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Prognostic and clinicopathological value of the controlling nutritional status (CONUT) score in patients with head and neck cancer: a meta-analysis

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Abstract

Background The efficiency of controlling nutritional status (CONUT) score in detecting the prognosis of head and neck cancer (HNC) patients has been investigated in some works, but no consistent findings are obtained. Therefore, this work focused on evaluating the precise prognostic role of CONUT for HNC patients through meta-analysis.

Methods The effect of CONUT on predicting the prognosis of HNC patients was evaluated through calculating combined hazard ratios (HRs) as well as 95% confidence intervals (CIs). The correlations of CONUT with clinicopathological features of HNC patients were investigated through combined odds ratios (ORs) and 95%CIs. This study used the random-effects model in the case of significant heterogeneity; or else, we selected the fixed-effects model.

Results There were eight articles involving 1,478 patients enrolled for the current meta-analysis. We adopted the fixed-effects model for OS and DFS analysis because of the non-significant heterogeneity. As demonstrated by our combined findings, high CONUT score could significantly predict the poor overall survival (OS) (HR = 1.94, 95%CI = 1.55–2.44, $p < 0.001$) and disease-free survival (DFS) (HR = 1.93, 95%CI = 1.45–2.56, $p < 0.001$) of HNC. In addition, higher CONUT score was significantly connected to T3-T4 stage (OR = 3.21, 95%CI = 1.94–5.31, $p < 0.001$) and N1-N3 stage (OR = 3.10, 95%CI = 1.74–5.53, $p < 0.001$).

Conclusion According to findings in the present meta-analysis, high CONUT score significantly predicted the prognosis of OS and DFS for HNC patients. Higher CONUT score was also correlated to larger tumor size and LN metastasis in HNC. Due to it is a cost-effective and easily available parameter, CONUT could serve as promising prognostic biomarker for HNC.

Keywords Controlling nutritional status score, Head and neck cancer, Meta-analysis, Evidence-based medicine, Nutrition

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Introduction

In the world, head and neck cancer (HNC) ranks the 7th place among cancers in terms of its morbidity, often affecting the mucosa of the oral cavity, pharynx, or larynx [1]. As reported by the Global Burden of Disease (GBD) study, there were 890 000 newly diagnosed HNC cases worldwide in 2017, which represented 5.3% of all cancers [2]. Infection with human papillomavirus (HPV), smoking and alcohol consumption are primary risk factors for HNC, and 95% of HNC patients develop head and neck squamous cell carcinoma (HNSCC) histopathologically [3]. Despite the advances obtained in surgery, chemotherapy, immunotherapy, and radiotherapy have been attained lately, HNC patients still have a low 5-year survival rate of 40–50%, as well as the distant and local metastasis risks of 30% and 60% separately [4]. Prognostic clinical factors and biomarkers play pivotal roles in improving clinical management of HNC cases [5]. Consequently, identifying novel and reliable biomarkers for the prognosis of patients with HNC is of urgent necessity.

In recent years, many studies have shown that nutritional status, systemic inflammation, and immune-compromised status influence tumor progression and development [6]. Many inflammation-nutritional parameters, such as platelet-to-lymphocyte ratio [7], lymphocyte-to-monocyte ratio [8], albumin-to-globulin ratio [9], and systemic immune-inflammation index [10] have been reported as significant prognostic factors for solid tumors. Controlling nutritional status (CONUT) score, including serum albumin (ALB), total lymphocyte count (TLC), and total cholesterol concentration, is previously reported as a novel biomarker for evaluating nutritional status [11]. The CONUT scores are 0–12 and high scores represent adverse nutritional conditions (Table 1). Previous studies have shown that low pretreatment ALB levels (< 3.5 g/dL) were associated with poor survival in patients with HNC [12–14]. Recent studies reported conflicting results on the prognostic value of TLC in patients with HNC [15–17]. The specific prognostic role of cholesterol in patients with HNC has not been reported according to current literature. CONUT is previously reported to be significant for predicting prognosis of different cancer types including colorectal cancer [18], diffuse large B-cell lymphoma [19], gastrointestinal stromal tumor [20], cholangiocarcinoma [21], and gastric cancer [22]. Its significance in predicting prognosis of HNC patients is widely analyzed, but no consistent findings are obtained [23–30]. For instance, high CONUT score is reported to significantly predict the HNC prognosis [26–28]. However, some studies report that CONUT is not significantly related to prognosis of HNC [23, 25, 29]. Therefore, we comprehensively retrieved the literature in this meta-analysis for identifying CONUT score's precise prognostic role in HNC. Moreover, correlations between CONUT score with clinicopathological characteristics in HNC were also explored.

Table 1 The scoring system for the CONUT

Variables	Degree			
	Normal	Light	Moderate	Severe
Albumin level (g/dl)	≥ 3.50	3.00-3.49	2.50–2.99	< 2.50
Score	0	2	4	6
Total lymphocyte count(/ml)	≥ 1600	1200–1599	800–1199	< 800
Score	0	1	2	3
Total cholesterol(mg/dL)	≥ 180	140–179	100–139	< 100
Score	0	1	2	3
CON UT score (total)	0–1	2–4	5–8	9–12

CONUT: controlling nutritional status

Materials and methods

Study guideline

The current meta-analysis was conducted according to the guideline of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Supplemental file 1) [31]. This meta-analysis was registered in INPLASY with the registration number INPLASY202480055. The link of the protocol is https://inplasy.com/inplasy-2024-8-0055/.

Ethics statement

Ethical approval was not needed in the current meta-analysis since it does not involve human or animal testing, nor does it include case reports.

