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Original Article

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Glasgow Prognostic Score is a Useful Predictive Factor for Palliative Surgery Outcomes in Advanced-stage Gastric Cancer

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BACKGROUND/AIMS
More than one million new gastric cancer cases have been reported in 2018. In many countries other than those in the Far East, gastric cancer could not be diagnosed at an early stage. Surgical options are limited in advanced-stage gastric cancer, and physicians have to make the right decision for the prolongation of patient survival. Surgery can prolong the survival even in advanced disease if the appropriate patient population is selected. The Glasgow prognostic score (GPS) was validated as a predictor of the prognosis in several cancer types. In this study, we aimed to test the hypothesis that GPS is useful to select the most suitable patients for surgical intervention in advanced-stage gastric cancer.

MATERIAL and METHODS
Data of 632 gastric cancer patients operated in our institute were investigated in this retrospective study. Eighty-four patients with gastric cancer who underwent palliative surgery and had complete clinical and follow-up data were included in this study.

RESULTS
Albumin levels were low in 46 patients. Forty-eight patients had high C-reactive protein (CRP) levels. Palliative gastrectomy was performed in 43 of 84 patients. Patients with a GPS of 2 survived a median 3 (95% confidence interval [CI]: 0.89-5.11) months, GPS of 1 for a median of 7 (95% CI: 4.50-9.50) months, and GPS of 0 for a median of 8 (95% CI: 3.31-12.70) months (p=0.047). Patients with modified GPS scores of 2 survived for a median of 3 (95% CI: 0.89-5.11) months, mGPS of 1 for a median of 3 (95% CI: 0.55-7.45) months, and mGPS of 0 for a median 8 (95% CI: 5.65-10.35) months (p=0.012). The mGPS values of patients with palliative gastric resection were compared; patients with mGPS of 0 had significantly longer survival times than those with mGPS 1 and 2.

CONCLUSION
The GPS and mGPS can be calculated prior to surgery using non-invasive and easily available laboratory tests. It has been shown in this study and other previous studies that mGPS can be particularly used easily to predict the prognosis in advanced-stage gastric cancer.

Keywords: Gastric cancer, prognosis, palliative surgery, glasgow prognostic score

INTRODUCTION

Gastric cancer is the third most common cause of cancer-related deaths. More than a million new gastric cancer patients were diagnosed in 2018 worldwide (1). In countries where routine screening is not performed, cases are unfortunately diagnosed in the late stage (2).

Curative surgery cannot be performed in patients with non-resectable tumor or peritoneal spread and/or multiple solid organ metastases. Patients often undergo palliative surgical intervention followed by chemotherapy. Although all patients in this group have advanced-stage disease, the survival time varies.

Recent studies have demonstrated that increased systemic inflammation in patients with advanced solid cancer is related to weight loss, decreased performance, and reduced survival (3-5).

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Abnormalities in C-reactive protein (CRP) and albumin levels are considered indicators of systemic inflammation. In 2005, the Glasgow Prognostic Score (GPS), which is calculated using (CRP) and albumin values, was introduced (6). GPS was validated in prognosis studies of advanced-stage solid organ cancers (7, 8). The purpose of the present study was to test the hypothesis that GPS is useful for predicting prognosis in gastric cancer patients undergoing palliative surgery.

PATIENTS and METHODS

Ethical approval was obtained from the ethical committee of Dokuz Eylul University medical study with the date and number of 2019/13-39. Oral informed consent was obtained from all the patients.

Patients

In total, data of 632 patients with gastric cancer who underwent curative surgical resection or palliative surgery at the Department of Surgery, Dokuz Eylul University Hospital, from September 2006 to December 2018 were retrospectively evaluated. Patients who died within 30 days of surgery, those with infection other malignancies, and those who received neoadjuvant chemotherapy that might have affected the CRP levels were excluded from this study. We excluded 53 of included 137 palliative surgery patients from the study due to incomplete clinical data. The remaining 84 patients included in the study had adequate clinical information and follow-up data.

