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Predictive role of the prognostic nutritional index for long-term prognosis among patients undergoing pancreatoduodenectomy: a meta-analysis

Ying Liu[1] and Keyu Li[1*]

Abstract

Purpose To identify the predictive role of the preoperative prognostic nutritional index (PNI) for long-term survival in patients undergoing pancreatoduodenectomy.

Methods The PubMed, EMBASE, Web of Science, Cochrane Library and CNKI databases were searched up to October 28, 2024. The primary outcomes included overall survival (OS) and disease-free survival (DFS). Hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated, and subgroup analyses by country, type of cancer and source of HR were performed.

Results Fifteen studies with 2106 patients were included. The pooled results demonstrated that a lower preoperative PNI was related to poorer OS (HR = 1.60, 95% CI: 1.38–1.86, $P < 0.001$) and DFS (HR = 1.44, 95% CI: 1.00–2.07, $P = 0.051$). Subgroup analysis stratified by country (China vs. non-China), type of cancer (pancreatic cancer vs. nonpancreatic cancer vs. mixed) and source of HR (univariate vs. multivariate analysis) revealed similar results.

Conclusion On the basis of the available evidence, the preoperative PNI might serve as a novel prognostic indicator in patients undergoing pancreatoduodenectomy, with a lower PNI predicting worse survival. However, more high-quality studies are needed to further verify the above findings.

Keywords Prognostic nutritional index, Pancreatoduodenectomy, Overall survival, Disease-free survival, Meta-analysis

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Introduction

Pancreaticoduodenectomy is a surgical procedure commonly used to treat malignant or complex benign diseases of the pancreas, bile duct, duodenum, and periampullary region. Globally, the most common indication for pancreaticoduodenectomy is pancreatic cancer, especially pancreatic head cancer [1]. The incidence of pancreatic cancer varies across regions and is generally higher in developed countries, such as North America and Europe [2, 3]. The number of new cases of pancreatic cancer reported annually is increasing worldwide, partly due to an aging population and changes in lifestyle factors [2, 3]. In recent years, with advances in surgical techniques and perioperative management, the perioperative mortality rate of pancreaticoduodenectomy has significantly decreased from historical levels of 20% to less than 5% today (even lower in centers with highly experienced teams) [4–6]. This procedure is also becoming increasingly common in large hospitals in Asian countries such as Japan and China, reflecting advancements in technical proficiency and accumulated experience. As the survival time of patients undergoing pancreaticoduodenectomy has increased, the need for more precise prediction of long-term postoperative survival has emerged as a new clinical issue, which is crucial for guiding postoperative management and treatment.

Currently, assessing the long-term prognosis of patients undergoing pancreaticoduodenectomy in clinical practice is challenging. Evaluations are commonly based on pathological characteristics of the tumor, such as tumor size, differentiation grade, invasion depth, resection margins, and the number of lymph node metastases, providing only a rough assessment with limited clinical application value [7–9]. However, recent studies have increasingly revealed that the nutritional status of patients is closely related to the prognosis of cancer patients and can effectively help predict long-term outcomes. The prognostic nutritional index (PNI) is a novel biological indicator calculated using the following formula: peripheral serum albumin level (g/L) + 5×absolute lymphocyte count in peripheral blood (10^9/L), and it has been confirmed to have prognostic value in various types of cancer [10–12]. Based on previous research, the preoperative PNI could serve as a reliable predictor of long-term survival in patients with cancer undergoing surgery [10–12]. However, its role in patients undergoing pancreaticoduodenectomy has not yet been well clarified. Although some studies have explored the prognostic role of the PNI among patients undergoing pancreaticoduodenectomy, their results have shown significant differences. It remains unclear whether the PNI can effectively predict the long-term prognosis of patients in this group.

Therefore, we conducted this meta-analysis, for the first time, to further clarify the predictive role of the preoperative PNI in long-term survival among patients undergoing pancreaticoduodenectomy on the basis of the current evidence.

Materials and methods

This meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (2020) [13].

