BJR

https://doi.org/10.1259/bjr.20201004

Received: 18 August 2020 | Revised: 02 September 2021 | Accepted: 08 December 2021

Cite this article as:
Sun W, Li G, Zhang J, Zhu J, Zhang Z. The role of nutritional assessment for predicting radiotherapy-induced adverse events in patients with gastric cancer. *Br J Radiol* 2022; **95**: 20201004.

FULL PAPER

The role of nutritional assessment for predicting radiotherapy-induced adverse events in patients with gastric cancer

[1,2]WENJIE SUN, [1,2]GUICHAO LI, [1,2]JING ZHANG, [1,2]JI ZHU and [1,2]ZHEN ZHANG

[1]Department of Radiation Oncology, Fudan University Shanghai Cancer Center, Shanghai, China
[2]Department of Oncology, Shanghai Medical College, Fudan University, Shanghai, China

Address correspondence to: Dr Zhen Zhang
E-mail: *zhenzhang6618@163.com*

Objective: The aim of this study was to investigate the role of nutritional factors in predicting radiotherapy-associated toxicities for gastric cancer patients.
Methods: A total of 285 gastric cancer patients who underwent radiotherapy in our hospital (Fudan University Shanghai Cancer Center) between 2010 and 2017 were included in this retrospective study. Nutritional status assessment included body weight loss (BWL), body mass index (BMI), serum albumin, nutrition risk screening 2002(NRS-2002), patient-generated subjective global assessment(PG-SGA) and nutritional risk index (NRI).
Results: Of all patients, 19.6% were underweight (BMI<18.5 kg/m^2), 25.6% were hypoalbuminemia (<35 g l^{-1}) and 48.8% lost ≥10% of body weight in the 6-month interval before radiotherapy(BWL). Meanwhile, 73.3%, 78.6 and 47.2% of the patients were diagnosed as malnutrition based on NRS-2002, PG-SGA and NRI, respectively. Hematological adverse events were present in 91.2% (≥Grade 1) and 20.4% (≥Grade 3) of the patients. Non-hematological adverse events occurred in 89.8% (≥Grade1) and 14.4% (≥Grade 3) of the patients. Multivariate analyses indicated that only hypoalbuminemia(<35 g l^{-1}) was independent predictor for Grade 3/4 hematological and non-hematological adverse events. Meanwhile, higher BWL(≥10%) was also independent predictor for Grade 3/4 non-hematological adverse events. NRS-2002, PG-SGA and NRI score were not associated with treatment-induced adverse events.
Conclusion: BWL and serum albumin are useful factors for predicting severe adverse events in gastric cancer patients who undergo radiotherapy.
Advances in knowledge: The use of nutritional factors in predicting severe adverse events enables implementation of individualized treatment strategies for early and intensive nutritional interventions in high-risk patients.

INTRODUCTION

Surgery combined with radiotherapy and chemotherapy is currently the main treatment modality in gastric cancer. Post-operative chemoradiotherapy should be considered for all gastric cancer patients at high risk for recurrence who have undergone curative resection, which may improve the local control rate and long-term survival of patients.[1] However, problems of treatment-related toxicities are gradually emerging, which often lead to dose reductions or treatment breaks.

Malnutrition is very common in gastric cancer patients.[2,3] Patients with gastric cancer are particularly susceptible to malnutrition for numerous reasons, mainly including tumor-induced metabolic abnormalities, decrease in dietary intake due to cancer-related gastrointestinal symptoms and treatment-related side-effects.[4–6] Malnutrition, which causes reduced tissue vitality and decreased wound healing, may be associated with the incidence of treatment-induced adverse events.[7,8] Severe adverse toxicities often lead to dose reductions, interruptions of treatment course or even treatment terminations, which eventually cause reduced treatment efficacy.[9,10] On the other hand, adverse toxicities may lead to decreased oral food intake and aggravation of malnutrition. Therefore, the assessment of malnutrition status and prediction of high-risk patients with severe adverse events, may play a key role in implementation of individualized treatment strategies. Early and intensive nutritional interventions might be given for high-risk patients in order to reduce treatment toxicities.

Some previous studies reported that malnutrition and weight loss were associated with poor treatment outcomes and severe toxicities in gastrointestinal cancer patients

undergoing surgery and chemotherapy.[11,12] Also, in most of these studies, the number of patients was too small to well analyze their intrinsic relevance. Therefore, the aim of our study was to evaluate the malnutrition status before radiotherapy and investigate the role of nutritional factors in predicting severe radiotherapy-induced toxicities for gastric cancer patients. To our knowledge, our study was the first report with a relatively large sample in this field.

