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ORIGINAL ARTICLE

Neutrophil–Lymphocyte Ratio and Clinical Outcome in Advanced Pancreatic Cancer Patients

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ABSTRACT

Background: Studies have been carried out to highlight the connection between the Neutrophil–Lymphocyte Ratio (NLR) and the prognosis of pancreatic cancer, still with controversial findings. This study retrospectively examined the relation between NLR and response to treatment, time to treatment failure (TTF), and overall survival (OS) among patients with advanced pancreatic cancer.**Subjects and methods:** This observational retrospective cohort study was carried out on 80 patients diagnosed with advanced pancreatic cancertreated with first-line chemotherapy. The NLR was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count. We evaluated the TTF and OS in all cases.**Results:**Using the 1-year survival as a time point to create the receiver operating characteristics (ROC) curve, the optimal cut-off value for baseline NLR was found to be 2.05 with an area under the curve (AUC) of 0.906. Patients with NLR ≤2.05 revealed a significantly longer OS (mean: 11.347 months) than patients with NLR >2.05 (mean: 6.707 months) with a significant p-value of <0.001. NLR had a sensitivity of 81.2% and specificity of 84.4% at a threshold value of 2.05 in predicting mortality.For patients with NLR ≤2.05, the average TTF was longer (7.075 months) compared with those with NLR >2.05 (6.670 months) but with no significant difference (P >0.05). Regarding response, progressive disease (PD) at first evaluation to 1st line chemotherapy at three months was significantly higher in cases who had NLR >2.05 (p=0.008). In addition, death at one year was significantly higher in patients who had NLR >2.05 (p<0.001). WBCs and platelets counts were considerably higher in cases that had NLR >2.05 than in patients with NLR ≤2.05. Whereas albumin, Albumin to globulin (AG) ratio.**Conclusions:** NLR could serve as a valuable prognostic and predictive biomarker in advanced pancreatic cancer, aiding treatment decision-making and patient management.**Keywords :**Neutrophil–Lymphocyte Ratio; Clinical Outcome; Advanced Pancreatic Cancer

INTRODUCTION

Worldwide, pancreatic cancer ranks third among cancer-related mortality in both sexes [1], having a survival rate of about 10% after five years [2]. In Egypt, 3.2 per 100,000 people in lower, middle, and upper Egypt, with corresponding incidence rates of 3.2 percent, 1.94 percent, and 3.6 percent, pancreatic cancer has long been believed to be a rare disease, accounting for approximately 2% of all cancers [3].

Unlikedeveloped countries where the disease predominantly occurs in the elderly population, an unexpectedly high prevalence of young-onset pancreatic cancer was observed in the East Nile Delta, with the disease detected at advanced stages and associated with a high mortality rate [٤].Pancreatic cancer patients have the best likelihood of extended survival after curative resection. Unfortunately, nearly 80% of patients were initially diagnosed with unresectable pancreatic cancer [٥].

For pancreatic cancer patients with advanced stages, chemotherapy is a standard treatment option. A median OS of 8.5-11.1 months is the result of conventional chemotherapy, which, however, has a negligible impact on disease progression and inadequate efficacy. Though prior studies have revealed a variety of predictors of chemotherapy response, there are currently no potential predictors that allow better risk assessment for response, hence prognosis in advanced pancreatic cancer patients [6]. There is a lot of interest in determining the role of systemic inflammation in the development, progression, and prognosis of pancreatic cancer since chronic inflammation is an essential etiologic element in the disease's onset and response [7].

No matter the etiology, chronic pancreatitis raises the risk of cancer. However, there seems to be a subset of people who were especially at risk. Elevated pancreatic cancer risk has been associated with hereditary pancreatitis, an uncommon autosomal dominant condition resulting from cationic trypsinogen gene mutations. This population has a worse survival rate and develops pancreatic inflammation at a much younger age [8].

NLR, calculated by dividing the absolute neutrophil count by the absolute lymphocyte count, is a simple, cheap, and easily quantitative indicator of systemic inflammation. Among the many cancers for which NLR is a useful adjunctive pretreatment, it stands out as a distinct prognostic indication linked to poor prognosis. [٩].Research on the correlation between NLR and pancreatic cancer prognosis has also been conducted, although the results have been met with controversial reviews[١٠].

So, this study aimedto retrospectively assess the relation between NLR and response to treatment, TTF, and OS among patients with advanced pancreatic cancer and to correlate between NLR and clinicopathological features in advanced pancreatic cancer patients.

