

# Controlling Nutritional Status (CONUT) Score Predicts Outcomes of Curative Resection for Gastric Cancer in the Elderly

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## Abstract

**Background** Preoperative nutritional status is considered to affect the short-term and long-term outcomes of cancer patients. The clinical value of the controlling nutritional status (CONUT) score in elderly patients undergoing gastrectomy for gastric cancer remains unknown.

**Methods** This study reviewed 211 elderly patients aged 75 years or over who underwent curative resection for gastric cancer from 2000 to 2015. Patients were grouped according to the preoperative CONUT score into those with normal nutrition (75 patients), light malnutrition (100 patients) and moderate or severe malnutrition (36 patients). The predictive value of the CONUT score for postoperative morbidity and survival was assessed.

**Results** Impaired nutrition was associated with cardiovascular disease ( $P = 0.012$ ) and chronic kidney disease ( $P = 0.014$ ), and worsened malnutrition was linked to advanced age ( $P = 0.004$ ), decreased body mass index ( $P = 0.008$ ) and advanced disease stage ( $P = 0.01$ ). Multivariate analysis showed the CONUT score as an independent predictor of procedure-unrelated infectious morbidity (odds ratio, 2.36; 95% confidence interval [CI], 0.99–5.40;  $P = 0.046$ ). Patients with a higher CONUT score had significantly shorter overall survival in both stage I and stage II/III gastric cancer ( $P = 0.044$  and  $P = 0.007$ , respectively) and reduced cancer-specific survival in stage II/III ( $P = 0.003$ ). The CONUT score was a strong predictor of overall survival (hazard ratio [HR], 2.12; 95% CI, 1.18–3.69;  $P = 0.012$ ) and cancer-specific survival (HR, 3.75; 95% CI, 1.30–10.43;  $P = 0.015$ ) independent of disease stage.

**Conclusions** The preoperative CONUT score is a simple and promising predictor of postoperative procedure-unrelated infectious morbidity and prognosis in elderly gastric cancer patients.

## Introduction

Gastric cancer is one of the leading causes of cancer deaths globally and is expected to continue to increase as populations in developed countries age [1]. The number of elderly patients with gastric cancer in Japan has risen every

year since records on it have been kept [2]. Gastrectomy is the main treatment for gastric cancer, but it can significantly diminish patients' quality of life. Postoperative morbidities also seriously impair health condition and lead to poor prognosis in the elderly [3, 4]. Elderly patients generally have poor health condition that adversely affects surgical outcomes and prolongs disability after surgery [5, 6]. However, physical status varies greatly among elderly individuals. Therefore, it is essential to identify a practical tool that can predict postoperative morbidity and survival, and guide the development of therapeutic strategies for elderly gastric cancer patients.

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**Table 1** Nutritional status assessment according to CONUT scoring system

Parameters	Malnutrition status			
	Normal	Light	Moderate	Severe
Serum albumin (g/dL)	≥3.50	3.00–3.49	2.50–2.99	<2.50
Score	0	2	4	6
Total lymphocyte count	≥1600	1200–1599	800–1199	<800
Score	0	1	2	3
Total cholesterol (mg/dL)	≥180	140–179	100–139	<100
Score	0	1	2	3
Total score	0–1	2–4	5–8	9–12