METHODS AND MATERIALS

Study patients

Gastric cancer patients who underwent radiation therapy in our hospital between April 2010 and February 2017 were included in this retrospective study. Patients who underwent radiation therapy outside of the gastric regions were eliminated. Patients who had other types of cancer and those who had poor physical performance level with ECOG score >2 (the Eastern Cooperative Oncology Group, ECOG) were also excluded. Patients who did not receive comprehensive nutritional assessments during radiotherapy were excluded. A total of 285 patients were included in this study. All patients received comprehensive clinical evaluations and nutritional assessments before initiation of radiation therapy. This study was ethically based on the Declaration of Helsinki and the principles of "good clinical practice". The study was approved by the Institutional Research and Ethics Committee.

Treatments and evaluation of adverse events

All patients were treated with intensity-modulated radiation therapy (IMRT) in daily fraction of 1.8 Gy, 5 days per week, total doses of 45–50.4 Gy. Most patients (89.1%) received concurrent chemotherapy during radiation therapy. Of these, 21.4% patients received Capecitabine (625 mg/m^2, bd, day 1–5/week) as chemotherapy protocol while 60.7% patients received S-1(Tegafur/Gimeracil/Oteracil) (25 mg/m^2, bd, day 1–5/week). Other concurrent chemotherapy protocols included XELOX (Oxaliplatin + Capecitabine), SOX (Oxaliplatin + S-1), FOLFIRI (Irinotecan+5 Fu). These data were shown in Table 1.

Table 1. Patients' characteristics (*N* = 285)

Patients' characteristics	N(%)
Age	
Median	57
Range	24–87
Sex	
Male	210 (73.7)
Female	75 (26.3)
T Stage	
T1-2	28 (9.8)
T3-4	257 (90.2)
N Stage	
Negative	11 (3.9)
Positive	274 (96.1)
Metastasis	
Negative	260 (91.2)
Positive	25 (8.8)
Radiotherapy	
45 Gy (25 Fx in 5 weeks)	251 (88.1)
50.4 Gy (28 Fx in 5.5 weeks)	20 (7.0)
Others	14 (4.9)
Chemotherapy regimen	
No concurrent chemo	31 (10.9)
Capecitabine	61 (21.4)
S-1	173 (60.7)
Others (XELOX; SOX; FOLFIRI)	20 (7.0)
Treatment type	
Neoadjuvant	67 (23.5)
Adjuvant	189 (66.3)
Palliative	29 (10.2)

FOLFIRI: Irinotecan + 5-Fu; SOX: Oxaliplatin + Tegafur;XELOX: Oxaliplatin + Capecitabine.

Treatment-associated adverse events were assessed and recorded by the guidelines of Common Terminology Criteria for Adverse Events (CTCAE, v. 3). The score of each side-effect was the highest score among measurements during the treatment period. Grade 3 and Grade 4 were considered severe adverse effects. Treatment outcomes were recorded, which included completion of prescribed radiotherapy and/or chemotherapy (received dose/cycles compared with prescribed dose/cycles) and occurrence of unscheduled breaks from radiotherapy (number of breaks, break duration and reason for the break).

Nutritional assessment

In our study, we used six nutritional parameters to evaluate the nutritional status of patients before radiation therapy, including body weight loss (BWL), body mass index (BMI), serum albumin, nutrition risk screening 2002 (NRS-2002), patient-generated subjective global assessment (PG-SGA) and nutritional risk index (NRI). BWL malnutrition was defined as a greater than 10% decrease in body weight in the 6-month interval immediately preceding radiation therapy. BMI was calculated and underweight was defined as BMI less than 18.5 kg/m^2. The value of serum albumin was considered "low" when below 35 g l^{-1}.[12] Furthermore, nutritional screening tools such as NRS-2002, PG-SGA and NRI were assessed. NRS-2002 score combined data from nutritional status, severity of disease and age, and NRS-2002 ≥3 was considered to have risk of malnutrition.[13] PG-SGA score was composed of two sections of numerical scores. The first section was a medical history section completed by the patient, and the second section was a physical examination section completed by medical staff. The sum scores of these two sections were classified as three grades: without or mild malnutrition (PG-SGA 0–3), moderate malnutrition (PG-SGA 4–8) and severe malnutrition (PG-SGA ≥9).[14]