METHODS

This observational retrospective cohort study wasconducted at theMedical Oncology department in Zagazig University Hospitals from January 2017 to December 2021. Weanalyzed data from 80patients who were diagnosed with advanced pancreatic cancer.

Inclusion criteria:Patients of both sexes were 18 years old or older and had radiographic

and histologic proof of pancreatic adenocarcinoma that had spread locally or across the body. Pancreatic cancer TNM staging was based on the 8th edition of the American Joint Committee on Cancer (AJCC) recommendations [١١], cases who had adequate bone marrow reservewhite blood cells (WBCs) to be ≥ 3 x 10^9/L, platelets to be ≥ 100 x 10^9/L, and hemoglobin to be ≥ 10 g/L), who had adequate kidney functions (Blood urea 20- 40 mg/dl and Serum creatinine < 1.2 mg/dl), who had adequate liver functions (Total bilirubin < 1.2 mg/dl and AST and ALT < 2.5 x upper normal range),and patients who underwent gemcitabine-based or fluoropyrimidine-based as1st line chemotherapy.

Exclusion criteria: We excluded all who had any of the following conditions: Incomplete data in the file,Patients who were planned for best supportive care or refused chemotherapy,and patients suffering from malignancy other than pancreatic cancer. Also,patients who were presented withresectable pancreatic cancer, who had prior chemotherapy and radiotherapy,who had medical contraindications for medical treatment, and women who were pregnant or lactating were not allowed to take part.

This study followed the guidelines [the World Medical Association's Code of Ethics (Declaration of Helsinki) for human studies]. All participants provided informed and written consent. The Institutional Review Board has approved this research (#9652).

Data collection

The following variables of patients were extracted anonymously from medical records and transcribed into an Excel spreadsheet: Personal data including age,gender, past medical history fordiabetes,diagnostic clinical staging according to the 8thversion of the TNM staging system developed by the AJCC, Eastern Cooperative Oncology Group (ECOG) performance status (PS) at the time of starting first-line chemotherapy [1٢], primary tumor location within the pancreas, tumor grade,chemotherapy regimen, and laboratory data, includingWBCs, neutrophil and lymphocyte, platelets, hemoglobin,total bilirubin, albumin, globulin, Albumin/globulin(AG) ratio, Within one week before the first treatment cycle, CA19.9 was acquired. Absolute neutrophil count/absolute lymphocyte count was the formula for NLR.Another inflammatory prognostic scoreisthe platelets to lymphocyte ratio(PLR),calculated by platelet count divided by absolute lymphocyte count, Odonera Prognostic nutritional index (PNI) (calculated as 10 × Albumin levels + 0.005 × lymphocyte levels)[١٣].

Endpoints

Primary endpoint: Time to treatment failure was calculated from the date of chemotherapy initiation to the date of chemotherapy discontinuation for various reasons, including treatment toxicity or disease progression.

Secondary endpoint:Overall survival was calculated from the beginning of chemotherapy until the last follow-up or death.

STATISTICAL ANALYSIS:

The statistical package for the social sciences, SPSS, version 20, was used for the data analysis. (Armonk, NY: IBM Corp").A chi-square test was used to examine how the two sets of ordinal data were related. The student t-test was used for normally distributed

quantitative variables and the Mann-Whitney U test for otherwise dispersed ones, and we compared the two sets of data.Kaplan Meier curves were created to evaluate OS and progression-free survival (PFS). Then, a Log Rank test was performed to determine if there was a statistically significant change between groups.The optimal cutoff value for a quantitative parameter utilized in diagnosing a health issue was determined using anROC curve.

RESULTS

Based on the data provided by patients' files, the age of diagnosis ranged from 35 to 65 years, with a mean age of 58.0± 7.0 years. Patients more than 60 years were the most typical age group found (43.75%), followed by the age group between 51 and 60 (42.5%), then the age group between 41 and 50 (10%), and the age group between 30 and 40 (3.75%). More than half of the patients (52.5%) were males. In comparison, 47.5% were females, with a male-to-female ratio of 1.1:1; PS is an independent prognostic factor for survival in patients with pancreatic cancer, and 57.5% were PS-I. In comparison, PS-II patients represented 42.5% of the patient population; 29 (36.3%) patients were known to be diabetic, as shown in (Table 1).

