Glasgow Prognostic Score (GPS) Can Be a Useful Indicator to Determine Prognosis of Patients With Colorectal Carcinoma

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The Glasgow Prognostic Score (GPS), an inflammation-based score, has been used to predict the biologic behavior of malignant tumors. The aim of the current study was to elucidate a further significance of GPS in colorectal carcinoma. Correlation of GPS and modified GPS (mGPS), which are composed of combined score provided for serum elevation of C-reactive protein and hypoalbuminemia examined before surgical treatment, with clinicopathologic features was investigated in 272 patients with colorectal carcinoma. Survival of GPS 1 patients was significantly worse than that of GPS 0 patients ($P = 0.009$), and survival of GPS 2 patients was significantly worse than that of GPS 1 patients ($P < 0.0001$). Similarly, survival of mGPS 1 patients was significantly worse than that of mGPS 0 patients ($P = 0.009$), and survival of mGPS 2 patients was significantly worse than that of mGPS 1 patients ($P = 0.0006$). Multivariate analysis demonstrated that GPS ($P < 0.0001$) as well as tumor stage ($P = 0.004$) and venous invasion ($P = 0.011$) were factors independently associated with worse prognosis. Both GPS and mGPS could classify outcome of patients with a clear stratification, and could be applied as prognostic indicators in colorectal carcinoma.

Key words: Colorectal carcinoma – Glasgow prognostic score (GPS) – Prognostic indicator

Although many tumor-environmental elements, including both tumor-related and host-related factors, have been linked with tumor progression, host inflammatory response is one of the more important factors that has a role in the progression and/or development of tumors.¹

Serum elevation of C-reactive protein (CRP), an acute phase protein, has been shown to be a prognostic indicator in a variety of neoplasms, including colorectal carcinoma.^{2–5} Moreover, hypoalbuminemia brought about by malnutrition and related to cachexic condition has been reported to

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Table 1 Relationship between GPS and patients' clinicopathologic characteristics

	GPS 0 (n = 179)	GPS 1 (n = 62)	GPS 2 (n = 31)	P value
Sex				
Male	105 (58.7)	35 (56.5)	20 (64.5)	0.756
Female	74 (41.3)	27 (43.5)	11 (35.5)	
Age	69.8 ± 11.0	70.4 ± 12.5	71.3 ± 9.1	0.130
Location of tumor				
Colon	121 (67.6)	47 (75.8)	25 (80.6)	0.212
Rectum	58 (32.4)	15 (24.2)	6 (19.4)	
Depth of tumor				
T1	31 (17.3)	3 (4.8)	0	<0.0001
T2	36 (20.1)	8 (12.9)	1 (3.2)	
T3	111 (62.0)	48 (77.5)	26 (83.9)	
T4	1 (0.6)	3 (4.8)	4 (12.9)	
Histology				
Well	60 (33.5)	15 (24.2)	7 (22.6)	0.127
Moderately	110 (61.5)	41 (66.1)	19 (61.3)	
Poorly	9 (5.0)	6 (9.7)	5 (16.1)	
Nodal metastasis				
No	107 (59.8)	33 (53.2)	12 (38.7)	0.083
Yes	72 (40.2)	29 (46.8)	19 (61.3)	
Lymphatic invasion				
No	107 (59.8)	40 (64.5)	13 (41.9)	0.103
Yes	72 (40.2)	22 (35.5)	18 (58.1)	
Venous invasion				
No	138 (77.1)	46 (74.2)	23 (74.2)	0.868
Yes	41 (22.9)	16 (25.8)	8 (25.8)	
Tumor stage				
I	59 (33.0)	10 (16.1)	0	0.0009
II	46 (25.7)	20 (32.3)	12 (38.7)	
III	59 (33.0)	21 (33.9)	12 (38.7)	
IV	15 (8.3)	11 (17.7)	7 (22.6)	
Resection				
Curative	164 (91.6)	51 (82.3)	24 (77.4)	0.025
Noncurative	15 (8.4)	11 (17.7)	7 (22.6)	
Proportion of lymphocytes in the peripheral blood, %	29.6 ± 9.1	24.4 ± 10.0	17.8 ± 7.0	<0.0001

GPS, Glasgow Prognostic Score.

Values in parentheses are percentages.

be correlated with an unfavorable prognosis of some gastrointestinal tumors.^{6,7}

The Glasgow prognostic score (GPS), which is a cumulative inflammation-based cancer-prognostic marker composed of serum elevation of CRP and decrease in albumin concentration, is likely to reflect host systemic inflammatory response and has been reported to be significant as a prognostic indicator in cancer-bearing patients.^{8–10}

Moreover, it has been found that hypoalbuminemia alone is unlikely to be associated with reduced survival likelihood in patients with colorectal carcinoma¹¹; therefore, the GPS has been modified (mGPS), providing a score of 1 only for a case with

serum elevation of CRP, and score of 0 for a case only with hypoalbuminemia or where neither was elevated. Although, until now, there have been some reports regarding the significance of GPS as a prognostic indicator in colorectal carcinoma,^{9,11–16} the aim of this study was to elucidate further the significance of GPS and mGPS in colorectal carcinoma.