Table 2. Nutritional status-related indices of the patients (*N* = 285)

Nutritional status	Neoadjuvant *N* = 67 n (%)	Adjuvant *N* = 189 n (%)	Palliative *N* = 29 n (%)
BWL (%)			
Mean	5.31	11.76	5.89
≥10%	12 (17.9)	120 (63.5)	7 (24.1)
<10%	55 (82.1)	69 (36.5)	22 (75.9)
BMI (kg/m^2)			
Mean	22.56	20.73	20.57
≥18.5	64 (95.5)	144 (76.2)	21 (72.4)
<18.5	3 (4.5)	45 (23.8)	8 (27.6)
Albumin (g/L)			
Mean	39.69	38.45	38.28
≥35	58 (86.6)	133 (70.4)	21 (72.4)
<35	9 (13.4)	56 (29.6)	8 (27.6)
NRS2002 score			
Mean	2.36	4.01	3.07
≥3	27 (40.3)	163 (86.2)	19 (65.5)
<3	40 (59.7)	26 (13.8)	10 (34.5)
PG-SGA score			
Mean	4.67	7.13	6.90
0–3	23 (34.3)	30 (15.9)	8 (27.6)
4–8	38 (56.7)	105 (55.6)	15 (51.7)
≥9	6 (9.0)	54 (28.6)	6 (20.7)
NRI score			
Mean	99.78	95.20	97.40
<83.5	5 (7.5)	32 (16.9)	6 (20.7)
83.5–97.5	18 (26.9)	70 (37.0)	7 (24.1)
>97.5	44 (65.7)	87 (46.0)	16 (55.2)

BMI: body mass index;BWL: body weight loss; NRI: nutritional risk index; NRS: nutrition risk screening; PG-SGA: patient-generated subjective global assessment.

NRI was calculated as follows: NRI= (1.519*serum albumin, g/L)+0.417*(present body weight /ideal body weight) *100. NRI scores were regrouped as three grades: major risk (NRI <83.5), moderate risk (NRI 83.5–97.5) and mild risk (NRI >97.5).[11]

Statistical analyses

Statistical analyses were performed using SPSS v. 18.0 (Chicago, IL). Categorical variables were expressed as counts and percentages. To analyze the associations between adverse events and clinical or nutritional variables, the χ^2 test was used for univariate analysis. Multivariate binary logistic regression was further computed to investigate the relationship between adverse events and these variables. Covariates used in each multivariate analysis were those which showed significance in univariate analysis. All tests were two-sided and were performed at a 5% level of significance.

RESULTS

Patients' characteristics

Clinical characteristics of the patients were presented in Table 1. This study included 210 (73.7%) males and 75 (26.3%) females. The median age was 57 years old (range 24–87). All patients received comprehensive evaluations at baseline and their clinical or pathological stages were shown as follows: for T stage, 28 (9.8%) and 257 (90.2%) patients were classified as T1-2 and T3-4, respectively. For N stage, 274 (96.1%) and 11 (3.9%) patients were classified as *N* + and N0, respectively. Of all patients, 25 (8.8%) patients were diagnosed as distant metastasis. For treatment type, most patients received adjuvant (66.3%) or neoadjuvant (23.5%) radiotherapy, and 89.1% patients received concurrent chemotherapy.

Evaluation of nutritional status

The results of nutritional status-related assessments at baseline were shown in Table 2. There were 139 (48.8%) patients who

Table 3. Hematological and non-hematological adverse events (*N* = 285)