More than half of patients (57.5%) received mFOLFIRINOX, while 42.5% received Gemcitabine monotherapy as the first line. The mean duration of 1stline chemotherapy was 4.28± 1.71 months and ranged from one month to 12 months. Only 30 (37.5%) patients received subsequentlines. The response to treatment at first evaluation at three monthsrevealed that 34 out of 80 cases(42.5%) had Stable disease (SD),18 cases achieved partial response (PR) (22.5%) while 28 patients(35.0%) reported progression. 52 out of 80 patients (65.0%) achieved a disease control rate (PR+SD). Regarding survival outcome, there were 32 (40%) cases alive within one year, while death was reported in 48 (60%) cases. TheOS of all studied patients was 8.795 months, as shown in (Table 2).

The best cut-off value for baseline NLR was discovered to be 2.05 with an AUC of 0.906, using the 1-year survival as a time point to produce the receiver ROC curve. Patients whose NLR was less than or equal to 2.05 had an OS rate of 11.347 months, while patients whose NLR was more significant than or equivalent to 2.05. Those with an NLR greater than 2.05 had a significantly poorer OS rate than patients with an NLR less than or equal to 2.05 (P <0.001).(Table 3).

The mean TTF among the studied pancreatic cancer patients was 6.932 months.For patients with NLR ≤2.05, the average TTF was 7.075 months, while for those with NLR >2.05, it was 6.670 months. TTF showed no significant difference in patients with NLR >2.05 compared to patients with NLR ≤2.05 (P >0.05).The PFS of all studied patients was 11.485 months. The PFS was 14.733 months for patients with NLR ≤2.05 and 7.410 months for patients with NLR >2.05. In comparison to those with NLR ≤2.05, PFS was significantly shorter in patients with NLR > 2.05 (P <0.001) (Table 4).

The NLR, PLR, PNI, AG ratio, and CA19.9 were evaluated using ROC analysis to predict mortality. With an AUC of 0.906, a sensitivity of 81.2%, and a specificity of 84.4% at a threshold value of 2.05, NLR was very significant (P< 0.001). PLR had 75% sensitivity and 78.1% specificity at a

threshold value of 117.3 with AUC = 0.798 and was highly significant (P< 0.001). PNI had 73.7% sensitivity and 96.9% specificity at a threshold value of 34.5 with AUC = 0.646 and was significant (P= 0.019). A/G ratio at a threshold value of 1.1 had 54.2% sensitivity& 75% specificity, with an AUC of 0.619 and was non-significant (P = 0.057). CA19.9 at a threshold value of 9 had 93.7% sensitivity& 31.2% specificity, with an AUC of 0.564 and was non-significant (P = 0.369)(Table 5 andFigure 1).

Regarding response, patients with an NLR greater than 2.05 had a significantly increased PD rate at the initial three-month assessment (p=0.008). In addition, patients with an NLR greater than 2.05 had a significantly increased risk of death at one year (p<0.001).WBCs, platelets count, and Platelets lymphocyte ratio were significantly higher in cases with NLR >2.05 compared to cases with NLR ≤2.05. In contrast, patients with an NLR equal to or more than 2.05 had significantly lower levels of albumin, AG ratio, length of first-line chemotherapy, PFS, and TTF compared to cases with an NLR less than or equal to 2.05 (Table 6).

Table (1): Characteristics of the studied pancreatic cancer patients.

		Studied patients (N= 80)	
		N	%
Gender	**Male**	42	52.5%
	Female	38	47.5%
Age (years)	**Mean± SD**	58.0± 7.0	
	Median	60.0	
	Range	35.0 – 65.0	
Age groups	**30- 40 years**	3	3.75%
	41- 50 years	8	10.0%
	51- 60 years	34	42.5%
	> 60 years	35	43.75%
ECOG performance status (PS)	**I**	46	57.5%
	II	34	42.5%
Diabetes Mellitus	**No**	51	63.7%
	Yes	29	36.3%

SD= standard deviation,

Table(2):1st line chemotherapy, response among the studied pancreatic cancer patients

		Studiedpatients(N=80)	
		N	%
1st line Chemotherapy	Gemcitabinemonotherapy	34	42.5%
	mFOLFIRINOX	46	57.5%
Durationof1st line chemotherapy(months)	Mean± SD	4.28± 1.71	
	Median	4.0	
	Range	1.0 –12.0	
2nd line Chemotherapy	No	50	62.5%
	Yes	30	37.5%
Treatment response	Partialresponse(PR)	18	22.5%
	Stable disease(SD)	34	42.5%
	Progressiondisease (PD)	28	35.0%
Disease control rate(DCR)**	No(Progression)	28	35.0%
	Yes(No progression)	52	65.0%

