REVIEW

# Prognostic Potential of the Preoperative Controlling Nutritional Status (CONUT) Score in Predicting Survival of Patients with Cancer: A Systematic Review

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## ABSTRACT

The nutritional status of a patient has prognostic potency concerning short- and long-term outcomes, including survival, in many diseases. The controlling nutritional status (CONUT) score is a method for assessing nutritional status and predicting outcomes of several diseases. This study sought to systematically identify the prognostic role of preoperative CONUT score on posttreatment overall survival (OS), recurrence-free survival (RFS), and cancer-specific survival (CSS) in patients with cancer. The PubMed, SCOPUS, and Google Scholar databases and Google were searched for all dates until December 2019. Original articles investigating the association of preoperative CONUT score with survival in cancer patients who underwent surgery were included. Duplicate and irrelevant reports were screened out and the remaining articles assessed for quality and data extracted during critical analysis. Results of multivariate analysis were used to evaluate the prognostic competence of CONUT score in predicting survival. The search method identified an initial 181 articles, of which 32 were included in the final analysis. Lower OS, CSS, and RFS rates were reported by 100%, 100%, and 87.0% of the included studies, respectively, in cancer patients with high CONUT scores. A prognostic role of the CONUT score for prediction of OS, CSS, and RFS in cancer patients was shown by 91.7%, 90.9%, and 52.6% of the studies, respectively. The receiver operating characteristic curve area under the curve (AUC) value of the CONUT score for predicting OS, CSS, and RFS was at an acceptable level (>0.5) in all studies with available AUC values ($n = 19$). Sixty percent (12 of 20) of the studies reported that high CONUT score was significantly related to lower BMI. The findings promote confidence that a high preoperative CONUT score is associated with poor survival rate and is an independent prognostic factor of OS and CSS in patients with various types of cancer. Evaluation of the preoperative CONUT score might help clinicians in decision-making with respect to surgical implications. *Adv Nutr* 2021;12:234–250.

Keywords: biomarker, cancer, cancer-specific survival, controlling nutritional status, overall survival, recurrence-free survival, prognosis

## Introduction

A biomarker is a biological feature that is measured to indicate the body's biological situation or condition, objectively, in relation to, e.g., normal or pathogenic processes, or pharmacologic reactions to a therapeutic approach (1). In clinical practice, biomarkers are often used for early diagnosis or monitoring of a disease; predicting the risk or outcome of a disease; measuring the effectiveness or harmfulness of a treatment regimen or other aspects of health; or screening of patients (2).

Prognostic biomarkers are baseline evaluations of disease features or patients' characteristics that can predict the risk or outcome of the disease in patients regardless of therapy (3). In cancers, a prognostic biomarker could be an attribute of the disease (such as size of the tumor or stage or grade of the cancer) or an individual characteristic of the patient (such as age, sex, or weight loss) that may influence the outcome. Prognostic biomarkers are beneficial in predicting the outcomes, developing a treatment plan, and decision-making regarding surgical or chemotherapy implications (4).

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Supplemental Table 1 is available from the "Supplementary data" link in the online posting of the article and from the same link in the online table of contents at https://academic.oup.com/advances.

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Abbreviations used: CA19-9, carbohydrate antigen 19-9; CEA, carcinoembryonic antigen; CONUT, controlling nutritional status; CSS, cancer-specific survival; DFS, disease-free survival; GPS, Glasgow Prognostic Score; NLR, neutrophil-to-lymphocyte ratio; OS, overall survival; PFS, progression-free survival; PLR, platelet-to-lymphocyte ratio; PNI, Prognostic Nutritional Index; RFS, recurrence/relapse-free survival; ROC, receiver operating characteristic.



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Malnutrition is prevalent in cancer patients, which can affect short- and long-term outcomes. Nutritional status has a prognostic capacity for posttreatment long-term outcomes, including disease progression and survival, in patients (5). The controlling nutritional status (CONUT) score is an efficient nutritional screening tool for assessing the nutritional status of patients and is useful for early detection of undernutrition in all hospital inpatients. This tool is computed from the 3 clinical parameters of serum albumin, total cholesterol concentration, and total peripheral lymphocyte counts (6).

Multiple investigations have recently examined the prognostic capacity of the CONUT score on posttreatment complications, clinicopathological factors, and long-term outcomes in several types of diseases such as heart failure, liver disease, hypertension, and cancer (7–10). However, to our knowledge, the prognostic value of the CONUT score with regards to long-term outcomes has not yet been systematically reviewed in patients with cancer. The research question was "Is controlling nutritional status useful as a prognostic biomarker of survival in cancer patients who underwent surgery?" Therefore, this study aimed to systematically identify the prognostic role of preoperative CONUT score on posttreatment long-term outcomes including overall survival (OS), recurrence-free survival (RFS), and cancer-specific survival (CSS) in patients with cancer.

## Methods

### Search strategy and selection criteria

This review was conducted according to the guidelines indicated in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses protocols, 2015 statement. The PubMed, Google Scholar, and SCOPUS databases and Google were searched for all dates until December 2019. Journal articles and observational studies were searched. Original articles and congresses (if information of interest was available) in the English language that investigated the association of preoperative CONUT score with survival in cancer patients who underwent surgery were included. Inclusion criteria were as follows: articles that studied cancer patients who underwent surgery, and availability of postoperative survival information in the article. Research that studied cancer patients who underwent chemotherapy, radiotherapy, or immunotherapy without surgery, or with an unclear treatment method was excluded. Studies with postoperative CONUT score were also excluded. Studies that applied neoadjuvant therapy along with an operation were included in the present study if the effect of adjuvant therapy was considered in the multivariate analysis, otherwise they were excluded. Reviews, conferences, animal studies, editorials, and letters were also excluded. The following search terms were used: "controlling nutritional status" (in title) AND "survival" (in title/abstract) AND "cancer OR tumor OR carcinoma OR malignant" (in title/abstract). Reference lists of the articles were manually reviewed to identify further studies.

### Screening of the articles

The extracted articles were saved in an EndNote file (Clarivate Analytics) and sorted to remove duplicate reports. The remaining titles and abstracts were reviewed to screen articles with the correct scope for the present review. The full texts of the screened articles were then critically analyzed separately for eligibility.