Literature search

The PubMed, EMBASE, Web of Science, Cochrane Library and CNKI databases were searched from inception to October 28, 2024, using the following terms: prognostic nutritional index, PNI, pancreatoduodenectomy and duodenopancreatectomy. In addition, MeSH terms and free texts were used during the search, and the references of the included publications were further reviewed.

Inclusion and exclusion criteria

Studies meeting the following criteria were included: ① patients underwent pancreatoduodenectomy due to pancreatic cancer, ampullary cancer or other adjacent cancers; ② the PNI was calculated before surgery according to the following formula: peripheral serum albumin level (g/L) + 5×absolute lymphocyte count in peripheral blood (10^9/L); ③ the association between the PNI and survival, including overall survival (OS) and disease-free survival (DFS), was explored; ④ hazard ratios (HRs) and 95% confidence intervals (CIs) were reported, or Kaplan–Meier survival curves were generated to calculate them; and ⑤ full texts were available.

Studies that met the following criteria were excluded: ① studies with insufficient, overlapping or duplicated data; ② no available HRs with 95% CIs even after contacting the authors; and ③ reviews, case reports, letters, editorials, meeting abstracts or animal trials.

Data collection

We collected the following information from the included publications: first author, publication year, country, sample size, type of cancer, PNI cutoff value, method of cutoff value determination, source of HR (univariate or multivariate), endpoint, HR and 95% CI.

Quality evaluation

In this meta-analysis, the methodological quality of the included studies was evaluated according to the Newcastle–Ottawa Scale (NOS) score, and studies with NOS scores ≥ 6 were regarded as high-quality studies [14].

Statistical analysis

Statistical analyses were conducted with STATA software (version 15.0). Heterogeneity among the included studies was calculated via I^2 statistics and the Q test.

When significant heterogeneity was detected, indicated by $P<0.1$ and/or $I^2>50\%$, the random effects model was applied; otherwise, the fixed effects model was applied [15]. HRs and 95% CIs were combined to identify the associations of the preoperative PNI with OS or DFS among patients who underwent pancreatoduodenectomy. Priority was given to the HRs and 95% CIs from multivariate analyses. If the HRs with 95% CIs were not reported in the manuscript, then they were obtained from the Kaplan–Meier survival curves. Subgroup analyses based on country (China vs. non-China), type of cancer (pancreatic cancer vs. nonpancreatic cancer vs. mixed) and source of HR (univariate vs. multivariate) were performed. Sensitivity analysis was conducted to assess the stability of the results of the meta-analysis. Begg's funnel plot and Egger's test were used to detect publication bias, with significant publication bias defined as $P<0.05$ [16, 17]. If significant publication bias was observed, the trim-and-fill method was applied to identify potentially unpublished studies and their impact on the overall results [18].

Results

Literature search and selection

The detailed process is shown in Fig. 1. Initially, 490 records were identified from the databases, and 75 duplicate records were removed. After reviewing the titles and abstracts, 353 and 34 records, respectively, were excluded. Eventually, 15 studies were included [19–33].

Basic characteristics of included studies

Among the 15 included studies, a total of 2106 patients were involved, and all the studies were high-quality studies, with NOS scores ≥ 6. Most studies were from China (9/15), focused on pancreatic cancer patients (11/15) and included multivariate analysis (13/15). The PNI cutoff values ranged from 36.948.85, and receiver operating characteristic (ROC) curve analysis was applied to determine the optimal PNI cutoff values in most studies (8/15). Other specific information is presented in Table 1.

Predictive role of preoperative PNI for OS in patients undergoing pancreatoduodenectomy

Fourteen studies explored the association between the preoperative PNI and OS in patients undergoing pancreatoduodenectomy [19–32]. The pooled results indicated that a lower preoperative PNI was significantly related