		Studiedpatients (N=80)	
		N	%
Survival within one year	Alive	32	40.0%
	Died	48	60.0%

Overallsurvival (OS)						
	Meansurvival(months)			Mediansurvival (months)		
	Estimate	95%CI		Estimate	95%CI	
Overall survival (OS)	8.795	7.914	9.676	9.676	8.014	9.986

CI :confidence interval

**: Response to 1st line chemotherapy was evaluated at three months and Survival among the studied pancreatic cancer patients within one year, and the overall survival analysis among the studied pancreatic cancer patients.*

***Disease control rate (DCR) is defined by cases achieving stable disease(SD) or partial response(PR) to Chemotherapy combined (SD+PR) so If DCR is (YES) means no progression on 1st evaluation to 1st line Chemotherapy and vice versa*

Table (3): Correlation between overall survival and NLR among thestudied pancreaticcancerpatients

Overallsurvival (OS)						
	Meansurvival(months)			Mediansurvival (months)		
	Estimate	95%CI		Estimate	95%CI	
NLR≤2.05	11.347	10.339	12.356	11.000	10.652	11.348
NLR>2.05	6.707	5.683	7.731	5.800	4.175	7.425
Comparisonof survivalcurves(Log ranktest)						
Chi-squared	24.38					
DF	1					
Significance	P<0.001*					

NLR :neutrophil-lymphocyte ratio DF : degree of freedom

CI :confidence interval p value: Probability value

**: Highlystatisticallysignificant atp≤0.01*

Table(4): CorrelationbetweenTime to treatment failureand Progression free survival withNLRamongthestudied pancreaticcancerpatients

Time to treatment failure (TTF)						
	Meansurvival(months)			Mediansurvival (months)		
	Estimate	95%CI		Estimate	95%CI	
NLR≤2.05	7.075	5.930	8.221	6.600	5.488	7.712
NLR>2.05	6.670	5.246	8.093	6.000	2.109	9.891
Comparisonof survivalcurves(Log ranktest)						
Chi-squared	0.022					
DF	1					
Significance	P=0.883*					
Progressionfreesurvival (PFS)						
	Meansurvival(months)			Mediansurvival (months)		
	Estimate	95%CI		Estimate	95%CI	
NLR≤2.05	14.733	1.014	12.746	16.720	.	.
NLR>2.05	7.410	1.106	5.242	9.578	4.200	1.016
All cases	11.485	.906	9.709	13.261	.	.
Comparisonof survivalcurves(Log ranktest)						
Chi-squared	13.752					
DF	1					
Significance	P<0.001**					

NLR :neutrophil-lymphocyte ratio DF : degree of freedom
CI :confidence interval p value: Probability value
**:Statistically non significantatp>0.05 **: Highlystatisticallysignificant atp≤0.01*

Table(5): Validity(AUC,sensitivity,specificity)forNLR,PLR,PNI,AGratioandCA19.9inpredi ctionofmortality

	Bestcut off	Sensitivity	Specificity	PPV	NPV	AUC	P-value
NLR	2.05	81.2%	84.4%	93.8%	81.8%	0.906	**<0.001****
PLR	117.3	75%	78.1%	77.4%	75.8%	0.798	**<0.001****
PNI	34.5	73.7%	96.9%	96%	78.7%	0.646	**0.019***
AGratio	1.1	54.2%	75%	68.4%	62%	0.619	0.057
CA19.9	9	93.7%	31.2%	57.7%	83.2%	0.564	0.369

AUC:AreaUndera Curve p value: Probability valueNPV:Negative predictivevaluePPV:Positivepredictivevalue
NLR :neutrophil-lymphocyte ratio PNI: prognostic nutritional index
PLR: platelets to lymphocytes ratio AG ratio: Albumin to globulin ratio
:Statistically significantatp≤0.05: Highlystatisticallysignificant atp≤0.01*

Table(6): Comparison betweenNLR, clinicopathologicalfeatures and other parameters in advanced pancreatic cancer patients

