

Original Research





Received: Sep 13, 2021 Revised: Nov 29, 2021 Accepted: Jan 7, 2022 Published online: Mar 15, 2022

§Corresponding Author:

Jianchun Yu

Department of General Surgery, Peking Union Medical College Hospital, Peking Union Medical College and Chinese Academy of Medical Sciences, No.1 Shuaifuyuan St., Dongcheng District, Beijing 100730, China. Tel. +86-10-69155193 Fax. +86-10-69155193 Email. yu-jch@163.com

*Xiao Liu and Zhigang Xue contributed equally to the current study.

©2022 The Korean Nutrition Society and the Korean Society of Community Nutrition
This is an Open Access article distributed under the terms of the Creative Commons
Attribution Non-Commercial License (https://creativecommons.org/licenses/by-nc/4.0/) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ORCID iDs

Kiao Liu ঢ

https://orcid.org/0000-0001-5173-6075 Zhigang Xue

https://orcid.org/0000-0002-5492-0553

Jianchun Yu https://orcid.org/0000-0002-8250-7475

Zhiqiang Ma (D

https://orcid.org/0000-0002-1982-323X Weiming Kang

https://orcid.org/0000-0002-6736-4728

Risk factors for cancer-specific survival in elderly gastric cancer patients after curative gastrectomy

Xiao Liu \bigcirc 1°, Zhigang Xue \bigcirc 2,3°, Jianchun Yu \bigcirc 28, Zhiqiang Ma \bigcirc 2, Weiming Kang \bigcirc 2, Xin Ye \bigcirc 2, and Zijian Li \bigcirc 2,3

¹Department of Surgery, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100730, China

²Department of General Surgery, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100730, China

³Graduate School, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100730, China

ABSTRACT

BACKGROUND/OBJECTIVES: This study aimed to investigate cancer-specific survival (CSS) and associated risk factors in elderly gastric cancer (EGC) patients.

SUBJECTS/METHODS: EGC patients (≥ 70 yrs) who underwent curative gastrectomy between January 2013 and December 2017 at our hospital were included. Clinicopathologic characteristics and survival data were collected. Receiver operating characteristic (ROC) analysis was used to extract the best cutoff point for body mass index (BMI). A Cox proportional hazards model was used to determine the risk factors for CSS.

RESULTS: In total, 290 EGC patients were included, with a median age of 74.7 yrs. The median follow-up time was 31 (1–77) mon. The postoperative 1-yr, 3-yr and 5-yr CSS rates were 93.7%, 75.9% and 65.1%, respectively. Univariate analysis revealed risk factors for CSS, including age (hazard ratio [HR] = 1.08; 95% confidence interval [CI], 1.01–1.15), intensive care unit (ICU) admission (HR = 1.73; 95% CI, 1.08–2.79), nutritional risk screening (NRS 2002) score ≥ 5 (HR = 2.33; 95% CI, 1.49–3.75), and preoperative prognostic nutrition index score < 45 (HR = 2.06; 95% CI, 1.27–3.33). The ROC curve showed that the best BMI cutoff value was 20.6 kg/m². Multivariate analysis indicated that a BMI ≤ 20.6 kg/m² (HR = 2.30; 95% CI, 1.36–3.87), ICU admission (HR = 1.97; 95% CI, 1.17–3.30) and TNM stage (stage II: HR = 5.56; 95% CI, 1.59–19.43; stage III: HR = 16.20; 95% CI, 4.99–52.59) were significantly associated with CSS.

CONCLUSIONS: Low BMI (≤ 20.6 kg/m²), ICU admission and advanced pathological TNM stages (II and III) are independent risk factors for CSS in EGC patients after curative gastrectomy. Nutrition support, better perioperative management and early diagnosis would be helpful for better survival.

Keywords: Stomach neoplasms; aged; risk factors; survival; body mass index

INTRODUCTION

Gastric cancer (GC) ranks fifth in morbidity and third in cancer-related mortality among malignancies worldwide [1], and it has a relatively higher prevalence in East Asian countries



Xin Ye 📵

https://orcid.org/0000-0001-8355-4516

https://orcid.org/0000-0001-9607-6664

Funding

This study was funded by Beijing Municipal Science and Technology Commission Program (No. D141100000414002, D171100006517002 and D171100006517004) and National Health Commission Program (No. 201502022).

Conflict of Interest

The authors declare that no potential conflicts of interests

Author Contributions

Conceptualization: Yu J, Ma Z, Kang W, Ye X; Data curation: Liu X, Xue Z, Li Z; Formal analysis: Liu X, Xue Z, Li Z; Funding acquisition: Yu J, Kang W; Investigation: Liu X, Xue Z, Li Z; Methodology: Liu X; Project administration: Ma Z, Ye X; Resources: Yu J, Ma Z, Kang W, Ye X; Software: Liu X; Supervision: Yu J, Kang W; Validation: Xue Z, Yu J; Visualization: Liu X; Writing - original draft: Liu X, Xue Z; Writing - review & editing: Xue Z, Yu J.

[2]. Cases of GC increase with increasing age, and the peak incidence occurs in the 7th decade of life, making GC that mainly affects the elderly population [3-5]. Generally, GC among elderly patients is more complex and severe, with a higher risk of frailty resulting from comorbidities and malnourishment [4,6], a higher risk of surgical complications [7,8], and a shorter life expectancy than in the young population.