**Table 2** Comparison of patient demographics according to CONUT score

Variables	Malnutrition status			P value
	Normal (n = 75)	Light (n = 100)	Moderate and severe (n = 36)	
Age (mean±SD)	78.3±3.5	79.0±3.7	80.9±4.4	0.004
Gender, n (%)				0.20
Male	50 (67)	68 (68)	23 (64)	
Female	25 (33)	32 (32)	13 (36)	
BMI	22.7±3.3	22.5±2.9	20.9±2.5	0.008
ASA score, n (%)				0.15
1	12 (16)	6 (6)	2 (6)	
2	50 (67)	71 (71)	24 (67)	
3	13 (17)	23 (23)	10 (27)	
Comorbidity, n (%)				
Cardiovascular disease	13 (17)	34 (35)	15 (42)	0.012
Cerebrovascular disease	10 (13)	10 (10)	6 (17)	0.55
Pulmonary disease	20 (27)	27 (27)	9 (25)	0.97
Chronic kidney disease	18 (24)	45 (45)	15 (42)	0.014
Liver disease	1 (1)	4 (4)	1 (3)	0.58
Diabetes mellitus	13 (17)	21 (21)	6 (17)	0.77
Tumor differentiation, n (%)				0.91
Differentiated	49 (65)	64 (64)	22 (61)	
Undifferentiated	26 (35)	36 (36)	14 (39)	
pStage, n (%)				0.01
I	54 (72)	60 (60)	18 (50)	
II	14 (19)	31 (31)	8 (22)	
III	7 (9)	9 (9)	10 (28)	

SD standard deviation, BMI body mass index, ASA American Society of Anesthesiologists

Nutritional status is thought to be associated with prognosis after oncologic surgery [7, 8]. Gastric cancer causes debilitating malnutrition due to decreased oral intake and blood loss from the primary tumor. Furthermore, the elderly tend to develop malnutrition as a result of decreases in both physical function and food intake [9]. The controlling nutritional status (CONUT) score was

developed to screen for nutritional impairment simply and objectively [10]. The CONUT score is calculated from serum albumin level, total lymphocyte count and total cholesterol level in the peripheral blood. Though the CONUT score has been reported to be useful as a prognostic indicator in patients with heart and liver disease [11, 12], few reports have studied the clinical value of

**Table 3** Comparison of operative characteristics and outcomes according to CONUT score

Variables	Malnutrition status			P value
	Normal (n = 75)	Light (n = 100)	Moderate and severe (n = 36)	
Surgical approach, n (%)				0.048
Open	36 (48)	59 (59)	26 (72)	
Laparoscopic	39 (52)	41 (41)	10 (28)	
Type of gastrectomy, n (%)				0.73
Total	20 (27)	29 (29)	8 (22)	
Partial (distal or proximal)	55 (73)	71 (71)	28 (78)	
Lymph node dissection, n (%)				0.14
≤ D1+	50 (67)	68 (68)	18 (50)	
D2	25 (33)	32 (32)	18 (50)	
Splenectomy, n (%)	5 (7)	11 (11)	5 (14)	0.44
Operation time (min), median (range)	304 (184–565)	296 (160–702)	313.5 (123–570)	0.96
Blood loss (g), median (range)	228 (10–1774)	220 (10–3281)	190 (10–2228)	0.74
Transfusion, n (%)	6 (8)	21 (21)	17 (47)	<0.001
Postoperative stay (days), median (range)	19 (10–99)	20.5 (8–131)	22 (15–179)	0.24
Mortality, n (%)	0 (0)	0 (0)	1 (3)	0.09
Morbidity, n (%)				
Overall morbidity	27 (36)	36 (36)	20 (56)	0.09
Infectious morbidity	19 (25)	26 (26)	16 (44)	0.08
Procedure-related	9 (12)	13 (13)	7 (19)	0.54
Procedure-unrelated	10 (13)	16 (16)	12 (33)	0.029
Pneumonia	5 (7)	14 (14)	8 (22)	0.06
Enterocolitis	1 (1)	0 (0)	1 (3)	0.31
Urinary tract infection	0 (0)	0 (0)	1 (3)	0.09
Biliary tract infection	2 (3)	0 (0)	0 (0)	0.16
Catheter-related infection	2 (3)	2 (2)	2 (6)	0.54
Noninfectious morbidity	13 (17)	15 (15)	6 (17)	0.91

CONUT score in cancer patients [13–17]. The value of the CONUT score in gastric cancer patients remains unknown.

The aim of this study was to investigate the predictive value of the preoperative CONUT score for postoperative morbidity and survival in elderly patients with gastric cancer.

