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Calf circumference-albumin index significantly predicts the prognosis of older patients with cancer cachexia: A multicenter cohort study

Pengxia Guo M.M., M.P.H. [a], Hongxia Xu M.D., Ph.D. [b], Min Weng M.D., Ph.D. [c], Fuxiang Zhou M.D., Ph.D. [d], Wen Hu M.D., Ph.D. [e], Suyi Li M.D., Ph.D. [f], Yuan Lin M.D., Ph.D. [g], Chunling Zhou M.D., Ph.D. [h], Hu Ma M.D., Ph.D. [i], Wei Li M.D., Ph.D. [j], Jiuwei Cui M.D., Ph.D. [j], Haoqing Cheng M.M., M.P.H. [a], Saba Fida M.M., M.P.H. [a], Hanping Shi M.D., Ph.D. [k,l], Chunhua Song M.D., Ph.D. [a,m,n,*], The Investigation on Nutrition Status and Its Clinical Outcome of Common Cancers (INSCOC) Group

[a] Department of Epidemiology and Statistics, College of Public Health, Zhengzhou University, Zhengzhou, Henan, China
[b] Department of Clinical Nutrition, Daping Hospital, Army Medical University (Third Military Medical University) , Chongqing, China
[c] Department of Clinical Nutrition, The First Affiliated Hospital of Kunming Medical University, Kunming, Yunnan, China
[d] Department of Radiation and Medical Oncology, Zhongnan Hospital of Wuhan University, Wuhan, Hubei, China
[e] Department of Clinical Nutrition, West China Hospital of Sichuan University, Chengdu, Sichuan, China
[f] Department of Nutrition and Metabolism of Oncology, Affiliated Provincial Hospital of Anhui Medical University, Hefei, Anhui, China
[g] Department of Gastrointestinal Surgery, Affiliated Tumor Hospital of Guangxi Medical University, Nanning, Guangxi, China
[h] Department of Clinical Nutrition, The Fourth Affiliated Hospital, Harbin Medical University, Harbin, Heilongjiang, China
[i] Department of Oncology, The Second Affiliated Hospital of Zunyi Medical University, Zunyi, Guizhou, China
[j] Cancer Center of the First Hospital of Jilin University, Changchun, Jilin, China
[k] Department of Gastrointestinal Surgery and Department of Clinical Nutrition, Beijing Shijitan Hospital, Capital Medical University, Beijing, China
[l] Key Laboratory of Cancer FSMP for State Market Regulation, Beijing, China
[m] Henan Key Laboratory of Tumor Epidemiology, Zhengzhou University, Zhengzhou, Henan, China
[n] State Key Laboratory of Esophageal Cancer Prevention & Treatment, Zhengzhou University, Zhengzhou, Henan, China

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ABSTRACT

Objectives: The aim of this study was to evaluate the combined prognostic value of calf circumference (CC) and serum albumin on mortality in patients with cancer cachexia aged ≥65 years.
Methods: This multicenter cohort study involved 5322 older patients in hospital with cancer cachexia. The combined indicator of CC and albumin was defined as the calf circumference-albumin (CCA) index. Harrell's C index, a time-dependent receiver operating characteristic curve analysis, was used to assess the prognostic performance of the CCA index and other indices. The optimal thresholds method was used to determine the cutoff values of CC and albumin, and the association between the CCA index and all-cause mortality was assessed using Kaplan-Meier analysis and Cox proportional hazard regression models.
Results: A total of 3875 men and 1447 women with a mean age of 72.0 years (range: 68.0–78.0 years) and a mean follow-up time of 55.0 months (range: 25.0–85.0 months) were included in the study. A total of 1269 patients were classified into the low CCA index group (0 score) by the optimal thresholds method. In the overall population, the CCA index showed better differentiating power at predicting mortality in older patients with cancer cachexia compared with CC or albumin alone (C index = 0.639; 95% CI: 0.612–0.666; $P < 0.05$). The time-dependent receiver operating characteristic curve showed that the CCA index had the highest prognostic value of all the measures studied ($P < 0.05$). In the overall population, male and female patients with a high CCA index (2 score) showed better performance than those with a low CCA index (0 or 1 score).
Conclusions: The CCA index could significantly predict the mortality of older patients with cancer cachexia, which might provide renewed assistance for future clinical management.

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*Corresponding author. Tel.: 0086-0371-67781454.
E-mail address: sch16@zzu.edu.cn (C. Song).

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Introduction

Cachexia is a multifactorial syndrome characterized by persistent loss of skeletal muscle mass (with or without loss of fat mass) that cannot be fully reversed with conventional nutritional support, leading to poor outcomes [1]. According to the World Health Organization, in 2020, there were approximately 10 million deaths as a result of different types of cancers—nearly one in six all-cause deaths. Cachexia has a high incidence and is associated with more than 50% of patients with cancer [2]. In China, approximately 37% of patients with cancer suffer from cachexia, and the top three cancers with a high prevalence rate include pancreatic cancer (62.8%), gastric cancer (56.4%), and esophageal cancer (51.8%). Prevalence in men is higher than in women (40.5% versus 32.7%), and the prevalence of cachexia is highest overall in northwest China (50.4%) [3].

Throughout the world, aging is an inevitable problem. Cancer and cancer cachexia are more likely to co-occur in individuals over 65 years of age, leading to increased morbidity and mortality. Thus, in this population mortality is higher than in patients with cancer in general [4], and cancer cachexia has been found in approximately 65% of older patients in studies [5]. The association between cachexia and cancers may be due to the fact that cachexia is always diagnosed at an advanced stage of cancer. It is related to the decline of food and nutrient intake, digestion and absorption ability, and is difficult to cure. Relevant studies have shown that cancer cachexia has a relatively high incidence at the end of any type of cancer [6]. If a new method could be developed to detect patients with cancer cachexia earlier, before the cancer progresses, it may be possible to improve the prognosis of patients with cancer and improve survival rates. Therefore, there is an urgent need to determine new indicators for predicting the prognosis of patients with cancer cachexia.

Malnutrition is very common in older patients with cancer [7], and all patients with cancer cachexia suffer from malnutrition [8,9]. The Asian Working Group for Sarcopenia added calf circumference (CC) to the diagnostic criteria for sarcopenia in 2019 [10] as the high success of CC in detecting lean body mass and sarcopenia of the extremities was confirmed. In Asian populations CC is positively associated with skeletal muscle mass and skeletal muscle index in the extremities, and could be used as a proxy for muscle mass in the diagnosis of sarcopenia [11–13].

Increased systemic inflammation is associated with frailty in the elderly, which in turn leads to increased mortality [14]. In patients with cancer cachexia, albumin levels are inversely associated with 1-year mortality, which could be an independent protective factor [15]. Albumin is an important marker of inflammation among many serum markers in aged populations [16]. Albumin is also included in many inflammatory indicators, such as the prognostic nutritional index (PNI) [17], nutritional risk index (NRI) [18], albumin-globulin ratio (AGR) [19], controlling nutritional status (CONUT) [20], and the C-reactive protein–albumin–lymphocyte (CALLY) index [21]. Inflammation and nutrition status affect the incidence and prognosis of cancer [22]; therefore, it is important to screen out appropriate prognostic indicators in patients with cancer, such as the combination of handgrip strength (HGS) and the cachexia index (CXI) [23], as well as the combination of triceps skinfold (TSF) and albumin measurements to form a new indicator, the triceps skinfold-albumin index [24]. From these studies, these combined indices may have better prognostic value.

