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Prognostic significance of preoperative prognostic nutritional index in hepatocellular carcinoma after curative hepatectomy: a meta-analysis and systemic review

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Background: The Prognostic Nutritional Index (PNI), which reflects both nutritional and immune status, has emerged as a potential predictor of survival outcomes in cancer patients. However, its role in forecasting the prognosis of hepatocellular carcinoma (HCC) following curative hepatectomy remains unclear. To further investigate the association between PNI and survival outcomes in HCC patients, we conducted a systematic review and meta-analysis.

Methods: We performed a comprehensive search across Web of Science, PubMed, Embase, Cochrane Library, and China National Knowledge Infrastructure to identify studies evaluating the prognostic value of PNI in HCC following curative hepatectomy. Overall survival (OS), recurrence-free survival (RFS), and disease-free survival (DFS) were extracted as primary outcomes. Pooled hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated using fixed-effect or random-effect models. Additionally, heterogeneity, publication bias, and sensitivity analyses were performed to evaluate the consistency and robustness of the obtained results.

Results: This systematic review and meta-analysis included 19 studies comprising a total of 9,830 patients. The results indicated that higher PNI was significantly associated with longer overall survival (OS) (n = 6,812; HR = 1.60; 95% CI: 1.44–1.77; $p < 0.001$) and recurrence-free survival (RFS) (n = 8,529; HR = 1.48; 95% CI: 1.30–1.69; $p < 0.001$). There was significant heterogeneity among studies for RFS (I^2 = 56.0%, p = 0.004). Subgroup analysis indicated that age, variations in PNI cutoff values and follow-up periods were the primary contributors to this heterogeneity. The trim-and-fill method indicated that publication bias did not impact the OS results, and Egger's test found no publication bias for RFS (p = 0.104). Sensitivity analysis further confirmed the stability of these results.

Conclusion: Preoperative PNI is a significant prognostic indicator in HCC patients undergoing curative hepatectomy, with higher PNI correlating with improved survival outcomes.

Systematic review registration: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42024530150, identifier CRD42024530150.

KEYWORDS

prognostic nutritional index, hepatocellular carcinoma, survival, prognosis, meta-analysis

1 Introduction

Hepatocellular carcinoma (HCC) is the most prevalent form of liver cancer, presenting a significant global health burden (1). Despite advancements in diagnostic and therapeutic strategies, the prognosis for HCC patients, especially those undergoing curative hepatectomy, remains variable and frequently uncertain (2). Therefore, identifying reliable prognostic factors for HCC is fundamentally crucial.

The prognosis of HCC is influenced by a number of factors, including tumor diameter, disease stage, liver function, alpha-fetoprotein (AFP), vascular invasion, cirrhosis, hepatitis B or C infection, alcoholic liver disease (1, 3). Notably, markers related to malnutrition and inflammation have proven to be reliable prognostic indicators. High levels of lymphocytes and tumor-infiltrating lymphocytes suggest a potent immune defense against cancer (4). In contrast, elevated neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios, along with programmed cell death-ligand 1 (PD-L1) expression, indicate inflammation and immune escape, which are associated with poorer cancer outcomes (5). Additionally, changes in body mass index, the prognostic nutritional index (PNI), serum albumin (ALB), and C-reactive protein levels crucially reflect a patient's nutritional and immune status. These indicators significantly impact cancer prognosis by revealing insights into malnutrition, systemic inflammation, and survival expectations (6).

Among various prognostic indicators, PNI has emerged as a potential factor influencing the prognosis of cancer patients, including those with HCC (7). PNI is calculated based on ALB levels and total lymphocyte counts in the blood, with the formula as follow: PNI = 10 × ALB (g/dL) + 0.005 × total lymphocyte count (/mm^3). Serum ALB, an acute-phase protein, has antioxidant and anti-inflammatory properties which can serve as an important indicator of both nutritional status and systemic inflammation (8). Lymphocytes play a vital role in cell-mediated immunity, inhibiting tumor cell proliferation and invasion through cytokine-mediated cytotoxicity (9, 10). Consequently, a low PNI serves as an indicator of insufficient nutritional and immune function in cancer patients. Various researches have shown that a low preoperative PNI is an independent negative prognostic factor for various digestive system neoplasms, including gastric and colorectal cancers (11), as well as for lung (12), breast (13), ovarian cancers (14), and gastrointestinal stromal tumors (15, 16).

However, the role of PNI in predicting prognosis for patients with HCC remains debated (17–19). Numerous studies suggested that a low PNI served as a prognostic indicator in patients with HCC following surgery (20–22). For example, the study of Hanxin Feng indicated that PNI was a significant prognostic markers for overall survival (OS), but not for disease-free survival (DFS) (23). Conversely, Xiaoxiao Fan's study revealed that HCC patients with a PNI below 45 had a poor recurrence-free survival (RFS) rate, though this association did not extend to OS (20).