## Materials and methods

### Patients

From January 2000 to December 2015, a total of 1149 patients underwent resection for gastric cancer at Kobe University Hospital. Of the 261 elderly patients defined as age 75 years or over, those who received preoperative chemotherapy or transfusion or had insufficient preoperative data or who were lost to follow-up were excluded. Two hundred and eleven patients who underwent curative

resection were analyzed using clinicopathological and treatment data extracted from medical charts. Disease status was diagnosed according to the Japanese Classification of Gastric Carcinoma [18]. Surgical procedures were performed according to the Japanese Gastric Cancer Treatment Guideline [19]. Postoperative morbidities  $\geq$  grade II on the Clavien–Dindo classification were defined as either infectious or noninfectious morbidities [20]. Infectious morbidities were divided into procedure-related and procedure-unrelated infectious morbidities. Procedure-related infectious morbidities included anastomotic leakage, pancreatic fistula, intra-abdominal abscess and wound infection. Procedure-unrelated infectious morbidities comprised organ infections such as pneumonia, enterocolitis, urinary tract infection, biliary tract infection and catheter-related infection. Noninfectious morbidities included anastomotic stricture, anastomotic hemorrhage, delayed gastric emptying, small bowel obstruction, arrhythmia, angina pectoris, venous thromboembolism and stroke. This study was

**Table 4** Logistic regression analyses for postoperative procedure-unrelated infectious morbidity

Variables	Univariate analysis			Multivariate analysis		
	Odds ratio	95% CI	<i>P</i> value	Odds ratio	95% CI	<i>P</i> value
Age $\geq$ 80 years	1.14	0.55–2.32	0.72			
Male gender	1.75	0.81–4.15	0.16			
BMI < 18.5	1.17	0.44–2.80	0.74			
ASA score 3	1.13	0.58–2.58	0.46			
CONUT score $\geq$ 5	2.87	1.25–6.38	0.014	2.36	0.99–5.40	0.046
Cardiovascular comorbidity	1.05	0.50–2.36	0.89			
Cerebrovascular disease	1.43	0.49–3.68	0.49			
Pulmonary disease	1.57	0.72–3.30	0.25			
Chronic kidney disease	1.93	0.95–3.95	0.07	2.00	0.96–4.20	0.07
Diabetes mellitus	1.70	0.72–3.79	0.22			
pStage II, III	1.88	0.92–3.84	0.08	1.25	0.55–2.85	0.59
Open-approach surgery	2.06	0.99–4.58	0.06	1.69	0.74–4.04	0.22
Total gastrectomy	1.31	0.66–2.97	0.49			
Splenectomy	1.98	0.66–5.27	0.21			
D2 Lymph node dissection	2.09	1.02–4.28	0.043	1.57	0.71–3.46	0.27
Operation time >300 min	1.82	0.89–3.82	0.11			
Blood loss >250 ml	1.42	0.70–2.88	0.33			

BMI body mass index, ASA American Society of Anesthesiologists, CI confidence interval

approved by the Institutional Review Board of the Graduate School of Medicine, Kobe University. Written informed consent was received from all patients.

### Preoperative nutritional assessment

The CONUT score is calculated as described in Table 1. Serum albumin level, total lymphocyte count and total cholesterol level in peripheral blood were each categorized into quartiles that were then assigned scores [10]. The total scores of three parameters represent four nutritional statuses: normal nutrition and light, moderate and severe malnutrition.