The aged are one of the most vulnerable groups, and there are many problems related to nutrition and sarcopenia, which in turn aggravate diseases associated with cancer cachexia in the elderly, leading to complications in this population [25]. CC is associated with survival rates of older patients, and albumin is an inflammatory marker in patients with cancer. However, the prognostic value of the combination of the two in older patients with cancer cachexia remains to be explored. The aim of this study was to evaluate the combined prognostic value of CC and serum albumin on mortality in patients aged ≥65 years with cancer cachexia.

Methods

Study design and population

The Investigation on Nutrition Status and its Clinical Outcome of Common Cancers (INSCOC) project was a hospital-based, multicenter, observational cohort study (chictr.org.cn, ChiCTR1800020329). Complete information on this project has been described in detail in previous articles. INSCOC enrolled more than 50 000 patients with cancer from more than 100 hospitals in more than 100 districts from 2013 to 2020. Once the patients were enrolled, they would be followed up. Informed consent was signed prior to inclusion and the study was approved by institutional review boards at all study sites. This study conformed to the Declaration of Helsinki and all data were analyzed anonymously. In our study we included patients older than 65 years of age who were followed up at least once and excluded others without critical data such as CC, albumin, and so on. Finally, 5322 patients were enrolled in the study, as shown in Figure S1.

Data acquisition

The researchers collected the following information by interview and physical examination within the first 48 hours of admission: gender, age, smoking status, alcohol status, family history, diabetes status, hypertension status, tumor, node, metastasis (TNM) stage, Karnofsky performance status (KPS) score, scored patient-generated subjective global assessment (PG-SGA) [26], Nutritional Risk Screening 2002 (NRS2002) [27], CC (left), albumin, mid-arm circumference (MAC), TSF, body mass index (BMI), HGS, mid-arm muscle circumference (MAMC), weight loss in 6 months, and other significant information.

Based on Chinese standards, BMI was divided into four categories: underweight (<18.5 kg/m^2), normal (18.5 to <24 kg/m^2), overweight (24 to <28 kg/m^2), or obese (≥28 kg/m^2) [28]. The PG-SGA score was also divided into four categories: 1 (0–1), 2 (2–3), 3 (4–8), and 4 (≥9). For the NRS2002 score, the higher the score, the worse the survival status.

Some information was collected by browsing the electronic medical record system. Biochemical test indices were measured within 48 h after admission using serum to measure albumin, prealbumin, total protein, creatinine, urea nitrogen, total bilirubin, C-reactive protein, total cholesterol, blood sugar, high- and low-density lipoprotein cholesterol, hemoglobin, leukocytes, neutrophils, platelets, etc. During CC measurement, the person being examined was placed in a sitting position with their knees and hips bent 90 degrees and feet naturally on the ground. Trained investigators placed a tape around the calf to obtain the maximum circumference twice and this was averaged. Patients with calf edema were excluded to ensure accuracy [29].

Follow-up and main outcome

The researchers followed up annually by telephone interviews or face-to-face communication to collect the survival status of patients with cancer cachexia. For this study, the main outcome was all-cause mortality at any time after enrollment. The overall

survival (OS) time was calculated as the time from first admission to the date of death or the last valid follow-up, or April 2020.

Definition of cancer cachexia

Three diagnostic criteria exist for cancer cachexia [1]: weight loss >5% over the past 6 months (in the absence of simple starvation); or BMI <20 kg/m^2 and any degree of weight loss >2%; or mid-upper–arm muscle area by anthropometry (<5th percentile; men <23.25 cm^2, women <18.75 cm^2); and any degree of weight loss >2%. Mid-upper–arm muscle area was used as a simple screening tool to diagnose skeletal muscle mass index, especially in men with sarcopenia, and was calculated by the following method: mid-upper–arm muscle area (cm^2) = (MAC (cm) - (3.14 × TSF (cm))^2/(4 × 3.14) [30].

Definition and grouping of the CCA index

First, using the optimal thresholds methods, CC and albumin were divided into two categories by gender, respectively. In this study focusing on the calf circumference-albumin (CCA) index, we combined the left CC level and albumin level, as the difference between the left CC and right CC was statistically significant. The optimal thresholds method was widely used for the continuous factor for OS.

Statistical analysis

First, univariate Cox regression analysis was used to analyze all variables and corresponding *P* values were obtained. Variables with $P < 0.05$ were included from multivariate Cox regression analysis to obtain meaningful variables. Because of the large number of variables and severe collinearity among variables, least absolute shrinkage and selection operator (LASSO) processing was performed to eliminate variables with severe collinearity and incorporate qualified variables into the model for subsequent analysis (Fig. S2A, B). The optimal thresholds method was used to determine the cutoff values of CC and albumin in males and females, respectively. After this, the population was divided into four groups: CC low, CC high, albumin low, and albumin high. Each group was assigned a low level of 0 and a high level of 1, combining the CC and albumin to form a combined indicator, the CCA index. Based on the CCA index, the population was divided into three groups: 0 (low CC and low albumin), 1 (low CC and high albumin, or high CC and low albumin), and 2 score (high CC and high albumin). The baseline characteristics of the population were analyzed according to the groups. Harrell's C index was used to predict the predictive ability and prognosis value of the CCA index in the population and this was compared with other prognostic indices such as PNI, NRI, and SII. Note that NRI = (1.519 × serum albumin, g/L) + (41.7 × present); PNI = 10 × serum albumin (g/dL) + 0.005 × total lymphocyte count (mm^3); and SII = peripheral platelet × neutrophil/lymphocyte counts [31]. The ability of the CCA index to determine prognosis was compared and evaluated by calculating the C index (calculated using R software, version 4.3.1) and the receiver operating characteristic (ROC) curve. The time-dependent C index improves its robustness through self-service cross-validation of 1000 samples and 10 iterations of 10-fold cross-validation. Kaplan-Meier curve analysis was used to analyze population, total population, male, female, patients with colorectal cancer, lung cancer, gastric cancer, and esophageal cancer groups.

All of the above analyses were performed using R software, version 4.3.1.

Results

Cohort overview

Among the 33 614 patients investigated, 5322 elderly patients with cancer cachexia were enrolled in this study (Fig. S1), of whom 1447 were female and 3875 were male. The median age of the older patients was 72.0 years (range: 68.0–78.0 years). A total of 1903 deaths were observed during a median survival time of 55.0 months (range: 25.0–85.0 months). Cancer types with the highest incidence included colorectal (21.0%), lung (21.0%), and gastric (21.0%). There were 1371 (26.0%) underweight patients, 3230 (61.0%) normal-weight patients, 671 (13.0%) overweight patients, and 50 (0.9%) obese patients. Additionally, 1338 (25.0%) patients were at clinical stage Ⅲ and 1380 (26.0%) patients at stage Ⅳ (Table 1).

Association of CC or albumin with OS

The results of univariate and multivariate analysis showed that most baseline characteristics were associated with an increased risk of death, and that CC and albumin were independent prognostic factors in older patients with cancer cachexia (Table S1).

Based on the optimal thresholds method, optimal thresholds for the CC index were determined to be 28.8 cm for females and 30.6 cm for males (Fig. 1A, C), with optimal thresholds for albumin determined to be 44.1 g/L for females and 36.4 g/L for males (Fig. 1B, D). Based on these thresholds, females and males were classified into low CC index, high CC index, low albumin, and high albumin groups. Kaplan-Meier curves showed that the low CC index and low albumin groups were associated with increased mortality across both gender strata (both $P < 0.001$, Fig. 2E–H).