Literature search

We systemically searched PubMed, Web of Sciences, Embase, and Cochrane library databases between inception and December 19, 2023 using search terms below, (controlling nutritional status OR CONUT) AND (nasopharyngeal OR oropharyngeal OR oral cavity OR laryngeal OR glottic OR pharynx OR mouth OR paranasal OR hypopharynx OR hypopharyngeal OR head OR neck OR sinonasal) AND (cancer OR carcinoma OR tumor OR neoplasm). The detailed search strategies for each database were provided in Supplemental file 2. Moreover, the study language was restricted to English. To identify eligible studies, the reference lists of enrolled articles were examined.

Eligibility criteria

Studies below were included: (1) studies enrolling patients with the pathology of primary HNC; (2) studies measuring pretreatment CONUT based on blood test; (3) studies reported relations of CONUT with survival of HNC; (4) studies with available or calculable hazard ratios (HRs) as well as 95% confidence

intervals (CIs); (5) the cut-off value was identified for determining low/high CONUT score; and (6) English publications. The following studies were excluded: (1) reviews, case reports, conference abstracts, letters, and comments; (2) patients suffered from other cancers besides NHC; (3) articles did not offer survival data; (4) studies included overlapped patients; and (5) animal studies.

Data collection and quality assessment

Data were collected in enrolled articles by two researchers (Y.W. and C.Q.) independently. Any disagreement between the two investigators was settled through mutual negotiation until consensus. Data below were collected in the enrolled articles: name of the first author, publication year, country, sample size, gender, age, study design, study period, cancer subtype, TNM stage, treatment, cut-off value of CONUT, survival outcomes, follow-up, survival analysis type, as well as HRs and 95%CIs. Our primary and secondary survival endpoints were overall survival (OS) and disease-free survival (DFS) separately. Study methodological quality was evaluated with the Newcastle–Ottawa Scale (NOS) [32] that covers 3 parts: selection, comparability, and outcome assessment, with the scores of 0–9. Articles of NOS scores ≥ 6 were thought to be of high quality.

Statistical analysis

We determined combined HRs and 95%CIs for evaluating the effect of CONUT on predicting the prognosis of patients undergoing HNC. Cochran's Q and Higgin's I^2 tests were employed to assess the heterogeneity, with I^2 greater than 50% indicating significant heterogeneity. This study used the random-effects model in the case of significant heterogeneity ($I^2 > 50\%$); or else, we selected the fixed-effects model. Subgroup analyses were also performed for exploring the heterogeneity source. Correlations of CONUT with clinicopathological characteristics of HNC patients were investigated by pooling odds ratios (ORs) as well as 95%CIs. The effect of each study data on the results was assessed via sensitivity analysis. Begg's and Egger's tests were carried out for assessing publication bias. Stata version 12.0 (Stata Corporation, College Station, TX, USA) was adopted for performing statistical analysis. When $p < 0.05$, the difference was of statistical significance.

Results

Process of literature search

From Fig. 1, there were 59 articles obtained initially, among which, 42 were retained after duplicates were removed. By title- and abstract-reviewing, 22 articles were removed due to irrelevance or animal studies, while the rest 20 articles were examined by reading their full-texts. Subsequently, 12 articles were eliminated because of not reporting CONUT ($n = 6$), no survival data ($n = 3$), review ($n = 1$), not focused on HNC ($n = 1$), and overlapped patients recruited ($n = 1$). Ultimately, altogether eight articles with 1,478 patients were enrolled for this meta-analysis [23–30] (Fig. 1; Table 2).

Enrolled article features

Table 2 shows basic characteristics of enrolled articles. The publication year was 2021–2023 [23–30]. One study was a prospective trial [23] and seven studies were of retrospective design [24–30]. Five studies were conducted in China [24, 26–28, 30] and three studies were carried in Japan [23, 25, 29]. The sample size was 78–427 (median, 112.5). Two studies recruited patients with HNC [23, 28], two studies enrolled patients with hypopharyngeal cancer (HPC) [26, 27], two studies included patients with laryngeal cancer (LC) [24, 30], and one each study involved patients with HNSCC [29] and oral squamous cell carcinoma (OSCC) [25], respectively. Six studies enrolled HNC patients with stage I-IV [23–26, 28, 30], one each included patients with stage III-IV [27] and recurrent/ metastatic (R/M) status [29]. Four studies used the cut-off value of ≥ 4 [23, 25, 26, 30], two studies applied ≥ 3 [27, 29], and two studies selected ≥ 2 [24, 28]. All eight studies mentioned the significance of CONUT score in the prediction of OS [23–30], while four provided the data on the correlation between CONUT and DFS in HNC [24, 27, 29, 30]. The HRs and 95%CIs in 5 articles were derived based on multivariate regression [24–27, 29] and those in 3 articles were obtained by univariate regression [23, 28, 30]. Among those enrolled articles, their NOS scores were 7–9 (median, 8), indicating their high quality (Table 2). The detailed NOS scores of each study were shown in Supplemental file 3.

CONUT and OS in HNC

All the eight studies with 1,478 patients [23–30] presented the association of CONUT with OS for HNC. We adopted the fixed-effects model because of the insignificant heterogeneity ($I^2 = 26.1\%$, $p = 0.221$). From combined findings of Fig. 2; Table 3, high CONUT score significantly predicted the poor OS in HNC (HR = 1.94, 95%CI = 1.55–2.44, $p < 0.001$). As revealed by subgroup analysis, CONUT's prognosis prediction value remained unaffected by sample size and survival analysis type ($p < 0.05$; Table 3). In addition, elevated CONUT score still significantly predicted the worse OS of subgroups below: studies in China ($p < 0.001$), retrospective design ($p < 0.001$), in HPC ($p < 0.001$), in LC ($p < 0.001$), TNM stage of I-IV ($p < 0.001$), treatment