### Statistical analysis

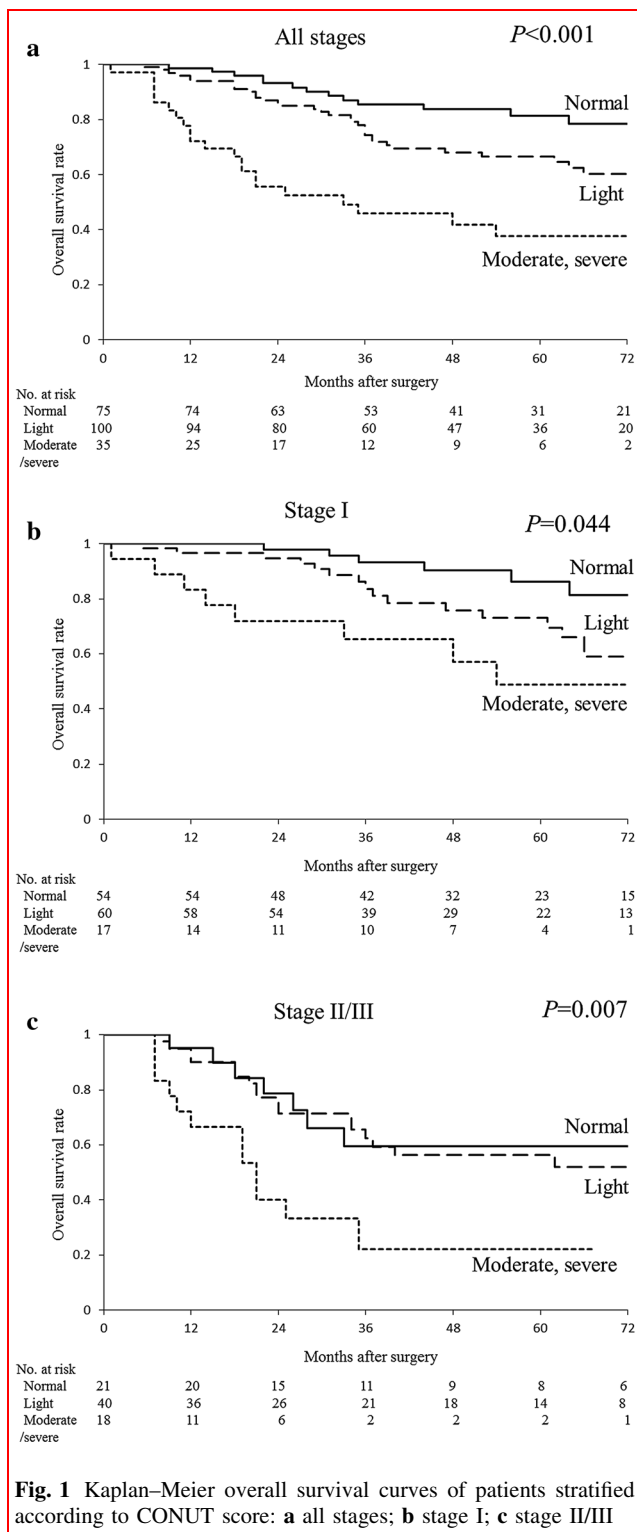
Statistical comparisons between groups were performed with the Mann–Whitney *U* test or Student's *t* test for continuous variables and with the Chi-square test or Fisher's exact test for categorical variables. Possible risk factors for postoperative morbidities were assessed using logistic regression analysis. Factors with a probability level  $\leq$ 0.1 were adopted for subsequent multivariate analysis and were considered as independent risk factors at a probability level <0.05. The cumulative survival rate was calculated by the Kaplan–Meier method, and survival curves were compared using the log-rank test. A Cox

proportional hazard regression model was constructed to identify independent prognostic factors. *P* values <0.05 were considered statistically significant. All statistical analyses were performed using JMP statistical software, version 11 (SAS institute Inc., Cary, NC, USA).

## Results

### Demographics and clinicopathologic characteristics

Based on their preoperative CONUT scores, there were 75 patients (36%) with normal nutrition, 100 (47%) with light malnutrition, 32 (15%) with moderate malnutrition and 4 (2%) with severe malnutrition. The patients were divided into three groups: normal nutrition, light malnutrition and moderate and severe malnutrition groups. A comparison of the clinicopathologic characteristics of the three groups is summarized in Table 2. Cardiovascular disease ( $P = 0.012$ ) and chronic kidney disease ( $P = 0.014$ ) were more prevalent in the malnutrition groups than in the normal group. Compared with patients with normal nutrition and light malnutrition, those with moderate or severe malnutrition demonstrated significantly older age ( $P = 0.004$ ), lower body mass index ( $P = 0.008$ ) and advanced disease stage ( $P = 0.01$ ).