Previous studies have shown that several clinicopathological factors, including tumor location in the entire stomach, tumor size, stage, vascular invasion, perineural invasion and adjuvant chemotherapy, are related to a poor prognosis in elderly GC patients [9]. Comorbidities may impact survival in cancer patients. Cancer-specific survival (CSS) was found to be reduced among patients with comorbidities in some studies [10]. However, other studies did not find associations between CSS and comorbidities [11,12]. The impact of comorbidities on CSS is not consistent and is likely to vary depending on the severity of the comorbidity, prognostic factors for the cancer, the stage of the cancer and the impact of treatment [12,13].

Moreover, elderly cancer patients have a high prevalence of malnutrition, ranging from 19% to 55% [14-16], and that proportion is even higher in GC patients, reaching up to 80% [17]. Malnutrition has been shown to be associated with poor survival in GC patients [18]. Recent studies have been dedicated to developing risk models for overall survival (OS) and CSS in GC patients after gastrectomy [19-21], which might be more beneficial and urgently needed in the elderly population. Therefore, we aimed to identify the potential risk factors for CSS in elderly GC patients after gastrectomy at an academic Chinese medical center.

SUBJECTS AND METHODS

Participants and study design

All patients included in our study were consecutively admitted to our hospital from January 2013 to December 2017. The inclusion criteria were as follows: (1) age \geq 70 yrs, (2) selective curative gastrectomy, and (3) pathological diagnosis of gastric adenocarcinoma. Patients who underwent emergency surgery, had other malignancies, had incomplete clinicopathological data or were lost to follow-up were excluded from the study. We defined age \geq 70 yrs as "elderly" in this study based on the published literature [22,23]. The primary endpoint was cancer-related death, and CSS was defined as the duration from operation to cancer-related death. All patients had regular follow-up visits, and the follow-ups were updated by January 31, 2020. The study protocol was reviewed and approved by the Institutional Review Board of Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, for a quick pass based on its retrospective nature. The IRB number is PUMCH-B117. Each patient provided written informed consent.

Data collection and evaluation

We collected clinicopathological data, including sex, age, history of smoking, Charlson comorbidity index (CCI) score without age adjustment [24], American Society of Anesthesiologists (ASA) score, ICU admission, perioperative blood transfusion, tumor differentiation grade and the tumor, node, and metastasis (TNM) stage based on postoperative pathological reports. Age was defined at the time of inpatient admission. The criteria for ICU admission were as follows: (1) postoperative need for hemodynamic monitoring and frequent nursing care; (2) a high risk of postoperative respiratory



complications requiring mechanical ventilation, such as patients with chronic obstructive pulmonary disease; and (3) cardiac function evaluated by cardiologists as being high risk and needing continuous monitoring and dose adjustment. GC staging was performed according to the 7th Union for International Cancer Control & American Joint Committee on Cancer (UICC & AJCC) staging system for gastric cancer [25].

Nutritional variables included preoperative body mass index (BMI), weight loss, Nutritional Risk Screening 2002 (NRS 2002) [26], Prognostic Nutrition Index (PNI) [15], and serum hemoglobin, albumin and prealbumin levels. BMI was defined by weight (kg)/height(m)² at admission. Preoperative weight loss was defined as losing at least 5% of one's total body weight within 12 mon before surgery. NRS 2002 is a widely used tool to screen nutritional risk in hospitalized patients from three dimensions, including severity of diseases, severity of malnutrition and age (see full chart in **Supplementary Table 1**) [26]. An NRS 2002 score \geq 3 indicated nutritional risk, and an NRS 2002 score \geq 5 indicated high nutritional risk. The PNI scores were calculated as follows: $10 \times \text{serum}$ albumin value (g/dL) + 0.005 \times peripheral lymphocyte count (/mm³) [15]. A PNI score < 45 indicated poor nutritional status.

We collected surgical data, including approaches to gastrectomy, dissection area of the stomach and perigastric lymph nodes, combined resection of organs, duration of operation, and intraoperative blood loss. The combined resection of organs refers to gastrectomy combined with surgical removal of the spleen, part of the transverse colon, or part of the pancreas. We used 240 min as the cutoff for the operation duration [27] and 400 mL as the cutoff for intraoperative blood loss [28]. Most patients had regular visits to our clinic annually; for those who did not visit us over one yr, we made phone calls to update their survival status. Death date and causes were reported by the families. Patients who died from causes other than GC were recorded as censored. CSS was defined as days from the operation date to the date of death, loss to follow-up or the end of the study.

Statistical analysis

Continuous variables are presented as the means \pm SD or medians with interquartile ranges. Categorical variables are described as numbers and percentages. We included all the clinicopathological, nutritional and surgical variables in the univariate analysis to identify the potential risk factors for CSS, then we assessed the effects of covariates on univariable association by multivariate analyses. Variables in univariate analyses with P < 0.05 were included in multivariate analysis, including age, ICU admission, TNM stage II, III, and all the nutritional variables. Hazard rations (HRs) and 95% confidence intervals (CIs) were calculated and reported both in the univariate and multivariate analyses. The Cox model was used to perform survival analysis to simultaneously assess the effects of several risk factors on survival time. A receiver operating characteristic (ROC) curve was used to identify the cutoff value for BMI. Survival curves were estimated by the Kaplan–Meier method using the log-rank test. P < 0.05 was regarded as statistically significant. All statistical analyses were performed using SPSS for Windows (version 20; IBM Corp., Armonk, NY, USA).

