Clinical utility of the modified Glasgow prognostic score in patients with advanced head and neck cancer

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ABSTRACT: *Background.* The purpose of this study was to evaluate the prognostic potential of the modified Glasgow prognostic score (mGPS), known to reflect the degree of tumor-associated inflammation and cancer cachexia, in patients with advanced head and neck cancer.

Methods. Patients with advanced head and neck cancer treated at the University of Tsukuba Hospital between January 2002 and December 2011 were retrospectively evaluated. They were categorized by their mGPS.

Results. A total of 210 patients were enrolled in this study. Patients with an mGPS of 0 had better overall survival and disease-free survival than did those with an mGPS of 1 or 2. Multivariate analysis revealed that the mGPS was a significant risk factor for overall survival and disease-free survival.

Conclusions. Our results suggest that the mGPS is useful for predicting outcome in patients with advanced head and neck cancer and should be included in their routine clinical assessment. © 2014 Wiley Periodicals, Inc. *Head Neck* **37:** 1745–1749, 2015

KEY WORDS: modified Glasgow prognostic score (mGPS), head and neck cancer, inflammation, cancer cachexia, prognostic indicator

INTRODUCTION

Head and neck cancer is estimated to represent around 4% of all malignancies.[1] Worldwide, more than half a million people are newly diagnosed with head and neck cancer each year.[2]

Progressive malignant disease is often associated with a complex biochemical and metabolic disturbance, which results in the syndrome of cancer cachexia.[3] Cachexia is associated with diminished quality of life, perioperative medical complications, poor response to treatment, and increased morbidity and mortality rates in patients with cancer.[2,4] A state of chronic inflammation plays a key role in the initiation, promotion, and progression of cancers.[5–7] C-reactive protein (CRP) is one of the most widely used markers of acute or chronic systemic inflammation, and its production is regulated by proinflammatory cytokines, particularly interleukin-6.[8] Recent studies have suggested that an elevated serum CRP level is associated with poor prognosis in patients with various cancers, such as esophageal cancer, gastric cancer, colorectal cancer, pancreatic cancer, lung cancer, renal cell carcinoma, breast cancer, hepatocellular carcinoma, and ovarian carcinoma.[9–13] Albumin is an important intravascular and extravascular protein responsible for transportation, osmotic pressure, free radical scavenging, platelet function inhibition, and antithrombotic effects.[14–16] Increased catabolism, chronic malnutrition and chronic inflammatory reaction because of cancer eventually lead to hypoalbuminemia, which has been shown to be associated with poor survival in various cancers.[17,18] High CRP and low albumin serum levels have been combined to form the modified Glasgow prognostic score (mGPS).[19] The mGPS has been reported to provide additional prognostic information in patients with advanced cancer of the lung,[20,21] breast,[22] esophagus,[23] or pancreas.[24]

To our knowledge, the utility of the mGPS in patients with head and neck cancer has not been investigated. The purpose of this study was to retrospectively evaluate the association between pretreatment mGPS and survival in a single-institution series of patients with advanced head and neck cancer to examine the clinical utility of the mGPS.

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MATERIALS AND METHODS

Patients

Patients with advanced head and neck cancer (stage III or IV) treated at the Department of Otolaryngology, University of Tsukuba Hospital, between January 2002 and December 2011, were enrolled in this study. The patients' files and an electronic database were analyzed, and the clinical data, retrospectively extracted. Routine laboratory measurements of albumin and CRP concentrations were carried out before treatment in our hospital. Patients with clinical evidence of acute infection, chronic active inflammatory diseases, or double cancer were excluded.

TABLE 1. Relationship between the modified Glasgow prognostic score and clinical characteristics.

Variables	mGPS 0 ($n = 155$)	mGPS 1 ($n = 11$)	mGPS 2 ($n = 44$)	p value
Age at first diagnosis				
<65 y	79	3	23	.461
65–74	53	7	11	
≥75	23	1	10	
Sex				
Male	130	11	40	.193
Female	25	0	4	
Tumor site				
Larynx	49	2	11	.45
Oropharynx	54	4	12	
Hypopharynx	37	4	18	
Oral cavity	15	1	3	
Tumor classification				
III	42	2	4	.04
IV	113	9	40	
T classification				
T1	14	0	1	.01
T2	32	0	3	
T3	58	3	6	
T4	51	8	34	
Lymph node involvement				
Negative	39	5	8	.157
Positive	111	6	36	
Treatment				
RT alone	33	5	12	.268
RT + OP	16	1	7	
Radical CRT	84	3	19	
Preoperative CRT + OP	23	2	5	
Death				
Cancer-specific	28	3	36	.01
Intercurrent disease	3	1	0	

Abbreviations: RT, radiation therapy; OP, operation; CRT, chemoradiotherapy.

