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Impact of inflammation-based prognostic score on survival after curative thoracoscopic esophagectomy for esophageal cancer

N. Hirahara*, T. Matsubara, H. Hayashi, K. Takai, Y. Fujii, Y. Tajima

Department of Digestive and General Surgery, Shimane University Faculty of Medicine, Japan

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Abstract

Background: Despite recent improvements in early detection, progress in surgical techniques, and development of chemoradiation therapies, prognosis of esophageal cancer remains poor. The aim of the present study was to assess whether Glasgow Prognostic Score (GPS), an inflammation-based prognostic score, has prognostic value independent of conventional clinicopathological criteria in patients undergoing curative resection for esophageal cancer, even in elderly patients.

Methods: We retrospectively reviewed the database of 141 consecutive patients with histologically verified esophageal squamous cell carcinoma who underwent potentially curative surgery in our institute, between January 2006 and December 2014. GPS and neutrophil lymphocyte ratio (NLR) were calculated.

Results: On multivariate analysis, TNM stage ($p < 0.0001$) and GPS ($p = 0.041$) were independently associated with worse prognosis in overall patients with esophageal cancer.

Multivariate analysis evaluated the prognostic factors in two different patient groups: patients younger than 70 years (non-elderly) and those aged 70 years or more (elderly).

Multivariate analysis demonstrated that TNM stage ($p = 0.0003$) was an only independent risk factor for a worse prognosis among non-elderly group. Meanwhile, multivariate analysis demonstrated that TNM stage ($p = 0.001$) and GPS ($p = 0.043$) were the independent risk factor for a worse prognosis among elderly group.

Conclusion: The present study demonstrated that GPS is associated with prognosis and can be considered as an independent prognostic marker in patients who underwent esophagectomy. Moreover, the GPS has the advantage of being simple to measure, routinely available and well standardized. But the present study failed to confirm the NLR as a significant predictor of survival following resection for esophageal cancer.

Keywords: Esophageal cancer; Glasgow Prognostic Score; Neutrophil lymphocyte ratio; Prognosis

Introduction

Despite recent improvements in early detection, progress in surgical techniques, and development of chemoradiation therapies, prognosis of esophageal cancer remains poor worldwide. Surgery is the mainstay treatment for esophageal cancer, but an appreciable proportion of patients with advanced esophageal cancer develop recurrence, even after curative resection. Therefore, accurately predicting the prognosis is needed to improve patient survival and to provide an appropriate preoperative patient counseling.

Host-related factors including performance status, weight loss, smoking, and comorbidity, in addition to tumor pathology, play an important role in cancer outcomes.[1] However, the use of weight loss as a prognostic factor remains problematic since it is often not well defined and subject to bias.[2,3] Furthermore, performance status is recognized to be subjective.[4]

There has been an increasing evidence that the cancer-associated systemic inflammatory response has a great

* Corresponding author. Department of Digestive and General Surgery, Shimane University Faculty of Medicine, 89-1 Enya-cho, Izumo, Shimane 693-8501, Japan. Tel.: +81 853 20 2232; fax: +81 853 20 2229.
E-mail address: norinorihirahara@yahoo.co.jp (N. Hirahara).

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influence on disease-related outcomes for many cancer sites.[5,6] Recent several studies have indicated that the systemic inflammatory response may be associated with poor outcome in patients with advanced cancer.[7–9] In particular, the GPS, an inflammation-based prognostic score that includes only the serum levels of C-reactive protein (CRP) and albumin, is one of the most useful scoring systems for prognostication of patients with various advanced cancers.[10–13] The GPS is simple, convenient and can be calculated easily at the time of admission. Moreover, recent reports have demonstrated the utility of NLR, which is calculated from the neutrophil count divided by the lymphocyte count.[14] NLR is also a measure of systematic inflammation and an elevated NLR was found to predict poor survival in breast cancer patients.[15]

The aim of the present study was to assess whether GPS, an inflammation-based prognostic score, has prognostic value independent of conventional clinicopathological criteria in patients undergoing a potentially curative resection for esophageal cancer, even in elderly patients.

Patients and methods

Patients

We retrospectively reviewed the database of 141 consecutive patients with histologically verified esophageal squamous cell carcinoma who underwent potentially curative esophagectomy with R0 resection in our institute, between January 2006 and December 2014. R0 resection was defined as a complete resection without microscopic involvement of margins. Thoracoscopic subtotal esophagectomy with a three-field lymph node dissection was performed in all patients, followed by laparoscopic gastric surgery with an elevation of gastric conduit to the neck via the posterior mediastinal pathway or retrosternal pathway with an end-to-end anastomosis of the cervical esophagus and gastric conduit. The patient's clinical characteristics, laboratory data, treatment, and pathological data were obtained from a retrospective review of the records. No patients had clinical signs of infection or other systemic inflammatory conditions preoperatively.