### Predictive value of the CONUT score for postoperative morbidity

Surgical procedures and outcomes are listed in Table 3. Open-approach surgery ( $P = 0.048$ ) and intraoperative

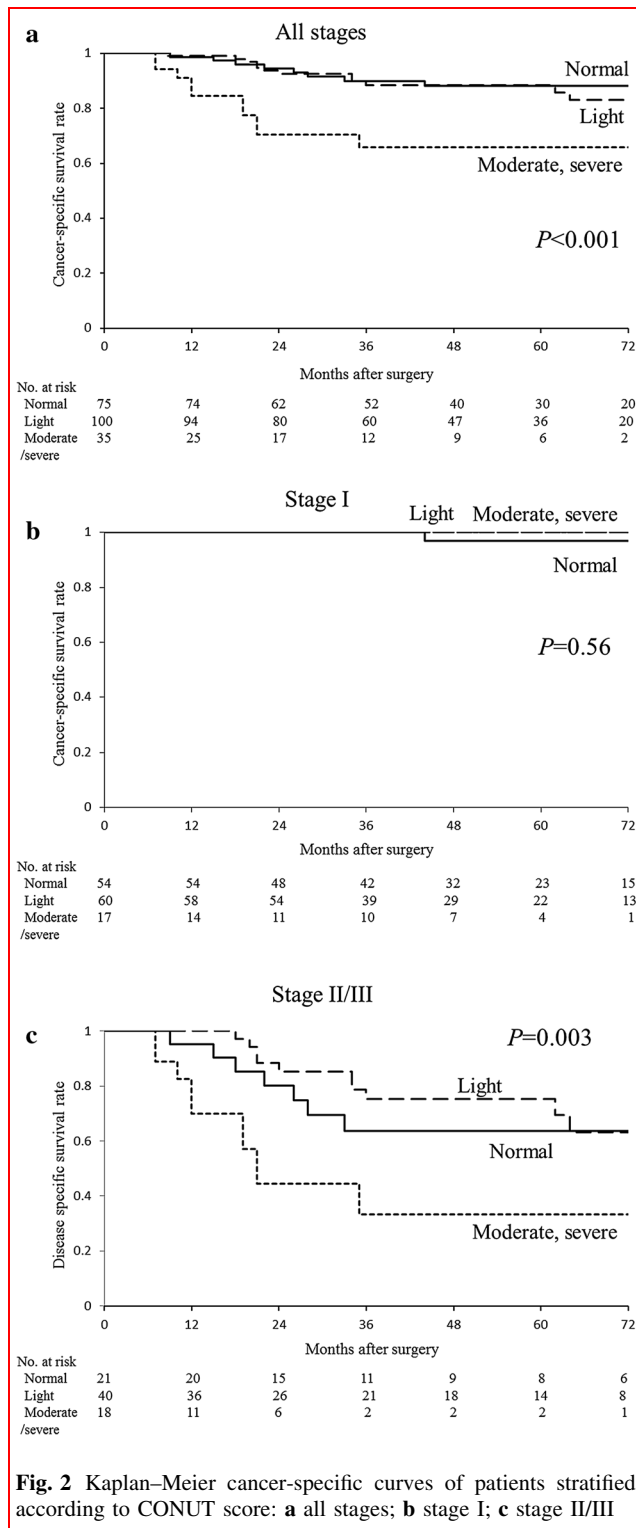
transfusion ( $P < 0.001$ ) were significantly more prevalent in moderate or severe malnutrition group, but there was no significant difference in the extent of gastrectomy or lymph node dissection, splenectomy or blood loss among the three groups. One patient with a high CONUT score died within 30 days of surgery. Postoperative morbidity developed in 83 patients (39%) after gastrectomy. Infectious morbidity developed in 61 patients (29%), and noninfectious morbidity occurred in 34 patients (16%). Patients with moderate or severe malnutrition experienced a higher tendency of any morbidity and infectious morbidity ( $P = 0.09$  and  $P = 0.08$ , respectively) and suffered from procedure-unrelated infectious morbidity ( $P = 0.029$ ) significantly more frequently. The incidence of postoperative pneumonia tended to increase with degree of impaired nutrition ( $P = 0.06$ ).