### Quality assessment of the articles

The Newcastle-Ottawa scale for cohort studies was used for assessment of the quality of the included studies (11). Articles were categorized as good quality (if 3 or 4 stars in the selection domain AND 1 or 2 stars in the comparability domain AND 1 or 2 or 3 stars in the outcome/exposure domain were gained), fair quality (if 2 stars in the selection domain AND 1 or 2 stars in the comparability domain AND 2 or 3 stars in the outcome/exposure domain were achieved), or poor quality (if 0 or 1 star in the selection domain OR 0 stars in the comparability domain OR 0 or 1 star in the outcome/exposure domain were attained).

### Data extraction

Full texts of the screened articles were carefully reviewed and data were extracted with regard to authors, year of publication, country, study design, type of cancer, type of treatment, number and age of patients, follow-up time, method and time of CONUT assessment, CONUT cutoffs, method of CONUT cutoff determination, efficacy of the CONUT score (sensitivity and specificity) for prognosis of survival, survival rates and their association with CONUT score, method of survival rate estimation, method of statistical analysis, confounding factors, and adjustments. Results of multivariate analysis were used to evaluate the prognostic effect of CONUT score on survival, in this review.

The time interval from surgery to radiological or histological detection of recurrence or metastasis or progression of disease was defined as RFS, disease-free-survival (DFS), or progression-free survival (PFS), which were all placed in 1 group (12, 13). The time interval from surgery to cancer-related death was defined as CSS (12, 14) and the time interval from surgery to overall death or last follow-up was defined as OS (12, 15). Studies that did not specify type of survival were considered as OS in this review.

## Results

As **Figure 1** shows, initially 181 titles and abstracts were found using the search method (173 by databases, 5 by Google, and 3 by reference list searching). After elimination of duplicate studies, 62 articles remained. During the screening stage, 50 studies were found to be relevant to the study subject. During critical analysis, 18 articles were excluded because of not being written in English ($n = 3$), being conference papers ($n = 2$), being generic studies ($n = 2$), similarity ($n = 1$), low quality ($n = 1$), unclear treatment method ($n = 2$), postoperative CONUT score ($n = 1$), and applying adjuvant therapy without considering it in the multivariate analysis ($n = 6$). Eventually, 32 original studies

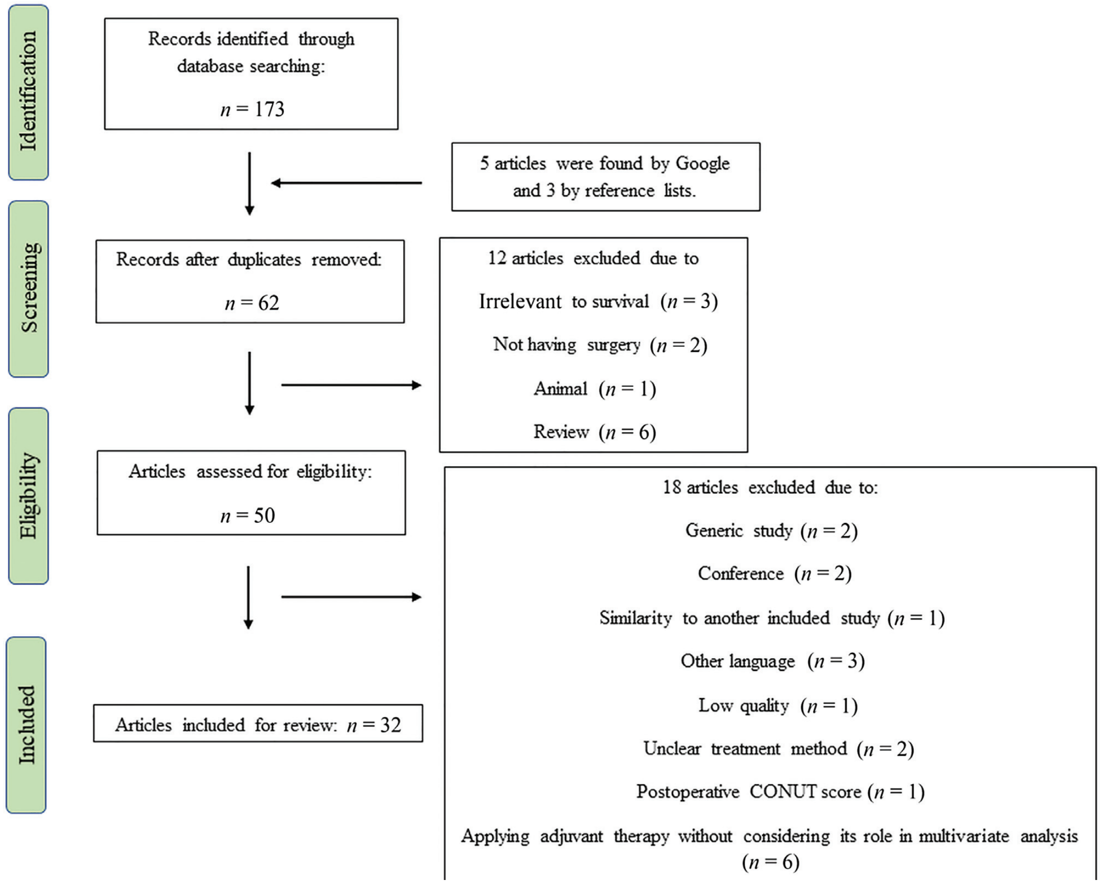


**FIGURE 1** Flow diagram of the study. CONUT, controlling nutritional status.

(10, 12, 16–45) (W Yang, C Shou, J Yu, Q Zhang, X Liu, H Yu, X Lin, unpublished results, 2019) matched the study scope and, thus, were comprised in the final review and analysis (Figure 1).

## Characteristics of the studies

As **Table 1** shows, 62.5% ($n = 20$) of the included studies were performed in Japan, 31.3% ($n = 10$) in China, and 6.3% ($n = 2$) in South Korea. All the studies included were retrospective cohort investigations except the report by Huang et al. (22), a prospective cohort study. Of the articles, 96.9% (31 of 32) were published between 2017 and 2019.

In all included studies the CONUT score was evaluated based on serum albumin concentration, total lymphocyte count, and total cholesterol concentration in each patient. Of the studies, 90.6% (29 of 32) used the Kaplan–Meier method and log-rank test to estimate survival rates and 96.9% (31 of 32) used Cox proportional hazards regression models to calculate HRs and 95% CIs.

The receiver operating characteristic (ROC) curve and the AUC were used to evaluate the efficacy of the CONUT score for predicting survival (65.6%, 21 of 32) and to determine the optimal cutoff for the CONUT score. The highest Youden index was used to attain the optimal cutoff of the CONUT score in 10 studies.