Permission to perform this retrospective study was obtained from the ethical board of our institution.

Inflammation-based prognostic scores

Laboratory measurements including the serum levels of CRP, albumin and total cholesterol, white blood cell (WBC) count, neutrophil count, and lymphocyte count were performed on the day of admission. GPS and NLR were calculated based on these clinical data. The GPS was constructed as previously described.[16] Briefly, patients with both an elevated C-reactive protein (>1.0 mg/dl) and hypoalbuminemia (<3.5 g/dl) were allocated a score of 2. Patients in whom only one of these biochemical abnormalities was present were allocated a score of 1. Patients in whom neither of these abnormalities was present were allocated a score of 0. NLR was defined as the absolute neutrophil count divided by the absolute lymphocyte count.[14] For the purposes of analysis, an NLR of ≧2.5 is allocated a score of 1, and <2.5 a score of 0.

TNM stage

The pathological classification of the primary tumor, the degree of lymph node involvement and the presence of organ metastasis were determined according to the TNM classification system (7th edition of the cancer staging manual of the American Joint Committee on Cancer[17]).

Statistical analysis

Means and standard deviations were calculated and differences were identified using Student's t test. Differences between categories were identified using the Chi-square test. Survival curves were produced using the Kaplan–Meier survival method. Two groups were compared with a two-sided log-rank test. Hazard ratios were calculated and univariate and multivariate analyses were performed using Cox proportional hazards regression models. The potential prognostic factors for esophageal cancer were as follows: age (<70 vs. ≧70); gender (male vs. female); albumin concentration (<3.5 g/dl vs. ≧3.5 g/dl), CRP (<1.0 mg/dl vs. ≧1.0 mg/dl), pStage (1, 2 vs. 3), tumor size (<3 cm vs. ≧3 cm), operation time (<600 min vs. ≧600 min), intraoperative blood loss (<500 ml vs. ≧500 ml), GPS (GPS 0 vs. GPS 1–2), and NLR (0 vs. 1). Medical records were retrospectively reviewed to examine these factors.

All statistical analyses were performed using IBM SPSS Statistics version 21 for Windows (IBM Corporation, Armonk, NY, USA), and a p values of less than 0.05 was considered statistically significant.

Results

Relationships between GPS and clinicopathological features in esophageal cancer

Relationships between GPS and clinicopathological features are shown in Table 1. Significant correlations were observed between GPS and such factors as neutrophil count ($p = 0.016$), albumin concentrations ($p < 0.0001$), C-reactive protein ($p < 0.0001$), depth of tumor ($p = 0.002$), TNM stage ($p = 0.04$), and NLR ($p = 0.001$).

Prognostic factors for survival in esophageal cancer

The univariate analysis demonstrated that albumin concentrations ($p = 0.003$), TNM stage ($p < 0.0001$), tumor size ($p = 0.007$), and GPS ($p = 0.003$) were the significant risk factor for a worse prognosis (Table 2).

Table 1
Relationships between GPS and clinicopathologic features of all patients.

	GPS 0 (n = 109)	GPS 1 (n = 23)	GPS 2 (n = 9)	*p* value
Age(years)	65.7 ± 8.1	66.3 ± 8.4	66.0 ± 7.2	0.988
Gender				0.620
Male	97	22	8	
Female	12	1	1	
Neutrophil count (mL)	3380.2 ± 1341.3	4252.5 ± 1874.2	4417.4 ± 1549.3	0.016
Lymphocyte count (mL)	1679.0 ± 573.2	1557.8 ± 707.5	1297.1 ± 879.4	0.054
Albumin (g/dL)	4.1 ± 0.3	3.5 ± 0.5	3.0 ± 0.4	<0.0001
CRP (mg/dL)	0.19 ± 0.14	0.90 ± 1.14	1.91 ± 0.63	<0.0001
Location of tumor				0.204
Ce	3	2	1	
Ut	6	1	2	
Mt	47	11	4	
Lt	43	5	2	
Ae	10	4	0	
Tumor size (mm)	4.2 ± 2.5	4.9 ± 2.5	4.8 ± 1.5	0.090
Depth of tumor				0.002
T1a–1b	57	4	1	
T2	10	1	3	
T3	35	13	4	
T4a–4b	7	5	1	
Lymph node metastasis				0.038
N0	65	8	2	
N1	27	11	5	
N2	10	1	2	
N3	7	3	0	
Pathological stage				0.004
1a–1b	52	2	1	
2a–2b	23	8	3	
3a–3c	34	13	5	
Operation time (min)	652.6 ± 162.9	662.0 ± 144.5	700.2 ± 163.5	0.6106
Intraoperative blood loss (mL)	670.1 ± 638.8	737.8 ± 666.9	810.0 ± 505.4	0.4485
NLR	2.16 ± 0.88	3.45 ± 2.70	5.09 ± 4.64	0.001