Patients and Methods

Patients, collection of blood samples, and laboratory measurement

Two hundred and seventy-two patients with colorectal carcinoma that had been treated by resection

Fig. 1 Comparison of the patients' survival between GPS 0, 1, and 2. Significant differences were observed between GPS 0 and GPS 1 patients ($P = 0.009$) and between GPS 1 and GPS 2 patients ($P < 0.0001$).

and lymph node dissection in our institute from 2003 to 2012 were included in this study. Patients who have had malignant tumors in other organs or have been suffering from other chronic inflammatory diseases causing serum elevation of CRP were excluded from this study.

Patient ages ranged from 24 to 90 years, with a mean of 70.4, and were composed of 160 men and 112 women. No neoadjuvant therapy had been given for the patients who had been enrolled in this study.

All blood samples were collected and the laboratory measurements of serum values of CRP and albumin were performed just before the operation.

Patients who had both a serum elevation of CRP (>1.0 mg/dL) and hypoalbuminemia (<3.5 g/dL) were allocated a GPS of 2. Patients with only one of the abnormal values were allocated a GPS of 1, and patients who had neither were allocated a GPS of 0.

Moreover, patients who had both abnormal values were allocated an mGPS of 2. Patients who had only serum elevation of CRP but not hypoalbuminemia were allocated an mGPS of 1, and patients who had neither or only hypoalbuminemia were allocated a mGPS of 0.

Correlation of preoperative values of GPS and mGPS with clinicopathologic characteristics were examined.

Clinicopathologic investigation

The clinicopathologic factors were determined according to the TNM classification of malignant tumors prescribed by the International Union Against Cancer.¹⁷

Follow-up for the patients

The follow-up for patients was continued until their death, and only patients who died of colorectal carcinoma were included in the tumor-related deaths. The period from the operation to the date of death was defined to be the survival time. The interval of the follow-up after operation ranged from 2 months to 8 years and 5 months.

Statistical analysis

All statistical analyses were performed using Stat-View (SAS Institute Inc, Cary, NC). Chi-square and t tests were used to compare the difference regarding values in each GPS score. Survival curves were made by the Kaplan-Meier method, and the Mantel-Cox test was used to analyze the equality of the survival curves. The Cox proportional hazards model in a forward stepwise manner was used in the multivariate analysis to determine the independent prognostic indicators. $P < 0.05$ was considered significant.

Results

The relationship between GPS and clinicopathologic features is shown in Table 1. Significant differences were observed regarding depth of tumor ($P < 0.0001$), stage of the tumors ($P = 0.0009$), and the proportion of curative resection ($P = 0.025$). Additionally, a significant correlation of GPS with the proportion of lymphocytes in the peripheral blood was also found ($P < 0.0001$).

The prognosis of GPS 1 patients (a 5-year survival rate of 74.9%) was significantly worse than that of GPS 0 patients [a 5-year survival rate of 92.6% ($P = 0.009$)]; the prognosis of GPS 2 patients (a 5-year survival rate of 35.2%) was significantly worse than that of GPS 1 patients ($P < 0.0001$; Fig. 1).

Next, the relationship between mGPS and clinicopathologic features is shown in Table 2. Similarly, significant differences were found for depth of tumor ($P < 0.0001$), stage of the tumors ($P = 0.0004$), the proportion of curative resection ($P =$

Table 2 Relationship between mGPS and patients' clinicopathologic characteristics

	mGPS 0 (n = 202)	mGPS 1 (n = 39)	mGPS 2 (n = 31)	P value
Sex				
Male	118 (58.4)	22 (56.4)	20 (64.5)	0.770
Female	84 (41.6)	17 (43.6)	11 (35.5)	
Age	70.2 ± 11.4	68.7 ± 11.7	71.3 ± 9.1	0.060
Location of tumor				
Colon	138 (68.3)	30 (76.9)	25 (80.6)	0.251
Rectum	64 (31.7)	9 (23.1)	6 (19.4)	
Depth of tumor				
T1	34 (16.8)	0	0	<0.0001
T2	38 (18.8)	6 (15.4)	1 (3.2)	
T3	128 (63.4)	31 (79.5)	26 (83.9)	
T4	2 (1.0)	2 (5.1)	4 (12.9)	
Histology				
Well	66 (32.7)	9 (23.1)	7 (22.6)	0.166
Moderately	125 (61.9)	26 (66.7)	19 (61.3)	
Poorly	11 (5.4)	4 (10.2)	5 (16.1)	
Nodal metastasis				
No	120 (59.4)	20 (51.3)	12 (38.7)	0.080
Yes	82 (40.6)	19 (48.7)	19 (61.3)	
Lymphatic invasion				
No	124 (61.4)	23 (59.0)	13 (41.9)	0.123
Yes	78 (38.6)	16 (41.0)	18 (58.1)	
Venous invasion				
No	155 (76.7)	29 (74.4)	23 (74.2)	0.918
Yes	47 (23.3)	10 (25.6)	8 (25.8)	
Tumor stage				
I	64 (31.7)	5 (12.8)	0	0.0004
II	53 (26.2)	13 (33.3)	12 (38.7)	
III	68 (33.7)	12 (30.8)	12 (38.7)	
IV	17 (8.4)	9 (23.1)	7 (22.6)	
Resection				
Curative	185 (91.6)	30 (76.9)	24 (77.4)	0.006
Noncurative	17 (8.4)	9 (23.1)	7 (22.6)	
Proportion of lymphocytes in the peripheral blood, %	29.5 ± 9.4	22.0 ± 8.4	17.8 ± 7.0	<0.0001