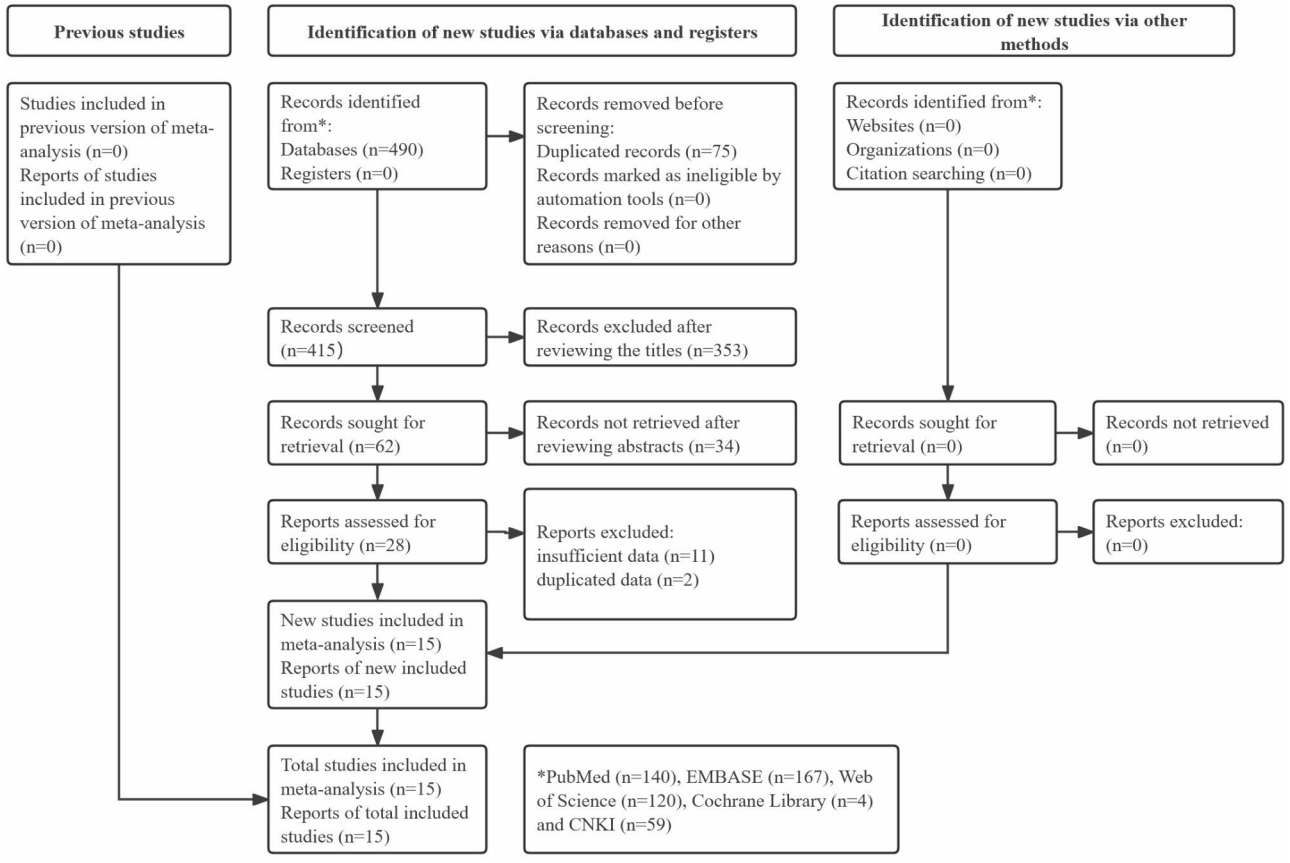

Fig. 1 Prisma flow diagram of this meta-analysis

Table 1 Basic characteristics of included studies

Author	Year	Country	Sample size	Type of cancer	Cutoff value of PNI	Determining method of cutoff value	Source of HR	Endpoint	NOS
Watanabe [30]	2016	Japan	46	PC	40	NR	U	OS	6
Onoe [26]	2019	Japan	165	PHA	38	Median	M	OS	6
Cai [19]	2020	China	85	PHC, PAC	48.4	ROC curve	M	OS	6
Yoo [33]	2020	South Korea	118	AVC	48.85	C-index	U/M	DFS	6
Wu [31]	2021	China	177	PHA	48.5	C-index	M	OS	6
Xiao [32]	2021	China	138	PA	46.63	ROC curve	M	OS	6
Cui [21]	2022	China	119	PDA	40.5	NR	M	OS	6
Jiang [24]	2022	China	251	PHC	45.1	ROC curve	M	OS	7
Chen [20]	2023	China	164	PHC	Continuous	-	M	OS, DFS	6
Huang [23]	2023	China	122	PC	44.6	ROC curve	M	OS	6
Ma [25]	2023	China	160	DC	42.275	ROC curve	M	OS	7
Hidaka [22]	2024	Japan	136	PHC	44.0	Median	U	OS, DFS	6
Sun [27]	2024	China	233	AA	45.3	ROC curve	M	OS, DFS	7
Suto [28]	2024	Japan	112	PC	36.9	ROC curve	M	OS	6
Utsumi [29]	2024	Japan	80	PC	45	ROC curve	M	OS	6