Figure 1 shows that both low CC and low albumin were also risk factors for the OS of older patients with cancer cachexia. Therefore, it was possible for us to establish a joint indicator to predict the prognostic value.

Relationship between CCA index and clinical characteristics

To determine whether the combination of CC and albumin could potentially provide better stratification of the prognosis of older patients with cancer cachexia, we constructed a new score system: the CCA score. This study assigned low CC a value of 0, low albumin a value of 0, high CC a value of 1, and high albumin a value of 1. The CC and albumin values were then added together. Ultimately, three groups emerged: a 0 score group (low CC + low albumin), a 1 score group (low CC + high albumin or high CC + low albumin), and a 2 score group (high CC + high albumin).

Most characteristics were shown to be statistically significant via the comparison of group characteristics, such as gender, age, smoking, alcohol, TNM stages, therapy methods, KPS, total protein, albumin, prealbumin, total bilirubin, hemoglobin, leukocytes, neutrophils, lymphocytes, erythrocytes, BMI, MAC, TSF, HGS, MAMC, CC, weight loss in 6 months, cancer site, PG-SGA stage, NRS2002, prognostic scores, and so on (all $P < 0.05$) (Table 1).

Prognostic value of the CCA index

Harrell's C index of the CCA index was statistically compared with those calculated for albumin, CC, NRS2002, PG-SGA, TSF, BMI, NRI, PNI, SII in the overall population, sex, and patient score of 0, 1, or 2. The results showed that the CCA index had the highest prognostic value in the overall population, with a C

Table 1
Baseline characteristics of the study population

Characteristic	Overall (n = 5322)	Calf circumference-albumin index			*P* value
		0 score (n = 1269)	1 score (n = 2395)	2 score (n = 1658)	
Gender, n (%)					<0.001
Male	3875 (72.8)	853 (67.2)	1520 (63.5)	1502 (90.6)	
Female	1447 (27.2)	416 (32.8)	875 (36.5)	156 (9.4)	
Age (years)	72.0 (68.0–78.0)	74.0 (69.0–79.0)	72.0 (68.0–78.0)	71.0 (68.0,76.0)	<0.001
Family history, yes, n (%)	620 (12.0)	131 (10.0)	257 (11.0)	232 (14.0)	0.002
Smoking, yes, n (%)	2894 (54.0)	661 (52.0)	1148 (48.0)	1085 (65.0)	<0.001
Alcohol, yes, n (%)	1422 (27.0)	311 (25.0)	564 (24.0)	547 (33.0)	<0.001
TNM stage, n (%)					<0.001
Ⅰ	382 (7.2)	60 (4.7)	168 (7.0)	154 (9.3)	
Ⅱ	884 (17.0)	158 (12)	387 (16)	339 (20)	
Ⅲ	1338 (25.0)	308 (24)	618 (26)	412 (25)	
Ⅳ	1380 (26.0)	390 (31)	608 (25)	382 (23)	
Operation, yes, n (%)	1974 (37.0)	384 (30.0)	916 (38.0)	674 (41.0)	<0.001
Radiation or chemotherapy, yes, n (%)	2256 (42.0)	537 (42.0)	1013 (42.0)	706 (43.0)	0.982
KPS	90.0 (80.0–90.0)	80.0 (70.0–90.0)	90.0 (80.0–90.0)	90.0 (80.0–90.0)	<0.001
Total protein (g/L)	66.9 (61.7–72.0)	62.7 (57.7–67.9)	66.3 (61.1–71.4)	70.1 (66.1–74.6)	<0.001
Albumin (g/L)	37.5 (33.8–41.1)	33.3 (30.2–35.6)	36.7 (33.4–40.0)	41.1 (38.8–44.0)	<0.001
Prealbumin (mg/L)	61.0 (0.0–188.9)	29.0 (0.0–141.1)	68.0 (0.0–185.0)	100.0 (0.0–224.0)	<0.001
Hemoglobin (g/L)	118.0 (103.3–132.0)	106.0 (92.0–120.0)	116.0 (103.6–128.0)	129.0 (116.0–141.0)	<0.001
Leukocyte ($*10^9$/L)	5.9 (4.6–7.8)	6.2 (4.6–8.7)	5.8 (4.5–7.6)	5.9 (4.7–7.4)	<0.001
Neutrophil ($*10^9$/L)	3.9 (2.7–5.7)	4.4 (2.8–6.9)	3.8 (2.6–5.7)	3.6 (2.7–5.1)	<0.001
Lymphocyte ($*10^9$/L)	1.3 (1.0–1.8)	1.2 (0.8–1.7)	1.3 (1.0–1.8)	1.4 (1.1–1.9)	<0.001
Erythrocyte ($*10^{12}$/L)	4.0 (3.5–4.4)	3.7 (3.2–4.1)	3.9 (3.5–4.3)	4.3 (3.9–4.7)	<0.001
Platelet ($*10^9$/L)	211.0 (156.0–273.3)	223.0 (158.0–295.0)	211.0 (155.0–277.0)	204.0 (156.0–255.0)	<0.001
BMI category, n (%)					<0.001
Underweight (<18.5 kg/m^2)	1371 (26.0)	700 (55)	535 (22)	136 (8.2)	
Normal (18.5–23.9 kg/m^2)	3230 (61.0)	534 (42)	1559 (65)	1137 (69)	
Overweight (24–27.9 kg/m^2)	671 (13.0)	33 (2.6)	284 (12)	354 (21)	
Obesity (≥28 kg/m^2)	50 (0.9)	2 (0.2)	17 (0.7)	31 (1.9)	
MAC (cm)	24.5 (3.3)	22.1 (3.2)	24.9 (3.3)	26.3 (3.5)	<0.001
TSF (cm)	10.0 (6.1)	8.9 (5.5)	11.2 (6.6)	11.6 (6.3)	<0.001
HGS (kg)	23.0 (9.7)	19.0 (8.0)	23.0 (10.0)	28.0 (11.0)	<0.001
MAMC (cm)	21.4 (2.7)	27.5 (2.4)	31.4 (3.3)	33.7 (2.5)	<0.001
CC (cm)	31.0 (3.2)	19.3 (3.1)	21.3 (3.2)	22.6 (3.4)	<0.001
Cancer site, n (%)					<0.001
Nasopharynx	164 (3.1)	47 (3.7)	58 (2.4)	59 (3.6)	
Esophagus	944 (18.0)	212 (17)	391 (16)	341 (21)	
Stomach	1107 (21.0)	283 (22)	467 (19)	357 (22)	
Colorectum	1133 (21.0)	205 (16)	534 (22)	394 (24)	
Liver	225 (4.2)	72 (5.7)	110 (4.6)	43 (2.6)	
Pancreas	130 (2.4)	38 (3.0)	61 (2.5)	31 (1.9)	
Lung	1094 (21.0)	283 (22)	472 (20)	339 (20)	
Breast	101 (1.9)	16 (1.3)	67 (2.8)	18 (1.1)	
Gynecological cancer	135 (2.5)	22 (1.7)	97 (4.0)	16 (0.9)	
Other cancer	206 (3.9)	53 (4.2)	94 (3.9)	59 (3.6)	
PG-SGA, n (%)					<0.001
0–1	108 (2.0)	14 (1.1)	52 (2.2)	42 (2.5)	
2–3	491 (9.2)	37 (2.9)	225 (9.4)	229 (14)	
4–8	1829 (34.0)	299 (24)	814 (34)	716 (43)	
≥9	2894 (54.0)	919 (72)	1304 (54)	671 (40)	
NRS2002, n (%)					<0.001
1	751 (14.0)	81 (6.4)	344 (14.0)	326 (20)	
2	908 (17.0)	121 (9.5)	445 (19)	342 (21)	
3	775 (15.0)	136 (11)	365 (15)	274 (17)	
4	1737 (33.0)	549 (43)	758 (32)	430 (26)	
5	758 (14.0)	306 (24)	310 (13)	142 (8.6)	
6	55 (1.0)	24 (1.9)	26 (1.1)	5 (0.3)	
Prognostic indices					
PNI	3757.6 (3391.0–4121.5)	3339.3 (3029.4–3573.8)	3673.5 (3353.4–4007.4)	4122.9 (3892.2–4405.6)	<0.001
NRI	98.7 (93.0–104.1)	92.1 (87.4–95.8)	97.4 (92.4–102.5)	104.1 (100.6–108.5)	<0.001
SII	588.0 (317.0–1129.9)	804.9 (375.6–1639.7)	580.0 (306.4–1120.1)	509.4 (284.9–863.1)	<0.001
Cost (10000CNY)	1.9 (1.0–4.9)	1.9 (1.0–4.8)	1.9 (1.0–4.7)	1.8 (0.9–5.4)	0.401