mGPS, modified Glasgow Prognostic Score.

Values in parentheses are percentages.

0.006), and lymphocyte proportion in the peripheral blood ($P < 0.0001$).

The prognosis of mGPS 1 patients (a 5-year survival rate of 72.9%) was significantly worse than that of mGPS 0 patients [a 5-year survival rate of 91.5% ($P = 0.009$)]; the prognosis of mGPS 2 patients (a 5-year survival rate of 35.2%) was significantly worse than that of mGPS 1 patients ($P = 0.0006$; Fig. 2).

While patients with GPS 0 or 1 are in accordance with those with mGPS 0 or 1, multivariate analysis was performed by dividing GPS 2 or mGPS 2 and others. This analysis revealed that GPS ($P < 0.0001$) as well as tumor stage ($P = 0.004$) and venous

invasion ($P = 0.011$) proved to be factors independently associated with a worse prognosis for the patient (Table 3).

Discussion

GPS, which comprises solely serum concentrations of CRP and albumin, has been established as an inflammation-based score to predict the extent of aggression of the tumor and/or the prognosis of patients. It is used for a variety of malignant tumors, including carcinomas of the gastrointestinal tract^{11,18} and other organs.^{19,20}

Fig. 2 Comparison of the patients' survival between mGPS 0, 1, and 2. Significant differences were observed between mGPS 0 and mGPS 1 patients ($P = 0.009$) and between mGPS 1 and mGPS 2 patients ($P = 0.0006$).

Initially, this combination of the clinical data of serum elevation of CRP and hypoalbuminemia was applied to possibly determine the prognosis of patients with inoperative lung cancer.²¹ Thereafter, to the best of the authors' knowledge, this criteria, termed GPS, has come to be used to assess the outcome of patients with malignant tumors.¹⁹

It has been reported that GPS is a marker for the incidence of distant metastasis in colorectal carcinoma¹⁴ and is also a significant prognostic indicator for colorectal carcinoma.^{9,12} However, in an investigation by McMillan et al.¹¹ regarding the significance of GPS in colorectal carcinoma, survival of patients with a GPS of 1 derived from hypoalbuminemia proved to be much better than that of patients with a GPS of 1 derived from serum elevation of CRP. Therefore, patients with hypoalbuminemia but without serum elevation of CRP were classified as GPS 0, and this criteria has been come to be used as a modified GPS (mGPS) to chiefly investigate the biologic behavior of colorectal carcinoma. A series of further investigations also demonstrated that mGPS has proven to be a significant prognostic indicator in colorectal carcinoma.^{11,13,15,16} In the current study, both GPS and mGPS proved to be significant as independent prognostic indicators in colorectal carcinoma.

Close correlation of serum elevation of CRP with a decrease in lymphocyte percentage in the peripheral blood,²² which was also shown in this study, and with a decrease in T lymphocyte infiltration in

Table 3 Factors independently correlated with the prognosis

Variable	Odds ratio (95% confidence interval)	P value
GPS, mGPS (0, 1 versus 2)	7.41 (3.66–15.2)	<0.0001
Stage of tumor (I, II versus III, IV)	3.94 (1.54–10.1)	0.004
Venous invasion	2.25 (1.15–4.41)	0.011

GPS, Glasgow Prognostic Score; mGPS, modified Glasgow Prognostic Score.

patients with colorectal carcinoma²³ was previously reported.

Although it should be appreciated that the identification of hypoalbuminemia in cancer-bearing patients depends on the systemic inflammatory response,¹⁸ and the independent significance of hypoalbuminemia in determining a prognosis in colorectal carcinoma might be less reliable,¹¹ it has been known to be associated with an impaired immune response through macrophage activation.²⁴ Additionally, in the current study, a significant correlation of GPS with a decrease in the proportion of lymphocytes in the peripheral blood of the patients was found. Taken together from the panel of our investigations, GPS also has an important significance as an indicator of the nutritional and immunologic host response in patients with colorectal carcinoma.

In conclusion, both GPS and mGPS could be easy and useful tools to predict the outcome of patients with colorectal carcinoma.

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