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Research Article

The Effect of the Modified Glasgow Prognostic Score and Neutrophil/Lymphocyte Ratio on Prognosis in Stage 4 Pancreatic Cancer

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Abstract

Objectives: To demonstrate that the neutrophil/lymphocyte ratio (NLR) and modified Glasgow Prognostic Score (mGPS) are negative prognostic factors for overall survival and mGPS is a more sensitive marker in patients diagnosed with stage 4 pancreatic cancer (PC).

Methods: A total of 68 patients with stage 4 PC were included in the study. Clinical and laboratory data were collected and evaluated in the form of retrospective file scanning. Analysis was performed using the SPSS database.

Results: The median age at diagnosis was 67 years, the median progression-free survival (PFS) was 5.2 months, and the median overall survival (OS) was 11.1 months. OS was 18.1 months in patients with low NLR and 10.4 months in patients with high NLR (*p=0.013). OS was 21.3 months in patients with an mGPS of 0, 10.3 months in patients with an mGPS of 1, and 5.5 months in patients with an mGPS of 2 (*p=0.001).

Conclusion: Eastern Cooperative Oncology Group (ECOG) performance status score, NLR, and mGPS are unfavorable prognostic factors for OS in stage 4 PC. mGPS is a more sensitive prognostic factor than both ECOG performance status score and NLR.

Keywords: Stage 4 pancreatic cancer, neutrophil/lymphocyte ratio, modified Glasgow prognostic score

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Pancreatic cancer (PC) ranks seventh among cancer-related deaths. More than 80% of patients are inoperable at the time of diagnosis.[1] Over the years, treatment options have changed from single-agent gemcitabine or 5-fluorouracil-containing regimens to doublet regimens containing gemcitabine (gemcitabine-platinum combinations, gemcitabine–nab-paclitaxel) followed by treatment regimens containing FOLFIRINOX.[2] However, despite increasing chemotherapy options, 5-year survival rates are still below 5%.[3] When deciding between treatment regimens, the patient's performance score is generally taken into account; it is predicted that making a decision based on performance alone may lead to misleading results. Therefore, there is a need for prognostic markers that predict survival.

Recently, inflammation has been reported to be closely associated with carcinogenesis and progression of PC. In clinical practice, prognostic indicators based on systemic inflammation have been developed to predict prognosis in patients with PC. Due to the simplicity of the calculation, NLR is one of the most frequently used parameters in this regard, but there are conflicting data regarding its effect on overall survival (OS).[4-6] In addition, various scoring systems

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are used to evaluate the parameters that support inflammation, such as the modified Glasgow Prognostic Score (mGPS).[7, 8] Most previous studies on inflammatory indices have been conducted on patients with early-stage disease undergoing surgical resection or chemoradiotherapy.

This study aimed to compare these two prognostic parameters in unresectable PC and to evaluate which one was more suitable for PC.

Methods

Sixty-eight patients who were diagnosed as having stage 4 PC in İzmir City Private Hospital between 2016 and 2021 were included in the study. This retrospective study complied with the standards of the Declaration of Helsinki. Patients' age, sex, primary tumor location, Eastern Cooperative Oncology Group (ECOG) performance status (PS) score, and laboratory parameters at the time of diagnosis were evaluated. Laboratory parameters including mGPS, NLR, C-reactive protein (CRP), and albumin levels were evaluated using blood samples at the first outpatient admission.

Univariate and multivariate analyses were used to identify predictive factors of OS in patients with unresectable PC. Analyzed factors were age, sex, tumor location, clinical stage, treatment, ECOG-PS score, mGPS, NLR, CRP, and albumin levels.

OS was evaluated using Kaplan-Meier analysis, and log-rank analysis was performed to confirm the significance of the variables. Cox regression analysis was used in the analysis of prognostic factors and hazard ratios (HR) and 95% confidence intervals (CI) were calculated. P values of <0.05 were considered statistically significant. All statistical analyses were performed using the SPSS statistics package, version 22.0 (IBM).