Moreover, multiple meta-analyses have identified the PNI as an independent risk factor for patients with liver cancer post-surgery (20, 24, 25). However, the previous meta-analyses only included studies published up to 2021. Since then, numerous studies on PNI in HCC had been published. Additionally, the value of PNI in peripheral blood may vary with different treatment methods, such as chemotherapy and immunotherapy, an aspect overlooked in previous analyses. In the systematic review, we analyzed the association between preoperative PNI in treatment-naive patients and cancer survival outcomes.

2 Materials and methods

2.1 Literature search

On April 3, 2024, a comprehensive literature search was conducted across Embase, PubMed, the Cochrane Library, Web of Science, and China National Knowledge Infrastructure (CNKI), without language restrictions. The search strategy incorporated keywords such as "PNI," "HCC," "prognosis," "survival," and "treatment outcome," alongside their respective Medical Subject Headings (MeSH) terms. This meta-analysis was designed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

2.2 Study selection

Our systematic review aimed to address the following research question: What is the relationship between PNI and cancer survival in patients with HCC? We employed the PICOS (Patient, Intervention, Comparison, Outcome, and Study Design) framework to define selection criteria, as follows: "P" (patient)—patients diagnosed with HCC; "I" (intervention)—not applicable; "C" (comparison)—comparison between groups with high and low PNI; "O" (outcome)—relevant indicators to evaluate the association between preoperative PNI and prognostic outcomes on peripheral blood analysis; and "S" (study design)—prospective and retrospective study. According to the PICOS principles, the inclusion criteria were as follows: (1) Studies evaluated the association between various indicators and predictive outcomes, including PNI; (2) the patients were categorized into high and low PNI groups based on PNI values; (3) studies reported the prognosis of PNI value using multivariate Cox regression analysis. The exclusion criteria were as follows: (1) reviews, case reports, letters, editorials, and meeting abstracts; (2) full text was not available; (3) animal or *in vitro* experiments rather than clinical studies; (4) absence of preoperative PNI measurements prior to curative liver resection; (5) patients who received antitumor therapy before surgery or biopsy, as well as these whose treatment history were unclear; (6) studies that did not directly provide hazard ratios (HR) and 95% confidence intervals (CI).

2.3 Data extraction

Three investigators independently extracted data following consistent criteria, with any disagreements resolved through

consensus. The data collected included the publication year, first author's name, country, median age, gender, number of patients, outcome endpoints, PNI cut off value, median follow-up period, and method for estimating HRs with CIs. This meta-analysis focused on three outcome endpoints: OS, RFS, and DFS.

2.4 Quality assessment

Three investigators independently assessed the quality of included studies using the Quality in Prognostic Studies (QUIPS) tool. The assessment encompassed: study participation, study attrition, prognostic factor measurement, outcome measurement, study confounding, and statistical analysis. Studies were classified as having a low risk of bias if more than four of these six criteria demonstrated a low risk of bias. Conversely, studies with two or more criteria showing a high risk of bias were categorized as high risk of bias. Studies that did not meet either threshold were classified as having a moderate risk of bias.

2.5 Statistical analysis

Statistical analysis was conducted using RevMan 5.4 (Informer Technologies, Los Angeles, CA, USA) and Stata version 14.0 (Stata Corporation, College Station, TX, USA). Pooled HRs and 95% CIs for OS, RFS, and DFS were calculated to evaluate the association between PNI and survival outcomes. Heterogeneity was assessed by the I^2 value derived from the Q test, with $p < 0.05$ or $I^2 > 50\%$ indicating significant heterogeneity. Effect models were selected based on the I^2 and p values: a random-effects model was applied if $I^2 > 50\%$ or $p < 0.05$; otherwise, a fixed-effect model was applied. Publication bias was evaluated with Egger's test and the trim-and-fill method. Sensitivity analysis was performed to assess the stability of results by sequentially excluding individual studies.

3 Results

3.1 Study selection

A total of 1,035 papers were initially identified. After removing duplicate literature and reading the title, abstract, and full text according to the study's inclusion and exclusion criteria, ineligible publications were excluded. Ultimately, 19 studies were identified, comprising 9,830 patients with HCC who underwent curative resection (7, 20, 23, 26–41). These studies were published between 2016 and 2024. The flow diagram for the study selection is presented in Figure 1.