According to the Newcastle-Ottawa scale, all studies achieved good quality scores (**Supplemental Table 1**).

## Relation between CONUT score and patients' survival

Twenty-four articles studied the OS rate in different CONUT groups, for which all the studies (100%) showed that patients with high CONUT scores had significantly shorter OS than those with low CONUT scores ($P < 0.05$). Twenty-four of the studies investigated the prognostic effect of high CONUT score with regards to OS. Based on the multivariate analysis, 91.7% (22 of 24) of the studies demonstrated that CONUT score was an independent prognostic factor of OS ($P < 0.05$).

Eleven studies investigated CSS, cancer-specific mortality (CSM), or disease-specific survival (DSS) rate in different CONUT groups and all the studies (100%) indicated that patients with a high CONUT score had significantly shorter CSS than those with a low CONUT score ($P < 0.05$). According to multivariate analysis, 90.9% (10 of 11) of the studies reported that CONUT score was an independent prognostic factor of CSS ($P < 0.05$).

Twenty-three studies investigated RFS, DFS, or PFS rate in different CONUT groups and 87.0% (20 of 23) of the

**TABLE 1** Characteristics of the studies included and findings on prognostic potential (according to multivariate analysis) and efficacy of the CONUT score in predicting survival[1]

| Reference | Country, study design | Type of cancer | Patients, *n* | Age, y | Follow-up time | CONUT score cut offs | Determination of optimal cutoff values for CONUT score/index | CONUT score efficacy for predicting survival | Calculation method of survival rate, HR, and CONUT score[2] | Findings | Relation of CONUT score and BMI |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Ahiko et al. (16) | Japan, retrospective cohort | Colorectal cancer (Stage I–IV), underwent surgery | 830 (470 males, 360 females) | Median (range): 78 (75–94) | ≥5 y | 0–1 ($n = 508$)<br>2–3 ($n = 249$)<br>≥4 ($n = 73$) | Not indicated. | Not indicated. | *¶◇ | Higher CONUT group had the lowest 5-y OS rate ($P < 0.0001$).<br>CONUT score was a significant prognostic factor of OS (≥4 vs. 0–1: HR: 2.24; 95% CI: 1.48, 3.30; $P < 0.001$) after adjustment for confounders. | BMI did not differ between CONUT groups. |
| Akamine et al. (17) | Japan, retrospective | Lung adenocarcinoma, underwent surgery | 109 (76 males, 33 females) | Mean (range): 72 (45–85) | 4–13 y | High: ≥1 ($n = 74$)<br>Low: 0 ($n = 35$) | ROC curve/— | AUC: 0.596<br>Sensitivity: 0.6711; specificity: 0.4375 | *¶◇ | High-CONUT group had lower 5-y OS ($P = 0.04$) and DFS ($P = 0.01$) rates.<br>CONUT score was independently associated with DFS (HR: 2.63; 95% CI: 1.33, 5.68; $P = 0.004$) and OS (HR: 2.64; 95% CI: 1.06, 7.80; $P = 0.04$). | High-CONUT group had lower BMI ($P = 0.025$). |
| Elghiaty et al. (12) | South Korea, retrospective cohort | Nonmetastatic clear cell renal cell carcinoma, underwent radical or partial nephrectomy | 1046 (745 males and 301 females) | Median (range): 56 (46–64) | Median (range): 63 (43–87) mo | High: >2 ($n = 115$)<br>Low: ≤2 ($n = 931$) | ROC curve/Youden Index | AUC (based on OS) = 0.633<br>Sensitivity = 46.4%; specificity = 73.7% ($P = 0.001$) | *¶◇ | High-CONUT group had lower 3- and 5-y RFS ($P < 0.001$), CSS ($P = 0.006$), and OS ($P < 0.001$) rates.<br>High CONUT score was an independent predictor of RFS (HR: 3.09; 95% CI: 1.45, 6.59; $P = 0.003$), CSS (HR: 4.66; 95% CI: 1.62, 13.39; $P = 0.004$), and OS (HR: 2.81; 95% CI: (1.44, 5.50; $P = 0.003$). | High-CONUT group had lower BMI ($P = 0.001$). |

(*Continued*)

**TABLE 1** (*Continued*)

| Reference | Country, study design | Type of cancer | Patients, *n* | Age, y | Follow-up time | CONUT score cut offs | Determination of optimal cutoff values for CONUT score/index | CONUT score efficacy for predicting survival | Calculation method of survival rate, HR, and CONUT score[2] | Findings | Relation of CONUT score and BMI |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Harimoto et al. (18) | Japan, retrospective cohort | Hepatocellular carcinoma, underwent hepatic resection | 2461 (1785 males, 676 females) | Mean ± SD: Low CONUT: 68.2 ± 10.1; High CONUT: 69.8 ± 9.2 | Not indicated | High: ≥4 ($n = 540$) Low: ≤3 ($n = 1921$) | ROC curve/Youden index | AUC (based on OS): 0.580 Sensitivity: 31.3%; specificity: 91.6% ($P < 0.01$) AUC (based on CSS): 0.563 Sensitivity: 30.0%; specificity: 80.1% ($P < 0.01$) AUC (based on RFS): 0.536 Sensitivity: 63.5%; specificity: 41.9% ($P < 0.01$). | *¶◇ | High-CONUT group had lower OS and RFS rates (both, $P < 0.01$). Higher CONUT score was an independent predictor of poor OS (HR: 1.22; 95% CI: 1.06, 1.41; $P = 0.006$) and RFS (HR: 1.22; 95% CI: 1.06, 1.40; $P = 0.006$). | High-CONUT group had low BMI ($P < 0.01$). |
| Harimoto et al. (19) | Japan, retrospective | Hepatocellular carcinoma, underwent hepatic resection | 357 (270 males, 87 females) | Mean ± SD: Low CONUT: 67.3 ± 10.7; High CONUT: 69.8 ± 8.5 | ≥5 y | High: >3 ($n = 69$) Low: ≤3 ($n = 288$) | ROC curve/Youden index | AUC (based on OS): 0.621 Sensitivity: 56.06%; specificity: 66.56% AUC (based on DSS): 0.651 Sensitivity: 65.7%; specificity: 59.5%. | *¶◇ | High-CONUT group had lower 5-y OS, RFS, and DSS rates ($P < 0.01$). Higher CONUT score was associated with poor OS (HR: 2.16; 95% CI: 1.25, 3.72; $P = 0.03$), but not with RFS. | BMI did not differ between CONUT groups. |
| Hirahara et al. (20) | Japan, retrospective | Esophageal cancer, underwent curative thoracoscopic esophagectomy | 148 (132 males, 16 females) | Mean ± SD: CONUT 0: 65.6 ± 8.2; CONUT 1: 67.5 ± 8.4; CONUT 2-3: 65.3 ± 8.9 | Not indicated | Normal nutrition: 0–1 ($n = 70$) Mild malnutrition: 2–4 ($n = 62$) Moderate–severe malnutrition: 5–12 ($n = 16$) | Not indicated. | Not indicated. | *¶◇ | CONUT was independently associated with worse prognosis for CSS (HR: 1.99; 95% CI: 1.07, 3.87), $P = 0.03$). | Not indicated. |