On multivariate analysis, TNM stage ($p < 0.0001$) and GPS ($p = 0.041$) were independently associated with worse prognosis (Table 2).

Relationships between GPS and clinicopathological features in non-elderly patients

Relationships between GPS and clinicopathological features in non-elderly patients younger than 70-year-old (non-elderly group) are shown in Table 3. Significant correlations were observed between GPS and such factors as neutrophil count ($p = 0.009$), albumin concentrations ($p = 0.015$), C-reactive protein ($p < 0.0001$), depth of tumor ($p = 0.036$), TNM stage ($p = 0.009$), and NLR ($p < 0.0001$).

Prognostic factors for survival in non-elderly patients

Among non-elderlies, the univariate analysis demonstrated that TNM stage ($p < 0.0001$), tumor size ($p = 0.004$), and GPS ($p = 0.031$) were significant associated with worse prognosis. Multivariate analysis

Table 2
Univariate and multivariate analysis to assess the prognostic factor for overall patients.

Variables	Patients (n = 138)	Category or characteristics	Univariate			Multivariate		
			HR	95%CI	*p* value	HR	95%CI	*p* value
Age	95/46	(<70/≧70)	1.522	0.803–2.789	0.192			
Gender	127/14	(male/female)	0.724	0.329–1.913	0.483			
Albumin	27/114	(<3.5/≧3.5)	3.170	1.543–6.123	0.003			
CRP	123/18	(<1.0/≧1.0)	1.986	0.856–4.063	0.104			
pStage	89/52	(1,2/3)	5.679	3.052–11.092	<0.0001	4.957	2.543–10.129	<0.0001
Tumor size	56/85	(<3/≧3)	2.408	1.255–4.997	0.007	1.168	0.562–2.576	0.685
Operation time	47/94	(<600/≧600)	0.582	0.320–1.058	0.076			
Intraoperative blood loss	57/84	(<500/≧500)	1.187	0.652–2.223	0.579			
GPS	109/32	(<0/≧1.2)	2.747	1.426–5.087	0.003	2.045	1.032–3.928	0.041
NLR	92/49	(0/1)	1.164	0.616–2.126	0.631			

Table 3
Relationships between GPS and clinicopathologic features of non-elderly patients.

	GPS 0 (n = 73)	GPS 1 (n = 17)	GPS 2 (n = 5)	*p* value
Age(years)	61.4 ± 5.7	62.5 ± 5.4	60.6 ± 4.0	0.721
Gender				0.224
Male	64	17	5	
Female	9	0	0	
Neutrophil count (mL)	3379.6 ± 1370.8	4620.5 ± 1812.5	3887.8 ± 1598.3	0.009
Lymphocyte count (mL)	1720.9 ± 614.3	1553.6 ± 750.6	874.8 ± 465.8	0.015
Albumin (g/dL)	4.2 ± 0.3	3.6 ± 0.5	2.9 ± 0.5	<0.0001
CRP (mg/dL)	0.17 ± 0.11	1.11 ± 1.25	2.22 ± 0.56	<0.0001
Location of tumor				0.630
Ce	2	2	1	
Ut	3	1	0	
Mt	34	8	3	
Lt	25	4	1	
Ae	9	2	0	
Tumor size (mm)	4.1 ± 2.7	5.3 ± 2.5	4.3 ± 1.7	0.263
Depth of tumor				0.036
T1a–1b	37	3	0	
T2	5	0	1	
T3	24	11	3	
T4a–4b	7	3	1	
Lymph node metastasis				0.269
NO	45	6	2	
N1	18	7	3	
N2	5	1	0	
N3	5	3	0	
Pathological stage				0.009
1a–1b	34	2	1	
2a–2b	15	5	1	
3a–3c	24	10	3	
Operation time (min)	648.8 ± 152.7	669.5 ± 161.7	650.4 ± 183.1	0.885
Intraoperative blood loss (mL)	588.4 ± 523.0	918.2 ± 688.6	614.0 ± 454.3	0.087
NLR	2.13 ± 0.88	3.79 ± 2.94	6.72 ± 5.94	<0.0001

demonstrated that TNM stage (p = 0.0003) was an only independent risk factor for a worse prognosis (Table 4).