Abbreviations: BMI, body mass index; CC, calf circumference; CNY, Chinese Yuan; HGS, hand grip strength; KPS, Karnofsky Performance Status; MAC, mid-arm circumference; MAMC, mid-arm muscle circumference; NRI, the nutritional risk index; NRS 2002, Nutritional Risk Screening 2002 score; PG-SGA, Patient-Generated Subjective Global Assessment score; PNI, prognostic nutritional index; SII, systemic immune-inflammation index; TNM, tumor, node, metastasis; TSF, triceps skinfold thickness.
Data are represented as median (25th percentile, 75th percentile) or number (percentage).

index of 0.639 (95% CI: 0.612–0.666) compared with albumin (0.567; 95% CI: 0.553–0.581), CC (0.519; 95% CI: 0.505–0.533), NRS2002 (0.551; 95% CI: 0.537–0.565), PG-SGA (0.569; 95% CI: 0.555–0.583), TSF (0.527; 95% CI: 0.513–0.541), BMI (0.521; 95% CI: 0.507–0.535), NRI (0.567; 95% CI: 0.553–0.581), PNI (0.567; 95% CI: 0.553–0.581), and SII (0.536; 95% CI: 0.522–0.550) (all $P < 0.001$) (Table 2). In the sex-specific analysis, the CCA index showed a higher prognostic value than

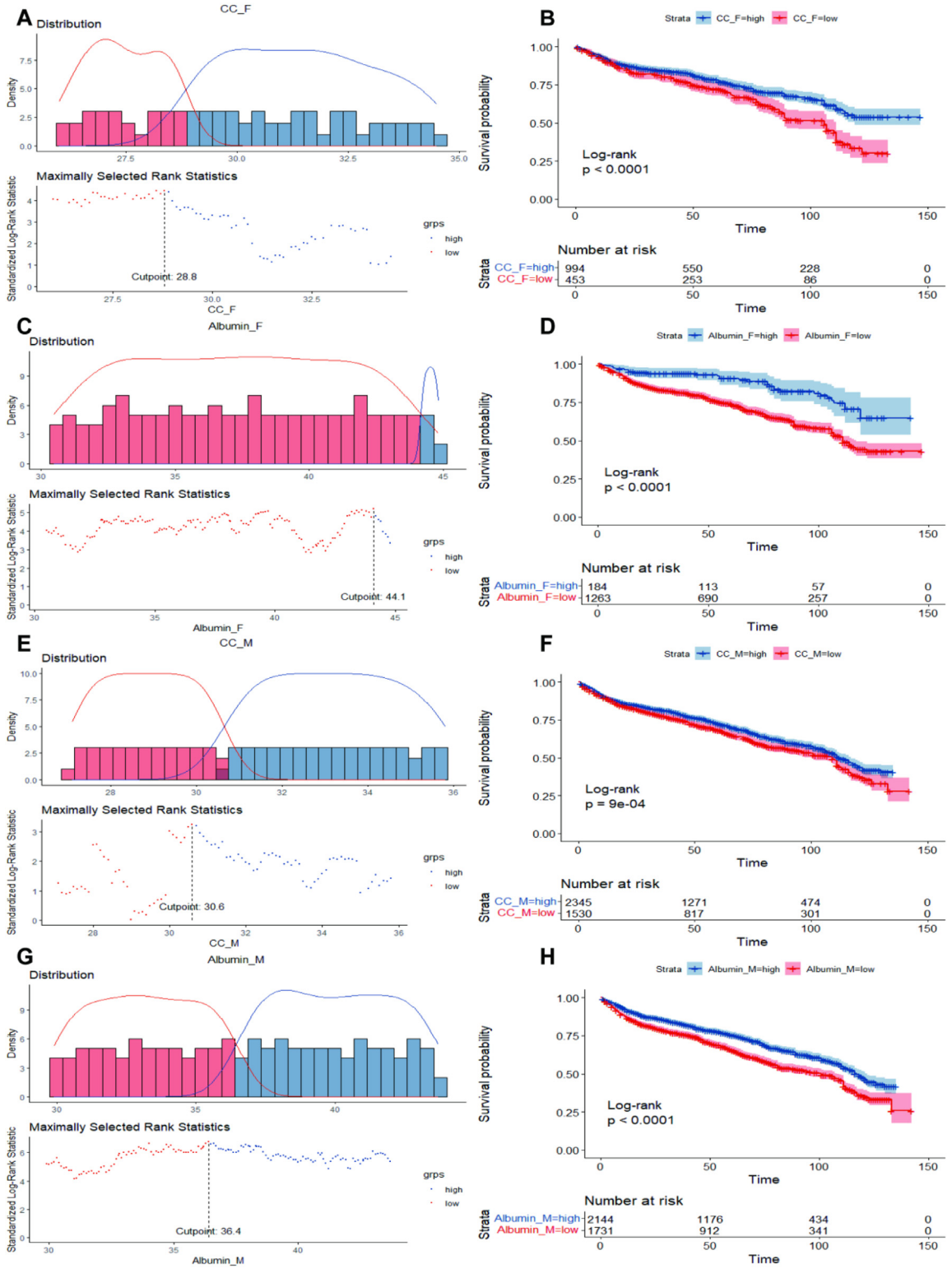

Figure 1. (A) Cutoff value of CC in females. (B) Kaplan-Meier curves of CC in females. (C) Cutoff value of albumin in females. (D) Kaplan-Meier curves of albumin in females. (E) Cutoff value of CC in males. (F) Kaplan-Meier curves of CC in males. (G) Cutoff value of albumin in males. (H) Kaplan-Meier curves of albumin in males. CC, calf circumference.

albumin, CC, NRS2002, PG-SGA, TSF, BMI, NRI, PNI, and SII (Fig. 2). Additionally, the CCA index had the best prognostic value in the patients with a score of 0 (0.597; 95% CI: 0.572–0.622), 1 (0.611; 95% CI: 0.591–0.631), and 2 (0.608; 95% CI: 0.581–0.635). Other evaluated parameters had lower C index values than the CCA index. This was repeated in males and females, respectively, and consistent results were obtained in the other three groups.