Events		Grade of treatment toxicity (No (%))					
		Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Grade 3 + 4
Hematological adverse events	Anemia	96 (33.7)	130 (45.6)	54 (18.9)	5 (1.8)	0 (0)	5 (1.8)
	Leucopenia	59 (20.7)	86 (30.2)	95 (33.3)	42 (14.7)	3 (1.1)	45 (15.8)
	Neutropenia	126 (44.2)	53 (18.6)	76 (26.7)	29 (10.2)	1 (0.4)	30 (10.5)
	Thrombocytopenia	136 (47.7)	82 (28.8)	56 (19.6)	11 (3.9)	0 (0)	11 (3.9)
	Total	25 (8.8)	75 (26.3)	127 (44.6)	55 (19.3)	3 (1.1)	58 (20.4)
Non-hematological adverse events	Anorexia	96 (33.7)	60 (21.1)	96 (33.7)	33 (11.6)	0 (0)	33 (11.6)
	Nausea	86 (30.2)	108 (37.9)	74 (26.0)	17 (6.0)	0 (0)	17 (6.0)
	Vomiting	159 (55.8)	68 (23.9)	51 (17.9)	7 (2.5)	0 (0)	7 (2.5)
	Diarrhea	231 (81.1)	41 (14.4)	13 (4.6)	0 (0)	0 (0)	0 (0)
	Constipation	194 (68.1)	69 (24.2)	21 (7.4)	1 (0.4)	0 (0)	1 (0.4)
	Abdominal pain	220 (77.2)	56 (19.6)	8 (2.8)	1 (0.4)	0 (0)	1 (0.4)
	Stomatitis	187 (65.6)	74 (26.0)	22 (7.7)	2 (0.7)	0 (0)	2 (0.7)
	Abdominal distension	195 (68.4)	45 (15.8)	44 (15.4)	1 (0.4)	0 (0)	1 (0.4)
	Intestinal obstruction	283 (99.3)	1 (0.4)	1 (0.4)	0 (0)	0 (0)	0 (0)
	Total	29 (10.2)	91 (31.9)	124 (43.5)	41 (14.4)	0 (0)	41 (14.4)

lost ≥10% of body weight in the 6-month interval before radiotherapy (BWL). Of all patients, 19.6% were underweight (BMI < 18.5 kg/m^2) and 25.6% were hypoalbuminemia (<35 $g l^{-1}$). Three nutritional screening tools were used in this study. Of all patients, 73.3% exhibited NRS-2002 score ≥3 which indicated the risk of malnutrition. The results of PG-SGA assessment showed that 55.4% of the patients were diagnosed as moderate malnutrition and 23.2% were diagnosed as severe malnutrition. Meanwhile, the results of NRI assessment showed that 32.5 and 14.7% of the patients were diagnosed as moderate and severe malnutrition, respectively.

Treatment-associated adverse events

Hematological and non-hematological adverse events of the patients were shown in Table 3. About 91% of the patients experienced hematological adverse events (≥Grade 1) and 20.4% of the patients had severe adverse events (Grade 3–4). The most common severe adverse events (Grade 3–4) were leucopenia (15.8%) and neutropenia (10.5%). About 90% of the patients experienced non-hematological adverse events (≥Grade 1) and 14.4% of the patients had adverse events with Grade 3. None of the patients experienced Grade 4 adverse events. The most common severe adverse events (Grade 3–4) were anorexia (11.6%) followed by nausea (6.0%).

93% of the patients (265/285) finished their radiotherapy as it was planned. However, about 2% of the patients (6/285) needed unplanned breaks in radiotherapy because of treatment toxicities. About 5% of patients (14/285) didn't finish their radiotherapy mainly because of treatment toxicities (other 2 patients because of their tumor progression). Meanwhile, 90% of patients (255/285) received concurrent chemotherapy during radiotherapy. About 27% of the patients (68/255) required drug dose reduction or treatment breaks because of their intolerable toxicities.

Prediction of treatment-associated adverse events

Association between different risk factors and hematological adverse events was analyzed and shown in Table 4. Based on the degree of hematological adverse events, patients were classified as those without or just with slight toxicities (Grade 0–2) and those with severe toxicities (Grade 3–4). Among these clinical and nutritional factors, higher BWL (≥10%), underweight (BMI<18.5 kg/m^2) and hypoalbuminemia (<35 $g l^{-1}$) demonstrated a statistically significant association with severe adverse events. Meanwhile, NRI score <83.5, NRS-2002 score ≥3 and PG-SGA score ≥9 were also found to be significant risk factors for severe adverse events. However, there was no statistical significance associated with other factors, including sex, age, metastasis, surgery prior to RT, chemotherapy prior to RT and concurrent chemotherapy. Multivariate analysis was further performed among these factors and the results showed that only hypoalbuminemia (<35 $g l^{-1}$) [odds ratio, OR 3.380; 95% confidence interval (CI) 1.398–8.173, $p = 0.007$] was significantly and independently related to severe toxicities.