Preoperative Radiological Evaluation

The patients were evaluated through a computerized tomography (CT) examination of the thorax and whole abdomen in the preoperative period. Investigations were performed using 16-section or 64section multidetector CT devices (Brilliance 16 or Brilliance 64, Philips Medical Systems, Eindhoven, Holland). In contrast-enhanced CT examinations, iodinated contrast agents were applied at a rate of 2 mL/kg (at least 100 mL). Arterial and portal phase images were obtained.

The computed tomography images were used for systemic evaluation of the following parameters: localization and extension of the primary tumor, possible tumor invasion, perigastric or retroperitoneal lymph node mapping, intra-abdominal suspicious implant, and distant lymph node or organ/structure metastases.

Surgical Procedure

Palliative gastrectomy was defined as the resection of the primary gastric lesion with or without regional lymph node dissection in patients with metastatic disease.

In this procedure, the resection of lesions in peritoneal implants and residual metastases of nonresectable lymph nodes, liver, or distant organs, was not performed. Gastrojejunostomy (GJ) for oral intake or placement of a feeding jejunostomy tube for enteral feeding was performed in nonresectable locally advanced gastric cancer.

Statistical Analysis

Statistical analysis was conducted using the Statistical Package for the Social Sciences version 22.0 software (IBM Corp.; Armonk, NY, USA). Age, gender, surgical method, preoperative disease stage, albumin, and CRP values, survival data were obtained. GPS and modified GPS (mGPS) were calculated (Table 1, 2). Kaplan–Meier survival analysis was applied to determine the factors affecting survival. Also, GPS and mGPS for predicting the prognosis were validated using the Kaplan–Meier survival analysis. Receiver Operating Characteristic (ROC) analysis was performed for GPS and mGPS.

RESULTS

The median age of the 84 patients was 63.5 years. The male/female ratio was 3/2. Palliative gastrectomy was performed

TABLE 1. GPS

	Score
CRP≤10 mg/L and albumin ≥3.5 g/dL	0
CRP≤10 mg/L and albumin <3.5 g/dL	1
CRP>10 mg/L and albumin ≥3.5 g/dL	1
CRP>10 mg/L and albumin <3.5 g/dL	2

GPS: Glasgow Prognostic Score; CRP: C-reactive protein

TABLE 2. Modified GPS

	Score
CRP≤10 mg/L and albumin ≥3.5 g/dL	0
CRP≤10 mg/L and albumin <3.5 g/dL	0
CRP>10 mg/L and albumin ≥3.5 g/dL	1
CRP>10 mg/L and albumin <3.5 g/dL	2

GPS: Glasgow Prognostic Score; CRP: C-reactive protein

TABLE 3. Patient characteristics and survival: Univariate analysis

	Patients (100%)	Survival, months (median, 95% CI)	p
Age, years			0.860
<65	46 (54)	7 (4.64-9.36)	
>65	38 (46)	5 (3.30-6.71)	
Gender			0.717
Female	34 (40)	4 (1.15-6.85)	
Male	50 (60)	7 (4.66-9.44)	
Albumin			0.204
≥3.5 g/dL	38 (46)	8 (4.68-11.32)	
<3.5 g/dL	46 (54)	5 (3.14-6.86)	
CRP			*0.003*
≤10 mg/L	36 (42)	8 (5.65-10.35)	
>10 mg/L	48 (58)	3 (1.18-4.82)	
GPS			*0.031*
0	23 (27)	8 (3.31-12.70)	
1	28 (34)	7 (4.50-9.50)	
2	33 (39)	3 (0.89-5.11)	

GPS: Glasgow Prognostic Score; CRP: C-reactive protein; CI: confidence interval

in 43 patients. The remaining patients underwent GJ bypass and/or feeding tube placement surgeries. Albumin levels were low in 46 patients (<3.5 g/dL). Forty-eight patients had high CRP (CRP>10 mg/L) levels. In the univariate analysis, GPS values were found to be effective in predicting prognosis (Table 3).