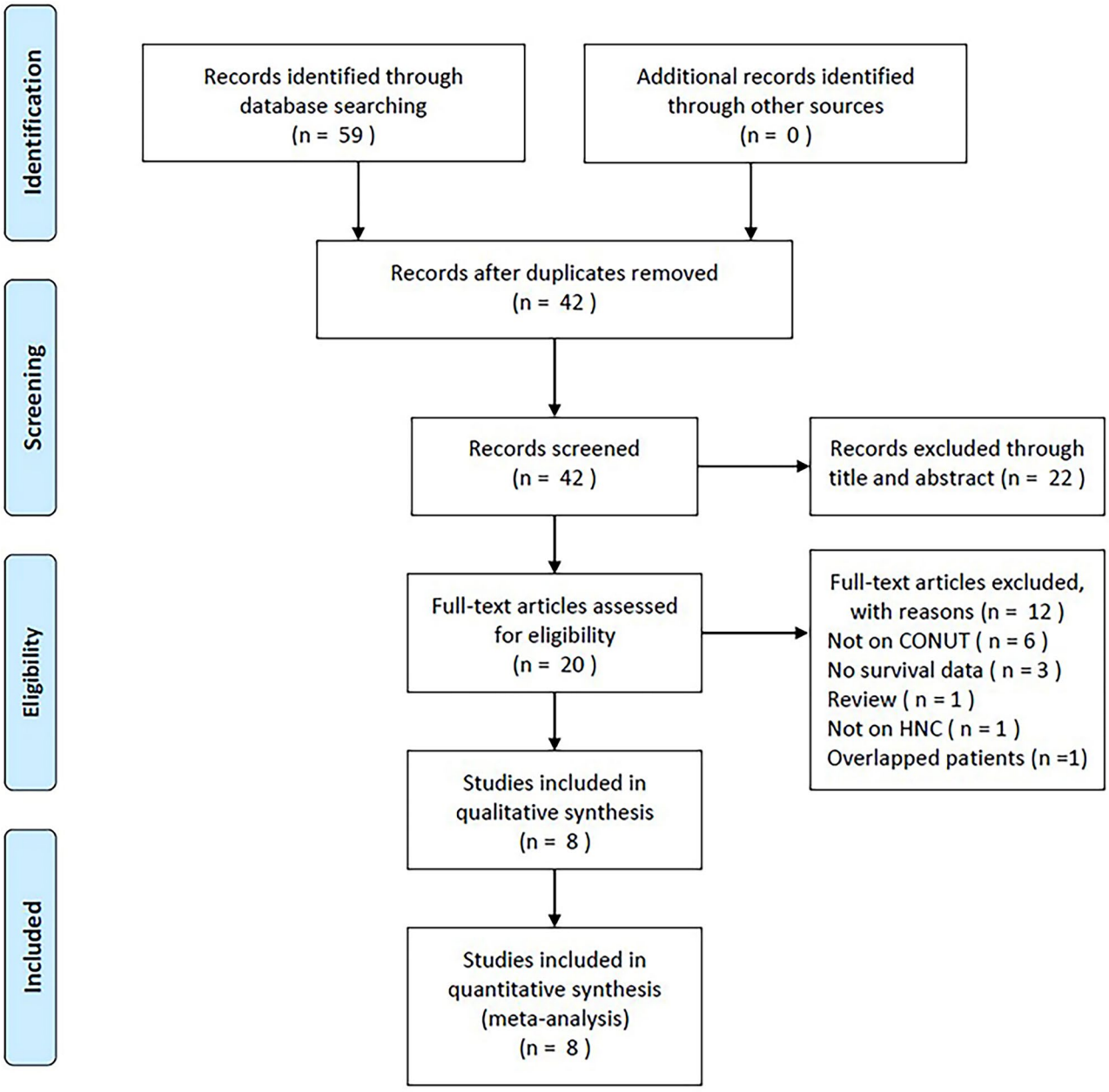

Fig. 1 The PRISMA flow chart of literature search strategies

of surgery ($p<0.001$) or radiotherapy ($p=0.012$), and CONUT cut-off value ≥4 ($p<0.001$) or ≥2 ($p=0.002$) (Table 3).

CONUT and DFS in HNC

Four studies involving 796 patients [24, 27, 29, 30] reported CONUT's role in predicting DFS in HNC. Pooled findings HR=1.93, 95%CI=1.45–2.56, and $p<0.001$ were obtained, indicating the significant correlation between increased CONUT score and poor DFS of HNC patients (Fig. 3; Table 4). According to subgroup analysis, increased CONUT score still could significantly predict the prognosis of the following subgroups: studies in China ($p<0.001$), sample size ≥150 ($p<0.001$), in HPC ($p=0.007$), in LC ($p<0.001$), TNM stage I-IV ($p<0.001$), treatment of surgery ($p<0.001$) or combined treatment ($p=0.007$), CONUT cut-off value ≥4 ($p<0.001$) or ≥2 ($p=0.011$), and univariate survival analysis ($p=0.001$) (Table 4).

CONUT and clinicopathological features in HNC

Four studies comprising 759 patients [24, 26–28] analyzed the correlation of CONUT with clinicopathological features of HNC. According to our pooled results,

Table 2 Baseline characteristics of included studies in this meta-analysis

Study	Year	Country	Sample size	Gender (M/F)	Age (years) Median(range)	Study design	Study duration	Cancer type	TNM stage	Treatment	Cut-off value	Survival endpoints	Follow-up (months) Median(range)	Survival analysis	NOS score
Ishii, R.	2021	Japan	78	54/24	79(70–97)	Prospective	Jan-Dec 2017	HNC	I-IV	Mixed	≥ 4	OS	1–40	Univariate	9
Lin, Q.	2022	China	154	147/7	60	Retrospective	2013–2016	LC	I-IV	Surgery	≥ 2	OS, DFS	1-100	Multivariate	7
Yoshimura, T.	2022	Japan	112	69/43	68(59–77)	Retrospective	2009–2015	OSCC	I-IV	Surgery	≥ 4	OS	44.5(28.3–60.8)	Multivariate	8
Ding, T.	2023	China	94	88/6	60.5(41–83)	Retrospective	2012–2020	HPC	I-IV	Surgery	≥ 4	OS	1-100	Multivariate	7
Lin, Q.	2023	China	113	107/6	61	Retrospective	2013–2017	HPC	III-IV	Mixed	≥ 3	OS, DFS	1-110	Multivariate	8
Pan, D.	2023	China	398	291/107	50.9	Retrospective	2005–2020	HNC	I-IV	Radiotherapy	≥ 2	OS	27.6	Univariate	7
Sakai, A.	2023	Japan	102	93/9	70(47–87)	Retrospective	2017–2022	HNSCC	Recurrent/ metastatic	ICIs	≥ 3	OS, DFS	13.5	Multivariate	8
Yi, H.	2023	China	427	407/20	60	Retrospective	2007–2017	LC	I-IV	Surgery	≥ 4	OS, DFS	77(1-160)	Univariate	8