Relationships between GPS and clinicopathological features in elderly patients

Relationships between GPS and clinicopathological features in elderly patients 70 years of age or older (elderly group) are shown in Table 5. Significant differences were observed regarding such factors as neutrophil count (p = 0.049), albumin concentrations (p < 0.0001), C-reactive protein (p = 0.004), location of tumor (p = 0.036), depth of tumor (p = 0.006), and intraoperative blood loss (p = 0.035).

Prognostic factors for survival in elderly patients

Among elderlies, the univariate analysis demonstrated that albumin concentrations (p = 0.010), TNM stage (p = 0.0005), and GPS (p = 0.019) were significant associated with worse prognosis (Table 6).

Table 4
Univariate and multivariate analysis to assess the prognostic factor for non-elderly patients.

Variables	Patients (n = 95)	Category or characteristics	Univariate			Multivariate		
			HR	95%CI	*p* value	HR	95%CI	*p* value
Gender	86/9	(male/female)	0.536	0.206–1.829	0.285			
Albumin	14/81	(<0.3.5/≧3.5)	2.424	0.885–5.700	0.081			
CRP	81/14	(<1.0/≧1.0)	2.208	0.869–4.963	0.091			
pStage	58/37	(1,2/3)	5.915	2.690–14.330	<0.0001	4.718	2.000–12.221	0.0003
Tumor size	40/55	(<3/≧3)	3.316	1.428–9.016	0.004	1.536	0.586–4.454	0.394
Operation time	33/62	(<600/≧600)	0.489	0.228–1.033	0.061			
Intraoperative blood loss	39/56	(<500/≧500)	1.455	0.683–3.283	0.336			
GPS	73/22	(0/≧1.2)	2.468	1.091–5.278	0.031	1.762	0.756–3.927	0.183
NLR	60/35	(0/1)	1.288	0.585–2.721	0.517			

Table 5
Relationships between GPS and clinicopathologic features of elderly patients.

	GPS 0 (n = 36)	GPS 1 (n = 6)	GPS 2 (n = 4)	*p* value
Age(years)	74.5 ± 4.1	77.3 ± 4.3	72.8 ± 2.5	0.145
Gender				0.530
Male	33	5	3	
Female	3	1	1	
Neutrophil count (mL)	3381.4 ± 1298.5	3209.8 ± 1782.6	5079.5 ± 1393.7	0.049
Lymphocyte count (mL)	1594.0 ± 476.1	1569.8 ± 631.7	1825.0 ± 1050.8	0.910
Albumin (g/dL)	4.1 ± 0.3	3.2 ± 0.2	3.2 ± 0.1	<0.0001
CRP (mg/dL)	0.22 ± 0.18	0.29 ± 0.33	1.51 ± 0.52	0.004
Location of tumor				0.036
Ce	1	0	0	
Ut	3	0	2	
Mt	13	3	1	
Lt	18	1	1	
Ae	1	2	0	
Tumor size (mm)	4.4 ± 2.2	4.1 ± 2.2	5.6 ± 0.9	0.309
Depth of tumor				0.006
T1a–1b	20	1	1	
T2	5	1	2	
T3	11	2	1	
T4a–4b	0	2	0	
Lymph node metastasis				0.107
N0	20	2	0	
N1	9	4	2	
N2	5	0	2	
N3	2	0	0	
Pathological stage				0.081
1a–1b	18	0	0	
2a–2b	8	3	2	
3a–3c	10	3	2	
Operation time (min)	660.1 ± 183.9	640.5 ± 86.3	762.5 ± 131.5	0.410
Intraoperative blood loss (mL)	835.9 ± 808.9	226.7 ± 319.8	1055.0 ± 511.6	0.035
NLR	2.23 ± 0.90	2.48 ± 1.71	3.06 ± 0.64	0.214

Multivariate analysis demonstrated that TNM stage ($p = 0.001$) and GPS ($p = 0.043$) were the independent risk factor for a worse prognosis.

Postoperative overall survival and GPS

There existed significant differences in overall survival between patients with GPS of 0 and 1 ($p = 0.004$) and between patients with GPS of 0 and 2 ($p = 0.002$), but no significant difference was observed between patients with GPS of 1 and 2 ($p = 0.615$) (Fig. 1).