Similarly, association between these risk factors and non-hematological adverse events was also analyzed and shown in Table 5. Higher BWL (≥10%) and hypoalbuminemia (<35 $g l^{-1}$) were significantly associated with severe adverse events. Meanwhile, NRI score <83.5 and PG-SGA score ≥9 were also demonstrated to be significant risk factors for severe toxicities. On the other hand, there was no significant relationship between severe adverse events and other factors, including sex, age, metastasis,

Table 4. Multivariate logistic regression analysis of risk factors for hematological adverse events (N = 285)

		Grade 0–2	Grade 3–4	Univariate	Multivariate	
		(N = 227)	(N = 58)	p- value	OR (95% CI)	p- value
Sex	Male	170 (81.0%)	40 (19.0%)	0.360		
	Female	57 (76.0%)	18 (24.0%)			
Age	≥60	101 (81.5%)	23 (18.5%)	0.507		
	<60	126 (78.3%)	35 (21.7%)			
Metastasis	Positive	17 (68.0%)	8 (32.0%)	0.130		
	Negative	210 (80.8%)	50 (19.2%)			
Surgery prior to RT	Yes	152 (80.4%)	37 (19.6%)	0.649		
	No	75 (78.1%)	21 (21.9%)			
Chemotherapy prior to RT	Yes	203 (78.4%)	56 (21.6%)	0.124		
	No	24 (92.3%)	2 (7.7%)			
Concurrent chemotherapy	Yes	204 (80.3%)	50 (19.7%)	0.424		
	No	23 (74.2%)	8 (25.8%)			
BWL	≥10%	99 (71.2%)	40 (28.8%)	0.001	1.58 (0.76–3.31)	0.220
	<10%	128 (87.7%)	18 (12.3%)		1	
BMI	≥18.5	188 (82.1%)	41 (17.9%)	0.038	1	0.702
	<18.5	39 (69.6%)	17 (30.4%)		1.16 (0.40–1.87)	
Albumin	≥35	187 (88.2%)	25 (11.8%)	<0.001	1	0.007
	<35	40 (54.8%)	33 (45.2%)		3.38 (0.12–0.72)	
NRI	≥83.5	207 (85.5%)	35 (14.5%)	<0.001	1	0.344
	<83.5	20 (46.5%)	23 (53.5%)		1.64 (0.59–4.54)	
NRS-2002	≥3	160 (76.6%)	49 (23.4%)	0.031	1.04 (0.41–2.60)	0.942
	<3	67 (88.2%)	9 (11.8%)		1	
PG-SGA	≥9	41 (62.1%)	25 (37.9%)	<0.001	2.00 (0.98–4.05)	0.057
	<9	186 (84.9%)	33 (15.1%)		1	

BMI: body mass index;BWL: body weight loss;CI, confidence interval; NRI: nutritional risk index; NRS: nutrition risk screening;OR, odds ratio; PG-SGA: patient-generated subjective global assessment.

surgery prior to RT, chemotherapy prior to RT, concurrent chemotherapy, BMI and NRS-2002 score. Furthermore, multivariate analysis was performed and the results showed that higher BWL (≥10%) (OR 4.900; 95% CI 1.677–14.322, p = 0.004) and hypoalbuminemia (<35 $g l^{-1}$) (OR 9.929; 95% CI 3.166–31.136, p < 0.001) were significantly and independently associated with severe adverse events.

DISCUSSION

There are various methods for screening and evaluating nutritional status of patients, but no consensus has been reached. In our study, we assessed the nutritional status of patients by several common methods and investigated the relationship between these nutritional factors and the toxicities of radiotherapy in gastric cancer. Firstly, we analyzed weight-associated factors including BMI and BWL. We observed that patients with ≥10% BWL had higher incidence of severe adverse events during radiotherapy compared with those without. Meanwhile, underweight patients (BMI<18.5 kg/m^2) also had higher incidence of severe toxicities. However, by multivariate analysis, we only found BWL (≥10%) was a significant and independent predictor for severe non-hematological adverse events. According to the results of our study, patients with obvious weight loss before radiotherapy had a significant increase in the probability of severe non-hematological toxicity of radiotherapy, but this phenomenon couldn't be observed for patients with low weight. Therefore, we think that it is more appropriate to evaluate the recent weight loss before radiotherapy for predicting severe toxicities of radiotherapy. Some studies also reported that greater BWL was associated with poor chemoradiotherapy compliance.[15,16] However, other studies indicated that underweight patients were also prone to having treatment-related toxicities. A recent Korean study pointed out that patients with low BMI were highly susceptible to severe hematological adverse events for gastric cancer patients who received chemotherapy.[12] Hu et al also demonstrated that postoperative complications were significantly associated with BWL and BMI before surgery.[17] It should be pointed out that these studies were aimed at toxicities

Table 5. Multivariate logistic regression analysis of risk factors for non-hematological adverse events (*N* = 285)