M: male; F: female; TNM: tumor (T), node (N), metastasis (M); HNC: head and neck cancer; LC: laryngeal cancer; OSCC: oral squamous cell carcinoma; HPC: hypopharyngeal cancer; HNSCC: head and neck squamous cell carcinoma; ICIs: immune checkpoint inhibitors; OS: overall survival; DFS: disease-free survival; NOS: Newcastle-Ottawa Scale

higher CONUT score was notably connected to T3-T4 stage (OR = 3.21, 95%CI = 1.94–5.31, $p < 0.001$) and N1-N3 stage (OR = 3.10, 95%CI = 1.74–5.53, $p < 0.001$) (Fig. 4; Table 5). But CONUT was not significantly correlated with gender (OR = 0.72, 95%CI = 0.45–1.15, $p = 0.174$) and TNM stage (OR = 1.83, 95%CI = 0.51–6.51, $p = 0.351$) in HNC (Fig. 4; Table 5).

Sensitivity analysis

Pooled results remained stable upon sensitivity analysis in which one study regarding OS and DFS was eliminated each time (Fig. 5).

Publication bias

We adopted Begg's and Egger's linear regression tests for determining any possible publication bias. As a result, significant publication bias was not detected in OS ($p = 1.000$ and 0.699 upon Begg's and Egger's tests) and DFS ($p = 0.734$ and 0.482 upon Begg's and Egger's tests) (Fig. 6).

Discussion

The effect of CONUT on predicting HNC prognosis has been previously investigated, but no consistent findings are reported [23–30]. In the present meta-analysis, results of 8 articles involving 1,478 patients were synthesized. Our results indicated that elevated CONUT score significantly predicted the poor OS and DFS of HNC. Moreover, higher CONUT score was remarkably related to advanced T stage and presence of lymph node (LN) metastasis. These findings were verified to be robust through sensitivity and publication bias analyses. Collectively, our results indicated CONUT score as the promising and reliable marker used to predict the short- and long-time survivals of HNC patients. Higher CONUT score was correlated to larger tumor size and LN metastasis in HNC. As we know, the present meta-analysis is the first to study the value of CONUT in the prediction of HNC prognosis.

The CONUT scoring system covers 3 parts - ALB, cholesterol, and TLC (Table 1). A high CONUT score can be caused by low levels ALB, cholesterol, and TLC. Although the precise mechanisms underlying the prognostic value of CONUT have not been completely clarified, they are interpreted as follows. First, the level of ALB in total serum protein reflects the body's nutritional status or illustrates systemic inflammation [33]. Low ALB levels are associated with increased inflammatory responses to tumors, poor nutritional status, and higher levels of cytokines [34]. Furthermore, there is evidence that a low ALB level is associated with an enhanced inflammatory response and an increase in cytokine release, which are all potentially indicating more aggressive tumor behavior [35]. Second, as a

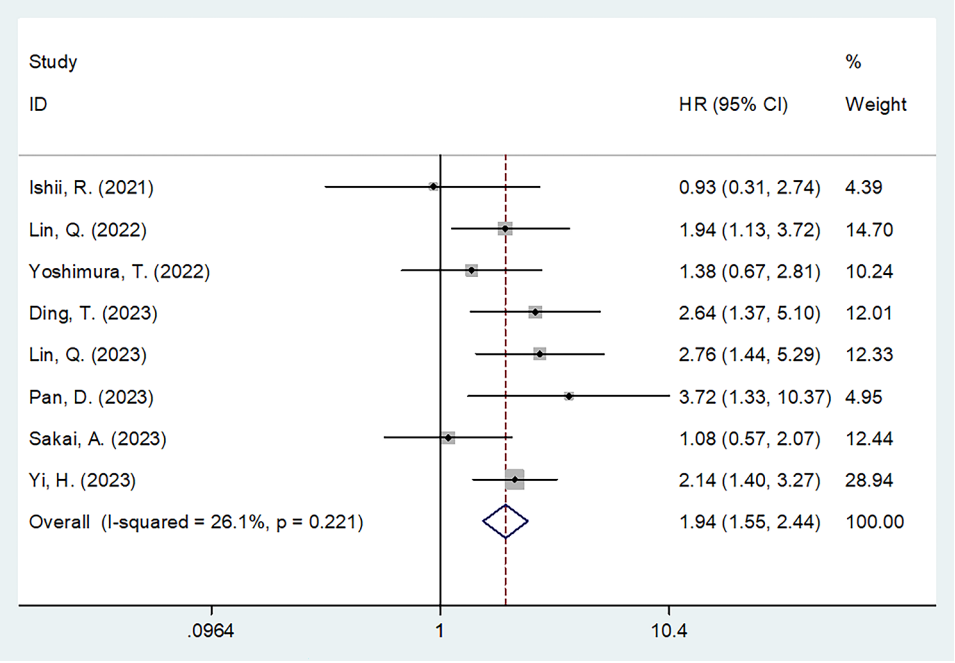

Fig. 2 Forest plot of correlation between CONUT score and overall survival in patients with HNC

fundamental component of cellular membranes, cholesterol also plays a critical role in the transmission of intracellular signals that maintain healthy cellular functions. The low cholesterol levels indicate inadequate energy storage and metabolic imbalance, which affects membrane structure and function, including membrane fluidity and protein activity [36, 37]. Hypocholesterolemia is significantly related to poor prognostic outcome among various cancers [38, 39]. Third, lymphocyte-dependent cellular immune response exerts an important effect on immunological destruction of tumor cells [40]. Tumor-infiltrating lymphocytes (TILs), the critical components of anticancer effect, are capable of inhibiting cancer cell growth and inducing cytotoxic cell death [41]. Perioperative lymphopenia is related to the poor cancer survival [42]. Therefore, CONUT is the reasonable marker used to predict HNC prognosis.