Results

Sixty-eight patients were included in our study. The median age at diagnosis was 67 years, the median progression-free survival (PFS) was 5.2 months, and the median OS was 11.1 months. Forty-one (60.3%) of the patients were male. The tumor location was the pancreas head in 73.5% (n=50) of the patients, and body and tail in 26.5% (n=18). All patients included in the study received first-line chemotherapy. Sixteen (23.5%) patients received single-agent gemcitabine, 36.8% (n=25) received dual chemotherapy regimens containing gemcitabine (gemcitabine-cisplatin, gemcitabine-carboplatin, gemcitabine–nab-paclitaxel), and 39.7% (n=27) received FOLFIRINOX.

The rate of those with albumin levels below 3.5 g/dL was 11.8% (n=8), and for those with CRP levels above 1 mg/L, it was 55.9% (n=38). The rate of patients with high NLR was 72.1% (n=49). The rate of mGPS scores of 0 was 44.1% (n=30), those with 1 were 48.5% (n=33), and those with 2 were 7.4% (n=5). Descriptive data are given in Table 1.

OS was 15.6 months in patients aged over 65 years and 13.7 months in those aged under 65 years (p=0.540). OS was 12.3 months in females and 16.4 months in males (p=0.197). OS was 22.4 months in patients with ECOG-PS-0, 13.5 months in those with ECOG-PS-1, and 9.1 months in patients with ECOG-PS-2 (*p=0.014).

OS was 8.7 months in patients with albumin levels below 3.5 g/dL, and 15.6 months in those with albumin levels above 3.5 g/dL (*p=0.029). OS was 9.7 months in patients with CRP levels above 1 mg/L and 21.3 months in those with CRP levels below 1 mg/L (*p=0.001).

OS was 18.1 months in patients with low NLR and 10.4 months in those with high NLR (*p=0.013). OS was 21.3 months in patients with an mGPS of 0, 10.3 months in pa-

Table 1. Number and percentage distribution of demographic and laboratory data

Variables	n	%	Variables	n	%
ECOG			CT		
0	15	22.1	Monotherapy	16	23.5
1	43	63.2	Doublet	25	36.8
2	10	14.7	Triplet	27	39.7
Sex			Albumin		
Female	27	39.7	>3.5 g/dL	60	88.2
Male	41	60.3	≤3.5 g/dL	8	11.8
Location			CRP		
Head	50	73.5	≤1 mg/L	30	44.1
Tail	18	26.5	>1 mg/L	38	55.9
NLR			Exitus		
Low	39	57.4	No	17	25
High	29	42.6	Yes	51	75

tients with an mGPS of 1, and 5.5 months in patients with an mGPS of 2 (*p=0.001). The mGPS-OS relationship is shown in Figure 1 by using the Kaplan-Meier plot.

Univariate and multivariate analyses of prognostic markers for OS are shown in Table 2.

Discussion

As a result of the evaluation with multivariate analysis, mGPS, ECOG-PS scores, and NLR were found to be unfavorable prognostic factors of OS, respectively. The mGPS score was identified as a more sensitive prognostic factor than NLR for OS.

Systemic inflammation is an important promoter of the proliferation, invasion, and metastasis of tumor cells.[9] The immune system also plays a vital role in cancer surveillance and elimination.

There are no standardized prognostic and predictive factors beyond the performance score (PS) for patients with unresectable or metastatic pancreatic adenocarcinoma. Poor PS, defined as 2 or more points by the ECOG, was associated with the detrimental effect of chemotherapy.[10] ECOG-PS scores are also an important prognostic parameter for survival.[11] We also confirmed in our study that the ECOG-PS score was a prognostic factor for OS.

