

Prognostic value of nutrition and inflammation based scores in patients with metastatic pancreatic cancer

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Cite this article as: Mutlu Özkan E, Fırat ST, İnanç M, et al. Prognostic value of nutrition and inflammation based scores in patients with metastatic pancreatic cancer. *Anatolian Curr Med J.* 2026;8(1):139-145.

Received: 03.12.2025

Accepted: 30.12.2025

Published: 06.01.2026

ABSTRACT

Aims: Pancreatic cancer is a highly aggressive malignancy, with most patients presenting at an advanced stage. Identifying reliable prognostic markers is essential to guide treatment decisions. This study evaluated the prognostic significance of inflammation and nutrition-based indices in metastatic pancreatic cancer.

Methods: A total of 162 patients with stage IV pancreatic cancer were retrospectively analyzed. Nutrition- and inflammation-based scores were calculated from baseline blood parameters. Progression-free survival (PFS) and metastatic overall survival (mOS) were evaluated using Kaplan–Meier and Cox regression analyses.

Results: The median PFS and mOS were 5.4 and 10.3 months, respectively. In the multivariate analysis, a high prognostic nutritional index (PNI) (HR: 0.72, p: 0.048) and a high platelet-to-lymphocyte ratio (ALI) (HR: 0.76, p: 0.005) were associated with favorable PFS, whereas a high systemic immune-inflammation index (SII) (HR: 1.84, p: 0.013) and a high systemic inflammation response index (SIRI) (HR: 2.11, p: 0.005) predicted poor PFS. High PNI (HR: 0.51, p: 0.002), ALI (HR: 0.73, p: 0.047), and hemoglobin-albumin-lymphocyte-platelet (HALP) index (HR: 0.72, p: 0.032) were significantly associated with longer mOS, whereas high SII (HR: 1.81, p: 0.007) and pan-immune inflammation value (PIIV) (HR: 1.87, p: 0.037) were associated with shorter mOS.

Conclusion: Inflammation-and nutrition-based scores are valuable prognostic biomarkers in metastatic pancreatic cancer. Their accessibility and low cost make them promising tools for risk stratification and individualized treatment planning in clinical practice.

Keywords: Pancreatic cancer, inflammation, survival, prognostic nutritional index

INTRODUCTION

Pancreatic cancer is one of the most common digestive system cancers worldwide and is a highly lethal malignancy, with a 5-year survival rate of approximately 3%.¹

Surgical treatment offers the only potential chance for cure; however, 80-85% of patients are diagnosed with metastatic disease. In metastatic disease, the primary goals of chemotherapy are symptom relief and prolongation of survival. Recently, the prognosis of advanced pancreatic cancer has improved with the use of fluorouracil, irinotecan, oxaliplatin, and leucovorin (FOLFIRINOX) chemotherapy. Therefore, prognostic factors play a crucial role, and precise identification of unfavorable prognostic indicators may assist in guiding more intensive treatment strategies for patients with pancreatic cancer. In a recent study, patients receiving FOLFIRINOX had a median overall survival (OS) of 11.3 months, whereas the control group treated with gemcitabine had a median OS of approximately 6.8 months, consistent

with previous studies.² Therefore, identifying prognostic markers that can help predict survival and guide optimal treatment in patients with advanced pancreatic cancer is of critical importance. Increasing evidence has shown that cancer prognosis is influenced not only by oncological characteristics but also by nutritional and immunological status.³ The advanced lung cancer inflammation index (ALI), first introduced in lung cancer and later investigated in various malignancies, serves as a prognostic biomarker reflecting both nutritional and inflammatory status.⁴ Likewise, several inflammation-based indices, including the PIIV, platelet-to-lymphocyte ratio (PLR), PNI, neutrophil-to-lymphocyte ratio (NLR), SII, systemic inflammation response index (SIRI), (HALP) score, have also been shown to be associated with survival across different cancer types.⁵⁻¹⁰ Although numerous inflammation- and nutrition-based indices such as NLR, SII, SIRI, PIIV, PNI, ALI, and HALP have individually