RESULTS

In our database of 1,446 consecutive EGC patients, 290 patients met the inclusion and exclusion criteria and were included in the study (**Fig. 1**). In this cohort, 290 patients had a median follow-up duration of 31 (1–77) mon. There were 86 deaths in total during the follow-up, including 68



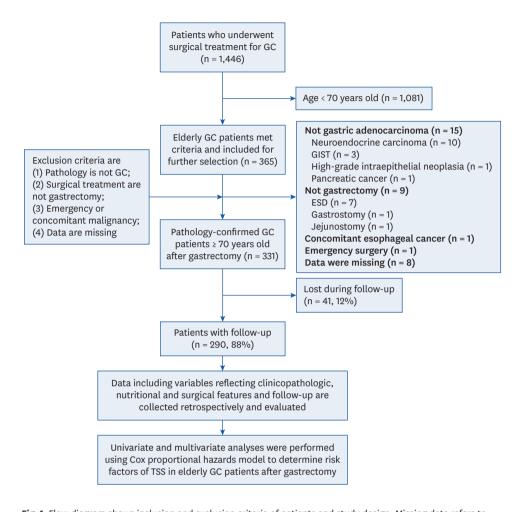


Fig. 1. Flow diagram shows inclusion and exclusion criteria of patients and study design. Missing data refers to loss of pathological, laboratory tests or surgical records. GC, gastric cancer; GIST, gastrointestinal stromal tumor; ESD, endoscopic submucosal dissection; TSS, tumor-specific survival.

tumor-related deaths. The postoperative 1-, 3-, and 5-yr CSS rates were 93.7%, 75.9% and 65.1%, respectively. The characteristics of these patients categorized into clinicopathologic, nutritional and surgical outcomes are summarized in **Tables 1, 2** and **3**, respectively.

Clinicopathologic characteristics at baseline and its associations with cancer-related death

Among the 290 EGC patients, the average age was 74.7 ± 3.6 yrs, and 77.6% were male. A total of 38 (13.1%) had CCI scores \geq 3, and 121 (41.7%) of all included patients were classified as ASA class \geq 3, indicating a relatively high percentage of patients with fragility as a cohort of elderly hospitalized populations. In total, 112 (38.6%) of the patients were admitted to the ICU after surgery, and 78 (26.9%) of the patients underwent perioperative blood transfusion. Pathological reports showed that 195 (67.2%) patients had locally advanced GC, and 181 (62.4%) had poorly differentiated GC. Univariate analysis demonstrated that the risk factors for CSS included age (HR = 1.08; 95% CI, 1.01–1.15), ICU admission (HR = 1.73; 95% CI, 1.08–2.79) and pathological TNM (pTNM) stage (stage II: HR = 4.23; 95% CI, 1.53–11.63; stage III: HR = 12.59; 95% CI, 5.00–31.73; **Table 1**).



Table 1. Clinicopathologic variables and risk factors of CSS in univariate analysis

Clinicopathologic variables	No. (%) or	Univariate analysis		
	mean ± SD	HR	95% CI	<i>P</i> -value
Sex		1.202	0.657-2.201	0.551
Male	225 (77.6)			
Female	65 (22.4)			
Age (yrs)	74.7 ± 3.6	1.08	1.014-1.151	0.017
Smoke history		1.3	0.802-2.108	0.287
Yes	104 (35.9)			
No	186 (64.1)			
CCI score		1.237	0.632-2.421	0.534
≥ 3	38 (13.1)			
0-2	252 (86.9)			
ASA class		1.128	0.689-1.847	0.632
≥ 3	121 (41.7)			
1-2	169 (58.3)			
ICU admission		1.733	1.077-2.788	0.024
Yes	112 (38.6)			
No	178 (61.4)			
Preoperative blood transfusion		1.48	0.884-2.476	0.136
Yes	78 (26.9)			
No	212 (73.1)			
Tumor differentiation				
Poor	181 (62.4)			
Moderate	87 (30.0)	0.799	0.471-1.353	0.403
Well	22 (7.6)	0.531	0.165-1.709	0.288
TNM stage				
1	95 (32.8)			
II	73 (25.2)	4.233	1.534-11.625	0.005
III	122 (42.0)	12.593	4.999-31.727	0.000

CSS, cancer-specific survival; CCI, Charlson comorbidity index; ASA, American Society of Anesthesiologists; ICU, intensive care unit; TNM, tumor node, and metastasis; HR, hazards ratio; CI, confidence interval.

Table 2. Nutritional variables and risk factors of CSS in univariate analysis

Nutritional variables	No. (%) or	Univariate analysis		
	mean ± SD	HR	95% CI	<i>P</i> -value
BMI (kg/m²)	23.1 ± 3.3	0.886	0.824-0.952	0.001
Preoperative weight loss		1.962	1.216-3.167	0.006
≥ 5%	100 (34.5)			
< 5%	190 (65.5)			
NRS 2002 score		2.331	1.448-3.753	0.000
≥ 5	101 (34.8)			
3-4	189 (65.2)			
Preoperative anemia		1.789	1.110-2.884	0.017
Yes	97 (33.4)			
No	193 (66.6)			
PNI score		2.058	1.273-3.327	0.003
< 45	96 (33.1)			
≥ 45	194 (66.9)			
Preoperative albumin (g/L)		2.161	1.258-3.711	0.005
< 35	51 (17.6)			
≥ 35	239 (82.4)			
Preoperative prealbumin (mg/L)*		2.426	1.485-3.965	0.000
< 200	117 (42.1)			
≥ 200	161 (57.9)			

CSS, cancer-specific survival; BMI, body mass index; NRS 2002, Nutritional Risk Screening 2002; PNI, Prognostic Nutrition Index; HR, hazards ration; CI, confidence interval.