Since the number of patients with GPS 1 and 2 was small, we compared the patients with GPS 0 to those with GPS 1–2 in non-elderly group and elderly group.

In non-elderly group, there existed significant difference in overall survival between patients with GPS of 0 and 1–2 ($p = 0.014$) (Fig. 2a).

In elderly group, there existed significant difference in overall survival between patients with GPS of 0 and 1–2 ($p = 0.003$) (Fig. 2b).

Discussion

Esophageal cancer is a disease of the elderly, with peak incidence occurring in patients in their 70 s, and the elderly population is rapidly increasing in worldwide.[18] Early detection and surgery confers the greatest chance of long-term survival in patients with esophageal cancer. Despite improvements in surgical techniques and perioperative care with reduced perioperative mortality in esophageal surgery, esophagectomy is still known to be associated with substantial surgical risks, especially in the elderly. Therefore, there is a continuing interest in prognostic factors to permit more accurate patient stratification and which will improve clinical decision making.

In this study, we examined the prognostic significance of the GPS and NLR in patients undergoing thoracoscopic subtotal esophagectomy for esophageal cancer. In addition, we also evaluated the significance of the GPS in both elderly and non-elderly esophageal cancer patients.

To date, several clinical factors including clinical stage, performance status, and pathological findings have been identified as independent predictors of survival in a variety of common solid tumors.[19] However, despite the use of high-resolution imaging systems, clinical staging is frequently inaccurate and performance status is rarely defined objectively.[4,20,21]

Generally the development of hypoalbuminemia is often occurred in elderly population. The progression of hypoalbuminemia is likely to be a secondary event following

Table 6
Univariate and multivariate analysis to assess the prognostic factor for elderly patients.

Variables	Patients (n = 46)	Category or characteristics	Univariate			Multivariate		
			HR	95%CI	*p* value	HR	95%CI	*p* value
Gender	41/5	(male/female)	1.453	0.397–9.373	0.610			
Albumin	13/33	(<3.5/≧3.5)	4.769	1.486–14.605	0.010			
CRP	42/4	(<1.0/≧1.0)	3.057	0.162–17.615	0.365			
pStage	31/15	(1,2/3)	6.267	2.235–19.130	0.0005	5.898	2.033–18.510	0.001
Tumor size	16/30	(<3/≧3)	1.265	0.459–4.018	0.660			
Operation time	14/32	(<600/≧600)	0.808	0.299–2.277	0.676			
Intraoperative blood loss	18/28	(<500/≧500)	0.767	0.283–2.162	0.605			
GPS	36/10	(<0/≧1.2)	4.470	1.314–13.719	0.019	3.805	1.046–12.965	0.043
NLR	32/14	(0/1)	0.965	0.304–2.657	0.947			

serum elevation of CRP, and it reflectes a systemic inflammatory response.[22,23] The GPS may thus reflect both the presence of ongoing systemic inflammatory response (CRP) and the progressive nutritional decline (albumin) of the elderly patients with esophageal cancer.

CRP is a non-specific but sensitive marker of systemic inflammatory response and elevated CRP value is accepted as a reliable indicator of prognosis for several cancers.[1,24,25] Although it is not fully understood why elevated CRP correlates with poor long-term outcomes in cancer patients, elevated CRP levels can accelerate angiogenesis based on increased level of circulating levels of vascular growth factors and interleukins in cancer patients.[6,26] Moreover, a systemic inflammatory response can impair the T-lymphocytic response to cancer, while the intratumoral T cell infiltration is a favorable prognostic factor by promoting proliferative activity and IFN-γ secretion.[27] Besides, the concomitant nutritional decline reduces tolerance to treatment toxicities and compliance in cancer patients. Additionally, elevated acute-phase response proteins, especially CRP, are associated with the nutrition status and development of cancer-related cachexia.