PHA: pancreatic head adenocarcinoma; PC: pancreatic carcinoma; PD: pancreatoduodenectomy; PHC: pancreatic head carcinoma; PAC: periampullary carcinoma; AC: ampullary carcinoma; AVC: ampulla of Vater carcinoma; PA: pancreatic adenocarcinoma; PDA: pancreatic ductal adenocarcinoma; DC: distal cholangiocarcinoma; AA: ampullary adenocarcinoma; ROC: receiver operator characteristic; NR: not reported; U: univariate; M: multivariate; OS: overall survival; DFS: disease-free survival; NOS: Newcastle-Ottawa Scale

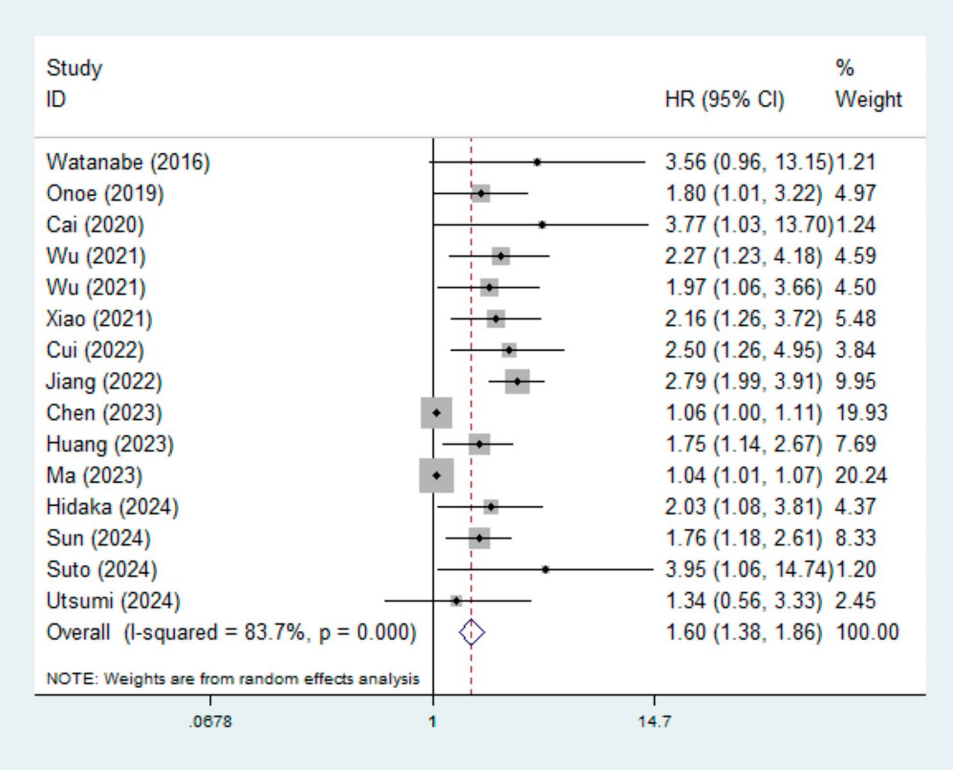

Fig. 2 Predictive role of preoperative prognostic nutritional index for overall survival among patients receiving pancreatoduodenectomy