^{*}Preoperative prealbumin value of 12 patients were missing.



Table 3. Surgical variables and risk factors of CSS in univariate analysis

Surgical variables	No. (%)		Univariate analysis		
		HR	95%CI	<i>P</i> -value	
Approach					
Laparoscopic surgery	114 (39.3)				
Conversion	13 (4.5)	0.362	0.049-2.679	0.320	
Open surgery	163 (56.2)	1.385	0.840-2.282	0.202	
Gastric dissection		1.479	0.894-2.445	0.127	
Total	83 (28.6)				
Partial	207 (71.4)				
Lymph node dissection		1.296	0.763-2.202	0.337	
D2	191 (65.9)				
< D2	99 (34.1)				
Combined resection of organs*		1.48	0.676-3.242	0.327	
Yes	22 (7.6)				
No	268 (92.4)				
Operation duration (min)		1.219	0.711-2.089	0.472	
≥ 240	69 (23.8)				
< 240	221 (76.2)				
Intraoperative blood loss (mL)		1.668	0.925-3.005	0.089	
≥ 400	42 (14.5)				
< 400	248 (85.5)				

CSS, cancer-specific survival; HR, hazards ration; CI, confidence interval.

Nutritional outcomes

In terms of the nutritional assessment, 100 (34.5%) patients had preoperative weight loss \geq 5%, 101 (34.8%) had an NRS 2002 score \geq 5 and 96 (33.1%) had a PNI score < 45. These three parameters had relatively high consistency, implying that over 1/3 of all elderly GC patients were at a high nutritional risk. In addition, the proportions of patients with anemia, hypoalbuminemia and low prealbumin levels were 33.4%, 17.6% and 42.1%, respectively. Single serum nutritional variables had large ranges of prevalence of nutritional risk. At baseline, BMI (HR = 0.89; 95% CI, 0.82–0.95), weight loss \geq 5% (HR = 1.96; 95% CI, 1.22–3.17), NRS 2002 score \geq 5 (HR = 2.33; 95% CI, 1.45–3.75), PNI score < 45 (HR = 2.06; 95% CI, 1.27–3.33), anemia (HR = 1.79; 95% CI, 1.11–2.88), an albumin level \leq 35 g/L (HR = 2.16; 95% CI, 1.15–4.28) and a prealbumin level < 200 mg/L (HR = 2.43; 95% CI, 1.49–3.97) were significantly associated with CSS in univariate analysis (**Table 2**). Furthermore, an ROC curve was generated, and a BMI of 20.6 kg/m² was determined to be the optimal cutoff value in our cohort of patients to categorize these patients into low and high BMI groups (**Fig. 2A**). The 5-yr CSS was significantly higher in patients with a BMI > 20.6 kg/m² than in those with a BMI \leq 20.6 kg/m² (72% vs. 39%; **Fig. 2B**).

Surgical outcomes

In total, 56.2% of patients underwent open surgery, 39.3% underwent laparoscopic surgery, and 4.5% underwent conversion from laparoscopic to open procedures. In terms of resection areas of the stomach, perigastric lymph nodes and surrounding organs, 28.6% received total gastrectomy, 65.9% underwent D2 lymphadenectomy, and 7.6% had combined resection of other organs (**Table 3**). However, none of these surgical variables were significantly associated with CSS.

Independent risk factors for CSS

In univariate analyses, we found that age, ICU admission, TNM stages II and III in **Table 1**, and all the nutritional variables in **Table 2** were associated with CSS. Then we included these

^{*}Combined resection of organs refers to gastrectomy combined with spleen, part of transverse colon, or part of pancreas.



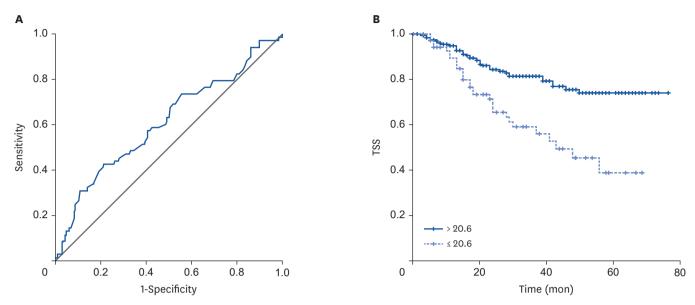


Fig. 2. (A) ROC curve showed the predictive accuracy of BMI values for tumor-specific survival. AUC was 0.61 (95% CI, 0.53–0.69, P = 0.006). Youden index was 0.21, sensitivity was 0.43 and specificity was 0.79. The BMI cut-off value was 20.65 kg/m². (B) TSS was compared between low BMI and high BMI groups using the novel cut-off value, 20.6 kg/m², in Kaplan-Meier method. Log-rank test was performed and χ^2 was 16.27, P < 0.001. ROC, receiver operating curve; BMI, body mass index; AUC, area under curve; CI, confidence interval; TSS, tumor-specific survival.

variables in multivariate analyses to identify independent risk factors for CSS by using a Cox proportional hazards model. It is demonstrated that a BMI \leq 20.6 kg/m² (HR = 2.30; 95% CI, 1.36–3.87), ICU admission (HR = 1.97; 95% CI, 1.17–3.30) and pTNM stage (stage II: HR = 5.56; 95% CI, 1.59–19.43, P = 0.007; stage III: HR = 16.202; 95% CI, 4.99–52.59) were significantly associated with CSS (**Table 4**). Therefore, these variables were identified as independent risk factors for poor CSS in EGC.