		NLR					
		NLR ≤2.05(n.= 36)		NLR>2.05 (n.= 44)		Chi-SquareTest	
		N	%	N	%	Testvalue	P-value
Gender	**Male**	17	47.2%	25	56.8%	0.731	0.393
	Female	19	52.8%	19	43.2%		
ECOG performancestatus(PS)	**I**	25	69.4%	22	50.0%	3.09	0.079
	II	11	30.6%	22	50.0%		
DiabetesMellitus	**No**	23	63.9%	28	63.6%	0.001	0.981
	Yes	13	36.1%	16	36.4%		
Stageat diagnosis	**Locallyadvanced**	1	1.25%	0	0.0%	4.298	**0.038**
	Distant Mets	35	97.2%	44	100%		
Grade	**GradeI**	2	5.6%	5	11.4%	4.109	0.128
	GradeII	22	61.1%	17	38.6%		
	GradeIII	12	33.3%	22	50.0%		
Livermetastasis	**No**	6	16.7%	1	2.27%	6.599	**0.010**
	Yes	30	83.3%	43	97.7%		
arcinomatosisperitonei	**No**	35	97.2%	31	70.45 %	5.657	**0.017**
	Yes	1	2.8%	13	29.5%		
Lung metastasis	**No**	36	100.0%	39	88.6%	4.364	**0.037**
	Yes	0	0.0%	5	11.4%		
Treatmentresponse at first evaluation	**PR**	10	27.8%	8	18.2%	9.721	**0.008**
	SD	20	55.6%	14	31.8%		
	PD	6	16.7%	22	50.0%		
Disease control rate(DCR)* at first evaluation at 3 month	**No(Progression)**	8	22.2%	24	54.5%	8.620	**0.003**
	Yes(Noprogression)	28	77.8%	20	45.5%		
Deathat oneyear	**No**	27	75.0%	5	11.4%	33.409	**<0.001**
	Yes	9	25.0%	39	88.6%		

	NLR					
	NLR≤2.05		NLR>2.05		Testvalue	P-value
	Mean	±SD	Mean	SD		
Age (years)	61.53	±9.45	59.41	±10.51	T=0.938	0.351

		NLR					
		NLR ≤2.05(n.= 36)		NLR>2.05 (n.= 44)		Chi-SquareTest	
		N	%	N	%	Testvalue	P-value
BMI(Kg/m2)	24.20	±9.61	24.68	±8.91		Z_{MWU}=0.397	1.692
WBCs(109×L)	6.51	±2.10	8.70	±2.79		T=3.882	**<0.001**
Hemoglobin(g/dl)	12.20	±1.65	11.63	±1.35		Z_{MWU}=1.685	0.092
Platelets(109×L)	204.81	±67.31	277.55	±95.56		Z_{MWU}=3.734	**<0.001**
Plateletslymphocyte ratio (PLR)	97.23	±35.93	173.19	±64.79		Z_{MWU}=5.237	**<0.001**
Totalbilirubin(mg/dl)	0.66	±0.33	0.64	±0.31		Z_{MWU}=0.214	0.831
Albumin(g/dl)	3.91	±0.51	3.51	±0.71		Z_{MWU}=2.965	**0.003**
Globulin(g/dl)	3.16	±0.81	3.31	±0.80		Z_{MWU}=1.706	0.088
AGratio	1.31	±0.32	1.15	±0.51		Z_{MWU}=2.829	**0.005**
CA19.9	951.81	±1971.84	379.91	±454.18		Z_{MWU}=0.005	0.996
PNI	4.46	±0.56	4.45	±0.57		Z_{MWU}=0.440	0.660
Durationof1stchemotherapy	5.01	±1.80	3.69	±1.39		Z_{MWU}=3.443	**0.001**
PFS(month)	7.38	±3.07	4.47	±2.56		Z_{MWU}=4.841	**<0.001**
TTF(months)	6.27	±2.91	4.32	±2.77		Z_{MWU}=3.497	0.883

P value< 0.05 is significant, P value< 0.01 is highly significant, SD: Standard deviation, ^{Z}MWU=Mann-WhitneyUtest,T:Student,WBCs: whitebloodcells, BMI: body mass index, NLR:neutrophil-to-lymphocyteratio, AG ratio: Albumin to globulin ratio, PNI: prognosticnutritionalindex, PFS: progression free survival, TTF: time to treatment failure.