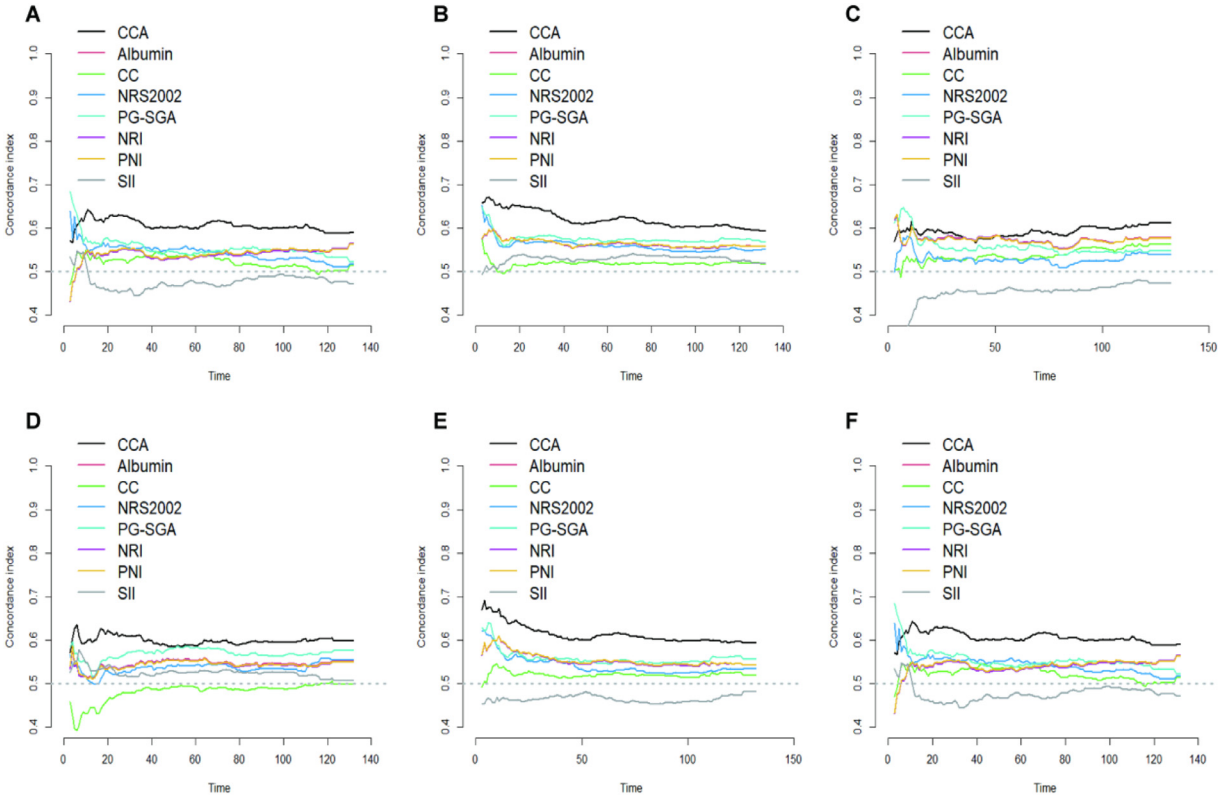

Figure 2. Time-dependent C index. (A) Time-dependent C index curves in the overall population. (B) Time-dependent C index in men. (C) Time-dependent C index curves in women. (D) Time-dependent C index at 0 score. (E) Time-dependent C index curves at 1 score. (F) Time-dependent C index curves at 2 score. BMI, body mass index; CC, calf circumference; CCA, calf circumference-albumin index; NRI, nutritional risk index; NRS 2002, Nutritional Risk Screening 2002 score; PG-SGA, Patient-Generated Subjective Global Assessment score; PNI, prognostic nutritional index; SII, systemic immune-inflammation index; TSF, triceps skinfold thickness

Kaplan-Meier and ROC curve analysis

As shown in Figure S3, in the overall population (Fig. S3A) and among males (Fig. S3B), females (Fig. S3C), and patients with scores of 0 (Fig. S3D), 1 (Fig. S3E), and 2 (Fig. S3F), the CCA index showed the highest values, revealing that the CCA index was a better predictor of older patients with cancer cachexia, respectively. The ROC values of the CCA index were higher than albumin, CC, NRS2002, PG-SGA, NRI, PNI, and SII values across the various subgroups.

Kaplan-Meier curves demonstrated that patients with a lower CCA index had a poorer OS than those in the higher CCA index group in the overall population ($P < 0.001$). Additionally, we replicated this analysis in different groups. The results show that the association observed in the overall population was similar between males and females, as well as those with lung cancer, colorectal cancer, gastric cancer, and other cancers (Figs. 3 and S4; all $P < 0.05$).

Association between CCA index and hazard ratio for mortality of patients with cancer cachexia and sensitivity analysis

The results of the Cox proportional risk model analysis are shown in Table 3. In this study, the CCA index was an independently protective factor. Thus, we used the group with the highest score as the reference to explore the risk of mortality in the lower score group, which is clearer and easier to understand. After

Table 2
Discrimination performance of the CCA index compared with albumin, CC, NRS2002, PG-SGA, TSF, BMI, NRI, PNI, and SII

Index	Harrell's C index (95% CI)						*P* value
	Overall (n = 5322)	Female (n = 1447)	Male (n = 3875)	0 score (n = 1269)	1 score (n = 2395)	2 score (n = 1658)	
CCA	0.639 (0.612–0.666)	0.590 (0.563–0.617)	0.620 (0.604-0.636)	0.597 (0.572–0.622)	0.611 (0.591–0.631)	0.608 (0.581–0.635)	<0.001
Albumin	0.567 (0.553–0.581)	0.572 (0.545–0.599)	0.563 (0.547–0.579)	0.546 (0.519–0.573)	0.552 (0.530–0.574)	0.541 (0.514–0.568)	<0.001
CC	0.519 (0.505–0.533)	0.538 (0.511–0.565)	0.518 (0.502–0.534)	0.487 (0.460–0.514)	0.520 (0.498–0.542)	0.525 (0.498–0.552)	<0.001
NRS2002	0.551 (0.537–0.565)	0.541 (0.512–0.570)	0.554 (0.538–0.570)	0.536 (0.511–0.561)	0.537 (0.515–0.559)	0.544 (0.517–0.571)	<0.001
PG-SGA	0.569 (0.555–0.583)	0.553 (0.524–0.582)	0.574 (0.558–0.590)	0.571 (0.546–0.596)	0.554 (0.532–0.576)	0.551 (0.524–0.578)	<0.001
TSF	0.527 (0.513–0.541)	0.521 (0.492–0.550)	0.524 (0.508–0.540)	0.530 (0.505–0.555)	0.518 (0.496–0.540)	0.507 (0.480–0.534)	<0.001
BMI	0.521 (0.507–0.535)	0.533 (0.504–0.562)	0.517 (0.501–0.533)	0.503 (0.478–0.528)	0.501 (0.479–0.523)	0.494 (0.467–0.521)	<0.001
NRI	0.567 (0.553–0.581)	0.572 (0.545–0.599)	0.563 (0.547–0.578)	0.544 (0.517–0.571)	0.552 (0.530–0.574)	0.541 (0.514–0.568)	<0.001
PNI	0.567 (0.553–0.581)	0.571 (0.544–0.598)	0.564 (0.548–0.580)	0.545 (0.518–0.572)	0.553 (0.533–0.573)	0.543 (0.516–0.570)	<0.001
SII	0.536 (0.522–0.550)	0.456 (0.427–0.485)	0.532 (0.516–0.548)	0.524 (0.497–0.551)	0.464 (0.444–0.484)	0.472 (0.447–0.497)	<0.001

BMI, body mass index; CC, calf circumference; CCA, calf circumference-albumin index; NRI, nutritional risk index; NRS 2002, Nutritional Risk Screening 2002 score; PG-SGA, Patient-Generated Subjective Global Assessment score; PNI, prognostic nutritional index; SII, systemic immune-inflammation index; TSF, triceps skinfold thickness.