We adopted Begg's test and Egger's test to evaluate potential publication bias in this meta-analysis. The results indicated that there was no significant publication bias in this study (Fig. 6), which suggested the robustness of the results. We performed subgroup analysis to investigate the prognostic value of CONUT in various populations of HNC patients (Tables 3 and 4). The subgroup variants were divided by clinicopathological features. The comparisons among various subgroups were independently conducted. We therefore did not performed adjustment due to the independence from each other.

Notably, HNC patients have a variety of factors that affect their prognosis, including the mode of treatment, the clinical stage, age, and basic disease. These factors are covariates which may influence the prognosis. We controlled the effects of covariates in two aspects. First, we extracted the HRs and 95%CIs by multivariate analysis from included studies, if they were provided. As multivariate analysis has considered the effects of covariates on the prognosis. The multivariate HRs and 95%CIs have spared out effects of these covariates. Second, we conducted the subgroup analysis to control the effects of covariates as shown in Tables 3 and 4. The effects of covariates in the prognostic value of CONUT in OS and DFS were analyzed in each subgroup. Moreover, during the development and treatment process, the items enrolled in the CONUT vary, so they only reflect the level during a given time period. We collected the pretreatment CONUT in this meta-analysis because it reflected the baseline inflammatory and nutritional status of HNC patients. The pretreatment CONUT was not influenced by various treatment strategies implementing for each individual patient.

Recently, CONUT has been widely suggested with prognostic significance in different cancer types by meta-analysis [43–46]. As revealed by Yin et al. in their meta-analysis involving 17 articles, elevated CONUT score was related to inferior OS and cancer-specific survival (CSS) of gastric cancer [43]. Peng and colleagues reported in their meta-analysis with 9 articles that the elevated CONUT score was correlated

Table 3 Subgroup analysis of the prognostic value of CONUT for OS in patients with HNC

Subgroups	No. of studies	No. of patients	Effects model	HR (95%CI)	*p*	Heterogeneity	
						I^2(%)	Ph
Total	8	1,478	Fixed	1.94(1.55–2.44)	< 0.001	26.1	0.221
Country							
China	5	1,186	Fixed	2.35(1.80–3.08)	< 0.001	0	0.790
Japan	3	292	Fixed	1.16(0.75–1.79)	0.516	0	0.810
Sample size							
< 150	5	499	Fixed	1.73(1.26–2.38)	0.001	44.5	0.125
≥ 150	3	979	Fixed	2.20(1.58–3.05)	< 0.001	0	0.551
Study design							
Prospective	1	78	-	0.93(0.31–2.76)	0.896	-	-
Retrospective	7	1,400	Fixed	2.01(1.59–2.54)	< 0.001	21.4	0.266
Cancer type							
HNC/HNSCC	3	578	Random	1.50(0.68–3.32)	0.320	56.7	0.099
HPC	2	207	Fixed	2.70(1.70–4.29)	< 0.001	0	0.924
LC	2	581	Fixed	2.07(1.47–2.93)	< 0.001	0	0.791
OSCC	1	112	-	1.38(0.67–2.81)	0.381	-	-
TNM stage							
I-IV	6	1,263	Fixed	2.02(1.55–2.63)	< 0.001	2.7	0.399
Recurrent/ Metastatic/ III-IV	2	215	Random	1.73(0.69–4.32)	0.242	74.9	0.046
Treatment							
Surgery	4	787	Fixed	2.03(1.53–2.69)	< 0.001	0	0.608
Mixed	2	191	Random	1.76(0.61–5.02)	0.294	64.6	0.093
Radiotherapy	1	398	-	3.72(1.33–10.39)	0.012	-	-
ICIs	1	102	-	1.08(0.57–2.07)	0.809	-	-
Cut-off value							
≥ 4	4	711	Fixed	1.93(1.42–2.63)	< 0.001	18.6	0.298
≥ 3	2	215	Random	1.73(0.69–4.32)	0.242	73.9	0.046
≥ 2	2	552	Fixed	2.29(1.37–3.83)	0.002	13.4	0.282
Survival analysis							
Univariate	3	903	Fixed	2.09(1.45–3.02)	< 0.001	40.2	0.188
Multivariate	5	575	Fixed	1.86(1.39–2.48)	< 0.001	32.0	0.208

TNM: tumor (T), node (N), metastasis (M); HNC: head and neck cancer; LC: laryngeal cancer; OSCC: oral squamous cell carcinoma; HPC: hypopharyngeal cancer; HNSCC: head and neck squamous cell carcinoma; ICIs: immune checkpoint inhibitors; OS: overall survival

with markedly shortened OS of breast cancer patients [44]. Another recent meta-analysis indicated that the increased CONUT score was evidently related to shortened OS and progression-free survival (PFS) of gynecological cancer [45]. As discovered by Zhang et al. in their meta-analysis with eight articles, cancer patients receiving immune checkpoint inhibitors (ICIs) with high CONUT score had poorer OS and PFS [47]. A recent meta-analysis involving 3,783 participants also suggested that the elevated CONUT score shows a significant relationship to worse OS, PFS, and CSS in esophageal cancer [48]. Our results in this meta-analysis on HNC were in line with results of CONUT's prognostic value in other cancer types.