DISCUSSION

In this study, we collected clinicopathological data from a cohort of EGC patients aged \geq 70 yrs. We aimed to investigate the potential risk factors for CSS in these patients. In particular, we focused on nutritional parameters in this cohort, since elderly patients may have worsened appetite and decreased food intake, leading to a poor nutritional status. Indeed,

Table 4. Independent risk factors of CSS were in multivariate analysis using Cox proportional hazards model

Factors	Multi-regression analysis			
	HR (95% CI)	<i>P</i> -value		
BMI (kg/m²)		0.002		
≤ 20.6	2.297 (1.362-3.874)			
> 20.6	1			
ICU admission		0.011		
Yes	1.965 (1.171-3.300)			
No	1			
TNM stage				
I	1			
II	5.560 (1.591-19.428)	0.007		
III	16.202 (4.991-52.591)	0.000		

Variables in univariate analyses with P < 0.05 were included in multivariate analyses using Cox model. CSS, cancer-specific survival; HR, hazards ratio; CI, confidence interval; BMI, body mass index; ICU, intensive care unit; TNM, tumor, node, and metastasis.



approximately one-third of these patients were at a high nutritional risk, whether using the NRS 2002 tool (34.8%) or the PNI (33.1%, **Table 2**). Additionally, 34.5% of these patients had weight loss \geq 5% within 12 mon before surgery. Multivariate analysis indicated that a BMI \leq 20.6 kg/m², ICU admission and advanced pTNM (stages II and III) were independent risk factors for CSS.

Our study demonstrated that a low BMI predicted poor survival in GC patients, which was consistent with some previous reports [29-31]. Kim et al. reported a cohort of 510 GC patients in whom a preoperative BMI \leq 18.5 kg/m² was an independent prognostic factor for CSS in the stage I/II group (HR = 13.52; 95% CI, 1.19–154.20) [29]. Liu et al. [30] and Feng et al. [31] both reported that a low BMI was associated with poor OS in GC patients. Zhao et al. [32] performed a meta-analysis of 12 studies including 12,626 GC patients and demonstrated that 15.1% had a low BMI (< 18.5 kg/m²) and that those with a low BMI had a significantly lower survival rate than patients with normal BMI. However, some studies did not find a relationship between BMI and survival [33,34]. Lee et al. [33] demonstrated that there was no significant difference in OS between the groups with low and normal preoperative BMI values (HR = 1.01; 95% CI, 0.72-1.40) in a study of 1,909 GC patients with a mean age of 58 yrs [31]. They found that patients with a low BMI had significantly lower OS than those with a high-normal BMI range (23.0 to 24.9). Interestingly, the subgroup analysis implied that the traditional BMI cutoff value is not as helpful as expected, and a better BMI cutoff value probably lies within the low-normal BMI range (18.5 to 22.9) [33]. Ejaz et al. [34] reported 775 GC patients in whom BMI was not related to CSS or OS, but patients who were underweight (BMI < 18.5 kg/m²) and had low albumin levels (< 35 g/L) had worse OS. However, researchers did not pay specific attention to elderly patients in these studies, and they used the low BMI cutoff value of 18.5 recommended by the World Health Organization.

BMI, which is an easily available index, is widely used as an indicator of nutrition in clinical practice, and a BMI < 18.5 kg/m² is used as an indication of underweight or malnutrition. Clinical researchers noticed that elderly patients probably had different BMI classifications due to reduced metabolic status [35]. However, there is no consensus about the BMI cutoff values in elderly patients. The Dutch Malnutrition Steering Group (DMSG) defines a low BMI for patients over 65 yrs as less than 20 kg/m² [36], and the European Society of Clinical Nutrition and Metabolism (ESPEN) recommends < 22 kg/m² as one of the malnutrition criteria for patients \geq 70 yrs [37]. These novel cutoff values were validated as predictors of short-term survival in the general hospitalized population [36]. In our study, we identified a BMI of 20.6 kg/m² to classify patients into low BMI and high BMI groups as a novel cutoff value. Moreover, BMI $\leq 20.6 \text{ kg/m}^2$ proved to be a significant independent risk factor for poor CSS in elderly GC patients after curative gastrectomy. This finding helped us to recognize that the novel BMI cutoff value, i.e., higher than 18.5, might be more suitable in elderly GC patients when evaluating their nutritional status, which is similar to the DMSG and ESPEN recommendations [36,37]. Further studies with larger sample sizes may be needed in the future. Prospective studies in elderly GC patients are also warranted.

Studies have reported that nutritional status might be associated with surgical mortality in GC patients. Based on the NRS 2002 score, all elderly GC patients were at nutritional risk, which is associated with surgical outcomes [38,39]. A PNI score < 45 might be a prognostic factor for survival in GC patients [40,41]. Anemia and low levels of albumin and prealbumin were reported to be related to cancer survival after surgery separately or combined in a model [42,43]. In our study, we found that weight loss \geq 5%, NRS 2002 score \geq 5, PNI score < 45,



anemia, and low albumin and prealbumin levels were associated with CSS in the univariate analysis. However, none of these variables were independent risk factors in the multivariate analysis. One possible explanation would be associations between low BMI and them based on the methodology.