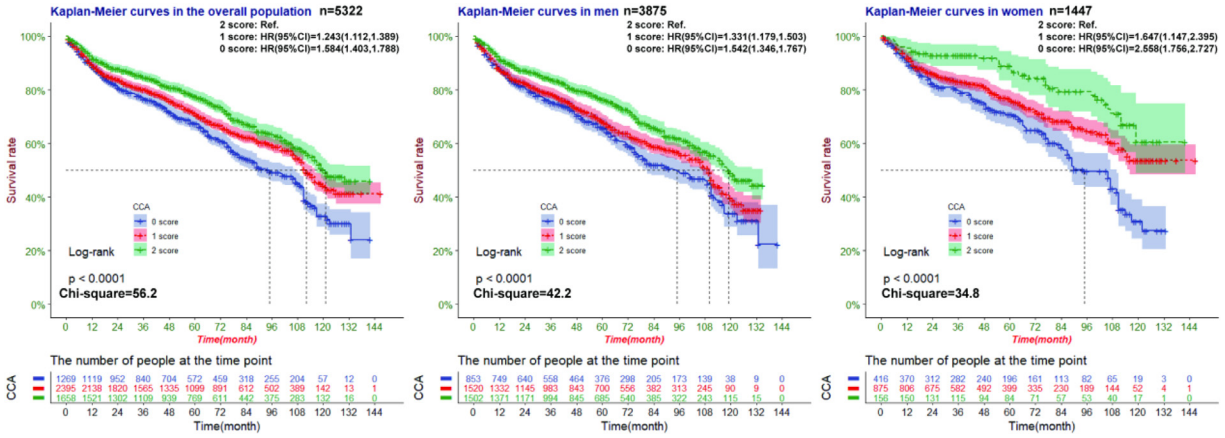

Figure 3. Analysis of the association of the calf circumference-albumin index with survival. (A) Kaplan-Meier curves in the overall population. (B) Kaplan-Meier curves in men. (C) Kaplan-Meier curves in women.

adjusting for sex, age, smoking, and other factors in Model 2, the lowest CCA score in the overall population was independently associated with an increased risk of death (hazard ratio [HR] = 1.553; 95% CI: 1.364–1.770). Consistent results were observed in males (HR = 1.478; 95% CI: 1.278–1.708) and females (HR = 2.233; 95% CI: 1.520–3.283), respectively. The sensitivity analysis, which excluded OS of less than 3 months, showed a consistent outcome.

Discussion

With a sample size of 5322 individuals (Fig. S1), this study was a multicenter, large-scale, multi-hospital study of patients over 65 years of age. Based on evidence from previous studies and this study, a joint indicator of the CCA index was proposed and its important prognostic value was confirmed in older patients with cancer cachexia. This study is the first to combine CC and albumin to evaluate the prognosis of older patients with cancer cachexia. Regarding this combined indicator, CC represents the muscle mass of older patients with cancer cachexia, and albumin partly provides information on inflammation and nutrition. Compared with a higher CCA index, a lower CCA index was associated with advanced TNM stage, long hospital stays, and shorter survival time. Compared with CC, albumin, PG-SGA, NRS2002, PNI, NRI, and SII, the CCA index had the best prognostic value and was able to predict patient outcomes in both the population as a whole and in male and female, and 0, 1, and 2 score groups. The lowest CCA score in the overall population was independently associated with an increased risk of death (Table 3).

This study used the method of optimal thresholds to obtain CC and albumin cutoff values in males and females, respectively, which can have certain implications for subsequent research. A previous study showed that higher CC predicted better survival outcomes for older patients with cancer cachexia [32]. Some studies also showed that CC played an important role in patients with cancer cachexia, which can reduce mortality [33,34]. However, the standard method of measuring human muscle mass was too complex. Under limited clinical conditions, more and more studies are using CC as a measure of human skeletal muscle and cancer cachexia [35]. Some studies have also demonstrated that albumin could predict the mortality of older patients with cancer cachexia [36,37]. Systemic inflammation affects the metabolic process of proteins in the liver, stimulates the production of inflammatory substances, increases protein content in the acute phase, reduces the synthesis of albumin, and increases the degradation of albumin, ultimately leading to a decline in albumin content [38]. In an inflammatory state protein synthesis is inhibited, which activates proteolysis and sarcopenia [39]. Albumin can reflect the immune

Table 3
Association between CCA and HR for mortality of patients with cancer cachexia and sensitivity analysis

CCA		Overall population (n = 5322), HR (95% CI)						Sensitivity analysis (n = 5156), HR (95% CI)	
		Model 0* HR (95% CI)	*P* value	Model 1† HR (95% CI)	*P* value	Model 2‡ HR (95% CI)	*P* value	Model 3§ HR (95% CI)	*P* value
Overall	2 Score	Ref.		Ref.		Ref.		Ref.	
	1 Score	1.243 (1.112–1.389)	<0.001	1.302 (1.162–1.460)	<0.001	1.252 (1.115–1.406)	<0.001	1.199 (1.063–1.352)	0.003
	0 Score	1.584 (1.403–1.788)	<0.001	1.616 (1.427–1.830)	<0.001	1.553 (1.364-1.770)	<0.001	1.483 (1.296–1.698)	<0.001
Male	2 Score	Ref.		Ref.		Ref.		Ref.	
	1 Score	1.331 (1.179–1.503)	<0.001	1.312 (1.161–1.483)	<0.001	1.264 (1.115–1.432)	<0.001	1.206 (1.059–1.374)	0.005
	0 Score	1.542 (1.346–1.767)	<0.001	1.508 (1.315–1.730)	<0.001	1.478 (1.278–1.708)	<0.001	1.397 (1.202–1.6 24)	<0.001
Female	2 Score	Ref.		Ref.		Ref.		Ref.	
	1 Score	1.647 (1.147–2.395)	<0.001	1.605 (1.110–2.321)	0.012	1.558 (1.077–2.256)	0.019	1.521 (1.044–2.217)	0.029
	0 Score	2.558 (1.756–2.727)	<0.001	2.346 (1.604–3.430)	<0.001	2.233 (1.520–3.283)	<0.001	2.198 (1.485–3.256)	<0.001

CCA, calf circumference-albumin index; CI, confidence interval; PNI, prognostic nutritional index; TSF, triceps skinfold thickness.
*Model 0 is the unadjusted crude model.
†Model 1 is adjusted by gender and age.
‡Model 2 is adjusted by gender, age, smoking, prealbumin, C-reactive protein, weight loss in 6 months, age over 70 years.
§Model 3 is adjusted for all covariates in Model 3, but excludes patients that died within the first 3 months after enrollment.

status of the body through $CD8^+$ cells. Studies have shown that, compared with a low level of albumin, a high level of albumin can inhibit distant metastasis of non-small-cell lung cancer and promote improvements in prognosis [40].