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**TABLE 1** (*Continued*)

| Reference | Country, study design | Type of cancer | Patients, *n* | Age, y | Follow-up time | CONUT score cut offs | Determination of optimal cutoff values for CONUT score/index | CONUT score efficacy for predicting survival | Calculation method of survival rate, HR, and CONUT score[2] | Findings | Relation of CONUT score and BMI |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Hirahara et al. (21) | Japan, retrospective cohort | Gastric cancer, underwent curative gastrectomy | 368 (254 males, 114 females) | Range: 36–91 | Median: 35.3 mo | High: ≥3 ($n = 105$) Low: ≤2 ($n = 263$) | ROC curve/— | AUC (based on 5-y OS): 0.625 Sensitivity: 65.0%; specificity: 57.9% | *¶◇ | High-CONUT group had lower 5-y OS rate ($P < 0.001$). Among all patients, OS was independently predicted by the CONUT score (HR: 2.25, $P = 0.001$). CONUT score was an independent prognostic factor for OS among the propensity score–matched subgroup (HR: 2.44; 95% CI: 1.46, 4.07; $P < 0.001$). | BMI did not differ between CONUT groups. |
| Huang et al. (22) | China, prospective cohort | Gastric cancer, underwent curative gastrectomy | 357 (275 males, 82 females) | Mean ± SD: 73.29 ± 5.24 | 1 y | Normal: 0–1 ($n = 153$) Light: 2–4 ($n = 168$) Moderate and severe: ≥5 ($n = 36$) | Not indicated. | Not indicated. | ¶◇ | CONUT score was an independent predictor of postoperative 1-y survival (OR: 2.91; 95% CI: 0.91, 9.31; $P = 0.02$). | Moderate–severe CONUT group had lower BMI ($P < 0.001$). |
| Iseki et al. (23) | Japan, retrospective | Colorectal cancer (Stage II/III), underwent curative surgery | 204 (112 males, 92 females) | Mean ± SD: High CONUT: 66.09 ± 9.23; Low CONUT: 71.13 ± 11.57 | 8 y or until their deaths | High: ≥3 ($n = 54$) Low: ≤2 ($n = 150$) | ROC curve/— | AUC (based on 5-y CSS): 0.624 ($P = 0.076$) Sensitivity: 0.5263; specificity: 0.7622 | *¶◇ | High-CONUT group had lower 5-y CSS ($P = 0.002$) and RFS ($P = 0.002$) rates. CONUT score was an independent risk factor for CSS (OR: 4.21; 95% CI: 1.21, 13.35; $P = 0.02$), but not for RFS. | Not indicated. |
| Ishihara et al. (24) | Japan, retrospective cohort | Localized urothelial carcinoma treated with radical nephroureterectomy | 107 (68 males, 39 females) | Mean ± SD: Low CONUT: 72.7 ± 9.98; High CONUT: 76.1 ± 8.65 | Mean ± SD: 46.1 ± 32.8; 25.5 ± 18.4 mo | High: ≥3 ($n = 24$) Low: <3 ($n = 83$) | ROC curve/Youden index | AUC (based on RFS): 0.588 | *¶◇ | High-CONUT group had lower 5-y RFS ($P = 0.04$), CSS ($P = 0.004$), and OS ($P = 0.01$) rates. | Not indicated. |

(*Continued*)

**TABLE 1** (*Continued*)

| Reference | Country, study design | Type of cancer | Patients, *n* | Age, y | Follow-up time | CONUT score cut offs | Determination of optimal cutoff values for CONUT score/index | CONUT score efficacy for predicting survival | Calculation method of survival rate, HR, and CONUT score[2] | Findings | Relation of CONUT score and BMI |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | CONUT score was an independent predictor of CSS (HR: 5.44; 95% CI: 1.95, 14.8; $P = 0.002$), OS (HR: 2.90; 95% CI: 1.18, 6.75; $P = 0.02$), and RFS (HR: 2.26; 95% CI: 0.97, 4.94; $P = 0.058$). | |
| Kang et al. (25) | Korea, retrospective cohort | Renal cell carcinoma, underwent surgery | 1881 (1361 males, 520 females) | Mean ± SD: Normal: 54.21 ± 12.17; Mild: 58.69 ± 12.80; Moderate to severe: 63.69 ± 12.83 | Median (range): 41 (6–178) mo | High: ≥2 ($n = 508$)<br>Low: 0–1 ($n = 1373$) | ROC curve/— | ROC curve | *¶◇ | High-CONUT group had shorter RFS ($P = 0.02$) and CSM ($P < 0.001$).<br>High CONUT score was an independent predictor of CSM (HR: 1.89; 95% CI: 1.12, 3.20; $P = 0.02$), but not for RFS. | High-CONUT group had lower BMI ($P < 0.001$). |
| Kato et al. (26) | Japan, retrospective | Pancreatic adenocarcinoma, underwent resection | 344 (207 males, 137 females) | Mean ± SD: 64.8 ± 9.9 | Median (range): 29.1 (0.6–178.5) mo | High: ≥4 ($n = 79$)<br>Low: <4 ($n = 265$) | ROC curve/— | AUC (based on 2-y survival): 0.614 (95% CI: 0.56, 0.67).<br>Sensitivity: 30.6%; specificity: 88.6% | *¶◇ | High-CONUT group showed lower OS ($P = 0.002$) but not RFS.<br>High CONUT score was an independent prognostic risk factor for OS (HR: 1.64; 95% CI: 1.19, 2.26; $P = 0.003$). | Not indicated. |
| Kuroda et al. (27) | Japan, retrospective cohort | Gastric cancer, underwent curative resection | 416 (267 males, 149 females) | Median (range): 67.2 (25–94) | Median (range): 61.2 (1–134) mo | High: ≥4 ($n = 62$)<br>Low: ≤3 ($n = 354$) | ROC curve/— | AUC (based on OS): 0.715 (95% CI: 0.68, 0.75)<br>AUC (based on RFS): 0.658 (95% CI: 0.62, 0.70)<br>AUC (based on CSS): 0.662 (95% CI: 0.61, 0.71) | *¶◇ | High-CONUT group had lower 5-y OS ($P < 0.001$), RFS ($P = 0.02$), and CSS ($P = 0.02$) rates.<br>CONUT was an independent prognostic factor for OS (HR: 2.72; 95% CI: 1.74, 4.25; $P < 0.001$), but not for RFS and CSS. | High-CONUT group had lower BMI ($P = 0.02$). |