3.2 Study characteristics and quality assessment

Table 1 in the meta-analysis presents the characteristics of the included studies, all of which were conducted in Asia, including 14 from China, 1 from Korea, and 4 from Japan, totaling 19 studies. Notably, in one study (40), the correlation between OS and PNI was separately discussed for patients with TNM stage I and TNM stage II. The sample sizes ranged from 100 to 2020 participants, with all studies being retrospective in design. Thirteen studies evaluated the impact of the PNI on OS, 12 on RFS, and 3 on DFS. The studies revealed that the median age of participants ranged from 49.63 to 70.46 years, with a higher prevalence of male participants. The majority of patients were in the early stages of disease, with 7,950 patients classified under the Barcelona Clinic Liver Cancer (BCLC) staging system as stages 0/A and 1,550 in advanced stages B/C/D. Most patients were affected by hepatitis B virus (HBV) or hepatitis C virus (HCV), and all underwent curative surgical excision. Follow-up periods varied, with median durations from 1.9 to 5.3 years. The median cut off values for PNI ranged from 44.35 to 53.95. Preoperative routine blood examinations were conducted, and HRs were calculated using multivariate regression analysis in all studies. According to the QUIPS checklist, 17 studies were assessed as having a low risk of bias, while 2 studies exhibited a moderate risk of bias.

3.3 The relation between PNI and OS in HCC patients

Thirteen studies were included in the meta-analysis of OS. A fixed effect model was used to calculate the pooled HRs and 95% CIs, as the heterogeneity test reported a p value of 0.08 and I^2 value of 37.1%. The results showed that patients with higher PNI had significantly longer OS (n = 6,812, HR = 1.60; 95% CI: 1.44–1.77; $p < 0.001$) (Figure 2).

3.4 The relation between PNI and RFS in HCC patients

A total of 12 studies reported the effects of PNI on RFS in the meta-analysis. Besides, 3 articles discussed DFS, which has a similar definition to RFS. Therefore, the HR of DFS was combined with RFS to obtain the final HR for the total 15 studies. A random effects model was used to calculate the pooled HRs and 95% CIs due to the relatively high heterogeneity (I^2 = 56.0%, p = 0.004). Our results demonstrated that a higher PNI was associated with improved survival outcomes (n = 8,529, HR = 1.48, 95% CI: 1.30–1.69, $p < 0.001$) (Figure 3).

Subgroup analyses of RFS were conducted based on several potential factors (age, sample sizes, cut off value of PNI, follow-up periods, and study quality) to investigate the heterogeneity (Table 2). The result indicated that age, cut off value of PNI and follow-up period were likely contributors to heterogeneity. The heterogeneity for studies with age < 60 (HR =1.41, 95% CI: 1.20–1.66, $p < 0.001$), PNI cut off value > 46 (HR = 1.41, 95% CI: 1.15–1.73, p = 0.001), and follow-up period >3 years (HR = 1.31, 95% CI: 1.04–1.64, p = 0.019) was notably high, with I^2 values of 59.1, 63.1 and 59.4%, respectively. In contrast, no significant heterogeneity was observed for studies with age ≥ 60 (HR =1.47, 95% CI: 1.13–1.91, $I^2 = 0$), PNI cut off value ≤46 (HR = 1.56, 95% CI: 1.35–1.80, I^2 = 31.6%), or a follow-up period ≤3 years (HR = 1.64; 95% CI: 1.34–2.00; $I^2 = 0$).

3.5 Publication bias and sensitivity analysis

Publication bias between studies was conducted using Egger's test. Results indicated publication bias was found between PNI and OS