Notably, all included studies in this meta-analysis were from Asian region, which may limit the applicability of our results in non-Asian HNC patients. Moreover, the methodological diversity of included studies also exists. Because the CONUT cut-off values, sample size, study period and some other study characteristics were not uniform in eligible studies, the methodological diversity could be a source of heterogeneity in this meta-analysis. Therefore, considering these factors, the generalizability of our results should be verified in future studies. In consideration of its disadvantages, CONUT could be integrated with other prognostic factors to build a prognostic penal for patients with HNC.

There are some limitations in this work. Firstly, many enrolled articles were retrospective studies. Therefore, selection bias may exist due to the inherent nature of retrospective studies. Secondly, our enrolled articles were conducted in Asia. Actually, we did not restrict the geographical regions of eligible studies and

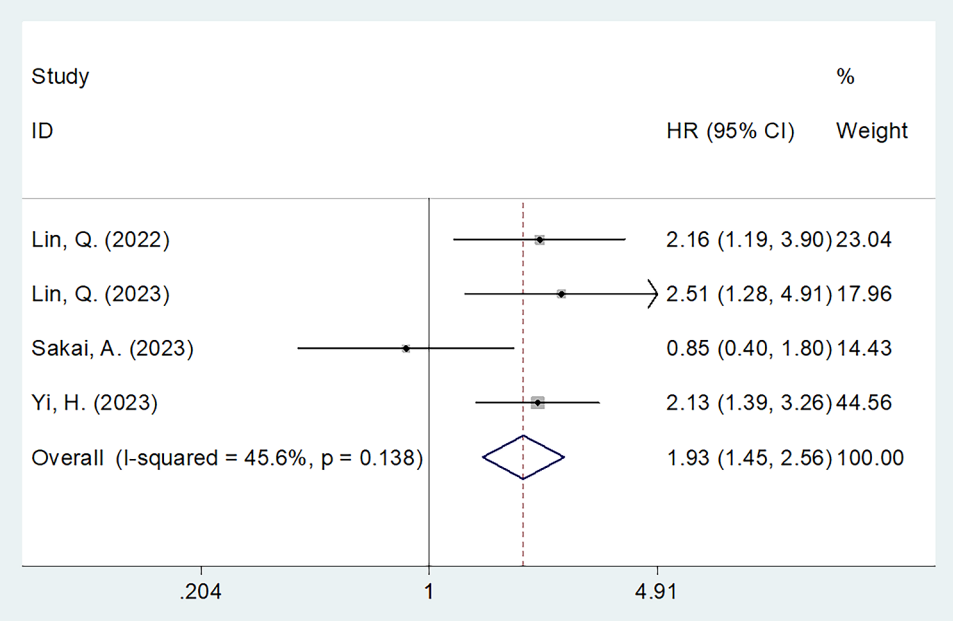

Fig. 3 Forest plot of correlation between CONUT score and disease-free survival in patients with HNC

Table 4 Subgroup analysis of the prognostic value of CONUT for DFS in patients with HNC

Subgroups	No. of studies	No. of patients	Effects model	HR (95%CI)	*p*	Heterogeneity I^2(%) Ph	
Total	4	796	Fixed	1.93(1.45–2.56)	< 0.001	45.6	0.138
Country							
China	3	694	Fixed	2.21(1.63–3.01)	< 0.001	0	0.917
Japan	1	102	-	0.85(0.40–1.80)	0.672	-	-
Sample size							
< 150	2	215	Random	1.48(0.51–4.27)	0.468	77.5	0.035
≥ 150	2	581	Fixed	2.14(1.51–3.02)	< 0.001	0	0.967
Cancer type							
HNC/HNSCC	1	102	-	0.85(0.40–1.80)	0.672	-	-
HPC	1	113	-	2.51(1.28–4.92)	0.007	-	-
LC	2	581	Fixed	2.14(1.51–3.02)	< 0.001	0	0.967
TNM stage							
I-IV	2	581	Fixed	2.14(1.51–3.02)	< 0.001	0	0.967
Recurrent/ Metastatic/ III-IV	2	215	Random	1.48(0.51–4.27)	0.468	77.5	0.035
Treatment							
Surgery	2	581	Fixed	2.14(1.51–3.02)	< 0.001	0	0.967
Mixed	1	113	-	2.51(1.28–4.92)	0.007	-	-
ICIs	1	102	-	0.85(0.40–1.80)	0.672	-	-
Cut-off value							
≥ 4	1	427	-	2.13(1.39–3.26)	0.001	-	-
≥ 3	2	215	Random	1.48(0.51–4.27)	0.468	77.5	0.035
≥ 2	1	154	-	2.16(1.19–3.91)	0.011	-	-
Survival analysis							
Univariate	1	427	-	2.13(1.39–3.26)	0.001	-	-
Multivariate	3	369	Random	1.71(0.92–3.18)	0.089	61.1	0.077

TNM: tumor (T), node (N), metastasis (M); HNC: head and neck cancer; LC: laryngeal cancer; HPC: hypopharyngeal cancer; HNSCC: head and neck squamous cell carcinoma; ICIs: immune checkpoint inhibitors; DFS: disease-free survival