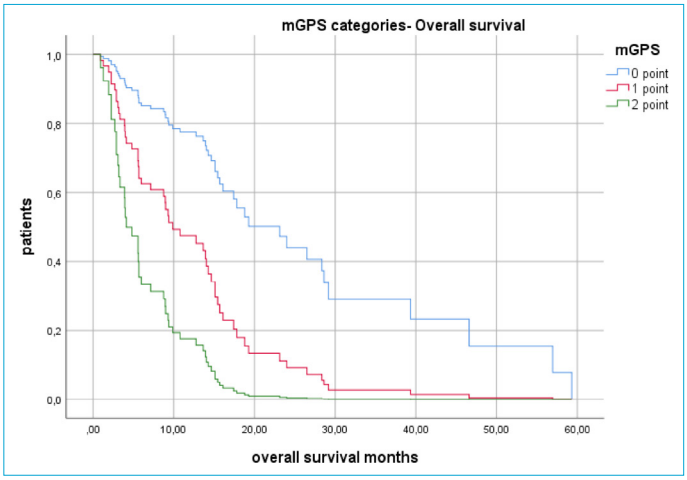

Figure 1. Representation of the mGPS-OS relationship with a Kaplan-Meier curve.

The mechanism of the relationship between NLR and prognosis in patients with unresectable PC has not yet been clarified. Neutrophils inhibit the immune response by lymphocytes, natural killer cells, or activated T cells, whereas lymphocytes reflect the host's immune response to infection or cancer. High pretreatment NLR has been identified as an adverse prognostic factor in many cancers, including colon cancer, gastric cancer, esophageal cancer, and breast cancer.[12-14] In addition, tumor-infiltrating lymphocytes are associated with a better prognosis in patients with pancreatic ductal adenocarcinoma. With this study, it was demonstrated once again that high NLR was an unfavorable prognostic factor in metastatic PC.

The GPS, a prognostic marker based on cumulative inflammation consisting of elevation of CRP levels and decrease in albumin concentrations, is likely to reflect the systemic inflammatory response in patients with cancer and has been reported to be important as a prognostic indicator.[15, 16] Studies are showing the effect of mGPS as a postoperative prognostic index in PC. mGPS is an independent prognostic factor in patients undergoing potentially curative surgery for PC. According to the mGPS result, there are suggestions such as administering anti-inflammatory treatment and delaying surgery to prevent complications.[8] On the other hand, although most patients with PC are diagnosed in the metastatic stage, few researchers have investigated the importance of the mGPS for stage 4 PC. Therefore, the benefit of mGPS in patients with stage 4 PC is not known.[17] This study clearly showed that mGPS was useful in predicting prognosis in patients with stage 4 PC. Although our study showed that the mGPS was useful in predicting survival, it was not designed to evaluate whether it would be helpful in drug selection in patients with metastatic PC.

Table 2. Univariate and multivariate analysis of factors affecting overall survival

Variables	Univariate analysis	(95% CI)	p	Multivariate analysis	(95% CI)	p
	HR			HR		
ECOG	0.45	(0.22-0.95)	0.03	0.39	(0.15-0.98)	0.045
Sex	1.33	(0.74-2.37)	0.34			
Location	0.82	(0.42-1.60)	0.56			
NLR	0.49	(0.28-0.89)	0.017	0.72	(0.37-1.39)	0.32
CT regimen	1.31	(0.69-2.50)	0.58			
Albumin	0.42	(0.19-0.94)	0.034	0.66	(0.24-1.78)	0.41
CRP	0.33	(0.17-0.62)	0.001	0.32	(0.15-0.66)	0.002
mGPS	0.13	(0.04-0.42)	0.001	0.3	(0.11-0.54)	0.001

There are some limitations to this study. It is a retrospective, single-center study with a small number of patients. Therefore, there is a need for multicenter prospective studies, which may confirm the results.

This study revealed that an increase in mGPS and NLR at the time of diagnosis might be an independent indicator of poor prognosis in patients with unresectable PC. The findings showed that mGPS was a factor with higher sensitivity than NLR.

Disclosures

Ethics Committee Approval: This retrospective study complied with the standards of the Declaration of Helsinki.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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