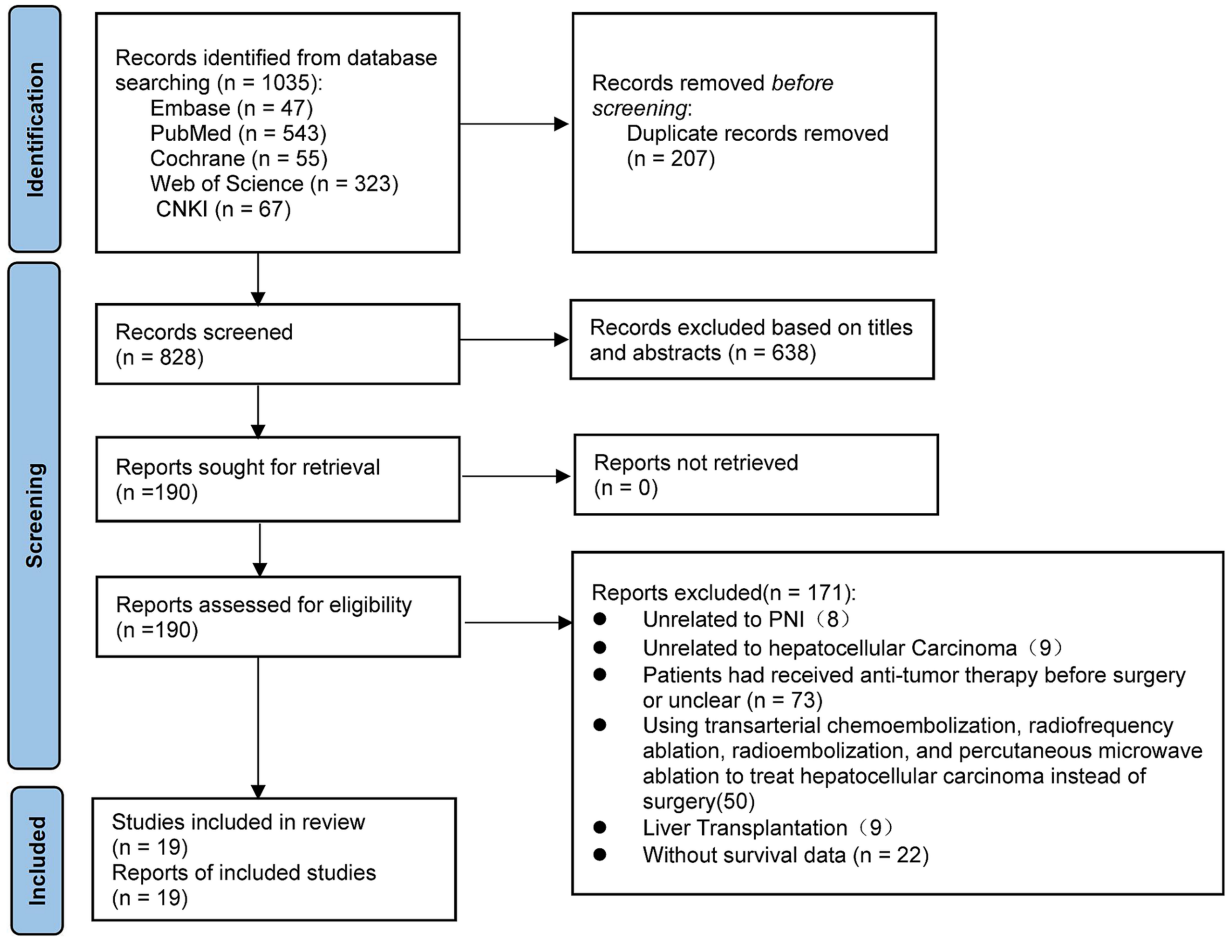

FIGURE 1
Flow diagram of study selection.

($p = 0.001$), while no publication bias was detected between PNI and RFS ($p = 0.104$) (Figure 4b). To further evaluate publication bias for OS, the trim-and-fill method was applied. The addition of six missing studies did not alter the overall effect (HR = 1.495; 95% CI: 1.361–1.642; $p < 0.001$) (Figure 4a), indicating that publication bias for OS did not impact the results and could be ignored. Sensitivity analysis demonstrated that no single study significantly influenced the conclusions of this meta-analysis (Figure 5).

4 Discussion

PNI was first proposed by Buzby et al. (42), and later validated by Onodera et al. (43) to predict the surgical risk in gastrointestinal malignancy. Due to its convenience and efficiency, the PNI has been investigated widely, with numerous studies demonstrating that a low PNI is an independent prognostic factor for both short-term postoperative complications and long-term outcomes across various cancers, such as gastric cancer (44), colorectal cancer (44), lung cancer (45), oral cancer (46), biliary tract cancer (47), and so on. In HCC, the PNI was first proposed as a potential prognostic maker by Pinato et al. (48), and its role in HCC treatment and prognosis continues to expand. Pretreatment PNI had been studied across diverse HCC patient groups, including these treated with curative therapies, radiofrequency ablation, microwave ablation (49), sorafenib (50), anti-PD1 therapy (51) and liver transplantation (52). More recently, researches have begun to explore the implications of post-treatment PNI (53). As studies on this topic continue to emerge, there is an urgent need to summarize and analyze the extensive research data to draw meaningful conclusions.

In this review, we comprehensively summarized the literature to date, providing supportive evidence for the prognostic significance of PNI in predicting outcomes for HCC patients following curative hepatectomy. This systematic review and meta-analysis included 19 studies with a total of 9,830 patients. The results indicated that the higher PNI was associated with significantly longer OS ($n = 6,812$, HR = 1.60; 95% CI: 1.45–1.77; $p < 0.001$) and RFS ($n = 8,529$, HR = 1.48, 95% CI: 1.30–1.68, $p < 0.001$), consistent with the previous meta-analyses (20, 24, 25). In the meta-analyses conducted by Guangliu Wu (24) and Xiaoxiao Fan (20), it remained unclear whether the patients received systemic antitumor therapy prior to hepatectomy, and the timing of PNI testing was ambiguous. Notably, Guangliu Wu's study did not clarify whether PNI was assessed preoperatively or postoperatively (24), and the most recent literature in Xiaoxiao Fan's study dated back to 2017 (20). Another related meta-analysis suggested that a lower preoperative PNI significantly predicted worse OS and DFS across HCC patients undergoing surgical resection,

TABLE 1 Characteristics of studies included in the meta-analysis.