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been associated with prognosis in various malignancies, their comparative evaluation within a single, well-defined cohort of patients with metastatic pancreatic cancer remains limited. The present study does not aim to introduce novel biomarkers; rather, it seeks to provide a simultaneous and systematic assessment of multiple established inflammation- and nutrition-based indices within the same real-world population. From a methodological perspective, the present analysis should be interpreted as exploratory and hypothesis-generating. The evaluated inflammation- and nutrition-based indices represent composite measures derived from correlated biological variables and were included to examine their prognostic behavior in parallel rather than to establish independent predictive effects. Given the absence of robust comparative data in metastatic pancreatic cancer, this approach was adopted to explore relative prognostic patterns within a homogeneous real-world cohort and to inform future confirmatory study designs. By evaluating their relative prognostic associations under uniform clinical conditions, this exploratory analysis aims to offer a clearer contextual understanding of how these indices perform alongside one another in metastatic pancreatic cancer, thereby generating hypotheses for future prospective and externally validated studies.

METHODS

The study has received ethical approval from the Kayseri City Hospital Non-Interventional Clinical Research Ethics Committee (Date: 18.11.2025, Decision no: 656). As this research was conducted retrospectively, the requirement for informed consent was waived. All patient data were anonymized and stored in secure, password-protected systems accessible only to authorized personnel. All procedures involving human participants were conducted in accordance with institutional and/or national ethical standards and the 1964 Helsinki Declaration and its later amendments.

Patients with metastatic pancreatic cancer (stage IV) who were able to receive at least 12 weeks of chemotherapy between January 2013 and February 2024 were included in the study. Patients with acute infection, a history of systemic steroid therapy within the past 3 months, or a known hematological disease were excluded from the study. Peripheral blood tests were performed 3 to 24 hours before chemotherapy. The following indices were derived according to the specified formulas:

NLR: Absolute neutrophil count (count/mm³)/Absolute lymphocyte count (count/mm³)

ALI: Serum albumin (g/dl) x BMI/NLR

SII: NLR x Platelet count (count/mm³)

PNI: [Absolute lymphocyte count (count/mm³) X 0.005]+[Serum albumin (g/dl) X 10]

PLR: Platelet count (count/mm³)/Absolute lymphocyte count (count/mm³)

SIRI: NLR x Absolute monocyte count (count/mm³)

PIIV: SIRI x Platelet count (count/mm³)

HALP: [Hemoglobin (g/dl)×albumin (g/dl)×Absolute lymphocyte count (count/mm³)]/Absolute platelet count (count/mm³).

Statistical Analysis

Statistical analyses were conducted using SPSS version 23, and receiver operating characteristic (ROC) analysis was performed to identify the optimal cut-off values for the inflammation scores. mOS and PFS were calculated as the time from the initiation of chemotherapy to death and to disease progression, respectively. ROC curve analyses were conducted using overall survival status (death vs. censored) as the endpoint for cut-off determination. Univariate mOS and PFS analyses were performed using the log-rank test and Kaplan-Meier method, whereas multivariate analyses were conducted using the Cox proportional hazards model. Associations between clinicopathological features and inflammation scores were assessed using the chi-square or Wilcoxon tests, and a two-sided p-value <0.05 was considered statistically significant.

RESULTS

A total of 190 patients were screened; however, patients with missing key laboratory values were excluded from the relevant analyses. Consequently, 162 patients were included in the final evaluation. The cohort consisted of 162 patients, including 98 males (60.5%) and 64 females (39.5%), with a median age of 61 years. The liver was the predominant site of metastasis (71.6%). Following hepatic involvement, the most frequent metastatic sites were non-regional lymph nodes, the lungs, and the peritoneum, respectively (**Table 1**). The area under the curve (AUC) values obtained from the ROC analysis were as follows: NLR (0.62), ALI (0.71), SII (0.71), PNI (0.74), PLR (0.63), PIIV (0.67), SIRI (0.73), and HALP (0.76), with HALP demonstrating the highest AUC value. The corresponding optimal cut-off values were ALI (31.5), NLR (2.85), HALP (28.7), PNI (46.5), PLR (167.6), SIRI (1.76), PIIV (445.6), and SII (821). Based on ROC curve analysis, the optimal cut-off value for HALP was determined to be 28.7, demonstrating a sensitivity of 83% and a specificity of 67%, with an AUC of 0.76. These values represented the highest combined sensitivity and specificity among the indices evaluated by ROC analysis.

