	14 (31.1)	35 (14.4)
Lee et al [19]	2019	England	Moderate risk 70.3±16.2; high risk 67±16.7	65±16.9	856	1212	SBO surgery	62(19.8)	38 (3.1)
Wang et al [20]	2019	China	Moderate risk 46.1+11.6; High risk 44.5+12.7	Low risk 45.2+13.2; no risk 45.3+12.7	46	102	Cardiac surgery	3 (13.1)	5 (10.0)
Kushiyama et al [21]	2018	Japan	80.3±3.8	79.0±3.6	190	158	Gastrectomy	2 (1.3)	0

1: GNRI = (1.489×serum albumin [g/L]) + (41.7×[current body weight / ideal body weight]); GNRI diagnostic criteria with Bouillanne O is high risk (GNRI<82), moderate risk (82≤GNRI<92), low risk (92≤GNRI≤98), and no risk (GNRI >98). GNRI: geriatric nutritional risk index SBO: small bowel obstruction, NSCLC: non-small cell lung cancer, POD: postoperative delirium

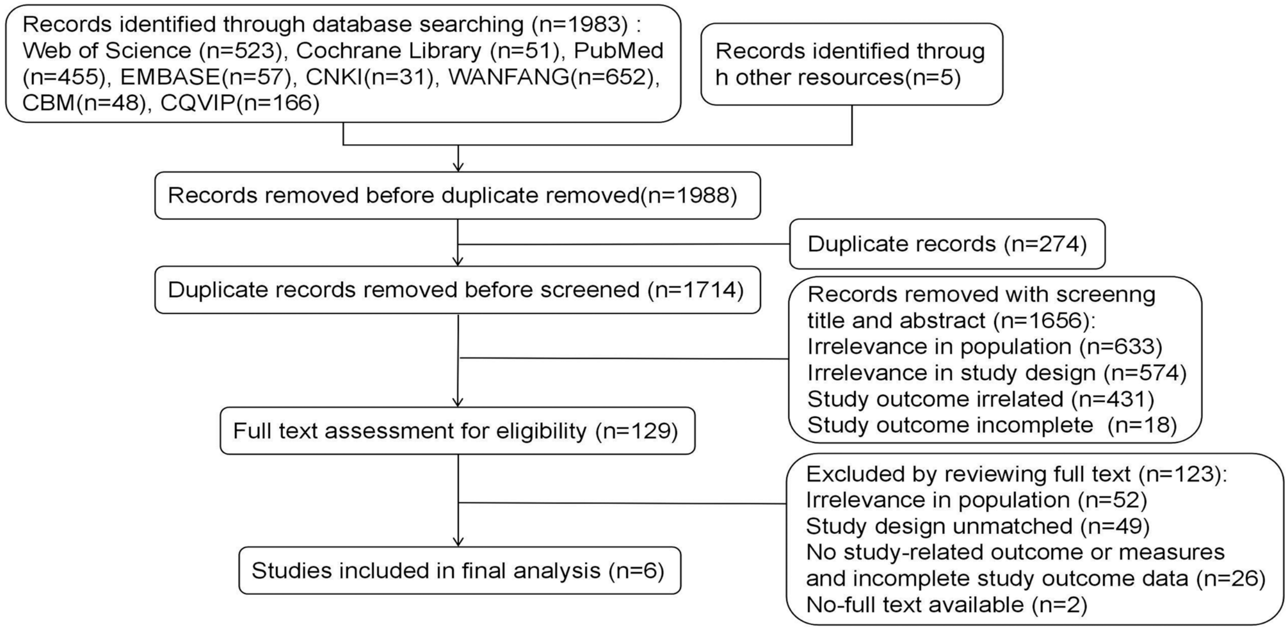

Figure 1 - Flowchart of the study.

Table 2 - Newcastle Ottawa Scale Rating of included studies

Included study	Selection of subjects			
	Representativeness of the exposed cohort	Representativeness of the control cohort	Ascertainment of the exposure	Lack of observatory indicator for the outcome of the study
Geng et al [16]	1	1	1	1
Takahashi et al[17]	1	1	1	1
Zhao et al[18]	1	1	1	1
Lee et al[19]	1	1	1	1
Wang et al[20]	1	1	1	1
Kushiyama et al[21]	1	1	1	1

Table 2 - Newcastle Ottawa Scale Rating of included studies (continuation).

Included study	Comparability between exposed and control cohorts	Outcome of measurement			Total score
		Independent evaluation of blinding	Sufficiency of follow-up	Completeness of follow-up	
Geng et al [16]	2	0	1	1	8
Takahashi et al[17]	2	1	1	1	9
Zhao et al[18]	2	0	1	1	8
Lee et al[19]	2	1	1	1	9
Wang et al[20]	2	0	1	1	8
Kushiyama et al[21]	2	1	1	1	9

distribution was roughly symmetrical, suggesting that the publication bias did not exist.