The combined index may have a better prognostic value. In this study on older patients with cancer cachexia, CCA had the highest C index (0.639; 95% CI: 0.612–0.666) compared with CC, albumin, PNI, NRI, and SII. Similar conclusions were reached in other studies on patients with cancer cachexia; for example, the triceps skinfold-albumin index showed a better discriminative performance to predict all-cause mortality than TSF or albumin alone [24]. Additionally, AGR, compared with other malnutrition evaluation tools, was able to effectively stratify the prognosis of patients with cancer cachexia [41]. In older patients, such as the combination of CC and albumin [42], the combination of Framingham Risk Score and CC, both combined indicators could better predict the all-cause mortality [29]. In patients with lung cancer, the prognostic indicator advanced lung cancer inflammation index was superior to other inflammation/nutrition-based indicators [31]. The CALLY index was independently associated with OS in patients with colorectal cancer and showed higher prognostic than classical factors [21]. The combination of CC and SII was also able to predict better prognostic value [43]. SII is an independent prognostic factor for patients with cancer and cardiovascular disease, and is significantly associated with the risk of death [17]. All of these studies showed that combined indices had better prognostic values than a single index. In this study, we found that a lower CCA index was associated with worse clinical outcomes, which may also suggest that CCA is a better prognostic factor in older patients with cancer cachexia.

Our study still has some limitations. First, the study selected older patients with cancer cachexia, so the results may vary among all patients with cancer and may not be applicable to all populations. Second, other clinical indicators related to inflammation were not measured, which may be confounding factors in this study. The study only included Asian populations, and the impact of the CCA index on prognosis needs to be reassessed while trialing this method in other ethnic groups, such as American or African individuals, due to differences in body composition between Asian and Western populations [10]. The C index showed that the highest CCA index value was 0.639, and other evaluated parameters also had lowers Harrel's C index values, which could be related to an insufficient sample size. Another explanation may be that the C index in this study analyzed a single indicator without considering other factors. Additionally, CC and albumin were measured only at admission, and more frequent assessment could more accurately predict prognosis in older patients with cancer cachexia. However, measurement of CC is more convenient, simple, non-invasive, and easy to accept, and cannot be replaced by machine inspection. It has a wide range of applications and is very easy to achieve in general hospitals and medical institutions. The value of CC may change in the course of disease progression in older patients with cancer cachexia, and timely monitoring is needed to evaluate prognostic benefits and outcomes accordingly. In future, it would be necessary to develop more convenient, faster, and accurate indicators that can reflect signs of obesity and muscle mass in patients to evaluate their cancer prognosis. In this study, due to the large number of research factors the model was adjusted during LASSO analysis and the variables with serious collinearity removed to make the results more accurate. INSCOC covered a multicenter, wide-ranging, and geographically representative cohort in China, which includes more than 100 territories across the country, and had a degree of generality; this study suggested that the CCA index as a combined indicator is of practical significance.

In summary, this study defines a new joint indicator, the CCA index, which combines information from two indicators, namely CC and albumin. This index can effectively reflect the nutritional, anthropometric, and inflammatory status of older patients with cancer cachexia, and it is also related to the subsequent survival status of patients. The CCA index is better than CC, albumin, PG-SGA, NRS2002, NRI, PNI, and SII alone at predicting mortality in older patients with cancer cachexia, both in the general population and in males and females. These results suggest that the CCA index may be a novel indicator that can provide effective prognostic information in older patients with malignant fluid and may provide a better approach for patient management.

Conclusion

The CCA index could significantly predict the mortality of older patients with cancer cachexia, which may provide new assistance for future clinical management.

Acknowledgments

All data were obtained from the Investigation on Nutrition Status and its Clinical Outcome of Common Cancers (INSCOC) project in China.

Ethical approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Medical Ethics Committee of First Affiliated Hospital of Sun yat-sen University (date: 2013-05-07, number: ChiCTR1800020329).

Consent to participate

Informed consent was obtained from all individual participants included in the study.

Declaration of competing interest

The authors declare that they have no conflicts of interest.

CRediT authorship contribution statement

Pengxia Guo: Writing – original draft, Software, Methodology, Conceptualization. **Hongxia Xu:** Resources, Investigation, Data curation. **Min Weng:** Resources, Investigation, Data curation. **Fuxiang Zhou:** Resources, Investigation, Data curation. **Wen Hu:** Resources, Investigation, Data curation. **Suyi Li:** Resources, Investigation, Data curation. **Yuan Lin:** Resources, Investigation, Data curation. **Chunling Zhou:** Resources, Investigation, Data curation. **Hu Ma:** Resources, Investigation, Data curation. **Wei Li:** Resources, Investigation, Data curation. **Jiuwei Cui:** Resources, Investigation, Data curation. **Haoqing Cheng:** Software, Formal analysis. **Saba Fida:** Software, Formal analysis. **Hanping Shi:** Writing – review & editing, Validation, Supervision, Conceptualization. **Chunhua Song:** Writing – review & editing, Validation, Supervision, Conceptualization.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.nut.2024.112594.