Kaplan-Meier analysis demonstrated a median PFS of 5.4 months and a median mOS of 10.3 months in the overall cohort. In the multivariate analysis, treatment with FOLFIRINOX (p=0.048), high PNI (p=0.048), and high ALI (p=0.005) were associated with favorable PFS. In contrast, high SII (p=0.013) and high SIRI (p = 0.005) were associated with poor PFS (**Table 2**). High PNI (p=0.002), ALI (p=0.047), and HALP (p=0.032) were associated with favorable mOS. Conversely, high SII (p=0.007) and high PIIV (p=0.037) were associated with poor mOS (**Table 3**).

In the multivariate analysis, the most statistically significant p-values for PFS were observed in the ALI and SIRI groups. The median PFS was 4.1 months in the low ALI group and 6.4 months in the high ALI group (HR: 0.76; 95% CI: 0.34-0.83; p=0.005) (**Figure 1A**). The median PFS was 6.7 months in the low SIRI group and 4.2 months in the high SIRI group (HR: 2.11; 95% CI: 1.25-3.55; p=0.005) (**Figure 1B**). For mOS, the

Table 1. Clinicopathological characteristics and inflammatory markers of patients

Variable	Categories	n: 162 (100%)	Median (min-max)
Age			61 (32–86)
Gender	Female	64(60.5%)	
	Male	98 (39.5%)	
Histopathology	Adenocarcinoma	162 (100%)	
Metastasis site	Liver	116 (71.6%)	
	Non-regional lymph node	25 (15.4%)	
	Lung	25 (15.4%)	
	Peritoneum	20 (12.3%)	
Albumin (g/L)			4 (2.20–5.38)
LDH (U/L)			206 (100-801)
Ca 19-9 (U/mL)			932 (0.6-65687)
ECOG PS	0-1	96 (59.3%)	
	≥2	66 (40.7%)	
First-line chemotherapy	FOLFIRINOX	26 (16%)	
	Platin+gemcitabine	136 (84%)	
PNI	<46.5	83 (51.2%)	
	≥46.5	79 (48.8%)	
NLR	<2.85	75 (46.2%)	
	≥2.85	87 (53.8%)	
ALI	<31.5	82 (50.6%)	
	≥31.5	80 (49.4%)	
SII	<821	67 (41.4%)	
	≥821	95 (58.6%)	
PIIV	<445.6	70 (43.2%)	
	≥445.6	92 (56.8%)	
SIRI	<1.76	79 (48.8%)	
	≥1.76	83 (51.2%)	
HALP	<28.7	85 (52.5%)	
	≥28.7	77 (47.5%)	
PLR	<167.6	64 (39.5%)	
	≥167.6	98 (60.5%)	

LDH: Lactate Dehydrogenase, ECOG PS: Eastern Cooperative Oncology Group Performance Status, FOLFIRINOX: Fluorouracil-irinotecan- oxaliplatin-leucovorin, PNI: Prognostic nutritional index, NLR: Neutrophil to lymphocyte ratio, ALI: Advanced lung cancer inflammation index, SII: Systemic immune-inflammation index, PIIV: Pan-immune inflammation value, SIRI: Systemic inflammation response index, HALP: Hemoglobin-albumin-lymphocyte-platelet, PLR: Platelet to lymphocyte ratio, Min: Minimum, Max: Maximum