Clinical management

After diagnosis, the treatment recommendations for each case were made after discussion at a multidisciplinary meeting according to various factors, including disease status, comorbidities, and patient wishes. Patients with resectable tumors received radical surgery after preoperative chemoradiotherapy (45 Gy over 5 weeks). Patients with good tumor response to chemoradiotherapy or without a wish for surgery received radical chemoradiotherapy. Tumors with carotid artery involvement, distant metastasis, or severe comorbidity were considered to be unresectable. The chemotherapy regimen consisted of S-1.

Modified Glasgow prognostic score

The pretherapeutic mGPS was calculated as follows: patients with elevated serum CRP serum (>10 mg/L) and hypoalbuminemia (<35 g/L) were allocated a score of 2, patients with elevated serum CRP levels (>10 mg/L) without hypoalbuminemia were allocated a score of 1, and patients with neither of these abnormalities were allocated a score of 0.[19]

Statistical analysis

The relationships between the mGPS and other variables were analyzed by the chi-square test. Univariate survival analysis was performed using the Kaplan–Meier method with the log-rank test. Additionally, the survivals of patients within advanced T classification (T3, T4) were analyzed. Multivariate survival analysis with calculation of hazard ratios (HRs) was performed using the Cox proportional hazards model. The results were analyzed for the end-points of disease-free survival and overall survival. The start date of the follow-up was set as the date of the initial treatment. Probability values below .05 were considered significant. We used SPSS 21.0 for Windows (SPSS 1.0; Chicago, IL) for the statistical analysis.

RESULTS

A total of 210 patients were enrolled in this study. Table 1 demonstrates the relationships between their clinical characteristics and the mGPS. The mean age of the patients was 64.1 years (range, 36–85 years); 50% of the patients were aged over 65 years. One hundred eighty-one patients (86.2%) were men and 29 (13.8%) were women. The primary tumor sites were the larynx in 62 patients (29.5%), the oropharynx in 70 patients (33.3%), the hypopharynx in 59 patients (28.1%), and the oral cavity in 19 patients (9%). Squamous cell carcinoma was pathologically diagnosed in all patients. The TNM classification of the tumors is shown in Table 2. Distant metastasis was present in 5 patients. An mGPS of 0 was allocated to 155 patients (73.8%), mGPS of 1 to 11 patients (5.2%), and mGPS of 2 to 44 patients (20.9%). The mGPS was associated with tumor stage, T classification, and cancer-specific death (chi-square test: $p < .05$). When the mGPS, T classification, N classification, tumor site, patients' age, and patients' sex were analyzed as prognostic scores for disease-free and overall survival by multivariate analysis, only the T classification and the mGPS were shown to be independent prognostic parameters in our study (Table 3). Kaplan–Meier curves for overall survival and disease-free survival broken down by the mGPS are shown in Figures 1 and 2, respectively. Patients with a higher mGPS showed poor disease-free survival and overall survival. The prognoses of patients with an mGPS of 1 or 2 were significantly poorer than those of patients with an mGPS of 0. Similarly, the prognoses of patients with an elevated mGPS were poorer than patients with an mGPS of 0 in advanced T classification (Figure 3A and 3B). Of all patients, 54 patients were treated with surgery (24 laryngeal cancers, 14 hypopharyngeal cancers, 9 oropharyngeal cancers, and 7 oral cavity cancers). Of those 54 patients, 37 had an mGPS of 0, 3 had an mGPS of 1, and 14 had an mGPS of 2. An elevated mGPS (1 or 2) also had a poorer prognosis than did an mGPS of 0 (see Figure 4).

TABLE 2. Patients' TNM classification.

N classification	No. of patients by T classification			
	T1	T2	T3	T4
N0	1		36	19
N1		9	3	3
N2	12	26	26	70
N3	2		2	1

TABLE 3. Multivariate survival analysis in 210 patients.