Discussion. This study showed that moderate and high-risk malnutrition increased the risk of POD by 2.04 times compared with low-risk and non-malnutrition. This finding is consistent with the study by Xiong et al,[22] which demonstrated the presence of malnutrition or the risk of malnutrition in patients as the risk factors for POD and the nutritional status to be inversely proportional to the possibility of POD. Given the scarcity of studies included in the meta-analysis, the findings should be substantiated through additional well-planned clinical trials in the future.

Study or Subgroup	Moderate and high risk malnutritionn Events	Total	Low risk and no malnutrition Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Geng 2022	38	239	66	676	37.8%	1.75 [1.14, 2.69]
Kushiyama 2018	2	190	0	158	0.7%	4.20 [0.20, 88.22]
Lee 2019	62	856	38	1212	38.1%	2.41 [1.60, 3.65]
Takahashi 2021	8	205	9	270	9.7%	1.18 [0.45, 3.11]
Wang 2019	3	46	5	102	3.8%	1.35 [0.31, 5.92]
Zhao 2020	14	45	35	243	9.8%	2.68 [1.30, 5.54]
Total (95% CI)		**1581**		**2661**	**100.0%**	**2.04 [1.58, 2.64]**
Total events	127		153			

Heterogeneity: $Chi^2 = 3.42$, df = 5 (P = 0.63); $I^2 = 0\%$
Test for overall effect: Z = 5.40 (P < 0.00001)

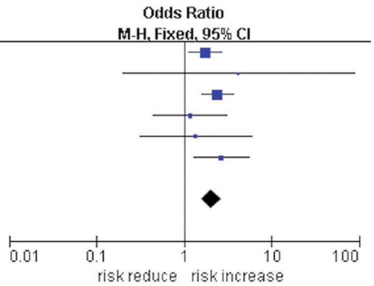

Figure 2 - Meta-analysis of the risk of POD in the patients with a moderate or high risk of malnutrition versus those with low risk or no malnutrition. CI: confidence interval, POD: postoperative delirium

Malnutrition as a complex body state has been widely accepted as a risk factor for the inferior prognosis of diseases. The poor nutrition state of patients contributes to frailty and sarcopenia, placing patients at a higher risk of POD.[23-26] The underlying mechanism has been hypothesized as the increased concentration of inflammatory factors in the blood of patients with malnutrition after surgery enters the brain through th e blood-brain barrier to induce an inflammatory response in the brain, which directly damages neurons to cause delirium.[27,28] Jayanama et al[29] showed that most nutritional parameters were associated with frailty, and the effect of individual parameters on mortality varied according to the degree of frailty. Many changes can occur with the aging process, such as lack of activity and malnutrition, which may lead to the development of various bone and muscle diseases to incite negative health impacts.[30,31] Studies have shown that GNRI is significantly associated with sarcopenia and physical function and can effectively predict the occurrence of sarcopenia in patients with liver cirrhosis.[32] Elderly hospitalized patients have a higher prevalence of malnutrition, frailty, and sarcopenia, which can markedly deteriorate body composition and function with age.[33,34]

Almost all prediction models of postoperative delirium use age as a predictor. However, the cut-off age differs slightly among these models.[35,36] According to the new age standard of WHO,[37] our study included those studies with an age range from 60 to 75 and found that patients over 60 with a moderate or high risk of malnutrition increased the risk of POD. The nutritional status of patients significantly impacts their surgical outcomes, so early diagnosis of malnutrition before surgeries makes the nutritional deficiency be corrected as early as possible to subsequently improve overall clinical outcomes.[38] Our study included both cardiovascular and non-cardiovascular surgeries, which showed that moderate and high GNRI increased the risk of POD in patients with non-cardiovascular surgery but could not predict the occurrence of delirium after cardiovascular surgery. Many studies have shown that nutritional status impacts the outcome and prognosis of cardiovascular surgery, so the study's results should be reviewed cautiously.[39-41]

This study only searched Chinese and English literature databases, so the language bias made our study only include 6 studies from China, Japan, and the United Kingdom, which did not fully reflect the differences among countries and regions. Moreover, due to the lack of well-designed randomized controlled trials in the included studies, selection, implementation, and measurement biases were unavoidable in this study. Remarkably, the number of included articles might be too small to deliver accuracy in the outcomes from various analyses.

In conclusion, this meta-analysis showed that GNRI had a predictive effect on POD, and moderate and high malnutrition increased the risk of POD during general anesthesia. However, due to the limited number of studies in our analysis, further research is needed to confirm the relationship between the GNRI and the risk of POD after general anesthesia in different age groups, types of surgery, and malnutrition groups.

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