The results of analysis for risk factors associated with procedure-unrelated infectious morbidities are shown in Table 4. Multivariate analysis showed that a high CONUT score was an independent risk factor for procedure-unrelated infectious morbidity (OR, 2.36; 95% CI, 0.99–5.40;  $P = 0.046$ ).

### Predictive value of the CONUT score for survival

Survival analysis after curative gastrectomy excluded one patient who died during hospitalization. The overall median follow-up period was 47 months (range 5–185 months). The survival curves stratified by preoperative nutritional status according to the CONUT score are demonstrated in Figs. 1 and 2. The overall survival (OS) in moderate or severe malnutrition group was significantly shorter than in normal nutrition and light malnutrition groups ( $P < 0.001$ ; Fig. 1a). In normal nutrition, light malnutrition and moderate and severe malnutrition groups, 5-year OS rates by disease status were as follows: stage I, 88, 76 and 51%; stage II/III, 64, 53 and 24%, respectively (Fig. 1b, c). A significant reduction in OS was also found for patients with moderate or severe malnutrition in both stage I and stage II/III groups ( $P = 0.044$  and  $P = 0.007$ , respectively). The patients with moderate or severe malnutrition also significantly shortened cancer-specific survival (CSS) than those with normal nutrition and light malnutrition ( $P < 0.001$ , Fig. 2a). CSS was significantly worse in patients with moderate or severe malnutrition than in those with normal nutrition and light malnutrition in stage II/III groups (5-year survival rates of 33% vs. 64% and 75%,  $P = 0.003$ ; Fig. 2c), but not in stage I group ( $P = 0.56$ ; Fig. 2b).

The results of the Cox regression hazard model for predictors of OS and CSS are shown in Tables 5 and 6. Multivariate analysis identified the CONUT score (hazard ratio [HR], 2.12; 95% CI, 1.18–3.69;  $P = 0.012$ ) and



procedure-unrelated infectious morbidities (HR, 2.53; 95% CI, 1.19–5.46;  $P = 0.016$ ) as independent prognostic factors for OS as well as age (HR, 2.14; 95% CI, 1.31–3.45;  $P = 0.003$ ), ASA score (HR, 1.90; 95% CI, 1.05–3.41;  $P = 0.035$ ) and disease stage (HR, 2.27; 95% CI,

1.35–3.83;  $P = 0.002$ ). High CONUT score (HR, 3.75; 95% CI, 1.30–10.43;  $P = 0.015$ ), great age (HR, 3.46; 95% CI, 1.54–7.95;  $P = 0.003$ ) and advanced disease stage (HR, 39.35; 95% CI, 7.32–73.3;  $P < 0.001$ ) were independently associated with worse CSS in multivariate analysis.

### Discussion

Our results linked high CONUT scores in elderly patients undergoing curative resection for gastric cancer to a reduced OS, and a poor CSS in advanced stage. Moreover, a high CONUT score was an independent risk factor for procedure-unrelated infectious morbidities that worsened prognosis. These results imply that the preoperative CONUT score may be a potential prognostic predictor for elderly gastric cancer patients and aid in the clinical decision-making process.

The underlying mechanisms responsible for the adverse effect of preoperative malnutrition on survival after oncologic surgery have not yet been fully clarified. Possible explanations focus on physical status and oncological behavior, respectively. First, impaired nutrition status defined by CONUT score was associated with the prevalence of cardiovascular disease and chronic kidney disease, which both adversely affect survival. Second, malnutrition may increase postoperative morbidities due to impaired physical status, causing elderly patients to experience further physical decline, and may lead to cancer-unrelated deaths. Third, postoperative infectious morbidity has been reported to be associated with poor long-term survival [4, 21, 22]. Tumor progression is influenced not only by tumor behavior but also by host status such as nutrition, inflammation and immunity. Infectious morbidities may amplify systemic inflammatory responses and accelerate the suppression of tumor immunity, leading to tumor progression [23]. Malnutrition also facilitates prolongation of inflammation and immunological deterioration and may contribute to tumor recurrence especially for advanced stage [6, 24]. Considering these findings together, malnutrition may result in an unfavorable prognosis.