References

[1] Fearon K, Strasser F, Anker SD, Bosaeus I, Bruera E, Fainsinger RL, et al. Definition and classification of cancer cachexia: an international consensus. Lancet Oncol 2011;12:489–95.
[2] Suzuki H, Asakawa A, Amitani H, Nakamura N, Inui A. Cancer cachexia—pathophysiology and management. J Gastroenterol 2013;48:574–94.
[3] Li X, Hu C, Zhang Q, Wang K, Li W, Xu H, et al. Cancer cachexia statistics in China. Precis Nutr 2022;1. https://doi.org/10.1097/PN9.0000000000000008.
[4] Pal SK, Katheria V, Hurria A. Evaluating the older patient with cancer: understanding frailty and the geriatric assessment. CA Cancer J Clin 2010;60:120–32.
[5] Dunne RF, Roussel B, Culakova E, Pandya C, Fleming FJ, Hensley B, et al. Characterizing cancer cachexia in the geriatric oncology population. J Geriatr Oncol 2019;10:415–9.
[6] Baracos VE, Martin L, Korc M, Guttridge DC, Fearon KCH. Cancer-associated cachexia. Nat Rev Dis Primers 2018;4:17105.
[7] Zhang X, Edwards BJ. Malnutrition in older adults with cancer. Curr Oncol Rep 2019;21:80.
[8] Muscaritoli M, Anker SD, Argiles J, Aversa Z, Bauer JM, Biolo G, et al. Consensus definition of sarcopenia, cachexia and pre-cachexia: joint document elaborated by Special Interest Groups (SIG) "cachexia-anorexia in chronic wasting diseases" and "nutrition in geriatrics. Clin Nutr 2010;29:154–9.
[9] Zhang X, Tang M, Zhang Q, Zhang KP, Guo ZQ, Xu HX, et al. The GLIM criteria as an effective tool for nutrition assessment and survival prediction in older adult cancer patients. Clin Nutr 2021;40:1224–32.
[10] Chen LK, Woo J, Assantachai P, Auyeung TW, Chou MY, Iijima K, et al. Asian Working Group for Sarcopenia: 2019 Consensus Update on Sarcopenia Diagnosis and Treatment. J Am Med Dir Assoc 2020;21. 300−7.e2.
[11] Kawakami R, Murakami H, Sanada K, Tanaka N, Sawada SS, Tabata I, et al. Calf circumference as a surrogate marker of muscle mass for diagnosing sarcopenia in Japanese men and women. Geriatr Gerontol Int 2015;15:969–76.
[12] Lim WS, Lim JP, Chew J, Tan AWK. Calf circumference as a case-finding tool for sarcopenia: Influence of obesity on diagnostic performance. J Am Med Dir Assoc 2020;21:1359–61.
[13] Borges K, Artacho R, Jodar-Graus R, Molina-Montes E, Ruiz-Lopez MD. Calf circumference, a valuable tool to predict sarcopenia in older people hospitalized with hip fracture. Nutrients 2022;14:4255.
[14] Zhang Q, Wang Z, Song M, Liu T, Ding J, Deng L, et al. Effects of systemic inflammation and frailty on survival in older cancer patients: Results from the INSCOC study. Front Immunol 2023;14:936904.
[15] Liu XY, Zhang X, Ruan GT, Zhang KP, Tang M, Zhang Q, et al. One-year mortality in patients with cancer cachexia: Association with albumin and total protein. Cancer Manag Res 2021;13:6775–83.
[16] Bullock AF, Greenley SL, McKenzie GAG, Paton LW, Johnson MJ. Relationship between markers of malnutrition and clinical outcomes in older adults with cancer: systematic review, narrative synthesis and meta-analysis. Eur J Clin Nutr 2020;74:1519–35.
[17] Cao Y, Li P, Zhang Y, Qiu M, Li J, Ma S, et al. Association of systemic immune inflammatory index with all-cause and cause-specific mortality in hypertensive individuals: Results from NHANES. Front Immunol. 2023;14:1087345.
[18] Ruan GT, Zhang Q, Zhang X, Tang M, Song MM, Zhang XW, et al. Geriatric Nutrition Risk Index: Prognostic factor related to inflammation in older patients with cancer cachexia. J Cachexia Sarcopenia Muscle 2021;12:1969–82.
[19] Go SI, Park MJ, Park S, Kang MH, Kim HG, Kang JH, et al. Cachexia index as a potential biomarker for cancer cachexia and a prognostic indicator in diffuse large B-cell lymphoma. J Cachexia Sarcopenia Muscle 2021;12:2211–9.
[20] Jin H, Zhu K, Wang W. The predictive values of pretreatment Controlling Nutritional Status (CONUT) Score in estimating short- and long-term outcomes for patients with gastric cancer treated with neoadjuvant chemotherapy and curative gastrectomy. J Gastric Cancer 2021;21:155–68.
[21] Yang M, Lin SQ, Liu XY, Tang M, Hu CL, Wang ZW, et al. Association between C-reactive protein-albumin-lymphocyte (CALLY) index and overall survival in patients with colorectal cancer: From the investigation on nutrition status and clinical outcome of common cancers study. Front Immunol 2023;14:1131496.
[22] Yang M, Zhang Q, Ge Y, Tang M, Hu C, Wang Z, et al. Prognostic roles of inflammation- and nutrition-based indicators for female patients with cancer. J Inflamm Res 2022;15:3573–86.
[23] Xie H, Ruan G, Wei L, Zhang H, Ge Y, Zhang Q, et al. Hand grip strength-based cachexia index as a predictor of cancer cachexia and prognosis in patients with cancer. J Cachexia Sarcopenia Muscle 2023;14:382–90.
[24] Yin L, Cui J, Lin X, Li L, Li N, Fan Y, et al. Triceps skinfold-albumin index significantly predicts the prognosis of cancer cachexia: A multicentre cohort study. J Cachexia Sarcopenia Muscle 2023;14:517–33.
[25] Dunne RF, Loh KP, Williams GR, Jatoi A, Mustian KM, Mohile SG. Cachexia and sarcopenia in older adults with cancer: A comprehensive review. Cancers (Basel) 2019;11:1861.
[26] Mauricio SF, Xiao J, Prado CM, Gonzalez MC, Correia M. Different nutritional assessment tools as predictors of postoperative complications in patients undergoing colorectal cancer resection. Clin Nutr 2018;37:1505–11.
[27] Kondrup J, Allison SP, Elia M, Vellas B, Plauth M. Educational and Clinical Practice Committee. European Society of Parenteral and Enteral Nutrition (ESPEN). ESPEN guidelines for nutrition screening 2002. Clin Nutr 2003;22:415–21.
[28] Zhang W, Chen Y, Chen N. Body mass index and trajectories of the cognition among Chinese middle and old-aged adults. BMC Geriatr 2022;22:613.
[29] Hsiang CH, Wu CJ, Kao TW, Chen WL. Calf circumference and risk of cardiovascular disease. Geriatr Gerontol Int 2020;20:1133–7.
[30] Hu FJ, Liu H, Liu XL, Jia SL, Hou LS, Xia X, et al. Mid-upper arm circumference as an alternative screening instrument to appendicular skeletal muscle mass index for diagnosing sarcopenia. Clin Interv Aging 2021;16:1095–104.
[31] Song M, Zhang Q, Song C, Liu T, Zhang X, Ruan G, et al. The advanced lung cancer inflammation index is the optimal inflammatory biomarker of overall survival in patients with lung cancer. J Cachexia Sarcopenia Muscle 2022;13(5):2504–14.
[32] Later W, Bosy-Westphal A, Kossel E, Gluer CC, Heller M, Muller MJ. Is the 1975 Reference Man still a suitable reference? Eur J Clin Nutr 2010;64:1035–42.
[33] Deutz NEP, Ashurst I, Ballesteros MD, Bear DE, Cruz-Jentoft AJ, Genton L, et al. The underappreciated role of low muscle mass in the management of malnutrition. J Am Med Dir Assoc 2019;20:22–7.
[34] Cederholm T, Jensen GL, Correia M, Gonzalez MC, Fukushima R, Higashiguchi T, et al. GLIM criteria for the diagnosis of malnutrition – A consensus report from the global clinical nutrition community. Clin Nutr 2019;38:1–9.
[35] Gonzalez MC, Mehrnezhad A, Razaviarab N, Barbosa-Silva TG, Heymsfield SB. Calf circumference: cutoff values from the NHANES 1999-2006. Am J Clin Nutr 2021;113:1679–87.
[36] Evans DC, Corkins MR, Malone A, Miller S, Mogensen KM, Guenter P, et al. The Use of Visceral Proteins as Nutrition Markers: An ASPEN Position Paper. Nutr Clin Pract 2021;36:22–8.
[37] Utech AE, Tadros EM, Hayes TG, Garcia JM. Predicting survival in cancer patients: the role of cachexia and hormonal, nutritional and inflammatory markers. J Cachexia Sarcopenia Muscle 2012;3:245–51.
[38] Baazim H, Antonio-Herrera L, Bergthaler A. The interplay of immunology and cachexia in infection and cancer. Nat Rev Immunol 2022;22:309–21.
[39] Soeters PB, Wolfe RR, Shenkin A. Hypoalbuminemia: Pathogenesis and Clinical Significance. JPEN J Parenter Enteral Nutr 2019;43:181–93.
[40] Li L-Y, Sun H-S, Chen X, Xu D-S, Chen N-F, Guo H-F, et al. Serum albumin as a prognostic predictor reflecting host immunity in patients with non−small cell lung cancer. J Nutr Oncol 9900:10.1097/JN9.0000000000000017.
[41] Xie HL, Zhang Q, Ruan GT, Ge YZ, Hu CL, Song MM, et al. Evaluation and validation of the prognostic value of serum albumin to globulin ratio in patients with cancer cachexia: Results from a large multicenter collaboration. Front Oncol 2021;11:707705.
[42] Zhang XM, Wu X, Ma Y, Zhu C, Cao J, Liu G, et al. Comparing the performance of calf circumference, albumin, and BMI for predicting mortality in immobile patients. Risk Manag Healthc Policy 2021;14. 2289−300.
[43] Liu YY, Ruan GT, Ge YZ, Li QQ, Zhang Q, Zhang X, et al. Systemic inflammation with sarcopenia predicts survival in patients with gastric cancer. J Cancer Res Clin Oncol 2023;149:1249–59.