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**TABLE 1** (*Continued*)

| Reference | Country, study design | Type of cancer | Patients, *n* | Age, y | Follow-up time | CONUT score cut offs | Determination of optimal cutoff values for CONUT score/index | CONUT score efficacy for predicting survival | Calculation method of survival rate, HR, and CONUT score[2] | Findings | Relation of CONUT score and BMI |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Liang et al. (28) | China, retrospective cohort | Soft-tissue sarcomas, underwent surgical resection | 658 (393 males, 265 females) | Median (range): 43 (5–85) | Median (range): 103 (61–147) mo | High: ≥2 ($n = 223$) Low: 0–1 ($n = 435$) | ROC curve/Youden index | ROC curve | *¶◇ | High-CONUT group had lower 5-y OS ($P < 0.001$) and DFS ($P < 0.001$) rates. High CONUT was an independent predictor of OS (HR: 1.86; 95% CI: 1.47, 4.14; $P < 0.001$) and DFS (HR: 1.63; 95% CI: 1.26, 2.11; $P < 0.001$). | Not indicated. |
| Lin et al. (29) | China, retrospective cohort | Hepatocellular carcinoma, underwent curative hepatectomy | 380 (333 males, 47 females) | Median (range): 50 (19–80) | Median: 48.5 mo | High: ≥2 ($n = 187$) Low: <2 ($n = 193$) | ROC curve/— | AUC (based on OS): 0.618 (95% CI: 0.567, 0.667) Sensitivity: 66.3%; specificity: 56.5% | *¶◇ | High-CONUT group had lower 5-y OS ($P < 0.001$) and RFS ($P = 0.02$) rates. High CONUT was an independent prognostic indicator of decreased OS (HR: 2.40; 95% CI: 1.74, 4.25; $P = 0.001$), but not decreased RFS (HR: 1.36; 95% CI: 1.00, 1.85; $P = 0.05$). | Not indicated. |
| Miyata et al. (30) | Japan, retrospective | Intrahepatic cholangiocarcinoma, underwent curative hepatectomy | 71 (45 males, 26 females) | Mean ± SD: Low CONUT: 64.8 ± 1.7; High CONUT: 69.1 ± 1.9 | Mean: 36.9 mo | High: ≥2 ($n = 31$) Low: <2 ($n = 40$) | Not indicated. | Not indicated. | *¶◇ | High-CONUT group had lower 1-, 3-, and 5-y OS ($P = 0.01$), but not RFS. High CONUT was an independent prognostic factor for OS (HR: 3.02; 95% CI: 1.4, 6.8; $P = 0.007$), but not for RFS. | High-CONUT group had lower BMI ($P = 0.009$). |
| Ryo et al. (31) | Japan, retrospective cohort | Gastric cancer, underwent gastrectomy | 626 (435 males, 191 females) | Mean ± SD: 67.9 ± 10.9 | Median: 49.2 mo or until death | High: ≥2 ($n = 289$) Low: <2 ($n = 337$) | ROC curve/— | AUC (based on DFS): 0.656 Sensitivity: 0.66; specificity: 0.58 | *¶◇ | High-CONUT group had shorter OS ($P < 0.0001$) and DFS ($P = 0.06$) times. CONUT score was an independent prognostic factor for OS (HR: 1.74; 95% CI: 1.26, 2.41; $P = 0.0007$). | High-CONUT group had lower BMI ($P < 0.0001$). |

(*Continued*)

**TABLE 1** (*Continued*)

| Reference | Country, study design | Type of cancer | Patients, *n* | Age, y | Follow-up time | CONUT score cut offs | Determination of optimal cutoff values for CONUT score/index | CONUT score efficacy for predicting survival | Calculation method of survival rate, HR, and CONUT score[2] | Findings | Relation of CONUT score and BMI |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Shoji et al. (32) | Japan, retrospective | Non–small cell lung cancer, underwent surgery | 138 (79 males, 59 females) | Mean (range): 68 (37–86) | Median (range): 58 (0–94) mo | High: ≥1 ($n = 79$)<br>Low: 0 ($n = 59$) | ROC curve/— | AUC (based on CSS): 0.703<br>Sensitivity = 91.67%; specificity = 46.07% | *¶◇ | High-CONUT group had lower 5-y RFS ($P = 0.046$), CSS, ($P = 0.01$), and OS ($P = 0.01$) rates.<br>CONUT score was an independent prognostic factor for CSS (RR: 6.06; 95% CI: 1.07, 113.94; $P = 0.04$). | Not indicated. |
| Song et al. (33) | China, retrospective cohort | Nonmetastatic renal cell carcinoma, underwent surgery | 325 (231 males, 94 females) | Median (IQR): 57 (47–66) | Median (IQR): 64 (56.5–69) mo | High: ≥3 ($n = 70$)<br>Low: <3 ($n = 255$) | ROC curve/Youden index | AUC (based on 5-y OS): 0.723, ($P < 0.001$)<br>Sensitivity: 51.28%; specificity: 82.52% | *¶◇ | High-CONUT group had lower 5-y OS ($P < 0.001$), CSS ($P < 0.001$), and DFS ($P < 0.001$) rates.<br>High CONUT was an independent risk factor for OS (HR: 3.36; 95% CI: 1.73, 6.56; $P < 0.001$), CSS (HR: 3.34; 95% CI: 1.59, 6.98; $P = 0.001$), and DFS (HR: 1.85; 95% CI: 1.07, 3.21; $P = 0.03$). | Not indicated. |
| Suzuki et al. (34) | Japan, retrospective | Gastric cancer, underwent curative resection | 211 (141 males, 70 females) | ≥75 | Median (range): 47 (5–185) mo | Normal nutrition: ($n = 75$)<br>Light malnutrition: ($n = 100$)<br>Moderate or severe malnutrition: ($n = 36$) | Not indicated. | Not indicated. | *¶◇ | Higher-CONUT group had shorter OS ($P < 0.001$) and CSS ($P < 0.001$).<br>CONUT score was an independent prognostic factor for OS (HR: 2.12; 95% CI: 1.18, 3.69; $P = 0.01$) and CSS (HR: 3.75; 95% CI: 1.30, 10.43; $P = 0.01$). | Higher CONUT group had lower BMI ($P = 0.008$). |