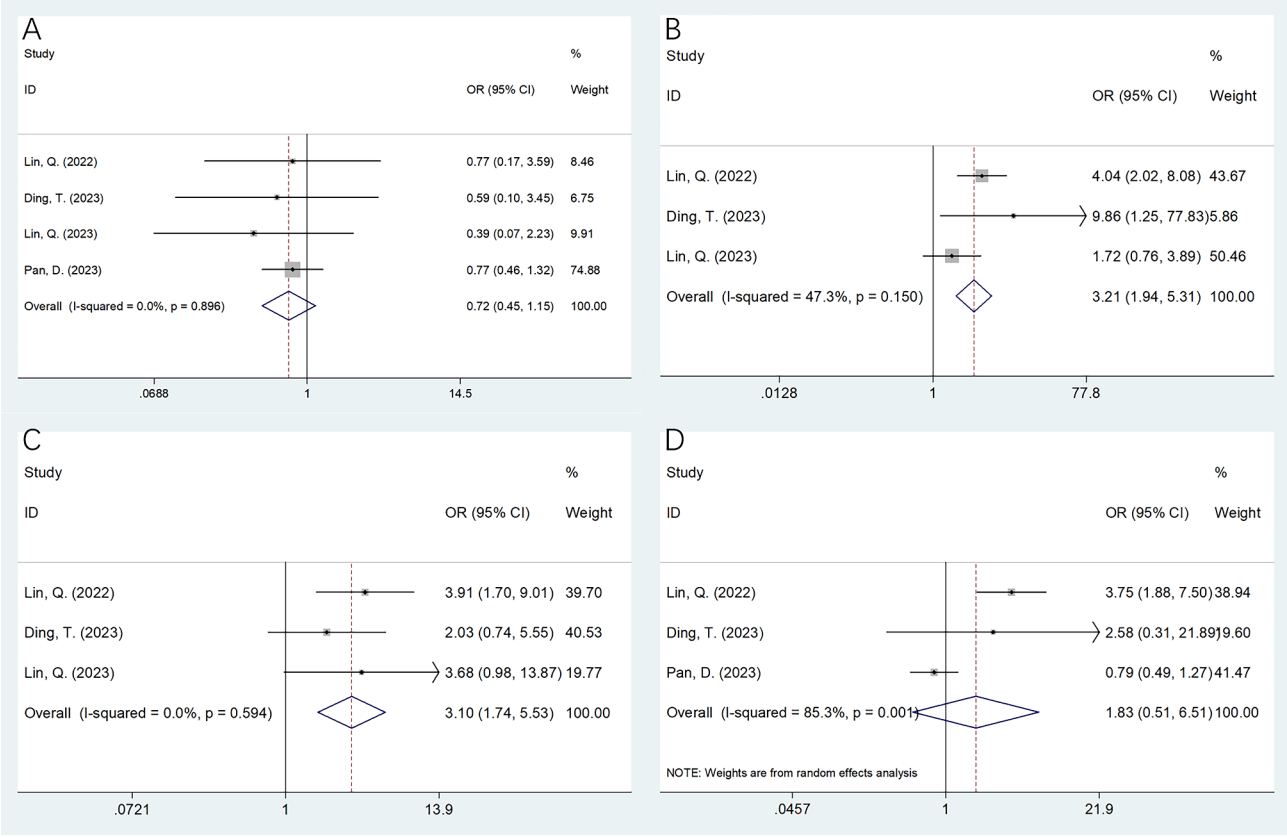

Fig. 4 The associations between CONUT score and clinicopathological characteristics in patients with HNC. (**A**) gender (male vs. female); (**B**) T stage (T3-T4 vs. T1-T2); (**C**) N stage (N1-N3 vs. N0); and (**D**) TNM stage (III-IV vs. I-II)

Table 5 The association between CONUT and clinicopathological features in patients with HNC

Variables	No. of studies	No. of patients	Effects model	OR (95%CI)	*p*	Heterogeneity	
						I^2(%)	Ph
Gender (male vs. female)	4	759	Fixed	0.72(0.45–1.15)	0.174	0	0.896
T stage (T3-T4 vs. T1-T2)	3	361	Fixed	3.21(1.94–5.31)	< 0.001	47.3	0.150
N stage (N1-N3 vs. N0)	3	361	Fixed	3.10(1.74–5.53)	< 0.001	0	0.594
TNM stage (III-IV vs. I-II)	3	646	Random	1.83(0.51–6.51)	0.351	85.3	0.001