most statistically significant p-values were observed in the PNI and SII groups. The median mOS was 6.1 months in the low PNI group and 11.9 months in the high PNI group (HR: 0.51; 95% CI: 0.34-0.77; $p=0.002$) (**Figure 2A**). The median mOS was 11.9 months in the high SII group and 6.6 months in the low SII group (HR: 1.81; 95% CI: 1.17-2.79; $p=0.007$) (**Figure 2B**). Multiple inflammation- and nutrition-based indices included in the multivariable models share overlapping biological components, which introduces a risk of multicollinearity and overfitting. Formal multicollinearity diagnostics (e.g., variance inflation factor or tolerance analyses) were not performed because the study was designed as exploratory and hypothesis-generating, with indices intentionally analyzed in parallel to describe relative associations rather than to establish independent prognostic effects.

DISCUSSION

In this study, we evaluated the prognostic value of a wide range of inflammation- and nutrition-based indices, including NLR, PLR, PNI, ALI, SII, SIRI, PIIV, and HALP, in patients with metastatic pancreatic cancer undergoing chemotherapy. Our findings highlight the importance of systemic inflammation and nutritional status in determining survival outcomes. Specifically, high PNI, ALI, and HALP values were associated with improved survival, whereas elevated SII, SIRI, and PIIV predicted poor prognosis. Among the investigated indices, HALP yielded the highest AUC value in the ROC analysis performed for cut-off determination. However, this finding should be interpreted descriptively rather than inferentially, as ROC/AUC analysis was not intended to establish prognostic superiority for survival outcomes, and no formal statistical comparison between indices was conducted. Accordingly, HALP should not be regarded as the strongest discriminative biomarker, but rather as one of several indices demonstrating potential prognostic relevance within the exploratory framework of this study.

The prognostic impact of nutritional and systemic inflammatory indices has been extensively reported in other malignancies. For instance, Hua et al.⁴ demonstrated in a meta-analysis that ALI is a reliable prognostic indicator across several cancer types, with high ALI consistently associated with longer survival.

Our findings are in line with this evidence, as patients with higher ALI had significantly better PFS and OS, suggesting that preserved nutritional reserves and lower systemic inflammation are critical for improved treatment response in pancreatic cancer as well. Similarly, PNI has been validated in multiple studies, particularly in lung and gastric cancer, as a strong predictor of survival outcomes.^{6,11} The association of high PNI with longer OS in our cohort supports the hypothesis that sufficient protein reserves and immune competence may enhance chemotherapy tolerance and disease control.

In contrast, markers reflecting a heightened inflammatory state, such as PIIV, SII, and SIRI, were significantly associated with poor outcomes in our study. Wei et al.⁷ reported similar findings in a large meta-analysis, in which elevated SIRI was consistently linked to worse survival across several tumor types.¹²

High SII, which integrates neutrophil, platelet, and lymphocyte counts, has also been shown to predict unfavorable prognosis in gastrointestinal cancers.^{8,13} In a pooled analysis of fifteen studies, patients with higher PIIV levels demonstrated significantly worse survival compared with those with lower levels.¹⁴ Our results underline the role of systemic inflammation in promoting tumor progression, immune suppression, and resistance to treatment in pancreatic cancer.

HALP, which combines inflammation and nutritional parameters, has emerged as a promising prognostic marker. Xu et al.¹⁰ demonstrated, through a meta-analysis of more than 13,000 patients, that HALP is significantly correlated with cancer survival across multiple tumor types.