(*Continued*)

**TABLE 1** (*Continued*)

| Reference | Country, study design | Type of cancer | Patients, *n* | Age, y | Follow-up time | CONUT score cut offs | Determination of optimal cutoff values for CONUT score/index | CONUT score efficacy for predicting survival | Calculation method of survival rate, HR, and CONUT score[2] | Findings | Relation of CONUT score and BMI |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Takagi et al. (35) | Japan, retrospective cohort | Hepatocellular carcinoma, underwent hepatectomy | 295 (241 males, 54 females) | Mean ± SD: 65.8 ± 10.4 | Mean: 42.3 mo | High: ≥3 ($n = 118$) Low: ≤2 ($n = 177$) | ROC curve/— | AUC = 0.59 | ∗¶◇ | High-CONUT group had lower 5-y RFS ($P = 0.01$) and OS ($P = 0.006$) rates. The CONUT score was an independent predictor of RFS (HR: 1.64; 95% CI: 1.15, 2.30; $P = 0.006$) and OS (HR: 2.50; 95% CI: 1.47, 4.23; $P = 0.001$). | BMI did not significantly differ between CONUT groups. |
| Takagi et al. (36) | Japan, retrospective cohort | Hepatocellular carcinoma, underwent hepatectomy | 331 (269 males, 62 females) | Median (range): 67 (60–74) | 1 mo | High: ≥5 ($n = 30$) Low: ≤4 ($n = 301$) | Not indicated. | Not indicated. | ¶◇ | High-CONUT group had higher incidence of 30-d mortality ($P < 0.001$). High CONUT score was an independent predictor of in-hospital mortality after hepatectomy (HR: 9.41; 95% CI: 1.15, 77.4; $P = 0.04$). | BMI did not differ between CONUT groups ($P > 0.05$). |
| Takamori et al. (37) | Japan, retrospective | Malignant pleural mesothelioma | 83 (66 males, 17 females) | Median (range): 59 (31–81) | — | High: ≥3 ($n = 31$) Low: ≤2 ($n = 52$) | ROC curve/— | AUC (based on 1-y survival): 0.772 Sensitivity: 73.1%; specificity: 64.0% | ∗¶◇ | High-CONUT group had lower OS and DFS rates (both, $P < 0.001$). High CONUT score was an independent predictive factor for OS (HR: 1.92; 95% CI: 1.17, 3.11; $P = 0.01$) and DFS (HR: 1.88; 95% CI: 1.14, 3.06; $P = 0.01$). High CONUT score was a prognostic factor of OS in patients who underwent surgery (HR: 4.86; 95% CI: 1.16, 19.14; $P = 0.03$). | Not indicated. |

(*Continued*)

**TABLE 1** (*Continued*)

| Reference | Country, study design | Type of cancer | Patients, *n* | Age, y | Follow-up time | CONUT score cut offs | Determination of optimal cutoff values for CONUT score/index | CONUT score efficacy for predicting survival | Calculation method of survival rate, HR, and CONUT score[2] | Findings | Relation of CONUT score and BMI |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Tokunaga et al. (38) | Japan, retro-spective | Colorectal cancer, underwent curative resection | 417 (247 males, 170 females) | Median (range): 68 (19–93) | Mean (range): 38.0 (1–115) mo | Normal: ($n = 246$) Light: ($n = 127$) Moderate: ($n = 33$) Severe: ($n = 11$) | Not indicated. | Not indicated. | *¶◇ | High-CONUT group (moderate/severe) had lower 5-y OS and RFS (both, $P < 0.001$). CONUT score was an independent prognostic factor for OS (moderate/severe vs. normal: HR: 5.92; 95% CI: 2.30, 14.92; $P < 0.001$; light vs. normal: HR: 2.74; 95% CI: 1.30, 5.87; $P = 0.008$), but not for RFS. | Moderate/severe CONUT group had lower BMI ($P = 0.005$). |
| Toyokawa et al. (39) | Japan, retro-spective | Lung squamous cell carcinoma, underwent surgery | 108 (96 males, 12 females) | Median (range): 71 (45–89) | ≥5 y | High: ≥2 ($n = 32$) Low: 0–1 ($n = 76$) | ROC curve/— | AUC (based on OS): 0.590 Sensitivity: 0.786; specificity: 0.385 | *¶◇ | High-CONUT group had lower 5-y DFS ($P = 0.02$) and OS ($P = 0.006$) rates. High CONUT score was an independent prognostic factor for DFS (HR: 1.90; 95% CI: 1.04, 3.37; $P = 0.04$) and OS (HR: 1.91; 95% CI: 0.92, 3.86; $P = 0.08$). | BMI did not differ between CONUT groups ($P > 0.05$). |
| Wang et al. (40) | China, retro-spective | Malignant peritoneal mesothe-lioma | 125 (46 males, 79 females) | Mean ± SD: 61.2 ± 9.3 | Median (range): 8 (0.6–53) mo | High: ≥3 ($n = 81$) Low: ≤2 ($n = 44$) | ROC curve/— | AUC (based on OS): 0.861 ($P < 0.001$) Sensitivity: 0.784; specificity: 0.821 | ¶◇ | CONUT score was an independent predictive factor for OS (RR: 1.26; 95% CI: 1.16, 1.38; $P < 0.001$). | BMI did not differ between CONUT groups ($P > 0.05$). |
| Yamamoto et al. (41) | Japan, retro-spective | Colorectal cancer (stage I–IV) underwent surgery | 522 (291 males, 231 females) | — | ≥5 y | High: ≥3 ($n = 158$) Low: <3 ($n = 364$) | ROC curve/— | AUC (based on OS): 0.627 ($P < 0.0001$) | *¶◇ | High-CONUT group had a lower 5-y OS rate ($P < 0.0001$). | Not indicated. |

(*Continued*)