The CONUT score is computed from three peripheral blood parameters. The serum albumin level is considered to be a dependable indicator of nutrition condition and systematic inflammation [25]. Although serum albumin concentration is associated with prognosis in gastric cancer, the prognostic value of albumin is considered to be secondary to systemic inflammatory response [26]. The predictive value of albumin was of debatable even among physically impaired elderly without inflammation [27]. The total lymphocyte count is known to reflect the host's immune responsiveness to a tumor [28]. The total cholesterol concentration has been reported to be associated with

**Table 5** Cox proportional hazard model for overall survival after curative gastrectomy

Variables	Univariate analysis			Multivariate analysis		
	HR	95% CI	<i>P</i> value	HR	95% CI	<i>P</i> value
Age $\geq$ 80 years	2.25	1.44–3.53	<0.001	2.14	1.31–3.45	0.003
Male gender	1.11	0.70–1.83	0.66			
BMI < 18.5	1.30	0.65–2.39	0.43			
ASA score 3	1.69	1.01–2.68	0.046	1.90	1.05–3.41	0.035
CONUT score $\geq$ 5	2.69	1.59–4.37	<0.001	2.12	1.18–3.69	0.012
Cardiovascular disease	1.53	0.96–2.38	0.07	1.05	0.63–1.82	0.84
Cerebrovascular disease	1.37	0.70–2.42	0.34			
Pulmonary disease	1.37	0.84–2.17	0.20			
Chronic kidney disease	1.23	0.76–1.94	0.37			
Diabetes mellitus	1.10	0.62–2.08	0.76			
Undifferentiated tumor	1.26	0.80–1.57	0.32			
pStage II, III	2.44	1.57–3.82	<0.001	2.27	1.35–3.83	0.002
Open-approach surgery	1.70	1.06–2.81	0.026	1.07	0.60–1.91	0.83
Total gastrectomy	2.17	1.37–3.39	0.001	1.67	0.91–2.93	0.10
Splenectomy	2.65	1.44–4.57	0.002	1.45	0.64–3.26	0.37
D2 lymph node dissection	1.69	1.07–2.63	0.024	1.09	0.61–1.99	0.77
Transfusion	2.35	1.44–3.74	<0.001	1.37	0.78–2.35	0.26
Postoperative morbidity	1.29	0.81–2.01	0.28			
Infectious morbidity	1.57	0.95–2.51	0.08	1.39	0.65–3.14	0.41
Procedure-related	1.15	0.61–2.48	0.68			
Procedure-unrelated	2.34	1.39–3.80	0.002	2.53	1.19–5.46	0.016
Noninfectious morbidity	1.18	0.66–1.99	0.56			

*BMI* body mass index, *ASA* American Society of Anesthesiologists, *CI* confidence interval

tumor progression and patient prognosis in various cancers [29, 30]. Low serum cholesterol level was correlated with worse survival possibly due to hypocholesterolemia resulting from depletion of cholesterol by tumor growth [31]. The CONUT score could therefore reflect not only nutritional status, but also systemic inflammation and an immune responsiveness, and may provide a more balanced assessment than other candidates such as prognostic nutritional index and the Glasgow prognostic score [13, 32].

The elderly population is a heterogeneous cohort with various physical statuses. Frailty represents a physical vulnerability of the elderly to surgical stressors and leads to increase adverse outcomes. The association between frailty and adverse surgical outcomes has been demonstrated in patients undergoing various type of surgery [33, 34]. Frailty assessment is essential for surgical risk assessment. Physical status is commonly assessed by chronological age and performance status (PS). However, chronological age does not necessarily reflect age-related physical changes in the elderly [35]. PS is a useful predictor of surgical outcomes, but can differ from one evaluator to the next.