Table 2. Univariate and multivariate analysis results in terms of PFS

Variables	Categories	Median PFS (months)	Univariate analysis HR 95% CI	p-value	Multivariate analysis HR 95% CI	p-value
Age, years	<65*	6.1				
	≥65	4.8	1.28 (0.90-1.81)	0.166		
Gender	Female*	5.2				
	Male	5.6	1.03 (0.72-1.46)	0.862		
ECOG PS	≥2*	3.6				
	0-1	5.8	0.91 (0.76-1.63)	0.562		
Hemoglobin (g/dl)	<12*	3.2				
	≥12	6.7	0.79 (0.55-0.93)	0.003	0.82 (0.32-2.32)	0.351
Metastases site	>1*	2.1				
	≤1	5.6	0.51 (0.55-1.13)	0.05		
Ca 19-9 (U/ml)	≥35*	3.4				
	<35	5.9	0.92 (0.74-1.79)	0.526		
LDH (U/L)	<250*	5.7				
	≥250	3.5	1.19 (1.12-3.21)	0.005	1.17 (0.76-2.56)	0.413
Chemotherapy groups	Platin+gemcitabin*	4.2				
	FOLFIRINOX	6.3	0.37 (0.20-0.66)	0.001	0.65 (0.22-0.92)	0.048
PNI	<46.5*	4				
	≥46.5	6.9	0.38 (0.27-0.54)	<0.001	0.72 (0.31-0.96)	0.048
NLR	<2.85*	5.8				
	≥2.85	5	1.55 (1.11-2.17)	0.009	1.34 (0.52-2.82)	0.232
ALI	<31.5*	4.1				
	≥31.5	6.4	0.61 (0.44-0.86)	0.004	0.76 (0.34-0.83)	0.005
SII	<821*	6.9				
	≥821	4.2	2.31 (1.63-3.26)	<0.001	1.84 (1.13-2.98)	0.013
PIIV	<445.6*	6.6				
	≥445.6	4.4	1.94 (1.38-2.73)	<0.001	1.17 (0.46-1.29)	0.325
SIRI	<1.76*	6.7				
	≥1.76	4.2	2.45 (1.73-3.45)	<0.001	2.11 (1.25-3.55)	0.005
HALP	<28.7*	4.5				
	≥28.7	6.3	0.59 (0.42-0.83)	0.002	0.96 (0.59-1.55)	0.887
PLR	<167.6*	6.6				
	≥167.6	4.6	1.61 (1.15-2.27)	0.005	1.09 (0.67-1.78)	0.720

*Reference category, PFS: Progression free survival, HR: Hazard ratio, CI: Confidence interval, ECOG PS: Eastern Cooperative Oncology Group Performance Status, LDH: Lactate Dehydrogenase, FOLFIRINOX: Fluorouracil-irinotecan- oxaliplatin-leucovorin, PNI: Prognostic nutritional index, NLR: Neutrophil to lymphocyte ratio, ALI: Advanced lung cancer inflammation index, SII: Systemic immune-inflammation index, PIIV: Pan-immune inflammation value, SIRI: Systemic inflammation response index, HALP: Hemoglobin-albumin-lymphocyte-platelet, PLR: Platelet to lymphocyte ratio

Our findings are consistent with this evidence and extend the prognostic role of HALP to metastatic pancreatic cancer. Given that HALP reflects both nutritional and inflammatory status, its superior predictive performance compared with individual clinical findings may stem from its ability to capture multiple aspects of host-tumor interactions. The loss of statistical significance of certain indices, such as HALP, in multivariate analyses for PFS despite strong univariate associations warrants careful interpretation. This attenuation may be explained by several factors. First, many inflammation-and nutrition-based indices share

overlapping hematological and biochemical components, leading to correlated information that may diminish apparent independent effects after multivariable adjustment. Second, PFS analyses were characterized by a relatively limited number of events, potentially resulting in reduced events-per-variable ratios and decreased statistical power. Finally, adjustment for correlated clinical and laboratory variables may further account for the shared prognostic variance observed in univariate models. Taken together, these findings suggest that univariate associations may capture composite biological signals that are partially redistributed across covariates in