No	Years	First author	Country	Sample size	PNI low/high	Age (mean or median, range)	Male/Female	Outcome	Cut off	Follow-up (year)	BCLC		Risk of bias
											0/A	B/C/D	
1	2024	Chengkun Yang	China	1,666	582/1084	<60	1419/247	OS, RFS	46	about 5	1,419	247	L
2	2023	Hikaru Hayashi	Japan	303	150/153	70.47	221/82	OS, RFS	46.2	about 0.2–11.75	221	82	L
3	2022	Wei Qian	China	661	193/468	51	572/89	OS, RFS	45	3 (1.6–3.2)	572	89	L
4	2022	Takashi Matsumoto	Japan	497	116/381	69 (38–87)	374/123	OS	45	4.3	374	123	L
5	2022	Hanxin Feng	China	283	100/183	58 (30–79)	223/60	OS, DFS	48.48	3.3 (0.2–8.9)	223	60	M
6	2021	Meilong Wu	China	88	20/68	NA	62/26	DFS	44.35	about 3	62	26	L
7	2021	Wu meilong	China	73	50/23	NA	57/16	OS	45.65	2.6 (0.2–4.7)	57	16	M
8	2021	Xiaoxiao Fan	China	187	65/122	57 (29–85)	165/22	OS, RFS	45	1.9 (0.1–5)	165	22	L
9	2021	Dong Wang	China	202	NA	50.4 (38.5–62.4)	168/34	OS, RFS	50.25	about 5	168	34	L
10	2021	Yu Saito	Japan	162	86/76	65.1	119/43	RFS	45	2.5 (0.02–8.0)	119	43	L
11	2021	Xie Liang	China	868	230/638	50.5 (38.5–62.6)	727/141	OS, DFS	46	about 3.4–8.3	727	141	L
12	2021	Ho Jeong	Korea	130	77/53	NA	111/19	RFS	52	2.9 (0.2–13.1)	111	19	L
13	2020	Jianxing Zeng	China	2020	1,552/468	51.4 (40.6–62.2)	1,765/255	RFS	53.95	3.9	1,765	255	L
14	2020	Junsheng Yang	China	238	81/157	59.1 (47.8–70.4)	195/43	RFS	48.05	3.1 (0.07–10.1)	195	43	L
15	2020	Z. X. Lin	China	380	189/191	50 (19–80)	333/47	RFS	50	4.1	333	47	L
16	2019	Tingting Zhang	China	401	170/231	52.1 (41.6–62.5)	354/47	OS	48.5	about 10–12.8	354	47	L
17	2019	Paoyuan Huang	China Taiwan	891	441/450	58.5 (46.9–70.1)	694/197	OS, RFS	45	5.3 (2.3–8.3)	694	197	L
18	2017	Yukiyasu Okamura-I	Japan	230	162/68	NA	183/47	OS	52	3.45 (0.5–10)	NA	NA	L
	2017	Yukiyasu Okamura-II	Japan	100	39/61	NA	NA	OS	47	3.45 (0.5–10)	NA	NA	L
19	2016	Sijia Wu	China	450	220/230	49.6 (17–81)	391/59	OS, RFS	48.28	3.8 (0.2–7.7)	391	59	L

OS, overall survival; RFS, recurrence-free survival; DFS, disease-free survival; L, Low-risk; M, Moderate-risk; NA, Not available.

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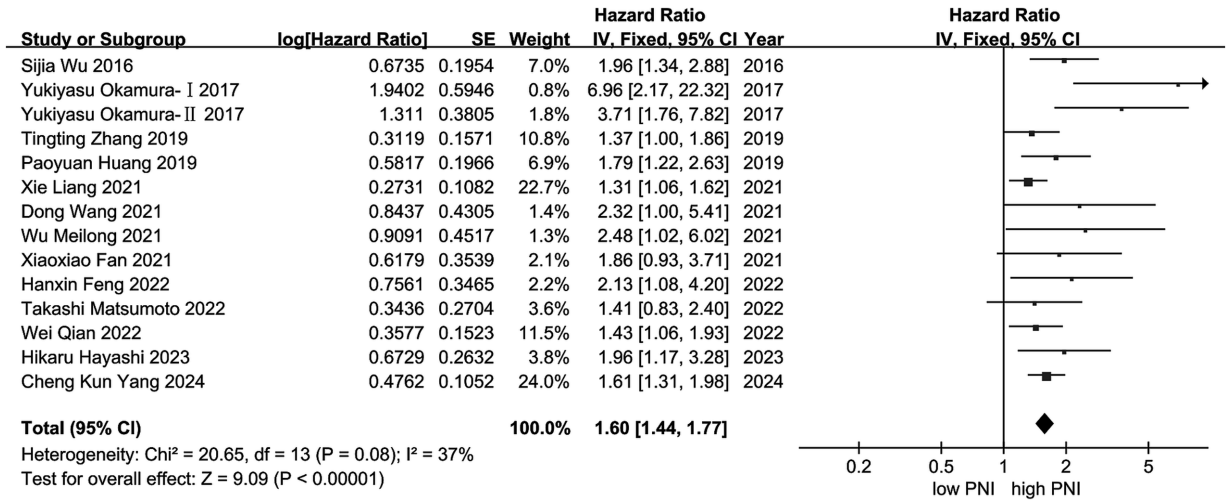