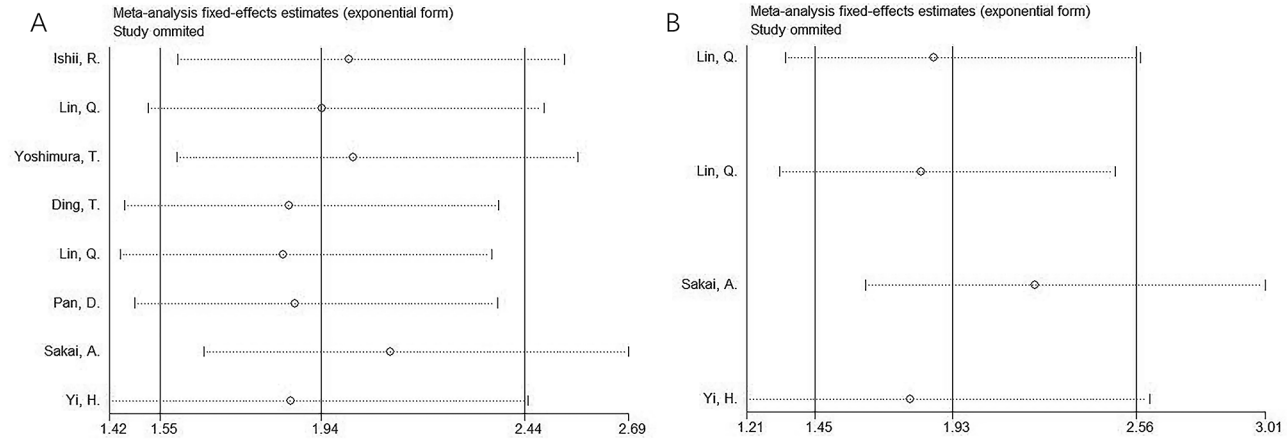

Fig. 5 Sensitivity analysis. (**A**) OS and (**B**) DFS

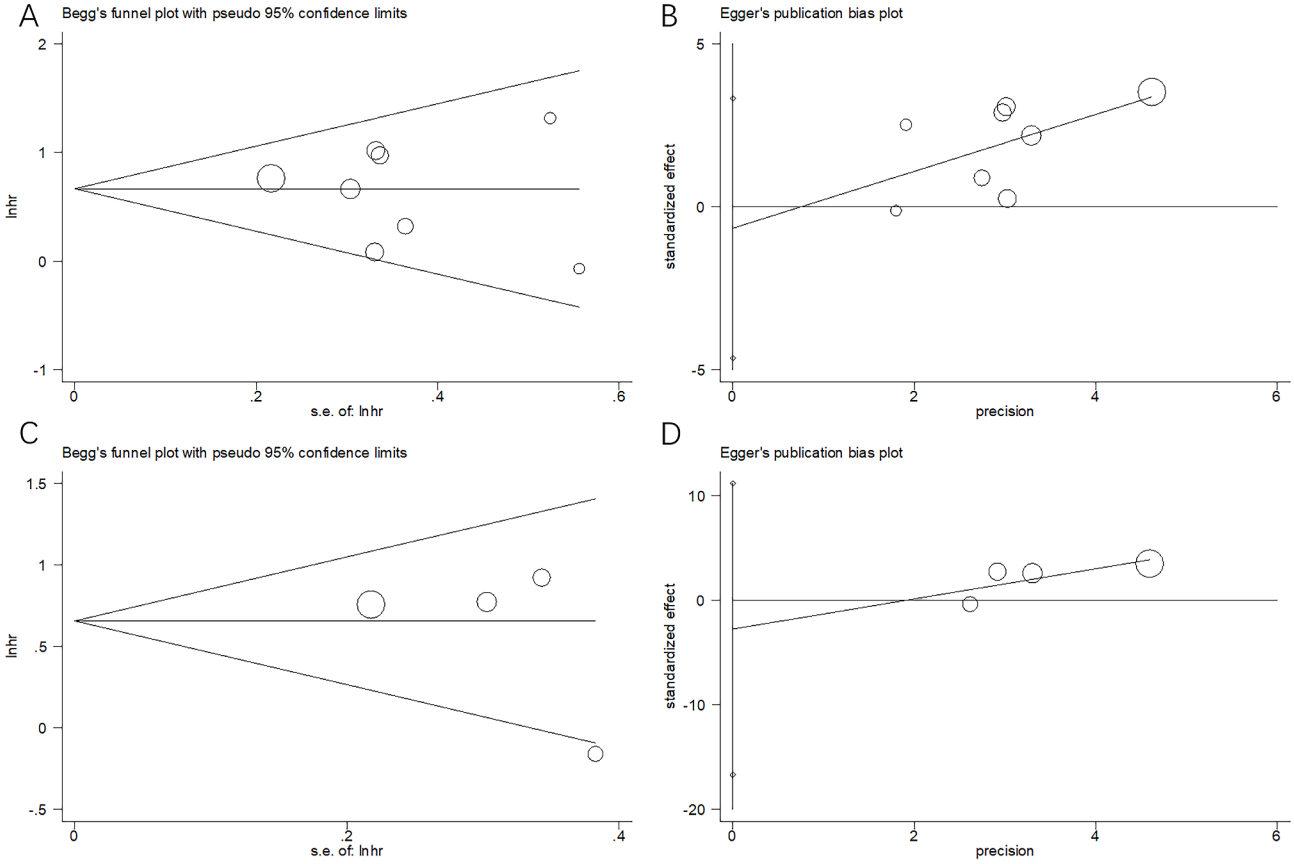

Fig. 6 Publication bias for OS and DFS. (**A**) Begg's test for OS, $p=1.000$; (**B**) Egger's test for OS, $p=0.699$; (**C**) Begg's test for DFS, $p=0.734$; and (**D**) Egger's test for DFS, $p=0.482$

we only included publications in English. However, after selection by the inclusion and exclusion criteria, all eligible studies are in Asia. Consequently, our findings might be applicable for Asian HNC cases. Thirdly, the CONUT threshold was not uniform in our enrolled articles, which was the potential heterogeneity source. Therefore, large-scale multi-center prospective studies should be carried out for validating our findings.

Conclusions

In summary, this meta-analysis demonstrated that high CONUT score significantly predicted OS and DFS of HNC patients. Higher CONUT score was also correlated to larger tumor size and LN metastasis in HNC. Due to it is a cost-effective and easily available parameter, CONUT could serve as promising prognostic biomarker for HNC in clinical practice.

Abbreviations

ALB	Albumin
CI	Confidence interval
CONUT	Controlling nutritional status
CSS	Cancer-specific survival
DFS	Disease-free survival
GBD	Global Burden of Disease
HNC	Head and neck cancer
HNSCC	Head and neck squamous cell carcinoma
HPC	Hypopharyngeal cancer
HPV	Human papillomavirus
HR	Hazard ratio
ICIs	Immune checkpoint inhibitors
LC	Laryngeal cancer
LN	Lymph node
NOS	Newcastle–Ottawa Scale
OR	Odds ratio
OS	Overall survival
OSCC	Oral squamous cell carcinoma
PFS	Progression-free survival
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
R/M	Recurrent/metastatic
TLC	Total lymphocyte count

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12957-024-03505-3.

Supplementary Material 1: The PRISMA checklist

Supplementary Material 2: The detailed search strategies for each database

Supplementary Material 3: The detailed NOS scores for each included study

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Author contributions
YW and CQ conceptualized, designed, and revised the manuscript; YW searched the literature, collected the data, organized the data, and drafted the manuscript; YW and CQ collected the data; YW performed the statistical analyses. All authors contributed to the article and approved the submitted version.

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Data availability
The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
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Competing interests
The authors declare no competing interests.

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