**Disease control rate (DCR) is defined by cases achieving stable disease or partial response to CHT combined (SD+PR) so If DCR is (YES) means no progression on 1st evaluation to 1st line CHT and vice versa*

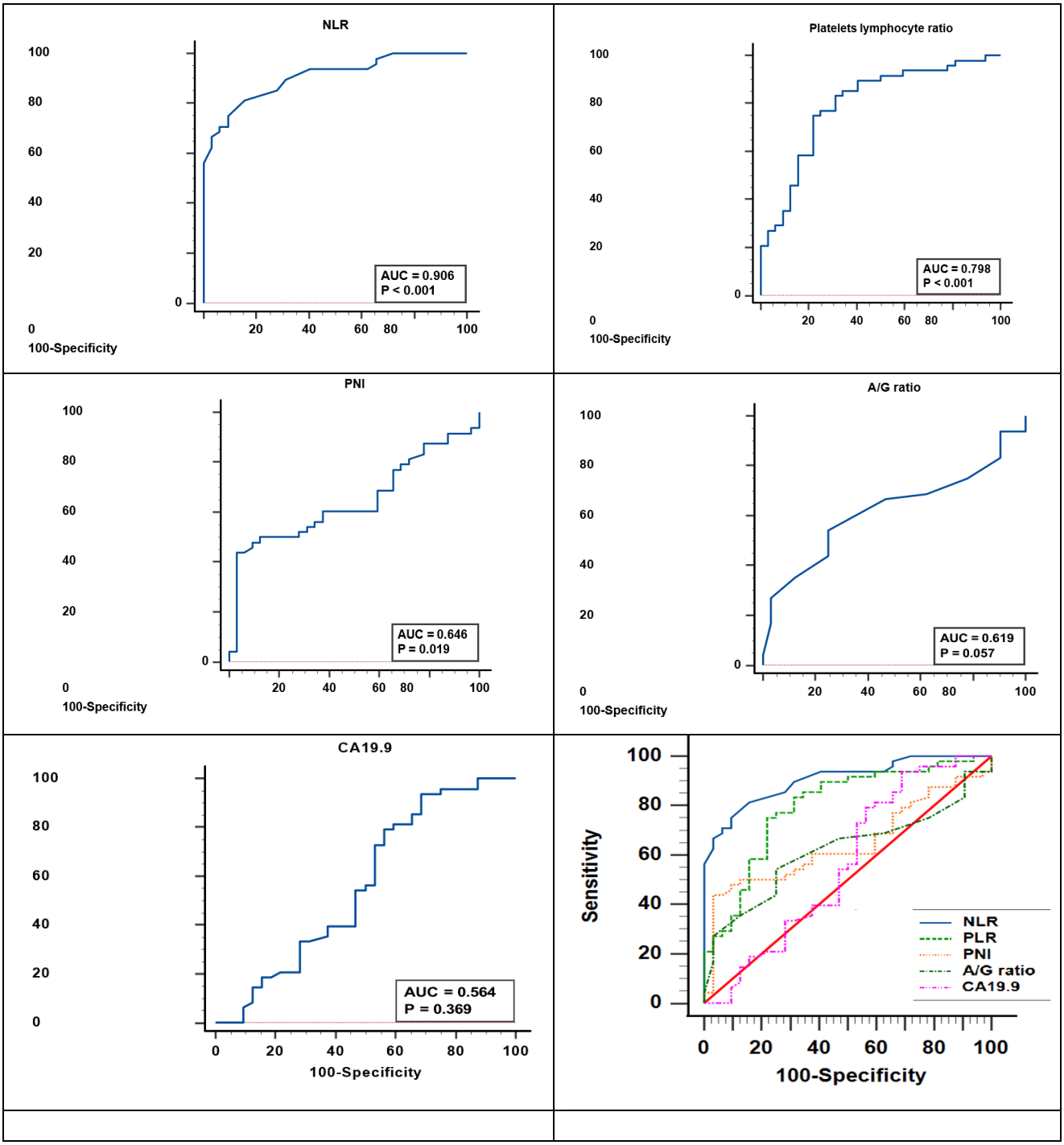

Figure (1) ROC curve showing (A): NLR in prediction of mortality, (B): PLR in prediction of mortality, (C): PNI in prediction of mortality, (D): A/G ratio in prediction of mortality, (E): CA19-9 in prediction of mortality, (F): NLR, PLR, PNI, AG ratio and CA19.9in prediction of mortality.