Table 3. Univariate and multivariate analysis results in terms of mOS

Variables	Categories	Median mOS (months)	Univariate analysis HR 95% CI	p-value	Multivariate analysis HR 95% CI	p-value
Age, years	<65*	10.3				
	≥65	7.4	1.13 (0.79-1.59)	0.488		
Gender	Female*	8.8				
	Male	9.1	1.15 (0.81-1.64)	0.409		
ECOG PS	≥2*	7.5				
	0-1	9.2	0.73 (0.78-1.63)	0.513		
Hemoglobin(g/dl)	<12*	7.3				
	≥12	8.7	0.79 (0.55-1.13)	0.209		
Metastases site	>1*	7.6				
	≤1	9.1	0.84 (0.57-1.2)	0.377		
Ca 19-9 (U/ml)	≥35*	6.7				
	<35	9.4	0.87 (0.54-1.41)	0.597		
LDH (U/L)	<250*	10.7				
	≥250	6.1	1.65 (1.11-2.46)	0.013	1.51 (0.98-2.31)	0.057
Chemotherapy groups	Platin+gemcitabin*	5.8				
	FOLFIRINOX	11.2	0.44 (0.24-0.78)	0.005	0.47 (0.23-1.37)	0.210
PNI	<46.5*	6.1				
	≥46.5	11.9	0.388 (0.27-0.54)	<0.001	0.51 (0.34-0.77)	0.002
NLR	<2.85*	10.7				
	≥2.85	7.5	1.55 (1.11-2.17)	0.009	1.12 (0.53-1.76)	0.670
ALI	<31.5*	7.4				
	≥31.5	10.6	0.61 (0.44-0.86)	0.005	0.73 (0.48-0.92)	0.047
SII	<821*	11.9				
	≥821	6.6	2.31 (1.63-3.26)	<0.001	1.81 (1.17-2.79)	0.007
PIIV	<445.6*	11.3				
	≥445.6	7	1.94 (1.38-2.73)	<0.001	1.87 (1.23-2.63)	0.037
SIRI	<1.76*	11.5				
	≥1.76	6.4	2.45 (1.73-3.45)	<0.001	1.58 (0.98-2.53)	0.057
HALP	<28.7*	7.4				
	≥28.7	10.5	0.59 (0.42-0.83)	0.002	0.72 (0.47-0.92)	0.032
PLR	<167.6*	10.9				
	≥167.6	7.7	1.61 (1.15-2.27)	0.005	1.12 (0.68-1.69)	0.071

*Reference category. mOS: Metastatic overall survival, HR: Hazard ratio, CI: Confidence interval, ECOG PS: Eastern Cooperative Oncology Group Performance Status, LDH: Lactate Dehydrogenase, FOLFIRINOX: Fluorouracil-irinotecan-oxaliplatin-leucovorin, PNI: Prognostic nutritional index, NLR: Neutrophil to lymphocyte ratio, ALI: Advanced lung cancer inflammation index, SII: Systemic immune-inflammation index, PIIV: Pan-immune inflammation value, SIRI: Systemic inflammation response index, HALP: Hemoglobin-albumin-lymphocyte-platelet, PLR: Platelet to lymphocyte ratio

multivariate models, particularly within an exploratory analytical framework.

Malnutrition is frequently observed in cancer patients and can negatively impact both treatment efficacy and overall quality of life. It may arise from the tumor itself, the host response, or adverse effects of cancer therapy. Unfortunately, malnutrition is often overlooked in many oncology departments and, when present across several cancer types, can have serious consequences if not addressed, including decreased tolerance to chemotherapy and poorer overall patient outcomes. Recent

studies have demonstrated that immune and nutritional status, together with clinicopathological features, are key predictors of cancer outcomes. Immunonutritional indices, which combine inflammatory markers with nutritional assessment, serve as important prognostic indicators in various types of cancer.^{15,16} Importantly, all of these indices are derived from routine blood tests, making them cost-effective, reproducible, and easily applicable in daily clinical practice.