to worse OS (HR = 1.60, 95% CI: 1.38–1.86, $P < 0.001$; $I^2 = 83.7\%$, $P < 0.001$) (Fig. 2). Subgroup analysis by country (China: HR = 1.52, 95% CI: 1.30–1.77, $P < 0.001$; non-China: HR = 1.99, 95% CI: 1.39–2.84, $P < 0.001$), type of cancer (pancreatic cancer: HR = 2.00, 95% CI: 1.43–2.79, $P < 0.001$; nonpancreatic cancer: HR = 1.30, 95% CI: 0.78–2.16, $P = 0.311$; mixed: HR = 3.77, 95% CI: 1.03–13.75, $P = 0.044$) and source of HR (univariate: HR = 2.26, 95% CI: 1.28–3.98, $P = 0.005$; multivariate: HR = 1.56, 95% CI: 1.34–1.81, $P < 0.001$) revealed similar results. Notably,

Table 2 Results of meta-analysis

Items	No. of studies	HR	95% CI	*P* value	I^2	*P* value of heterogeneity
Overall survival	14	1.60	1.38–1.86	<0.001	83.7%	<0.001
Country						
China	9	1.52	1.30–1.77	<0.001	87.3%	<0.001
Non-China	5	1.99	1.39–2.84	<0.001	0.0%	<0.001
Type of cancer						
Pancreatic cancer	11	2.00	1.43–2.79	<0.001	84.2%	<0.001
Non-pancreatic cancer	2	1.30	`0.78–2.16	0.311	85.1%	0.010
Mixed	1	3.77	1.03–13.75	0.044	-	-
Source of HR						
Univariate	2	2.26	1.28–3.98	0.005	0.0%	0.448
Multivariate	12	1.56	1.34–1.81	<0.001	84.7%	<0.001
Disease-free survival	4	1.44	1.00-2.07	0.051	73.0%	0.011

HR: hazard ratio; CI: confidence interval

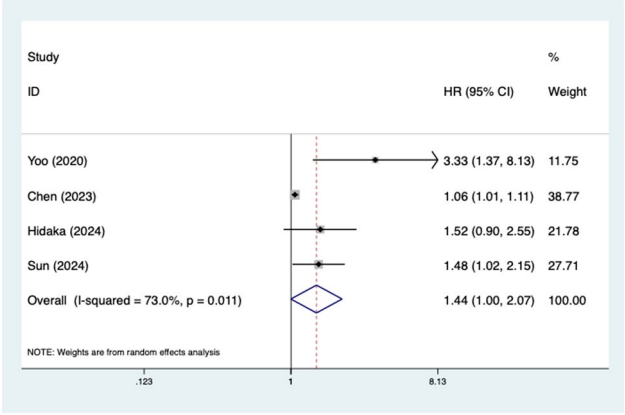

Fig. 3 Predictive role of preoperative prognostic nutritional index for disease-free survival among patients receiving pancreatoduodenectomy

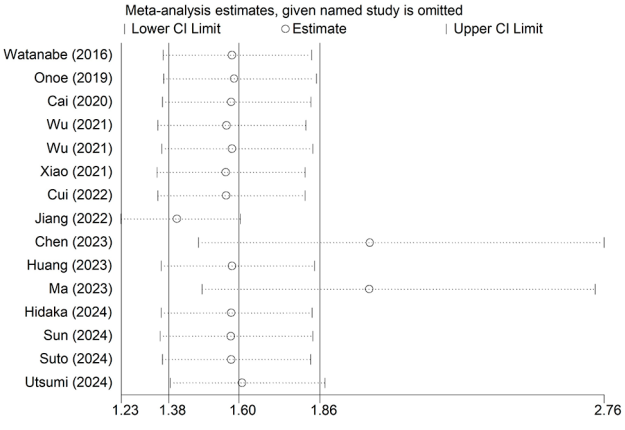

Fig. 4 Sensitivity analysis about the predictive role of preoperative prognostic nutritional index for overall survival among patients receiving pancreatoduodenectomy

although the predictive role of the PNI for OS in non-pancreatic cancer patients did not reach statistical significance, the two included studies both reported positive results (HR = 1.04, 95% CI: 1.01–1.07; HR = 1.76, 95% CI: 1.18–2.61) [25, 27] (Table 2).