DISCUSSION

Our study found that the age of diagnosis ranged from 35 to 65 years, with a mean age of 58.0± 7.0 years. Patients more than 60 years were the most typical age group found (43.75%), followed by the age group between 51 and 60 (42.5%), then the age group between 41 and 50 (10%), and the age group between 30 and 40 (3.75%). More than half of the patients (52.5%) were males, while 47.5% were females, with the male-to-female ratio being 1.1:1.

In agreement with our results, Wuet al. [14] who aimed to determine whether patients with advanced pancreatic cancer had a better chance of survival based on their C-reactive

protein to albumin ratio. The participants' ages ranged from 26 to 85, with a median of 62. Finding patients older than 60 was the most common age group (52.4 percent). There were 156 male patients (66.0%) and 77 female patients (33.0%).

Our study found that regarding PS, more than half of patients (57.5%) were PS-I, while PS-II patients represented 42.5% of the patient population. Our results in keeping with, As stated by Toledano-Fonseca et al. [15], our objective was to assess the predictive power of integrating NLR and PLR with circulating liquid biopsy indicators linked to unfavorable survival outcomes in patients with metastatic pancreatic cancer. More than half of the patients (51.7%) were classified as PS-I, according to the PS report, whereas 13.8% were classified as PS-II.

In our study, we found that regarding comorbidities, 29 (36.3%) patients were known to be diabetic. Our results agreed withFormica et al. [16],who aimed to investigate the predictive value of NLR in metastatic pancreatic cancer patients. They reported that regarding comorbidities, 25 (24.7%) patients were known to be diabetic.

Our study found that regarding first-line chemotherapy regimens, more than half of patients (57.5%) received mFOLFIRINOX, while 42.5% received Gemcitabine monotherapy. The mean duration of 1st chemotherapy was 4.28± 1.71 months and ranged from one month to 12 months. Only 30 (37.5%) patients received 2nd linechemotherapy. Also,Toledano-Fonseca et al. [15]found that regarding chemotherapy regimens, 2 (3.4%) received Gemcitabine monotherapy, and 11 (19%) received mFOLFIRINOX in the first line. In contrast with our results, Dogan et al. [17]reported that regarding chemotherapy regimens, only (1.6%) received mFOLFIRINOX while 34.9% received Gemcitabine monotherapy as the first line. These discrepancies may be attributed to variations in patient populations.

In our study, we found that regarding the response to treatment to 1st line chemotherapy at first evaluation at three months, 34 out of 80 cases SD 18 cases achieved PR (22.5%), while 28 patients reported progression(35.0%). 52 out of 80 patients (65.0%) achieved a disease control rate (PR+SD).Our results agreed withVivaldi et al. [18],who reported that regarding the response to treatment, For the entire population, there was one full response (0.6%) and fifty-two partial responses (38%), resulting in an overall ORR of 38.6%. At the initial assessment, 32 patients (or 33.6% of the total) had progressed, whereas 46 patients (or 33.6%) had successfully stabilized their condition. The overall disease control rate (DCR) for the people was 72.2%.

In our study, we found that regarding survival outcome, there were 32 (40%) cases alive within one year, while death was reported in 48 (60%) cases. Our results followedToledano-Fonseca et al. [١٥],who found that regarding survival outcome, there were 17 (29.3%) cases alive, while death was reported in 41 (70.7%) cases.

Our study found that the OS was 11.347 months for patients with NLR ≤2.05 and 6.707 months for patients with NLR >2.05. OS was significantly lower in patients with NLR >2.05 compared to patients with NLR ≤2.05 (P <0.001).Our results were in agreement withDogan et al. [17],who reported that the subgroup with low NLR (3.0) had a median OS of 8.7 months (95 percent CI: 6.7-10.8) and the subgroup with high NLR (>3.0) had a median OS of 4.9 months (95 percent CI: 3.3-6.6). The statistical significance of this difference was found to be p = 0.003.

As wellour results wereconsistent withMartin et al. [19],who reported that OS was significantly lower in patients with NLR >5 compared to patients with NLR ≤ 5 (P <0.001).Also, our results were consistent withToledano-Fonseca et al. [15],who found that patients with higher NLR (>5.52) had significantly poorer OS (108 versus 335 days; $p < 0.0001$)

Our study found that TTF is the interval from chemotherapy initiation to premature discontinuation due to the progression of unaccepted toxicity. The mean TTF among the studied pancreatic cancer patients was 6.932 months. The mean TTF was 7.075 months for patients with NLR ≤2.05 and 6.670 months for patients with NLR >2.05. Time to treatment failure showed no significant difference within patients with

NLR >2.05 compared to patients with NLR ≤2.05 (P >0.05).