FIGURE 2
Forest plot of HR with 95% CI for correlation between expression of PNI and OS.

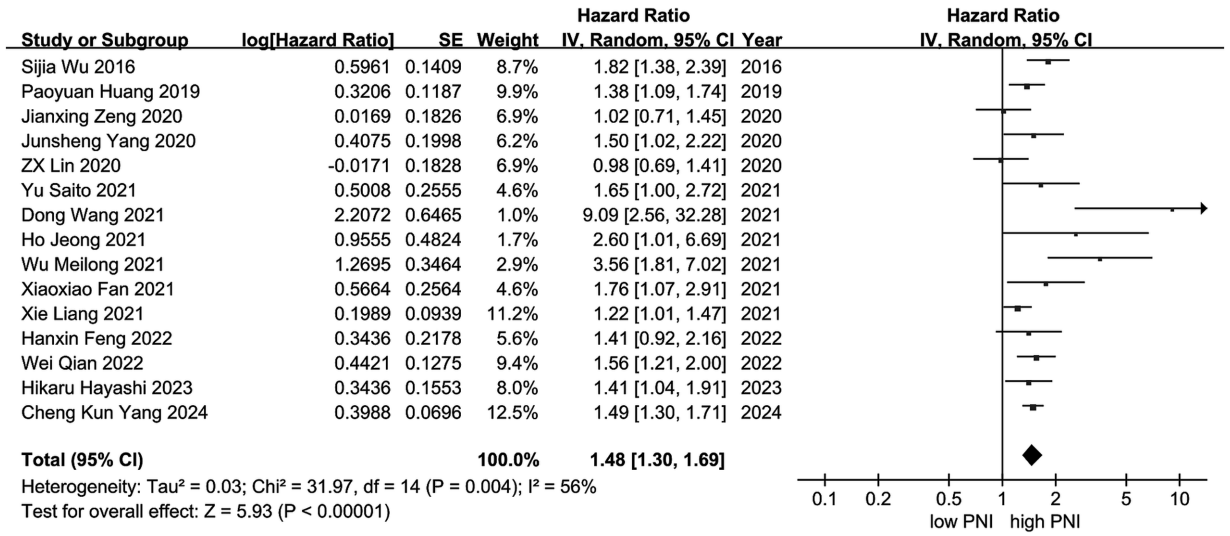

FIGURE 3
Forest plot of HR with 95% CI for correlation between expression of PNI and RFS.

transcatheter arterial chemoembolization, and non-surgical treatment (25). In our meta-analysis, we only included treatment-naive patients prior to surgery to eliminate the effect of antitumor treatment on PNI. Moreover, the literature included in this paper is relatively new and up to 2024, which provides a more comprehensive understanding of the relationship between PNI and survival outcomes.

The significant statistical heterogeneity was found in RFS. Although the factors of heterogeneity of PNI are very complex, the results of subgroup analyses could partially explain these heterogeneous factors. Subgroup analysis demonstrated that there were significant differences in age, cut-off values of PNI, and follow-up period. Firstly, heterogeneity generation is related to the age. Generally, the elderly are more susceptible to malnutrition due to decreased physiologic function and metabolic level, which in turn may influence PNI. Particularly, the related research also showed that poor nutritional status in HCC patients over 65 years was associated with worse prognoses (54). Consistently, broad age range from 49.6 to 70.5 median years was observed in our study, which may contribute to the heterogeneity. Secondly, the cut off value significantly influences the delineation of specific groupings, which were closely associated with the calculated method. Indeed, three different sources of cut-off value were involved among all the included articles with "previous literature" (7, 20, 29), "survminer" package (30, 35), and ROC data. Thirdly, the follow-up period is also a source of heterogeneity. One study focused on the psoas muscle index (PMI), an indicator similar to PNI, indicated that PMI was an independent prognostic factor for 1-year treatment outcomes but not effective for predicting 6-month outcomes (55). Unfortunately, the absence of precise median follow-up times in six of the studies included in this paper limited the potential for further in-depth analysis. Additionally, differences in multivariate

TABLE 2 Subgroup analysis of RFS included in the meta-analysis.