**TABLE 1** (*Continued*)

| Reference | Country, study design | Type of cancer | Patients, *n* | Age, y | Follow-up time | CONUT score cut offs | Determination of optimal cutoff values for CONUT score/index | CONUT score efficacy for predicting survival | Calculation method of survival rate, HR, and CONUT score[2] | Findings | Relation of CONUT score and BMI |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Yang C et al. (42) | China, retrospective | Colorectal cancer, underwent curative resection | 160 (90 males, 70 females) | Mean ± SD: 58.4 ± 11.8 | Median (range): 30 (6–42) mo | High: ≥3 ($n = 74$) Low: <3 ($n = 86$) | ROC curve/Youden index | AUC (based on CSS): 0.759 ($P < 0.001$) Specificity: 0.821; sensitivity: 0.625 | ∗¶⋄ | High CONUT score was correlated with poor RFS ($P < 0.001$) and CSS ($P < 0.001$). CONUT score was an independent prognostic factor for RFS (HR: 2.02; 95% CI: 1.19, 3.43; $P = 0.01$) and CSS (HR: 3.45; 95% CI: 1.68, 7.10; $P = 0.001$). | Not indicated. |
| W Yang, C Shou, J Yu, Q Zhang, X Liu, H Yu, X Lin, unpublished results, 2019 | —, retrospective | Gastrointestinal stromal tumors, underwent resection | 455 (222 males, 233 females) | Median (range): 57 (20–80) | Median (range): 110 (7–232) mo | Normal: 0–1 ($n = 219$) Light undernutrition: 2–4 ($n = 196$) Moderate–severe undernutrition: ≥5 ($n = 40$) | Not indicated. | Not indicated. | ∗¶⋄ | Higher-CONUT group had a lower RFS rate ($P = 0.001$). CONUT score was an independent prognostic factor for RFS (COUNT ≥5 vs. CONUT = 0–1: HR: 2.83; 95% CI: 1.46, 5.50; $P = 0.002$). | Not indicated. |
| Zhang et al. (43) | China, retrospective cohort | Metastatic prostate cancer, underwent surgery | 94 males | Median (range): 71 (53–84) | Median (range): 16.31 (4.6–55.10) mo | High: ≥3 ($n = 42$) Low: 0–2 ($n = 52$) | X-tile program | Using the X-tile software | ∗⋄ | High-CONUT group had shorter PFS before surgery ($P < 0.05$). High CONUT score was an independent prognostic factor for PFS (HR: 3.97; 95% CI: 1.05, 11.43; $P = 0.004$). | BMI did not differ between CONUT groups ($P > 0.05$). |
| Zheng Z-F et al. (44) | China, retrospective | Gastric cancer, underwent radical gastrectomy | 532 (403 males, 129 females) | Mean ± SD: 61.1 ± 11.5 | Median (range): 60 (2–76) mo | Normal nutrition: $n = 291$ Light malnutrition: $n = 183$ Moderate or severe malnutrition: $n = 58$ | Not indicated. | Not indicated. | ∗¶⋄ | Higher-CONUT group had the lowest 5-y OS ($P = 0.006$) and RFS ($P = 0.02$) rates. CONUT score was not associated with 5-y OS and RFS. | Higher-CONUT group had low BMI ($P = 0.01$). |

(*Continued*)

TABLE 1 (*Continued*)

| Reference | Country, study design | Type of cancer | Patients, *n* | Age, y | Follow-up time | CONUT score cut offs | Determination of optimal cutoff values for CONUT score/index | CONUT score efficacy for predicting survival | Calculation method of survival rate, HR, and CONUT score[2] | Findings | Relation of CONUT score and BMI |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Zheng Y et al. (45) | China, retrospective | Renal cell carcinoma, underwent nephrectomy | 635 (400 males, 235 females) | Mean ± SD: 61.71 ± 12.51 | Median (range): 48.4 (29.3–80.1) mo | High: ≥2 ($n = 349$) Low: <2 ($n = 286$) | X-tile program | X-tile program | ∗¶⋄ | High-CONUT group had shorter OS and CSS (both, $P < 0.0001$). CONUT score was an independent risk predictor of OS (HR: 3.01; 95% CI: 1.52, 5.95; $P = 0.001$) and CSS (HR: 3.00; 95% CI: 1.29, 6.98; $P = 0.01$). | High-CONUT group had low BMI ($P < 0.001$). |

[1]CONUT, controlling nutritional status; CSS, cancer-specific survival; DFS, disease-free survival; OS, overall survival; PFS, progression-free survival; RFS, recurrence/relapse-free survival; ROC, receiver operating characteristic.
[2]∗Survival rate, ¶HR, ⋄CONUT score. The Kaplan–Meier method and log-rank test were used to estimate survival rates. The Cox proportional hazards regression model was used to calculate HRs and 95% CIs. CONUT score was calculated from serum albumin and total cholesterol concentrations and total peripheral lymphocyte counts.

studies indicated that patients with a high CONUT score had significantly shorter RFS than those with a low CONUT score ($P < 0.05$). Nineteen studies evaluated the correlation between CONUT score and RFS. According to multivariate analysis, 52.6% (10 of 19) of the studies reported that the CONUT score was an independent prognostic factor for RFS ($P < 0.05$).

### Efficacy of the CONUT score in prognosis of survival

Fourteen studies reported AUC values of ROC curves for OS, of which the minimum and maximum values were 0.58 and 0.86, respectively, among the studies. Eleven studies reported the sensitivity and specificity of CONUT score cutoffs for detection of OS. The minimum and maximum values of sensitivity were 30.6% and 82.0%, respectively, and for specificity were 38.5% and 91.6%, respectively, among the studies.

Four studies reported AUC values of ROC curves for RFS, ranging from 0.54 to 0.66 among the studies. Two studies reported CONUT score cutoffs' sensitivity (ranging from 63.5% to 66.0% among the studies) and specificity (ranging from 41.9% to 58.0% across the studies) for detection of RFS.

Six studies reported AUC values of ROC curves for CSS with minimum and maximum values of 0.56 and 0.76, respectively, across the studies. Five studies reported CONUT score cutoffs' sensitivity (ranging from 30.0% to 91.7% across the studies) and specificity (ranging from 46.1% to 80.1% across the studies) for detection of CSS.

### Relation between BMI and CONUT score

Twenty studies measured the relation of BMI to CONUT score; 60.0% ($n = 12$) of the studies reported that the high-count group had significantly lower BMI ($P < 0.05$).