Elderly patients may be divided into three categories for cancer treatment. Some patients have sufficiently healthy status to enable them to receive the same treatment as nonelderly patients; some patients are vulnerable enough to indicate something less aggressive than standard treatment, and the remainders are too frail to be treated aggressively. Health status stratified according to the CONUT scoring system may conform to this category. A CONUT score of 0 or 1 represents healthy condition, a CONUT score of 3 or 4 represents some vulnerability and a CONUT score  $\geq$ 5 represents frailty. Hence, the CONUT score may serve to identify those frail patients who require intensive perioperative care to gastric cancer surgery. For elderly patients with high CONUT score, we have to plan the therapeutic strategy not to worsen postoperative outcome with meticulous care. Limited lymph node dissection should be considered to be adopted to prevent procedure-unrelated infectious morbidity. Aggressive perioperative nutritional therapies such as preoperative immunomodulating nutrition need to be offered to reduce postoperative morbidity [36–38], and these nutritional supports should be collaborated closely with ERAS program [39, 40]. Moreover,

**Table 6** Cox proportional hazard model for cancer-specific survival after curative gastrectomy

Variables	Univariate analysis			Multivariate analysis		
	HR	95% CI	<i>P</i> value	HR	95% CI	<i>P</i> value
Age $\geq$ 80 years	2.88	1.38–6.21	0.005	3.46	1.54–7.95	0.003
Male gender	1.68	0.79–3.49	0.17			
BMI $<$ 18.5	3.43	0.67–61.07	0.14			
ASA score 3	1.21	0.48–2.71	0.66			
CONUT score $\geq$ 5	3.82	1.70–8.07	0.008	3.75	1.30–10.43	0.015
Cardiovascular disease	1.87	0.88–3.89	0.10			
Cerebrovascular disease	1.18	0.42–4.54	0.78			
Pulmonary disease	1.33	0.57–2.83	0.49			
Chronic kidney disease	1.03	0.49–2.32	0.93			
Diabetes mellitus	1.14	0.47–3.38	0.79			
Undifferentiated tumor	2.32	1.18–4.93	0.024	1.17	0.51–2.72	0.72
pStage II, III	60.1	12.8–107.1	$<$ 0.001	39.35	7.32–73.3	$<$ 0.001
Open-approach surgery	7.86	2.49–29.6	$<$ 0.001	2.11	0.65–9.54	0.23
Total gastrectomy	4.28	2.06–9.18	0.001	1.72	0.59–4.60	0.31
Splenectomy	5.75	2.93–12.02	$<$ 0.001	3.06	0.90–11.5	0.07
D2 lymph node dissection	3.69	1.75–8.27	$<$ 0.001	1.57	0.57–4.47	0.38
Transfusion	2.90	1.33–6.06	0.009	1.51	0.60–4.03	0.39
Postoperative morbidity	1.79	0.85–3.74	0.12			
Infectious morbidity	2.30	1.07–4.79	0.034	1.20	0.45–3.15	0.72
Procedure-related	1.33	0.60–3.77	0.37			
Procedure-unrelated	1.90	0.71–4.26	0.16			
Noninfectious morbidity	1.19	0.4–2.76	0.70			

*BMI* body mass index, *ASA* American Society of Anesthesiologists, *CI* confidence interval

prehabilitation consisting of preoperatively correcting the declined nutritional, physical and neurophysiological function of patients may contribute to improved postoperative outcome [41, 42].

This study has several potential limitations because of its retrospective nature and enrollment of a limited number of patients at a single institution. The median follow-up period of only 47 months may be too short to form valid conclusions about long-term survival. Prospective studies of perioperative nutritional support based on the preoperative CONUT score are therefore required to better clarify the clinical value of the CONUT score in gastric cancer.

In conclusion, our results implied that the CONUT score was associated with prognosis after curative gastrectomy in elderly gastric cancer patients. Assessment of preoperative nutrition status according to the CONUT score may be of benefit in developing effective therapeutic strategies for gastric cancer.

#### Compliance with ethical standards

**Conflict of interest** All authors have no conflicts of interest or financial to disclose.

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