		Grade 0–2	Grade 3–4	Univariate	Multivariate	
		(*N* = 244)	(*N* = 41)	*p*- value	OR (95% CI)	*p*- value
Sex	Male	179 (85.2%)	31 (14.8%)	0.762		
	Female	65 (86.7%)	10 (13.3%)			
Age	≥60	110 (88.7%)	14 (11.3%)	0.191		
	<60	134 (83.2%)	27 (16.8%)			
Metastasis	Positive	21 (84.0%)	4 (16.0%)	0.768		
	Negative	223 (85.8%)	37 (14.2%)			
Surgery prior to RT	Yes	157 (83.1%)	32 (16.9%)	0.086		
	No	87 (90.6%)	9 (9.4%)			
Chemotherapy prior to RT	Yes	220 (84.9%)	39 (15.1%)	0.394		
	No	24 (92.3%)	2 (7.7%)			
Concurrent chemotherapy	Yes	217 (85.4%)	37 (14.6%)	0.803		
	No	27 (87.1%)	4 (12.9%)			
BWL	≥10%	103 (74.1%)	36 (25.9%)	<0.001	4.90 (1.68–14.32)	0.004
	<10%	141 (96.6%)	5 (3.4%)		1	
BMI	≥18.5	200 (87.3%)	29 (12.7%)	0.094		
	<18.5	44 (78.6%)	12 (21.4%)			
Albumin	≥35	205 (96.7%)	7 (3.3%)	<0.001	1	<0.001
	<35	39 (53.4%)	34 (46.6%)		9.90 (0.03–0.32)	
NRI	≥83.5	227 (93.8%)	15 (6.2%)	<0.001	1	0.062
	<83.5	17 (39.5%)	26 (60.5%)		2.85 (0.95–8.57)	
NRS-2002	≥3	174 (83.3%)	35 (16.7%)	0.060		
	<3	70 (92.1%)	6 (7.9%)			
PG-SGA	≥9	48 (72.7%)	18 (27.3%)	0.001	1.08 (0.44–2.71)	0.862
	<9	196 (89.5%)	23 (10.5%)		1	

BMI: body mass index;BWL: body weight loss;CI, confidence interval; NRI: nutritional risk Index; NRS: nutrition risk screening;OR, odds ratio; PG-SGA: patient-generated subjective global assessment.

or complications of chemotherapy and surgery, but our study focused on the adverse events of radiotherapy, which might lead to difference in results. Of course, our conclusions still need to be further verified.

Serum albumin is a common nutritional evaluation index in clinical settings. Previous studies found that hypoalbuminemia was closely associated with poor cancer prognosis.[18,19] Furthermore, prognostic nutritional index calculated based on serum albumin and lymphocytes was reported as a prognostic marker in gastric cancer patients.[20] However, few recent studies found a potential correlation between serum albumin and treatment-associated adverse events, which might help physicians to apply individualized therapy strategies in clinical practice.[12,17] Seo et al indicated that hypoalbuminemia was a sensitive factor to predict chemotherapy-associated hematological side-effects, the most frequently occurring neutropenia. However, no significant association was observed for serum albumin with non-hematological adverse events in this study.[12] Another study also demonstrated that hypoalbuminemia significantly predicted post-operative complications and the hypoalbuminemia group had significantly longer total hospital stay.[17] In our study, we found that about 25% of patients had hypoalbuminemia, and we also found that hypoalbuminemia was the only significant and independent marker in predicting both hematological and non-hematological radiotherapy-associated toxicities, even by multivariate analysis. Gastric cancer patients are prone to hypoalbuminemia before radiotherapy due to various reasons including the decrease of patients' intake, treatment-related side-effects, and tumor-induced metabolic abnormalities. Hypoalbuminemia may cause reduced tissue vitality and decreased wound healing,[7,8] which may lead to the aggravation of radiotherapy toxicity. Therefore, serum albumin might be a promising marker to predict treatment complications and would be applied in individualized therapy strategies.