TABLE 4. Modified GPS and survival: Univariate Analysis

	Patients (100%)	Survival, months (median, 95% CI)	p
mGPS			*0.011*
0	36 (42)	8 (5.65-10.35)	
1	15 (19)	3 (0.55-7.45)	
2	33 (39)	3 (0.89-5.11)	

mGPS: modified Glasgow Prognostic Score; CI: confidence interval

When the survival rates were examined, 9 patients were known to be alive. The median survival was 21.5 (6-50) months for the alive patients. The median survival was 5 (1-69) months for the other patients.

With regard to albumin values, patients with albumin levels ≥3.5 g/dL survived for a median of 8 (95% confidence interval [CI]: 4.68-11.32) months, and those with albumin <3.5 g/dL patients survived for a median 5 (95% CI: 3.14-6.86) months in the postoperative period (Figure 1). With regard to CRP values, patients with CRP≤10 mg/L survived for a median 8 (95% CI: 5.65-10.35) months, and those with CRP>10 mg/L survived for a median 3 (95% CI: 1.18-4.82) months in the postoperative period (Figure 2).

The GPS scores were compared, and patients with GPS 2 survived for a median 3 (95% CI: 0.89-5.11) months, GPS 1 for a median of 7 (95% CI: 4.50-9.50) months, and GPS 0 for a median of 8 (95% CI: 3.31-12.70) months (p=0.047; Figure 3). The area under the curve (AUC) in the ROC analysis was 0.613 for GPS (Figure 4).

Patients with mGPS 2 survived for a median of 3 (95% CI: 0.89-5.11) months, those with mGPS 1 for a median of 3 (95% CI: 0.55-7.45) months, and those with mGPS 0 for a median of 8 (95% CI: 5.65-10.35) months (p=0.012; Table 4; Figure 5). The AUC in the ROC analysis was 0.628 for the mGPS (Figure 6).

The mGPS values of patients with palliative gastric resection were examined, and those with mGPS=0 had significantly longer survival times compared to those with mGPS 1 and 2 (Figure 7).

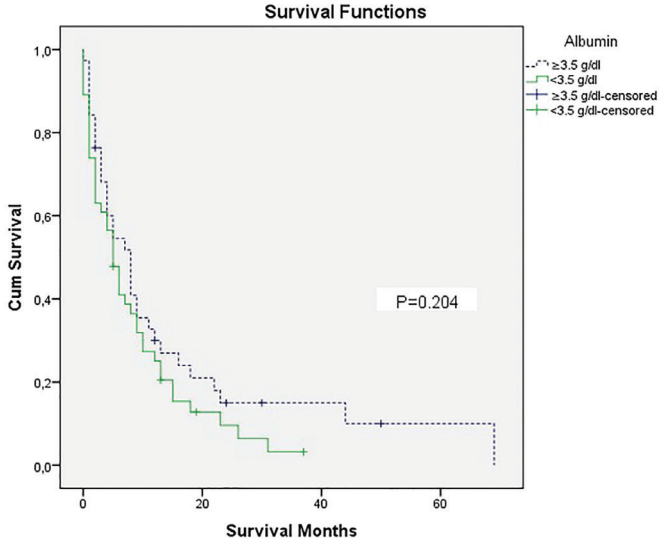


FIGURE 1. Kaplan–Meier survival curves of patients with gastric cancer who underwent palliative surgery according to albumin levels (p=0.204). The p value was calculated using the log-rank test