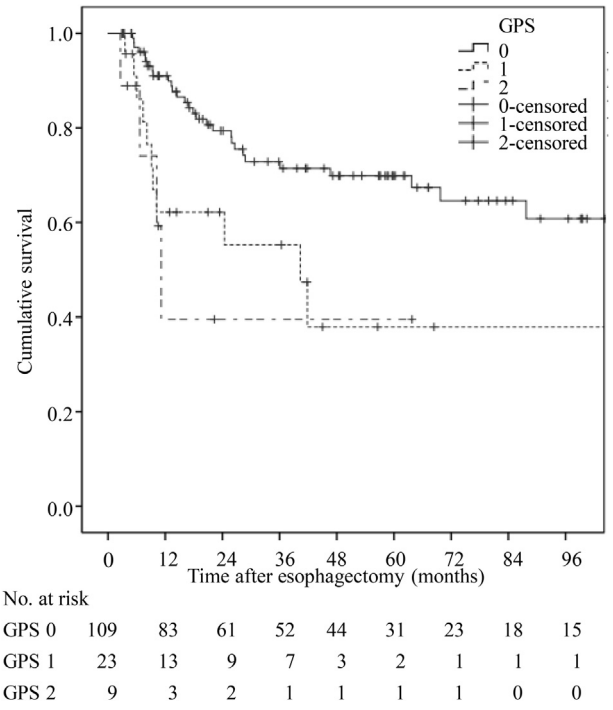

Figure 1. Kaplan–Meier survival curves showing the relationship between GPS levels (GPS = 0: solid line, GPS = 1: dotted line, GPS = 2: dashed line) and overall survival after esophagectomy in all patients with esophageal cancer.

While the GPS was a significant predictor of overall survival in patients with esophageal cancer in this study, TNM stage remained a significantly more powerful predictor of survival since the Hazard Ratio (HR) for TNM stage was 4.957 compared with HR of 2.045 for GPS on multivariate analysis. Therefore, the results of the present study suggested that the GPS and TNM stage are the significant and complementary factor predicting the survival in patients with esophageal cancer. But the survival data in this study is small sample, the data needs to be interpreted with caution.

Systemic inflammatory responses are associated with alterations in circulating white blood cell distribution with a neutrophilia and relative lymphopenia.[28] On the basis of ex vivo findings, neutrophils significantly modify the tumor microenvironment via their production of cytokines and chemokines, which influence inflammatory cell recruitment and activation. Additionally, products secreted from neutrophils, such as reactive oxygen species and proteinases, have specific roles in regulating tumor cell proliferation and metastasis.[29] The NLR was calculated from the neutrophil count divided by the lymphocyte count.[14] The NLR, a biomarker of the host systemic inflammatory response, has been shown to be highly promising in stratifying outcome in large cohorts of patients with cancers arising from unselected sites, with a higher pre-treatment ratio associated with a poor prognosis.[30,31] The relationship between a high NLR and poor prognosis is probably complex and still unclear. Recently, many studies have shown that a high NLR may indicate an impaired host immune response to the tumor.[32] In this study, NLR did not seem to affect the prognosis, which may due to retrospective small sample size and short follow-up duration of the study. However, other components of the systemic inflammatory response including platelet

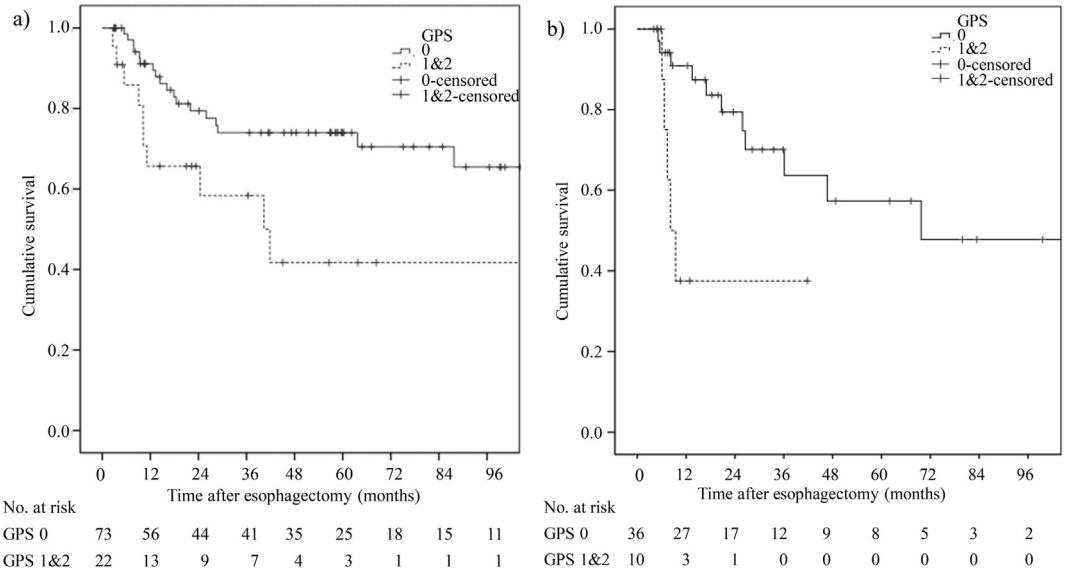

Figure 2. Kaplan–Meier survival curves showing the relationship between GPS levels (GPS = 0: solid line, GPS = 1–2: dotted line) and overall survival after esophagectomy in (a) non-elderly patents with esophageal cancer, (b) elderly patients with esophageal cancer.

counts, albumin and CRP levels are prognostically important in some studies.[33] Further examination will need to be performed to confirm these predicting markers.