There are various screening methods to be used in nutritional assessment of cancer patients. In our study, we chose and

analyzed three common nutritional screening tools including NRS-2002, PG-SGA and NRI. NRS-2002 score combined data from nutritional status, severity of disease and age. PG-SGA score was composed of two sections: medical history section completed by patients and physical examination completed by medical staff. NRI score was calculated based on serum albumin and body weight. In our study, 73.3%, 78.6% and 47.2% of the patients were diagnosed as malnutrition based on NRS-2002, PG-SGA and NRI, respectively. Patients who were assessed as malnutrition based on these three screening tools had higher incidence of severe toxicities, but there was no significant association by multivariate analyses. Some studies also reported similar results. Seo et al indicated that there was no significant relationship of PG-SGA and NRI with hematological or non-hematological adverse events for gastric cancer patients who received chemotherapy.[12] Kono et al also could not find a statistically significant association between nutritional tools (NRI and NRS-2002) and severe radiotherapy-associated toxicities for head and neck cancer patients.[21] However, some other studies had come to different conclusions. Barret et al indicated that severe malnutrition assessed by NRI was shown to increase the adverse events and reduce the survival rate in metastatic colon cancer patients.[22] Another study suggested that higher PG-SGA score increased incidence of treatment complication and hospitalization.[15] The presumable reasons for these different results were as follows: because of the weak specificity of NRS-2002, this tool might be more suitable for primary malnutrition risk screening, not for further nutritional assessment of cancer patients. On the other hand, PG-SGA score was affected by subjective factors of patients, which might affect the accuracy of malnutrition conclusion to a certain extent. Therefore, although NRS-2002, PG-SGA and NRI are all validated approaches successfully applied in clinical settings as nutritional assessment tools, the role of their prediction for treatment-associated adverse events needs to be further verified.

There were several limitations to this study. This was a retrospective study with different treatment modalities, which rendered assessment and analyses difficult. In this study, we analyzed the association between treatment toxicities and different treatment modalities, but we did not find statistically significant difference. However, the heterogeneity of these various factors still might affect the accuracy and reliability of the results. Therefore, further prospective, well-designed future studies are required. Based on the preliminary results of this study, our institution is also carrying out a multicenter prospective nutrition assessment study, I believe there will be a more convincing conclusion in the future. Furthermore, recent progress has been made in the treatment strategy and nutritional management, further analyses for evaluating new original indices for gastric cancer are also required.

CONCLUSIONS

In our study, both BWL and serum albumin were useful factors for predicting severe adverse events in gastric cancer patients who underwent radiotherapy. However, some frequently used nutritional screening tools (NRS-2002, PG-SGA and NRI) were unable to predict radiotherapy-associated adverse events. We believe that our results will help the implementation of aggressive nutritional interventions to high-risk patients prior to radiotherapy, improving treatment compliance. However, further prospective, well-designed studies should also be performed in the future.

REFERENCES

1. Macdonald JS, Smalley SR, Benedetti J, Hundahl SA, Estes NC, Stemmermann GN, et al. Chemoradiotherapy after surgery compared with surgery alone for adenocarcinoma of the stomach or gastroesophageal junction. *N Engl J Med* 2001; **345**: 725–30. https://doi.org/10.1056/NEJMoa010187
2. Pressoir M, Desné S, Berchery D, Rossignol G, Poiree B, Meslier M, et al. Prevalence, risk factors and clinical implications of malnutrition in french comprehensive cancer centres. *Br J Cancer* 2010; **102**: 966–71. https://doi.org/10.1038/sj.bjc.6605578
3. Pan H, Cai S, Ji J, Jiang Z, Liang H, Lin F, et al. The impact of nutritional status, nutritional risk, and nutritional treatment on clinical outcome of 2248 hospitalized cancer patients: a multi-center, prospective cohort study in chinese teaching hospitals. *Nutr Cancer* 2013; **65**: 62–70. https://doi.org/10.1080/01635581.2013.741752
4. Bernstein IL, Sigmundi RA. Tumor anorexia: a learned food aversion? *Science* 1980; **209**: 416–18. https://doi.org/10.1126/science.6930106
5. Bosaeus I, Daneryd P, Svanberg E, Lundholm K. Dietary intake and resting energy expenditure in relation to weight loss in unselected cancer patients. *Int J Cancer* 2001; **93**: 380–83. https://doi.org/10.1002/ijc.1332
6. Jin D, Phillips M, Byles JE. Effects of parenteral nutrition support and chemotherapy on the phasic composition of tumor cells in gastrointestinal cancer. *JPEN J Parenter Enteral Nutr* 1999; **23**: 237–41. https://doi.org/10.1177/014860719902300423
7. Magnano M, Mola P, Machetta G, Maffeis P, Forestiero I, Cavagna R, et al. The nutritional assessment of head and neck cancer patients. *Eur Arch Otorhinolaryngol* 2015; **272**: 3793–99. https://doi.org/10.1007/s00405-014-3462-z
8. Chandra RK. Nutrition and the immune system: an introduction. *Am J Clin Nutr* 1997; **66**: 460S-463S. https://doi.org/10.1093/ajcn/66.2.460S
9. Dewys WD, Begg C, Lavin PT, Band PR, Bennett JM, Bertino JR, et al. Prognostic effect of weight loss prior tochemotherapy in cancer patients. *Am J Med* 1980; **69**: 491–97. https://doi.org/10.1016/S0149-2918(05)80001-3
10. Andreyev HJ, Norman AR, Oates J, Cunningham D. Why do patients with weight loss have a worse outcome when undergoing chemotherapy for gastrointestinal malignancies? *Eur J Cancer* 1998; **34**: 503–9. https://doi.org/10.1016/s0959-8049(97)10090-9
11. Schiesser M, Kirchhoff P, Müller MK, Schäfer M, Clavien P-A. The correlation of nutrition risk index, nutrition risk score, and bioimpedance analysis with postoperative complications in patients undergoing