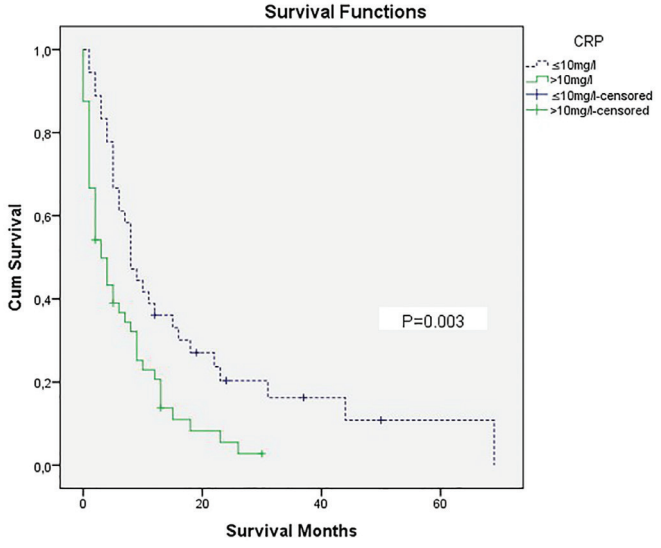


FIGURE 2. Kaplan–Meier survival curves of patients with gastric cancer who underwent palliative surgery according to the CRP levels (p=0.003). The p value was calculated using the log-rank test. CRP, C reactive protein

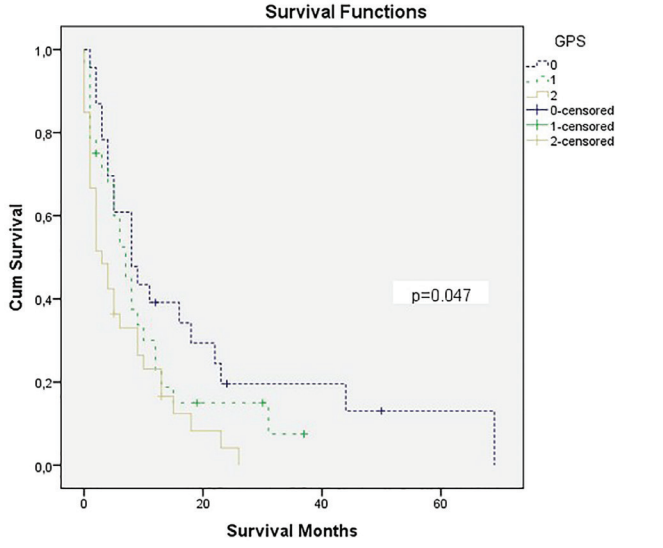


FIGURE 3. Kaplan–Meier survival curves of patients with gastric cancer who underwent palliative surgery according to GPS (p=0.047). The p value was calculated using the log-rank test. GPS, Glasgow Prognostic Score

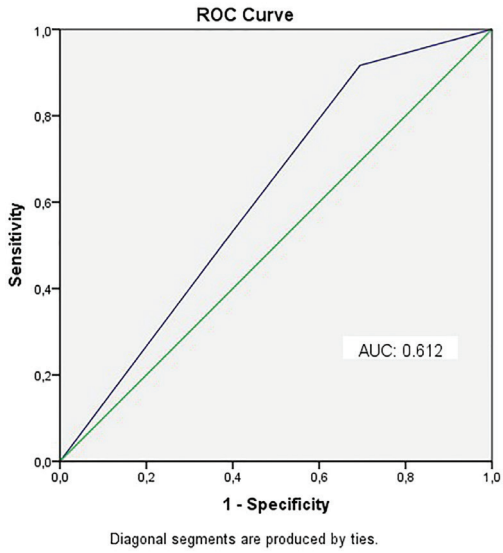


FIGURE 4. ROC curves of GPS of patients with gastric cancer with palliative surgery. The AUC of GPS was 0.612. GPS, Glasgow Prognostic Score; ROC, receiver operating characteristics; AUC, area under the curve