Subgroup	HR (95% CI)	*p*	Heterogeneity		Studies
			p	I^2	
Age					
≥ 60	1.47 (1.13–1.91)	0.004	0.599	0	2
< 60	1.41 (1.20–1.66)	<0.001	0.009	59.1%	10
NA	2.21 (1.18–4.15)	0.014	0.026	72.6%	3
PNI Low/High					
> 1	1.44 (1.07–1.94)	<0.001	0.123	48.0%	4
< 1	1.45 (1.27–1.65)	0.015	0.034	50.2%	10
NA	9.09 (2.52–32.70)	NA	NA	NA	1
Sample size					
>350	1.36 (1.19–1.56)	<0.001	0.031	56.7%	7
≤350	1.83 (1.40–2.39)	<0.001	0.044	51.5%	8
Cut off of PNI					
>46	1.41 (1.15–1.73)	0.001	0.006	63.1%	9
≤46	1.56 (1.35–1.80)	<0.001	0.199	31.6%	6
Follow-up period					
>3 years	1.31 (1.04–1.64)	0.019	0.043	59.4%	5
≤3 years	1.64 (1.34–2.00)	<0.001	0.761	0	4
NA	1.60 (1.26–2.04)	<0.001	0.003	72.6%	6
Study quality					
Low-risk	1.49 (1.30–1.71)	<0.001	0.003	59.1%	14
Moderate-risk	1.41 (0.92–2.16)	NA	NA	NA	1

HR, hazard ratio; CI, confidence interval; NA, Not available.

analysis models may also contribute to heterogeneity, as models based on different postoperative inflammatory indicators and clinicopathological factors exhibit varying HRs and 95% CIs (30).

The PNI incorporates measurements, such as ALB levels and lymphocyte count, that reflect both nutritional and immunological status. ALB (56) helps regulate blood volume and pressure, crucial for transporting nutrients, hormones, and immune cells (56). It's also linked to cancer prognosis, particularly in patients with HCC (57, 58). Lymphocytes, another part of the PNI, can prevent tumor growth and recurrence by supporting immune function (59). Additionally, a low PNI is associated with poor survival rates in metastatic intrahepatic cholangiocarcinoma (ICC) (6). Moreover, it also helps predict outcomes for patients undergoing immunotherapy (60), targeted therapy (50), and radiochemotherapy (61, 62).

There are several reasons why a low preoperative PNI may be associated with a poor prognosis in patients with HCC following curative hepatectomy. Firstly, the PNI serves as an indicator of nutritional status. A low preoperative PNI suggests a compromised nutritional state, which negatively impacts prognosis. Secondly, the study of Pinato noted that PNI correlated significantly with raised AFP, liver functional reserve, and the presence of portal vein thrombosis, suggesting that a high-risk PNI correlated with a more aggressive disease phenotype (48). Additionally, both ALB levels and lymphocyte counts could explain the phenomenon. ALB levels are linked to liver function and have been correlated with survival outcomes across various cancer types, including HCC. The lymphocyte count, an accessible and cost-effective biomarker of inflammation, plays a crucial role in assessing immune function and infection status.

Besides the PNI, patient prognosis may also be influenced by other factors, such as TNM staging (63), BCLC staging (26), age, sex (64), follow-up time (55). The study found that while PNI did not predict OS in HCC cases generally (HR = 1.855, 95% CI: 0.927–3.711; $p = 0.081$), it was an independent prognostic factor for OS in HCC patients who underwent curative hepatectomy at TNM stage I (HR = 2.305, 95% CI: 1.008–5.268; $p = 0.048$) (20). Unfortunately, most of the articles included in this study did not provide staging information, leaving insufficient data for further analysis. Across all 19 studies included, the number of BCLC (0/A) stage patients was greater than that of BCLC (B/C/D) stage patients, and the number of male patients was greater than that of female patients, which makes the conclusions of this paper more applicable to early-stage male liver cancer patients. Notably, most of the patients included had HBV, and antiviral treatment had a considerable impact on the conclusions, as it is known to produce biochemical and virological improvements in chronic HBV patients, including elevated serum ALB levels and increased peripheral T-lymphocyte counts (65). Studies shown that the use of antiviral treatment was associated with higher PNI (66).