gastrointestinal surgery. *Surgery* 2009; **145**: 519–26. https://doi.org/10.1016/j.surg.2009.02.001

12. Seo SH, Kim S-. E, Kang Y-. K, Ryoo B-. Y, Ryu M-. H, Jeong JH, et al. Association of nutritional status-related indices and chemotherapy-induced adverse events in gastric cancer patients. *BMC Cancer* 2016; **16**(1): 900. https://doi.org/10.1186/s12885-016-2934-5
13. 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. https://doi.org/10.1016/s0261-5614(02)00214-5
14. Bauer J, Capra S, Ferguson M. Use of the scored patient-generated subjective global assessment (pg-sga) as a nutrition assessment tool in patients with cancer. *Eur J Clin Nutr* 2002; **56**: 779–85. https://doi.org/10.1038/sj.ejcn.1601412
15. Hill A, Kiss N, Hodgson B, Crowe TC, Walsh AD. Associations between nutritional status, weight loss, radiotherapy treatment toxicity and treatment outcomes in gastrointestinal cancer patients. *Clin Nutr* 2011; **30**: 92–98. https://doi.org/10.1016/j.clnu.2010.07.015
16. Li Q, Li G, Wang Y, Long Z, Liu X, Zhang Z. Association of nutrition with treatment compliance and toxicities in patients undergoing chemoradiation after gastrectomy. *Zhonghua Wei Chang Wai Ke Za Zhi* 2013; **16**: 529–33.
17. Hu W-. H, Cajas-Monson LC, Eisenstein S, Parry L, Cosman B, Ramamoorthy S. Preoperative malnutrition assessments as predictors of postoperative mortality and morbidity in colorectal cancer: an analysis of acs-nsqip. *Nutr J* 2015; **14**: 91. https://doi.org/10.1186/s12937-015-0081-5
18. Di Fiore F, Lecleire S, Pop D, Rigal O, Hamidou H, Paillot B, et al. Baseline nutritional status is predictive of response to treatment and survival in patients treated by definitive chemoradiotherapy for a locally advanced esophageal cancer. *Am J Gastroenterol* 2007; **102**: 2557–63. https://doi.org/10.1111/j.1572-0241.2007.01437.x
19. Matsumoto Y, Zhou Q, Kamimura K, Moriyama M, Saijo Y. The prognostic nutrition index predicts the development of hematological toxicities in and the prognosis of esophageal cancer patients treated with cisplatin plus 5-fluorouracil chemotherapy. *Nutr Cancer* 2018; **70**: 447–52. https://doi.org/10.1080/01635581.2018.1445765
20. Nozoe T, Ninomiya M, Maeda T, Matsukuma A, Nakashima H, Ezaki T. Prognostic nutritional index: a tool to predict the biological aggressiveness of gastric carcinoma. *Surg Today* 2010; **40**: 440–43. https://doi.org/10.1007/s00595-009-4065-y
21. Kono T, Sakamoto K, Shinden S, Ogawa K. Pre-therapeutic nutritional assessment for predicting severe adverse events in patients with head and neck cancer treated by radiotherapy. *Clin Nutr* 2017; **36**: 1681–85. https://doi.org/10.1016/j.clnu.2016.10.021
22. Barret M, Malka D, Aparicio T, Dalban C, Locher C, Sabate J-M, et al. Nutritional status affects treatment tolerability and survival in metastatic colorectal cancer patients: results of an ageo prospective multicenter study. *Oncology* 2011; **81**: 395–402. https://doi.org/10.1159/000335478