	Disease-free survival		Overall survival	
	p value	HR (95% CI)	*p* value	HR (95% CI)
mGPS	< .001	2.50 (1.87–3.08)	< .001	2.40 (1.87–3.07)
T classification (T1, T2, T3, T4)	.004	1.55 (1.14–2.11)	.003	1.58 (1.16–2.14)
N classification (N0, N1, N2, N3)	.211	1.17 (0.91–1.51)	.263	1.15 (0.89–1.49)
Site	.318	1.10 (0.91–1.32)	.252	1.11 (0.92–1.34)
Age, y	.598	1.12 (0.72–1.75)	.941	1.00 (0.97–2.14)
Sex	.941	0.84 (0.38–1.75)	.498	0.76 (0.34–1.67)

Abbreviations: mGPS, modified Glasgow prognostic score; HR, hazard ratio; 95% CI, 95% confidence interval.

DISCUSSION

The mGPS, based on the combined serum levels of CRP and albumin, is an established, cheap, and readily available tool for the pretherapeutic assessment of prognosis for various cancers.[3,22,24–27] This retrospective analysis demonstrated that the mGPS is also highly predictive of the prognosis for patients with advanced head and neck cancer.

CRP is a nonspecific but very sensitive marker of the systemic inflammatory response expressed by certain tumors.[3,22,24–27] Serum CRP levels have been reported to correlate with tumor size, vascular invasion, lymph node metastasis, and tumor recurrence, resulting in poor prognosis in various cancers.[9–11,13,28–30] Although the reason why elevated CRP correlates with poor prognosis is not fully known, several proinflammatory cytokines expressed in the tumor environment, such as interleukin (IL)−1, IL-6, and tumor necrosis factor-α (TNF-α), may affect the malignant potential of tumor cells. On the other hand, patients with head and neck cancer often have underlying chronic malnutrition because of poor nutritional habits or alcohol or tobacco abuse. Additionally, the head and neck tumor may obstruct the aerodigestive tract or cause odynophagia or dysphagia, which reduces nutrient intake. Therefore, the patients with head and neck cancer tend to have hypoalbuminemia because of malnutrition. Furthermore, hypoalbuminemia is a consequent presentation of systemic inflammation.[18]

On multivariate analysis, the T classification and mGPS were independently associated with cancer-specific death and overall survival. In our study, the HR associated with the mGPS (HR, 2.40) was significantly greater than the T classification (HR, 1.58) for overall survival. Therefore, our results indicate that the mGPS might become a predictor of poor prognosis in addition to the TNM classification for patients with advanced head and neck cancer. In the present study, we also investigated the mGPS in patients treated with surgery. Among those patients, those with an elevated mGPS (1 or 2) also had a poorer prognosis than did patients with an mGPS of 0.

Patients with an elevated mGPS are considered to have precachexia.[31] Because cancer precachexia or cachexia is a multifactorial process, the treatment approach for cancer precachexia is multimodal. Recent reports suggested an importance of nutritional support for patients with cancer. Mantovani et al[32] analyzed 332 patients and found that a combination of dietary micronutrients, ω-3 fatty acids, and pharmacologic agents improved lean body mass and fatigue more than did a single intervention. Yeh et al[33] reported that the addition of several micronutrients and probiotics to an ω-3 fatty acids containing oral nutritional supplement improved the maintenance of body weight, and of serum albumin and prealbumin levels in patients with head and neck cancer cachexia. The improvement of the mGPS by multimodal therapy, including nutritional support, may help improve the condition and survival rates of patients with head and neck cancer.

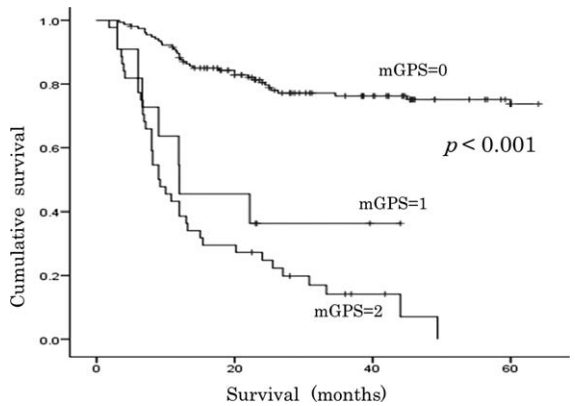

FIGURE 1. Patients with a higher modified Glasgow prognostic score (mGPS) showed poor overall survival.