## Discussion

Lower OS, CSS, and RFS rates in cancer patients with high CONUT scores were reported by 100%, 100%, and 86.7% of the studies, respectively. A prognostic role of the CONUT score for prediction of OS, CSS, and RFS in cancer patients was suggested by 91.7%, 90.9%, and 52.6% of the studies, respectively. The prognosis of outcomes (including tumor proliferation, patients' survival, and posttreatment complications) in patients with cancer has been demonstrated to be strongly correlated with aspects of the host's nutritional situation such as BMI, visceral obesity, and sarcopenia (46–49). The CONUT score is a nutritional assessment tool that is easily, cheaply, and objectively estimated from serum albumin, total cholesterol, and total lymphocyte count (6). A prognostic impact of the CONUT score on survival has also been reported in hospitalized elderly people (50) and in patients with heart failure (7), end-stage liver disease (8), hypertension (9), and peritoneal dialysis (51).

The AUC value of the ROC curve for the CONUT score was at an acceptable level (>0.5) for predicting OS, CSS, and RFS in all of the studies where AUC values were presented (12, 18, 27). This indicates that the preoperative CONUT score is a reliable and independent prognostic marker of survival in cancer patients. Although sensitivity and specificity of the CONUT score for the prediction of survival were at an acceptable level (>50%) in most of the studies, the difference across the studies was possibly due to the adoption of various CONUT score cutoffs. It appears that a cutoff ≥3 has acceptable sensitivity and specificity in predicting survival.

Several studies have shown that the AUC of the CONUT score, according to the ROC curve, was significantly higher than the AUC of each component of CONUT including serum albumin and total cholesterol concentrations and total lymphocyte count (23, 27, 31, 38, 45). Furthermore, numerous studies have reported that individual components of the CONUT score, against the CONUT score itself, were not independent predictors of survival in patients with various types of cancers (18, 19, 23, 45, 52). Taken together, it may be interpreted that the CONUT score is a more valuable factor than its individual components for predicting survival.

In addition, several studies have compared prognostic accuracy of the CONUT score in predicting survival with other nutritional prognostic factors such as the Prognostic Nutritional Index (PNI) (29, 33, 53, 54). The PNI is calculated from the serum albumin concentration and total peripheral lymphocyte count. The prognostic value of the PNI for predicting survival in cancer patients has been confirmed in numerous studies (55–59). However, various studies have shown that the CONUT score had a higher ROC curve AUC for the prediction of survival than the PNI (29, 33, 53, 54). Moreover, contrary to the CONUT score, many studies have shown that the PNI was not an independent predictor of survival in patients with cancer (30, 36, 60). Iseki et al. (23) reported that the PNI was not an independent predictor of CSS in patients with colorectal cancer, whereas CONUT score was. Takagi et al. (35) also reported that the PNI, against CONUT score, was not an independent predictor of survival in patients with hepatocellular carcinoma. Y Zheng et al. (45) also demonstrated that the PNI was not an independent predictor of survival in patients with renal cell carcinoma, whereas CONUT score was. Collectively, considering the results of all the aforementioned studies, it is concluded that the CONUT score has higher prognostic accuracy than, and is preferable to, the PNI in predicting survival in different types of cancer.

The platelet-to-lymphocyte ratio (PLR), neutrophil-to-lymphocyte ratio (NLR), and Glasgow Prognostic Score (GPS) are inflammatory factors that have recently been suggested as prognostic factors for predicting inflammation and survival in many diseases and/or cancers (61–65). Multiple studies have compared the prognostic accuracy of the CONUT score with the inflammatory markers in predicting survival. Li et al. (53) indicated that CONUT had a higher AUC (of ROC) for the prediction of survival than the NLR in patients with breast cancer. Leem et al. (54) reported that the CONUT had a higher ROC curve AUC than the GPS in patients with lung cancer. Lin et al. (29) showed that the CONUT score had a higher AUC value than the inflammatory parameters (NLR and PLR) in patients with hepatocellular carcinoma. Song et al. (33) reported that the CONUT AUC score for 5-y OS was higher than that of the NLR in patients with renal cell carcinoma. Toyokawa et al. (52) showed that the AUC of CONUT for predicting 3-y OS was higher than the AUCs of the PLR, NLR, and GPS in patients with esophageal cancer. Moreover, many studies have shown that the PLR, NLR, and GPS, against CONUT score, were not independent predictors of survival in patients with cancer (20, 29, 43, 45, 52). Putting together all the findings, it is suggested that the CONUT score, in comparison with the inflammatory markers, has higher prognostic accuracy and is superior in predicting survival in different types of cancer.

Carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA19-9) are 2 cancer markers with prognostic significance for prediction of survival in patients with cancer (66, 67). CEA is a protein commonly produced in very low concentrations in the blood of adults. The blood concentration of CEA may be raised in some types of cancer (68, 69). CA19-9 is a blood type antigen and it may be increased in patients with gastrointestinal cancers (69). None of the included studies compared the prognostic accuracy (AUC value of the ROC curve) of these markers with that of the CONUT score in predicting survival in cancer patients. However, several of the included studies showed that CEA and CA19-9, against CONUT score, were not independent predictors of survival in patients with cancer (10, 23, 26, 30, 32, 38, 42, 60). More investigations are needed to clarify the prognostic accuracy of the CONUT score in predicting survival compared with the CEA and CA19-9 markers in patients with cancer.

## Conclusions

The findings of the present study promote confidence that a preoperative high CONUT score is associated with a poor survival rate and is an independent prognostic factor of OS and CSS after surgery in patients with cancer.

### *Application of the findings.*

This study suggests that the CONUT score is an easy and inexpensive indicator which not only could be used for evaluating nutritional status, but can also be beneficial as a prognostic marker of patients' survival in various types of cancer. Evaluation of the CONUT score might help clinicians in decision-making with respect to surgical implications.

### *Strengths of the study.*

All the studies had good quality and, except 1, were published in the last 3 y. Nearly all of the studies used the same method to estimate survival rate and to analyze the correlation between CONUT score and survival. Further, in all studies included, the roles of main confounding factors including age, gender, BMI, stage of disease, tumor site, tumor number, tumor grade, tumor size, lymph node metastasis, presence of high-grade disease, adjuvant chemotherapy, immunohistochemistry, and operative procedures were considered in the analysis.

*Limitations of the study.*

All included studies were from East Asia (Japan, China, and South Korea), which may restrict the utilization of the findings among other nations and ethnic groups. Most of the studies did not indicate the role of BMI as a nutritional factor in prediction of survival. Several of the studies did not indicate the value of the AUC of the CONUT score for prediction of survival. The optimal cutoff of the CONUT score varied across the different studies.

*Suggestions for future research.*

The optimal cutoff of the CONUT score must be homogenized before its utilization in clinical practice. More investigations are needed to clarify the prognostic accuracy of the CONUT score in predicting survival compared with CEA and CA19-9 markers in patients with cancer.

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