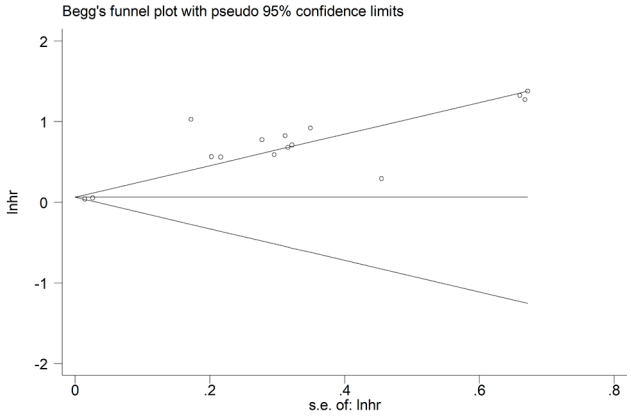

Fig. 5 Begg's funnel plot about the predictive role of preoperative prognostic nutritional index for overall survival among patients receiving pancreatoduodenectomy

Predictive role of preoperative PNI for DFS in patients undergoing pancreatoduodenectomy

Four studies explored the relationship between the PNI and DFS in patients receiving pancreatoduodenectomy [20, 22, 27, 33]. The pooled results demonstrated that a lower preoperative PNI was associated with worse DFS (HR = 1.44, 95% CI: 1.00–2.07, $P = 0.051$; $I^2 = 73.0\%$, $P = 0.011$) (Fig. 3; Table 2).

Sensitivity analysis and publication bias

According to the sensitivity analysis (Fig. 4), which was performed by excluding each study at one time, the pooled results of this meta-analysis were stable, and none of the included studies had a significant impact on the overall results.

Significant publication bias was detected according to the asymmetric Begg's funnel plot (Fig. 5) and Egger's test ($P < 0.001$). Therefore, the trim-and-fill method was applied, and nine potentially unpublished studies were identified (Fig. 6). However, these nine studies did not

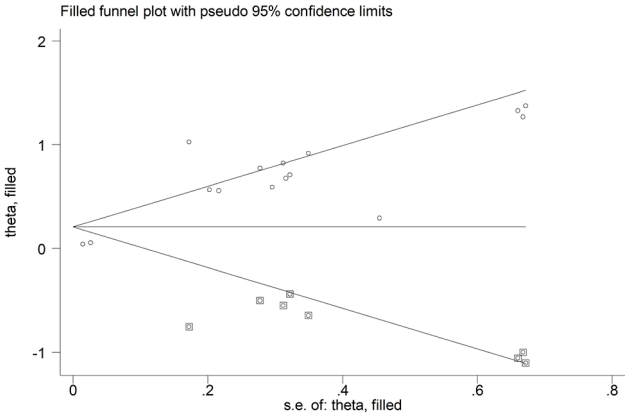

Fig. 6 Filled funnel plot about the predictive role of preoperative prognostic nutritional index for overall survival among patients receiving pancreatoduodenectomy

affect the overall conclusions (HR = 1.23, 95% CI: 1.07–1.42; $P = 0.004$).

Discussion

On the basis of the currently available evidence, our meta-analysis demonstrates for the first time that the preoperative PNI could serve as a novel and reliable predictive indicator of the long-term prognosis of patients undergoing pancreatoduodenectomy and suggests that patients with a lower preoperative PNI are more likely to experience worse survival. Further subgroup analysis supported the above findings. However, more prospective high-quality studies are needed to verify these findings due to the limitations of this meta-analysis.

In the subgroup analysis for OS by type of cancer, the association between the preoperative PNI and OS in patients with nonpancreatic cancer did not reach statistical significance ($P = 0.311$). However, the two included studies both reported positive results [25, 27]. Therefore, the PNI may also serve as a prognostic indicator among nonpancreatic cancer patients undergoing pancreatoduodenectomy; however, this finding should be verified by more studies.