The CCI is associated with surgical outcomes, both in terms of postoperative morbidities and long-term survival, particularly in elderly patients [44,45]. As a common tool used in geriatric units, a CCI score \geq 3 was recently reported by Iwai *et al.* [46] to be associated with OS (HR = 7.88; 95% CI, 4.50–13.80) in elderly GC patients. However, we did not find similar results, although ICU admission was an independent risk factor. ICU admission often results from a high risk of cardiac and/or pulmonary dysfunction, which can be quite common in elderly patients with multiple comorbidities. In our study, we found that ICU admission was an independent predictor of CSS (HR = 1.97; 95% CI, 1.17–3.30), which could be related to complex comorbidities in elderly GC patients. Additionally, a higher pTNM stage indicated a poor CSS (stage II: HR = 5.56; 95% CI, 1.59–19.43; stage III: HR = 16.202; 95% CI, 4.99–52.59), which is widely recognized.

There are some limitations of the present study. First, this is a retrospective study with a relatively small sample size. Second, we did not collect data on surgical morbidity and quality of life, which are important in elderly GC patients. Third, patients may have other lifestyle exposures, such as alcohol use, that were unaccounted for in the study, and some patients may receive other forms of treatment. Moreover, the patients were from a single academic medical center in China, and caution should be exerted when extrapolating the results to various other populations. To the best of our knowledge, the BMI cutoff value of 20.6 kg/m^2 is a novel finding, and a low BMI was determined to be an independent predictor of poor CSS in elderly GC patients. Future studies may examine the efficacy of the predictive value of these cutoff values for survival (20.6 vs. 18.5) in elderly surgical patients.

In conclusion, we found that a low BMI (\leq 20.6 kg/m²), postoperative ICU admission and advanced pathological TNM stages (II and III) were independent risk factors for CSS in elderly GC patients after gastrectomy. These findings may help optimally and efficiently evaluate and identify patients at high risk of poor outcomes. Survival in elderly GC patients could be improved by enhancing their nutritional status, treating their comorbidities and early diagnosis.

ACKNOWLEDGMENTS

We appreciated Dr. Guangyu Hu, from Institution of Medical Information, Chinese Academy of Medical Sciences and Peking Union Medical College, for his thoughtful supervision of statistical analyses.

SUPPLEMENTARY MATERIALS

Supplementary Table 1

NRS 2002: Initial screening

Click here to view



Supplementary Table 2

NRS 2002: Final screening

Click here to view

REFERENCES

 Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018;68:394-424.

PUBMED | CROSSREF

- Van Cutsem E, Sagaert X, Topal B, Haustermans K, Prenen H. Gastric cancer. Lancet 2016;388:2654-64.
 PUBMED | CROSSREF
- 3. Chen WQ, Zheng RS, Zhang SW, Zeng HM, Zou XN, He J. Analysis of cancer incidence and mortality in elderly population in China, 2013. Zhonghua Zhong Liu Za Zhi 2017;39:60-6.
- Leo S, Accettura C, Gnoni A, Licchetta A, Giampaglia M, Mauro A, Saracino V, Carr BI. Systemic treatment of gastrointestinal cancer in elderly patients. J Gastrointest Cancer 2013;44:22-32.

 PUBMED I CROSSREF
- Saito H, Osaki T, Murakami D, Sakamoto T, Kanaji S, Tatebe S, Tsujitani S, Ikeguchi M. Effect of age on prognosis in patients with gastric cancer. ANZ J Surg 2006;76:458-61.

 PUBMED | CROSSREF
- Hall PS, Lord SR, Collinson M, Marshall H, Jones M, Lowe C, Howard H, Swinson D, Velikova G, Anthoney A, et al. A randomised phase II trial and feasibility study of palliative chemotherapy in frail or elderly patients with advanced gastroesophageal cancer (321GO). Br J Cancer 2017;116:472-8.
 PUBMED | CROSSREF
- Takama T, Okano K, Kondo A, Akamoto S, Fujiwara M, Usuki H, Suzuki Y. Predictors of postoperative complications in elderly and oldest old patients with gastric cancer. Gastric Cancer 2015;18:653-61.
 PUBMED | CROSSREF
- Takeuchi D, Koide N, Suzuki A, Ishizone S, Shimizu F, Tsuchiya T, Kumeda S, Miyagawa S. Postoperative complications in elderly patients with gastric cancer. J Surg Res 2015;198:317-26.
 PUBMED I CROSSREF
- Kim DH, Kim SM, Hyun JK, Choi MG, Noh JH, Sohn TS, Bae JM, Kim S. Changes in postoperative recurrence and prognostic risk factors for patients with gastric cancer who underwent curative gastric resection during different time periods. Ann Surg Oncol 2013;20:2317-27.
 PUBMED | CROSSREF
- Sarfati D, Blakely T, Pearce N. Measuring cancer survival in populations: relative survival vs cancerspecific survival. Int J Epidemiol 2010;39:598-610.

PUBMED | CROSSREF

11. Edwards BK, Noone AM, Mariotto AB, Simard EP, Boscoe FP, Henley SJ, Jemal A, Cho H, Anderson RN, Kohler BA, et al. Annual report to the nation on the status of cancer, 1975-2010, featuring prevalence of comorbidity and impact on survival among persons with lung, colorectal, breast, or prostate cancer. Cancer 2014;120:1290-314.