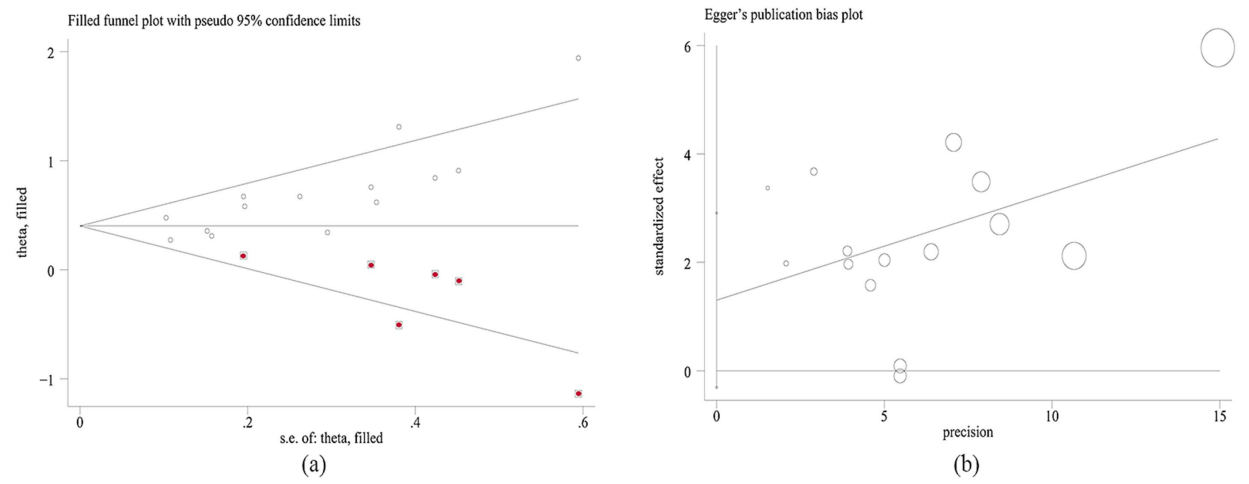

FIGURE 4
Result of Publication bias. **(a)** Funnel diagram of OS after filled six studies. **(b)** Egger' s test of RFS.

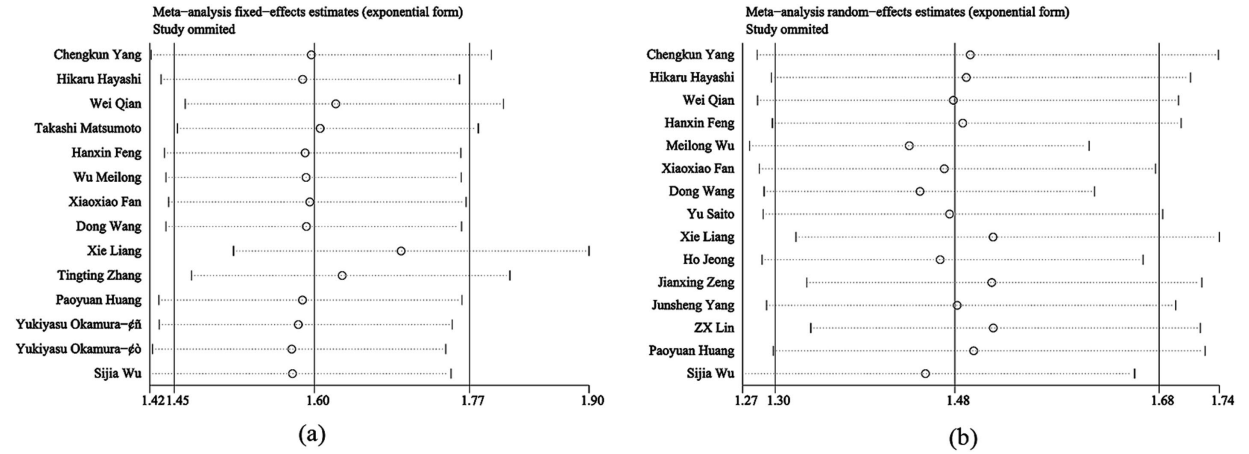

FIGURE 5
Consequence of sensitivity analysis. **(a)** OS. **(b)** RFS.

However, the included studies did not specify whether patients received HBV treatment or provide details of the treatment regimen, limiting the investigation of the relationship between antiviral treatment and PNI.

There were limitations in this meta-analysis. Firstly, we were unable to perform a subgroup analysis for each TNM stage and gender because of the limited number of included studies. Secondly, the cut off value of PNI was not completely consistent between studies, leading to the potential sources of heterogeneity. Finally, all the studies included were retrospective studies, lacking the prospective study. Additionally, all the studies are based in Asia. The lack of research from Europe and America means that the conclusions are only applicable to Asian patients.

5 Conclusion

In summary, this meta-analysis and systematic review endeavor to provide a definitive assessment of the prognostic significance of the preoperative PNI in HCC patients undergoing curative hepatectomy. Moreover, based on the conclusion, we speculated that HCC patients could benefit from preoperative treatment, such as enteral nutrition support and preoperative non-steroid anti-inflammatory drugs, to help HCC patients reach a satisfied PNI value.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

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Validation, Visualization, Writing – review & editing. DL: Writing – review & editing, Validation. JL: Data curation, Formal analysis, Funding acquisition, Investigation, Project administration, Resources, Writing – original draft, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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