The PNI can predict the long-term survival of patients undergoing pancreaticoduodenectomy, mainly because it reflects the patient's nutritional status and immune function, both of which play critical roles in postoperative recovery and long-term prognosis. A good nutritional status contributes to tissue repair, postoperative recovery, and resistance to infection, whereas postoperative malnutrition can lead to an increase in complications such as poor wound healing and infections, thereby affecting long-term survival rates [34, 35]. The PNI reflects a patient's nutritional and immune status through the serum albumin level and lymphocyte count, which are particularly important for postoperative recovery. Lymphocytes are a vital component of the immune system and participate in antitumor immune responses. A lower lymphocyte count is often associated with decreased immune function, which can increase the risk of recurrence and metastasis [36, 37]. The inclusion of the lymphocyte count in the PNI helps reflect a patient's immune capacity, indirectly indicating their ability to resist tumor recurrence [36, 37]. Notably, although peripheral blood lymphocyte counts may not fully reflect the role of lymphocytes in the tumor microenvironment and there may be some differences, on the basis of current research progress, the peripheral blood lymphocyte count can still serve as an effective indicator for assessing overall immune function and nutritional status. This is of significant help in predicting patient prognosis in a simple and effective manner in clinical practice. Low serum albumin levels are often linked to chronic inflammation and the progression of malignant tumors. A state of chronic inflammation can promote tumor growth and spread [18, 38]. Therefore, in the PNI, the albumin level not only serves as a marker of nutritional status but also reflects the inflammatory state of the body, which is important for patient prognosis.

Our results indicate that the PNI could serve as a reliable indicator for predicting the long-term prognosis of patients undergoing pancreaticoduodenectomy. Specifically, it can be applied in clinical practice in the following ways. The PNI can be used preoperatively to assess the nutritional and immune status of patients, helping physicians identify high-risk patients with malnutrition or impaired immune function. Providing nutritional support and immune-enhancing treatment (such as protein, vitamin, and mineral supplementation) to these patients before surgery may help improve postoperative recovery and reduce the occurrence of complications. Postoperative PNI values can assist physicians in determining the focus of postoperative management. Patients with a lower PNI may require closer monitoring and more proactive interventions, such as enhanced nutritional support and immune modulation, to reduce the risk of postoperative complications and disease recurrence. The PNI can also be used as an auxiliary decision-making tool to identify patients who may benefit from more aggressive postoperative adjuvant therapies (such as chemotherapy or radiotherapy). Patients with a poor nutritional and immune status might need special support to improve their tolerance and the efficacy of these treatments. However, these strategies still require further validation through additional studies. Furthermore, there are several similar nutritional and immune prognostic indicators, such as the controlling nutritional status (CONUT) score, the geriatric nutritional risk index (GNRI) and the C-reactive protein-to-albumin ratio (CAR), which have been reported to be predictive of long-term survival among

cancer patients [18, 39, 40]. A combination of these indices may demonstrate greater clinical applicability.

There are several limitations that should be noted. First, the sample sizes were relatively small, and most studies were from China or Japan, which might cause some bias. Second, the heterogeneity among the included studies was significant, but we were unable to identify the specific source of heterogeneity, which might affect the generalizability of our findings. Third, although most of the included studies performed multivariate analysis, and we also conducted subgroup analyses based on the source of HR, the variables included in the multivariate analyses differed across the studies. Some important variables, such as age, comorbidities, tumor stage, and resection margins, may affect the prognostic value of the PNI. However, owing to the lack of original data, we were unable to perform further subgroup analyses of these variables. Fourth, the PNI cutoff values for the prediction of long-term prognosis differed across the included studies. However, we were unable to further determine the optimal PNI cutoff values in our study because of the lack of original data, which is a common issue in meta-analyses.

Conclusion

According to the results of this meta-analysis, the preoperative PNI might serve as a novel prognostic indicator for patients undergoing pancreatoduodenectomy, and a lower PNI is a predictor of worse survival. However, more high-quality studies are needed to further verify our findings.

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None.

Author contributions
Keyu Li designed the study. Ying Liu and Keyu Li established the process of literature selection and screened the abstracts and articles. Ying Liu analyzed data and wrote the main manuscript. All authors reviewed and approved the final manuscript.

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Data availability
All data generated or analyzed during this study are included in this published article.

Declarations

Ethical approval
The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in studies that involved human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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