Several meta-analyses have consistently demonstrated that inflammation- and nutrition-based indices such as ALI,

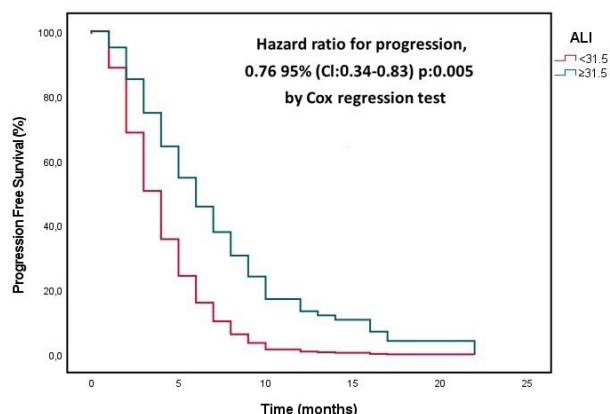


Figure 1A. Progression free survival outcomes according to ALI

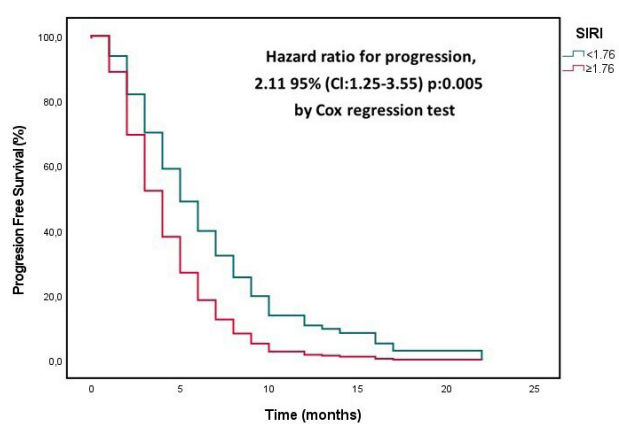


Figure 1B. Progression free survival outcomes according to SII

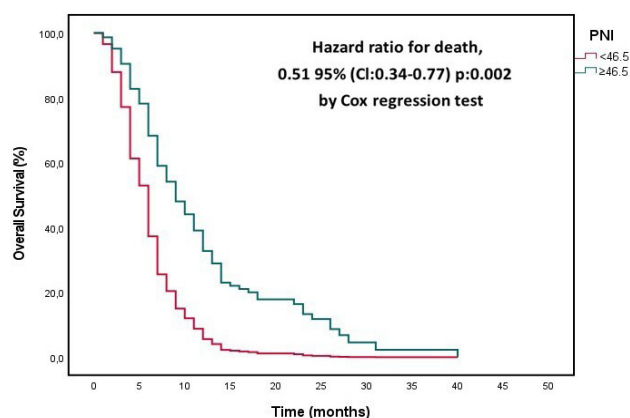


Figure 2A. Overall survival outcomes according to PNI

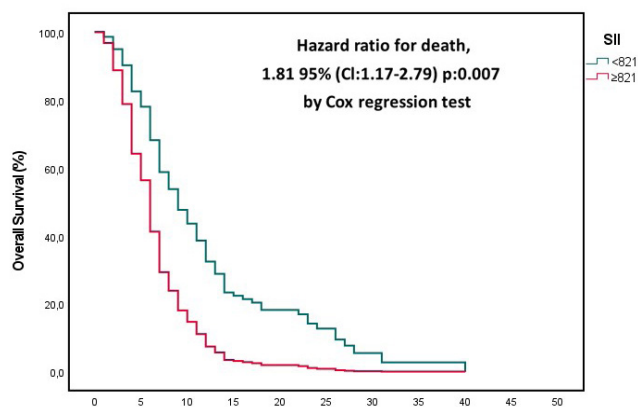


Figure 2B. Overall survival outcomes according to SII

PNI, SII, SIRI, PIIV, and HALP are associated with cancer prognosis across multiple tumor types, albeit with substantial heterogeneity between studies^{4,7,10,14}. Rather than reiterating individual survival results, the present findings should be interpreted within the context of existing aggregated evidence. Accordingly, this study was designed as an exploratory, hypothesis-generating analysis in which multiple inflammation- and nutrition-based indices were intentionally evaluated in parallel. Given that these indices reflect overlapping but not identical aspects of systemic inflammation and nutritional status, their concurrent assessment was aimed at exploring relative prognostic associations rather than establishing independent predictive effects. This approach acknowledges the potential for collinearity and is intended to provide a comparative exploratory framework to inform future confirmatory research in metastatic pancreatic cancer. In line with these reports, our results suggest that indices reflecting preserved nutritional status and lower systemic inflammation tend to be associated with more favorable outcomes, whereas markers of heightened inflammatory burden correlate with poorer survival. However, unlike large pooled analyses, the current study is limited by its retrospective design, single-center setting, and the inclusion of multiple biologically correlated indices within the same multivariable models, which introduces risks of multicollinearity, overfitting, and selection bias. Moreover, the absence of correction for multiple comparisons and the use of cohort-specific cut-off values further underscore the exploratory nature of the analysis. Accordingly, these findings should not be interpreted as establishing independent prognostic superiority of any single index, but rather as generating comparative signals that warrant confirmation in prospective, multicenter studies with predefined hypotheses and robust statistical modeling. Given the retrospective, single-center, and exploratory design, the evaluated inflammation- and nutrition-based indices cannot be considered tools for immediate clinical application, individualized treatment planning, or direct treatment decision-making. Rather than implying actionable clinical guidance, the observed associations highlight potential prognostic signals that may be relevant for future research. Accordingly, all interpretations are confined to hypothesis generation, emphasizing the need for prospective, multicenter studies with predefined analytical frameworks to determine whether and how these indices could meaningfully contribute to clinical risk stratification or decision-support models in metastatic pancreatic cancer. From a clinical perspective, the evaluated inflammation- and nutrition-based indices may offer practical advantages due to their derivation from routinely available laboratory parameters. While the present findings do not support direct clinical implementation, they suggest that such indices could be explored in future prospective studies as complementary tools for prognostic stratification or for identifying patient subgroups in clinical research settings. Their low cost and accessibility make them attractive candidates for further validation rather than immediate clinical application.