PUBMED | CROSSREF

12. Sarfati D, Koczwara B, Jackson C. The impact of comorbidity on cancer and its treatment. CA Cancer J Clin 2016;66:337-50.

PUBMED | CROSSREF

13. Lee L, Cheung WY, Atkinson E, Krzyzanowska MK. Impact of comorbidity on chemotherapy use and outcomes in solid tumors: a systematic review. J Clin Oncol 2011;29:106-17.

PUBMED | CROSSREF

- 14. Lacau St Guily J, Bouvard É, Raynard B, Goldwasser F, Maget B, Prevost A, Seguy D, Romano O, Narciso B, Couet C, et al. NutriCancer: a French observational multicentre cross-sectional study of malnutrition in elderly patients with cancer. J Geriatr Oncol 2018;9:74-80.
 - PUBMED | CROSSREF

PUBMED | CROSSREF

15. Kim CY, Kim SY, Song JH, Kim YS, Jeong SJ, Lee JG, Paik HC, Park MS. Usefulness of the preoperative prognostic nutritional index score as a predictor of the outcomes of lung transplantation: a single-institution experience. Clin Nutr 2019;38:2423-9.



 Fukuda Y, Yamamoto K, Hirao M, Nishikawa K, Maeda S, Haraguchi N, Miyake M, Hama N, Miyamoto A, Ikeda M, et al. Prevalence of malnutrition among gastric cancer patients undergoing gastrectomy and optimal preoperative nutritional support for preventing surgical site infections. Ann Surg Oncol 2015;22 Suppl 3:S778-85.

PUBMED | CROSSREF

17. Rosania R, Chiapponi C, Malfertheiner P, Venerito M. Nutrition in patients with gastric cancer: an update. Gastrointest Tumors 2016;2:178-87.

PUBMED | CROSSREF

18. Zheng HL, Lu J, Li P, Xie JW, Wang JB, Lin JX, Chen QY, Cao LL, Lin M, Tu R, et al. Effects of preoperative malnutrition on short- and long-term outcomes of patients with gastric cancer: can we do better? Ann Surg Oncol 2017;24:3376-85.

PUBMED | CROSSREF

- Kurita N, Miyata H, Gotoh M, Shimada M, Imura S, Kimura W, Tomita N, Baba H, Kitagawa Y, Sugihara K, et al. Risk model for distal gastrectomy when treating gastric cancer on the basis of data from 33,917 Japanese patients collected using a nationwide web-based data entry system. Ann Surg 2015;262:295-303.
 PUBMED | CROSSREF
- Kunisaki C, Miyata H, Konno H, Saze Z, Hirahara N, Kikuchi H, Wakabayashi G, Gotoh M, Mori M. Modeling preoperative risk factors for potentially lethal morbidities using a nationwide Japanese web-based database of patients undergoing distal gastrectomy for gastric cancer. Gastric Cancer 2017;20:496-507.

 PUBMED | CROSSREF
- 21. Kikuchi H, Miyata H, Konno H, Kamiya K, Tomotaki A, Gotoh M, Wakabayashi G, Mori M. Development and external validation of preoperative risk models for operative morbidities after total gastrectomy using a Japanese web-based nationwide registry. Gastric Cancer 2017;20:987-97.

 PUBMED | CROSSREF
- Hartgrink HH, van de Velde CJ, Putter H, Bonenkamp JJ, Klein Kranenbarg E, Songun I, Welvaart K, van Krieken JH, Meijer S, Plukker JT, et al. Extended lymph node dissection for gastric cancer: who may benefit? Final results of the randomized Dutch gastric cancer group trial. J Clin Oncol 2004;22:2069-77.

 PUBMED | CROSSREF
- 23. Liu X, Xue Z, Yu J, Li Z, Ma Z, Kang W, Ye X, Jiang L. Risk factors for postoperative infectious complications in elderly patients with gastric cancer. Cancer Manag Res 2020;12:4391-8.

 PUBMED | CROSSREF
- Hall WH, Ramachandran R, Narayan S, Jani AB, Vijayakumar S. An electronic application for rapidly calculating Charlson comorbidity score. BMC Cancer 2004;4:94.
 PUBMED | CROSSREF
- Washington K, 7th edition of the AJCC cancer staging manual: stomach. Ann Surg Oncol 2010;17:3077-9.
 PUBMED | CROSSREF
- 26. Kondrup J, Rasmussen HH, Hamberg O, Stanga Z; Ad Hoc ESPEN Working Group. Nutritional risk screening (NRS 2002): a new method based on an analysis of controlled clinical trials. Clin Nutr 2003;22:321-36.

PUBMED | CROSSREF

27. Park HA, Park SH, Cho SI, Jang YJ, Kim JH, Park SS, Mok YJ, Kim CS. Impact of age and comorbidity on the short-term surgical outcome after laparoscopy-assisted distal gastrectomy for adenocarcinoma. Am Surg 2013;79:40-8.

PUBMED | CROSSREF

28. Mizuno A, Kanda M, Kobayashi D, Tanaka C, Iwata N, Yamada S, Fujii T, Nakayama G, Sugimoto H, Koike M, et al. Adverse effects of intraoperative blood loss on long-term outcomes after curative gastrectomy of patients with stage II/III gastric cancer. Dig Surg 2016;33:121-8.