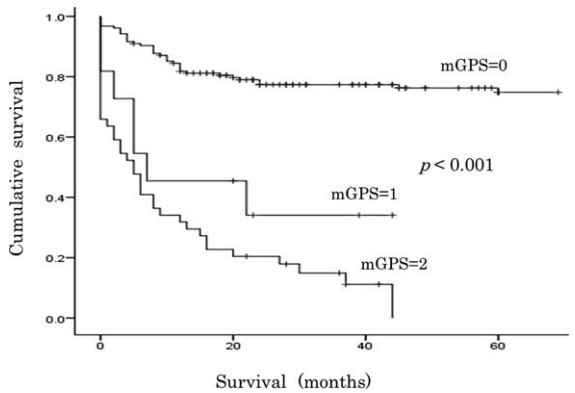

FIGURE 2. Patients with a higher modified Glasgow prognostic score (mGPS) showed poor disease-free survival.

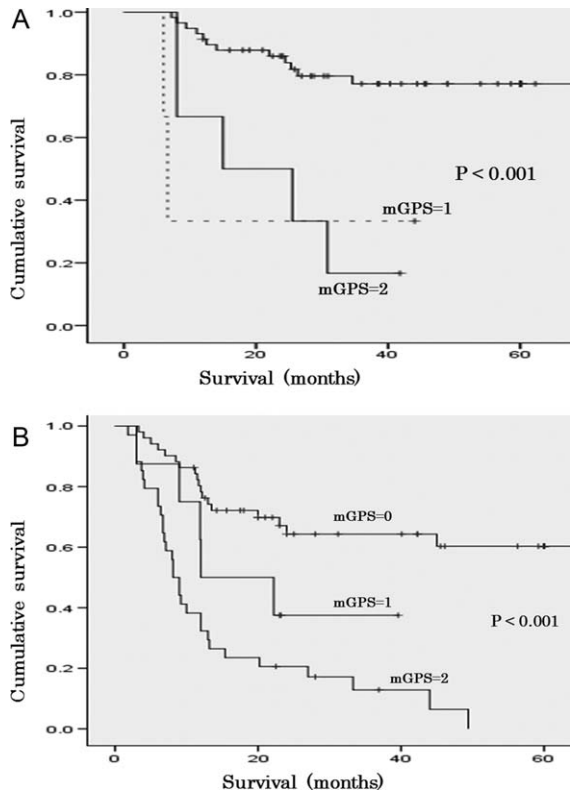

FIGURE 3. (A) Patients with a higher modified Glasgow prognostic score (mGPS) showed poor overall survival in T3. (B) Patients with a higher mGPS showed poor overall survival in T4.

Some limitations of this study should be acknowledged. First, this study was a retrospective study, conducted in a single institute, and was not blinded or controlled. Second, the number of patients studied was small, and the patients comprised a mixed group of head and neck cancers. In the future, larger prospective studies with long follow-up are needed to include the entire range of head and neck cancers and to establish the significance of the mGPS in advanced head and neck cancers.

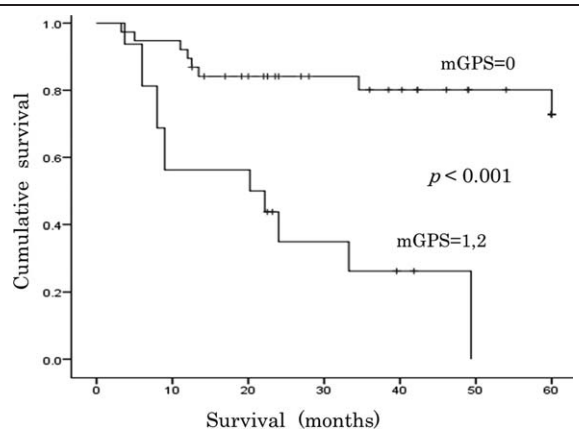

FIGURE 4. An elevated modified Glasgow prognostic score (mGPS) had a poorer prognosis than did an mGPS of 0.

CONCLUSIONS

Our study revealed that the mGPS is an objective prognostic marker for survival in patients with advanced head and neck cancer and provides additional value to other conventional, routinely available information. Further studies are needed to provide a better understanding of the mechanisms underlying the relationship between high mGPS and poor survival outcomes in patients with head and neck cancer.

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