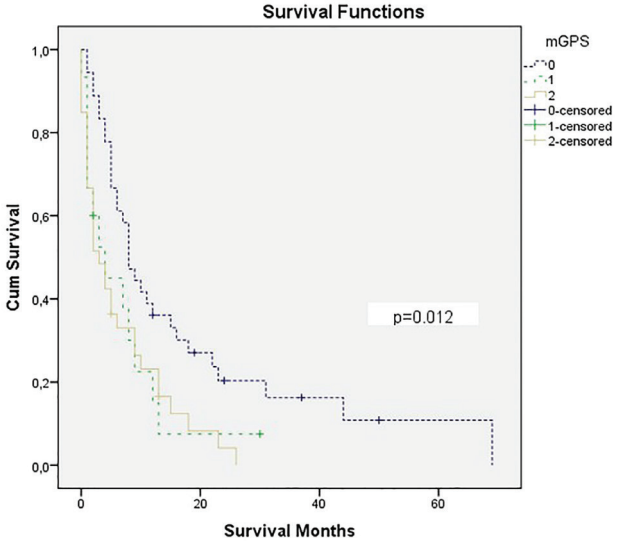


FIGURE 5. Kaplan–Meier survival curves of patients with gastric cancer who underwent palliative surgery according to mGPS (p=0.012). The p value was calculated using the log-rank test. mGPS, modified Glasgow Prognostic Score

DISCUSSION

Palliative surgical interventions in stage IV gastric cancer are performed if obstruction, bleeding, mass compression, intense acid, and perforation are observed. Although there is no consensus yet, there are reports that a combination of palliative resection and chemotherapy prolongs the survival in stage IV gastric cancer (9). However, some criteria should be considered to provide the expected benefit in these applications where patient selection is important. Parameters, such as the presence of comorbid diseases and general performance scores, prior to surgical intervention will guide in this regard. In contrast, cancer biology directly affects prognosis. Inflammation, which is considered the response (the host) to cancer and is frequently

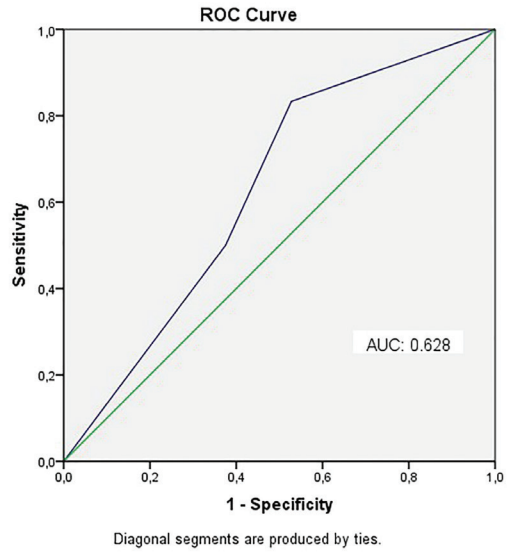
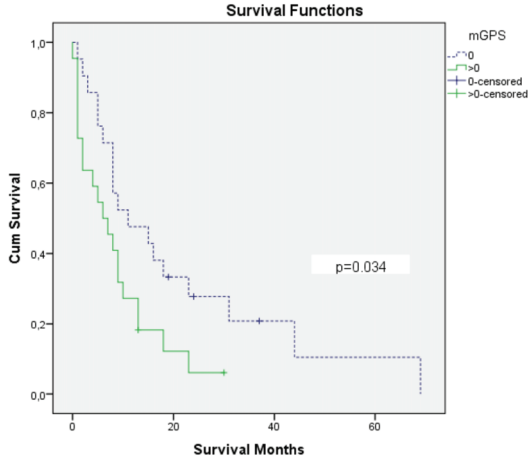


FIGURE 6. ROC curves of mGPS of patients with gastric cancer who underwent palliative surgery. The AUC of mGPS was 0.628. mGPS, modified Glasgow Prognostic Score; ROC, receiver operating characteristics; AUC, area under the curve