PUBMED | CROSSREF

 Kim CH, Park SM, Kim JJ. The impact of preoperative low body mass index on postoperative complications and long-term survival outcomes in gastric cancer patients. J Gastric Cancer 2018;18:274-86.
 PUBMED | CROSSREF

 Liu BZ, Tao L, Chen YZ, Li XZ, Dong YL, Ma YJ, Li SG, Li F, Zhang WJ. Preoperative body mass index, blood albumin and triglycerides predict survival for patients with gastric cancer. PLoS One 2016;11:e0157401.

PUBMED | CROSSREF

31. Feng F, Zheng G, Guo X, Liu Z, Xu G, Wang F, Wang Q, Guo M, Lian X, Zhang H. Impact of body mass index on surgical outcomes of gastric cancer. BMC Cancer 2018;18:151.

PUBMED | CROSSREF



32. Zhao B, Zhang J, Zhang J, Zou S, Luo R, Xu H, Huang B. The impact of preoperative underweight status on postoperative complication and survival outcome of gastric cancer patients: a systematic review and meta-analysis. Nutr Cancer 2018;70:1254-63.

PUBMED | CROSSREF

33. Lee HH, Park JM, Song KY, Choi MG, Park CH. Survival impact of postoperative body mass index in gastric cancer patients undergoing gastrectomy. Eur J Cancer 2016;52:129-37.

34. Ejaz A, Spolverato G, Kim Y, Poultsides GA, Fields RC, Bloomston M, Cho CS, Votanopoulos K, Maithel SK, Pawlik TM. Impact of body mass index on perioperative outcomes and survival after resection for gastric cancer. J Surg Res 2015;195:74-82.

PUBMED | CROSSREF

35. Bahat G, Tufan F, Saka B, Akin S, Ozkaya H, Yucel N, Erten N, Karan MA. Which body mass index (BMI) is better in the elderly for functional status? Arch Gerontol Geriatr 2012;54:78-81.

PURMED I CROSSREE

36. Rondel ALMA, Langius JAE, de van der Schueren MAE, Kruizenga HM. The new ESPEN diagnostic criteria for malnutrition predict overall survival in hospitalised patients. Clin Nutr 2018;37:163-8.

37. Cederholm T, Bosaeus I, Barazzoni R, Bauer J, Van Gossum A, Klek S, Muscaritoli M, Nyulasi I, Ockenga J, Schneider SM, et al. Diagnostic criteria for malnutrition - an ESPEN consensus statement. Clin Nutr 2015;34:335-40.

PUBMED | CROSSREF

38. Guo W, Ou G, Li X, Huang J, Liu J, Wei H. Screening of the nutritional risk of patients with gastric carcinoma before operation by NRS 2002 and its relationship with postoperative results. J Gastroenterol Hepatol 2010;25:800-3.

PUBMED | CROSSREF

39. Qiu M, Zhou YX, Jin Y, Wang ZX, Wei XL, Han HY, Ye WF, Zhou ZW, Zhang DS, Wang FH, et al. Nutrition support can bring survival benefit to high nutrition risk gastric cancer patients who received chemotherapy. Support Care Cancer 2015;23:1933-9.

PUBMED | CROSSREF

 Jiang N, Deng JY, Ding XW, Ke B, Liu N, Zhang RP, Liang H. Prognostic nutritional index predicts postoperative complications and long-term outcomes of gastric cancer. World J Gastroenterol 2014;20:10537-44.

PUBMED | CROSSREF

PUBMED | CROSSREF

41. Sakurai K, Ohira M, Tamura T, Toyokawa T, Amano R, Kubo N, Tanaka H, Muguruma K, Yashiro M, Maeda K, et al. Predictive potential of preoperative nutritional status in long-term outcome projections for patients with gastric cancer. Ann Surg Oncol 2016;23:525-33.

42. Tateishi R, Yoshida H, Shiina S, Imamura H, Hasegawa K, Teratani T, Obi S, Sato S, Koike Y, Fujishima T, et al. Proposal of a new prognostic model for hepatocellular carcinoma: an analysis of 403 patients. Gut 2005;54:419-25.

PUBMED | CROSSREF

43. Esfahani A, Makhdami N, Faramarzi E, Asghari Jafarabadi M, Ostadrahimi A, Ghayour Nahand M, Ghoreishi Z. Prealbumin/CRP based prognostic score, a new tool for predicting metastasis in patients with inoperable gastric cancer. Gastroenterol Res Pract 2016;2016:4686189.

PUBMED | CROSSREF

Eujisaki M. Shinahara T. Hanyu N. Vawana S. Tanak

44. Fujisaki M, Shinohara T, Hanyu N, Kawano S, Tanaka Y, Watanabe A, Yanaga K. Laparoscopic gastrectomy for gastric cancer in the elderly patients. Surg Endosc 2016;30:1380-7.

PUBMED | CROSSREF

45. Frenkel WJ, Jongerius EJ, Mandjes-van Uitert MJ, van Munster BC, de Rooij SE. Validation of the Charlson comorbidity index in acutely hospitalized elderly adults: a prospective cohort study. J Am Geriatr Soc 2014;62:342-6.

PUBMED | CROSSREF

46. Iwai N, Dohi O, Naito Y, Inada Y, Fukui A, Takayama S, Ogita K, Terasaki K, Nakano T, Ueda T, et al. Impact of the Charlson comorbidity index and prognostic nutritional index on prognosis in patients with early gastric cancer after endoscopic submucosal dissection. Dig Endosc 2018;30:616-23.

PUBMED | CROSSREF