Consistent with prior studies of esophageal cancer, the following factors were also associated with worse overall survival: older age, male sex, comorbidities, more advanced tumor stage, and worse tumor differentiation. The prognosis of patients diagnosed with operable esophageal cancer, even with active treatment, remains poor. Our study demonstrated that GPS is associated with prognosis and can be considered as an independent prognostic marker in patients who underwent esophagectomy. Moreover, the GPS has the advantage of being simple to measure, routinely available and well standardized. But the present study failed to confirm the NLR as a significant predictor of survival following resection for esophageal cancer. In summary, our study showed that preoperative GPS is a significant predictor of overall survival in patients with esophageal cancer and that the GPS is superior to NLR as a predictive factor for survival. Therefore pre-operative measurement of the GPS may be useful to decide the therapeutic strategy. We should examine pre-operative or post-operative adjuvant chemotherapy and/or radiotherapy for patients with poor prognosis identified by GPS score.

There were several potential limitations in our study. The prognostic analysis was a retrospective, small sample size, short follow-up periods study in a single institution. Furthermore, we excluded patients who had received adjuvant chemotherapy and/or radiotherapy, which may have influenced our analysis. Thus, larger prospective studies will need to be performed to confirm these preliminary results.

Conflict of interest statement

All authors have no conflicts of interest to declare.

References

1. Roxburgh CS, McMillan DC. Role of systemic inflammatory response in predicting survival in patients with primary operable cancer. *Future Oncol* 2010;**6**:149–63.
2. Morgan DB, Hill GL, Burkinshaw L. The assessment of weight loss from a single measurement of body weight: the problems and limitations. *Am J Clin Nutr* 1980;**33**:2101–5.
3. Rowland ML. Self-reported weight and height. *Am J Clin Nutr* 1990; **52**:1125–33.
4. Ando M, Ando Y, Hasegawa Y, et al. Prognostic value of performance status assessed by patients themselves, nurses, and oncologists in advanced non-small cell lung cancer. *Br J Cancer* 2001;**85**:1634–9.
5. Guthrie GJ, Charles KA, Roxburgh CS, et al. The systemic inflammation-based neutrophil-lymphocyte ratio: experience in patients with cancer. *Crit Rev Oncol Hematol* 2013;**88**:218–30.
6. McMillan DC. Systemic inflammation, nutritional status and survival in patients with cancer. *Curr Opin Clin Nutr Metab Care* 2009;**12**: 223–6.
7. McMillan DC, Elahi MM, Sattar N, et al. Measurement of the systemic inflammatory response predicts cancer-specific and non-cancer survival in patients with cancer. *Nutr Cancer* 2001;**41**:64–9.
8. Erlinger TP, Platz EA, Rifai N, et al. C-reactive protein and the risk of incident colorectal cancer. *JAMA* 2004;**291**:585–90.
9. Guillem P, Triboulet JP. Elevated serum levels of C-reactive protein are indicative of a poor prognosis in patients with esophageal cancer. *Dis Esophagus* 2005;**18**:146–50.
10. Forrest LM, McMillan DC, McArdle CS, et al. A prospective longitudinal study of performance status, an inflammation-based score (GPS) and survival in patients with inoperable non-small-cell lung cancer. *Br J Cancer* 2005;**92**:1834–6.
11. Brown DJ, Milroy R, Preston R, et al. The relationship between an inflammation based prognostic score (GPS) and changes in serum biochemical variables in patients with advanced lung and gastrointestinal cancer. *J Clin Pathol* 2007;**60**:705–8.
12. Glen P, Jamieson NB, McMillan DC, et al. Evaluation of an inflammation-based prognostic score in patients with inoperable pancreatic cancer. *Pancreatology* 2006;**6**:450–3.
13. Ramsey S, Lamb GW, Aitchison M, et al. Evaluation of an inflammation-based prognostic score in patients with metastatic renal cancer. *Cancer* 2007;**109**:205–12.