Means and Medians for Survival Time

	Mean[a]				Median			
			95% Confidence Interval				95% Confidence Interval	
VAR00002	Estimate	Std. Error	Lower Bound	Upper Bound	Estimate	Std. Error	Lower Bound	Upper Bound
0	20.678	4.960	10.957	30.399	11.000	5.340	0.533	21.467
>0	8.530	1.802	4.998	12.062	6.000	2.345	1.403	10.597
Overall	15.145	3.034	9.199	21.092	8.000	0.937	6.164	9.836

[a]Estimation is limited to the largest survival time if it is censored

FIGURE 7. Kaplan–Meier survival curves of patients with gastric cancer who underwent palliative gastrectomy according to mGPS (mGPS=0 and mGPS>0; p=0.034). The p value was calculated using the log-rank test. mGPS, modified Glasgow Prognostic Score

the focus of several studies in recent years, has been defined as a parameter of prognostic significance, particularly for advanced-stage cancer (10). GPS using the elevation in the CRP value and a decrease in albumin value, which are considered to be indicators of increased inflammation, were reported by Forrest et al. This scoring system was first described to predict the prognosis of inoperable non-small cell lung cancers. GPS used for estimating the prognosis was examined in various cancers and found beneficial (7, 8, 11).

When the results of the current study were evaluated, it was observed that the decrease in albumin and the increase in CRP values were found to be associated with shorter survival times (Table 3; Figure 1, 2). GPS using these parameters was found to be effective in predicting the prognosis in advanced gastric cancer (Figure 3). These results were consistent with those of Elahi and Mimatsu studies.

In our study, albumin decrease without CRP elevation was associated with shortened survival, but no statistically significant result was found. It was believed that the low levels of albumin alone could be caused by loss of appetite and relative malnutrition in the preoperative period rather than being the marker of the inflammatory process. The AUC in the ROC analysis for the GPS and the mGPS were 0.613 and 0.628, respectively (Figure 4-6). These results were similar to those of other validation studies for predicting prognosis in cancer patients using GPS and mGPS (8, 12, 13).

When the mGPS scores of the patients who underwent palliative gastric resection were examined in terms of survival, patients with an mGPS of 0 had a mean 20.68 (±4.96) months of survival and those with mGPS>0 had a mean of 8.53 (±1.80) months of survival (p=0.034). In other words, as mGPS scores increased, the prognosis was shorter (Figure 5). When the results of this study were evaluated together with the arguments of the researchers who suggested that palliative gastric resection for patients with stage IV gastric carcinoma would contribute positively to the prognosis, it was thought that a significant increase in the survival rate could be achieved by selecting appropriate patients with an mGPS of 0 and having other positive prognostic markers.

The number of patients and retrospective design are the most important limitations fort his study. Although the single-center design of the study benefits in terms of the homogeneity of the data, it can be considered a limitation due to a lower number of patients.

The mGPS can be calculated prior to surgery using non-invasive and easily available laboratory tests. Particularly, in advanced-stage gastric cancer, it can be easily used for predicting the prognosis of patients and choosing the treatment to be applied with other known prognostic markers.

Ethics Committee Approval: Ethics committee approval was received for this study from Dokuz Eylul University Ethical Committee. (Approval Date: 22.05.2019, Approval Number: 2019/13-39).

Informed Consent: Informed consent was obtained from the patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author contributions: Concept - S.D., T.E., K.A.; Design - S.D., T.E., A.Ç., I.B., S.Ü.; Supervision - K.A., Ö.S.; Resource - K.A., Ö.S., I.B., S.Ü., S.D.; Materials - S.D., I.B., S.Ü., Ö.S.; Data Collection and/or Processing - S.D., A.Ç., T.E., I.B.; Analysis and/or Interpretation - S.D., A.Ç., T.E., I.B., S.Ü.; Literature Search - S.D., I.B., T.E., A.Ç., S.Ü.; Writing - S.D., I.B., T.E., A.Ç.; Critical Reviews - K.A., Ö.S.

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Conflict of Interest: The authors have no conflicts of interest to declare.

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