Limitations

Despite the promising results, several limitations must be acknowledged. The study's retrospective, single-center design may introduce selection bias and limit the generalizability of the findings. Additionally, the cut-off values obtained from ROC analysis in our cohort may not be directly applicable to other populations. This represents an important limitation of the study. Multiple inflammation- and nutrition-based indices share overlapping biological components, introducing a risk of multicollinearity and overfitting; therefore, formal multicollinearity diagnostics were not performed, as the analysis was exploratory and aimed at describing relative associations rather than establishing independent prognostic effects. A further limitation is that the Events Per Variable (EPV) thresholds may not have been fully satisfied, particularly in progression analyses. Differences in baseline characteristics and treatment regimens among patients may also affect the reproducibility of these threshold values. Therefore, external validation through prospective, multicenter studies with larger sample sizes is necessary before these markers can be routinely implemented in clinical practice.

CONCLUSION

Our study demonstrates that inflammation- and nutrition-based indices, particularly HALP, PNI, ALI, PIIV, SII, and SIRI, provide valuable prognostic information in metastatic pancreatic cancer. These markers not only reflect the systemic inflammatory response but also highlight the importance of host nutritional and immune status in influencing survival outcomes. Given the retrospective, single-center, and exploratory design, the evaluated inflammation- and nutrition-based indices cannot be considered tools for immediate clinical application, individualized treatment planning, or direct treatment decision-making. However, they may provide informative insights into the contribution of patients' nutritional and inflammatory status to treatment effectiveness.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study has received ethical approval from the Kayseri City Hospital Non-Interventional Clinical Research Ethics Committee (Date: 18.11.2025, Decision no: 656).

Informed Consent

As this was a retrospective study, formal written informed consent was not required and was therefore not obtained.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

Financial Disclosure

The authors received no financial support for the conduct or publication of this research.

Author Contributions

Concept: E.M.Ö., S.T.F.; Design: E.M.Ö., M.İ., R.C.; Control: M.İ., E.D, İ.B.; Data collection: E.D., E.G. İ.B.; Analysis and interpretation: S.T.F., E.M.Ö., R.C.; Literature Review: E.M.Ö., M.İ.; Article writing: E.M.Ö., S.T.F., İ.B.; Critical review: All authors.

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