14. Kao SC, Pavlakis N, Harvie R, et al. High blood neutrophil-tolymphocyte ratio is an indicator of poor prognosis in malignant mesothelioma patients undergoing systemic therapy. *Clin Cancer Res* 2010;**16**:5805–13.
15. Azab B, Bhatt V, Phookhan J, et al. Usefulness of the neutrophiltolymphocyte ratio in predicting short- and long-term mortality in breast cancer patients. *Ann Surg Oncol* 2012;**19**:217–24.
16. Forrest LM, McMillan DC, McArdle CS, et al. Evaluation of cumulative prognostic scores based on the systemic inflammatory response in patients with inoperable non-small-cell lung cancer. *Br J Cancer* 2003;**89**:1028–30.
17. Sobin LH, Gospodarowicz MK, Wittekind C. *TNM classification of malignant tumors*. 7th ed. Oxford: Wiley-Blackwell; 2010.
18. Saif MW, Makrilia N, Zalonis A, et al. Gastric cancer in the elderly: an overview. *Eur J Surg Oncol* 2010;**36**:709–17.
19. Forrest LM, McMillan DC, McArdle CS, et al. Comparison of an inflammation-based prognostic score (GPS) with performance status (ECOG) in patients receiving platinum-based chemotherapy for inoperable non-small-cell lung cancer. *Br J Cancer* 2004;**90**:1704–6.
20. Ahn HS, Lee HJ, Yoo MW, et al. Diagnostic accuracy of T and N stages with endoscopy, stomach protocol CT, and endoscopic ultrasonography in early gastric cancer. *J Surg Oncol* 2009;**99**:20–7.
21. Lee HH, Lim CH, Park JM, et al. Low accuracy of endoscopic ultrasonography for detailed T staging in gastric cancer. *World J Surg Oncol* 2012;**15**(10):190. http://dx.doi.org/10.1186/1477-7819-10-190.
22. McMillan DC, Watson WS, O'Gorman P, et al. Albumin concentrations are primarily determined by the body cell mass and the systemic inflammatory response in cancer patients with weight loss. *Nutr Cancer* 2001;**39**:210–3.
23. Al Shaiba R, McMillan DC, Angerson WJ, et al. The relationship between hypoalbuminaemia, tumor volume and the systemic inflammatory response in patients with colorectal liver metastases. *Br J Cancer* 2004;**91**:205–7.
24. Koike Y, Miki C, Okugawa Y, et al. Preoperative C-reactive protein as a prognostic and therapeutic marker for colorectal cancer. *J Surg Oncol* 2008;**98**:540–4.
25. Crumley AB, Stuart RC, McKernan M, et al. Comparison of an inflammation-based prognostic score (GPS) with performance status (ECOG-ps) in patients receiving palliative chemotherapy for gastroesophageal cancer. *J Gastroenterol Hepatol* 2008;**23**:e325–329.
26. Krzystek-Korpacka M, Matusiewicz M, Diakowska D, et al. Acute-phase response proteins are related to cachexia and accelerated angiogenesis in gastroesophageal cancers. *Clin Chem Lab Med* 2008;**46**:359–64.
27. Schumacher K, Haensch W, Roefzaad C, et al. Prognostic significance of activated CD8(+) T cell infiltrations within esophageal carcinomas. *Cancer Res* 2001;**61**:3932–6.
28. Gabay C, Kushner I. Acute-phase proteins and other systemic responses to inflammation. *N Engl J Med* 1999;**340**:448–54.
29. Gregory AD, Houghton AM. Tumor-associated neutrophils: new targets for cancer therapy. *Cancer Res* 2011;**71**:2411–6.
30. Proctor MJ, Morrison DS, Talwar D, et al. A comparison of inflammation-based prognostic scores in patients with cancer. A Glasgow Inflammation Outcome Study. *Eur J Cancer* 2011;**47**:2633–41.
31. Proctor MJ, McMillan DC, Morrison DS, et al. A derived neutrophil to lymphocyte ratio predicts survival in patients with cancer. *Br J Cancer* 2012;**107**:695–9.
32. Walsh SR, Cook EJ, Goulder F, et al. Neutrophil-lymphocyte ratio as a prognostic factor in colorectal cancer. *J Surg Oncol* 2005;**91**:181–4.
33. Proctor MJ, Horgan PG, Talwar D, et al. Optimization of the systemic inflammation-based Glasgow prognostic score: a Glasgow Inflammation Outcome Study. *Cancer* 2013;**119**:2325–32.