Our results followed Xue et al. [20],who focused on determining the predictive significance of NLR in patients undergoing palliative treatment for advanced pancreatic adenocarcinoma. Two groups were formed based on the patients' pretreatment NLR values (≤5 or >5).There were 212 patients in group A with pretreatment NLR values of 5 or below and 40 patients in group B with NLR values greater than 5. (group B). The researchers found that group B had a lower TTF (3.1 vs. 8.7 months, P < 0.01) than group A.

Our study found that PFS, which is defined as the time from initiation of treatment to the occurrence of disease progression or death for any cause in all studied patients, was 5.77 months. For patients with NLR ≤2.05, the PFS was 7.38 months, while for individuals with NLR >2.0, it was 4.47 months. Patients whose NLR was more significant than 2.05 had a substantially shorter PFS than patients whose NLR was less than or equal to 2.05 (P <0.001).

Our results agreed withDogan et al. [17], who reported that the median time to PFSwas 4.9 months (95% CI: 3.6-6.1). For the subgroup with low NLR (<3.0), the median PFS was determined to be 6.2 months (95 percent CI: 4.5-7.9), but for the cohort with high NLR (>3.0), it was 3.7 months (95 percent CI: 2.3-5.1) (p = 0.04).

Also, our results were in agreement with Toledano-Fonseca et al. [15], who found that patients with higher NLR (>5.52) had significantly poorer PFS (85 versus 232 days; *p* = 0.0101) rates.

In our study, we found that ROC and NLR had 81.2% sensitivity and 84.4% specificity at a threshold value of 2.05 with AUC = 0.906 and was highly significant (P< 0.001). PLR had 75% sensitivity and 78.1% specificity at a threshold value of 117.3 with AUC = 0.798 and was highly significant (P< 0.001). PNI had 73.7% sensitivity and 96.9% specificity at a threshold value of 34.5 with AUC = 0.646 and was significant (P= 0.019). A/G ratio at a threshold value of 1.1 had 54.2% sensitivity& 75% specificity, with an AUC of 0.619 and was non-significant (P = 0.057). CA19.9 at a threshold value of 9 had 93.7% sensitivity& 31.2% specificity, with an AUC of 0.564 and was non-significant (P = 0.369).

Our result was consistent with that of Han et al. [21], who aimed to assess pretreatment NLR's role in predicting the prognosis of patients with advanced pancreatic cancer. Statistical sensitivity and specificity were considered, as well as clinical importance; they concluded that a pretreatment value of 2.5 was the optimal cutoff value. In comparison to patients in the NLR < 2.5 group, individuals in the NLR > 2.5 group had a significantly shorter median OS, according to their data.

Additionally, our results agreed withJing et al. [22], whoassessed the relevance of inflammation-based prognostic indicators among pancreatic cancer patients, such as NLR, PLR, lymphocyte-monocyte ratio (LMR), albumin (ALB), and a combination of these markers. In 50 patients with pancreatic cancer that has spread to other parts of the body, the researchers found that the best inflammatory marker cut-off was 4.5 (AUC=0.840, 95 percent CI:0.732-0.948, P<0.001), PLR=138 (AUC=0.671, 95%*CI*:0.517-0.826, *P*=0.038), LMR=4.0(AUC=0.873,95% CI:0.770-0.975, P<0.001), respectively. However, the difference in optimal cutoff value may be attributed to differences in population and inclusion criteria.

Also, our results agreed withDogan et al. [17],who reported that The PLR and PNI areas under the ROC curves were 0.610 and 0.624, respectively, with a 95% confidence interval of 0.391-0.826 and 0.362-0.887, respectively. Regarding PLR, the ROC curve analysis suggested a cut-off value of 141, and for PNI, 51.2. Regarding PLR, the sensitivity rate was 60%, and the specificity rate was 66.7%, whereas when it came to PNI, the rates were 67.4% and 73.4%, respectively. High PLR (>141) was present in over half of the patients (57.5 percent).

Regarding response, progressive disease at first evaluation at three months was significantly higher in cases who had NLR >2.05 (p=0.008). In addition, death at one year was significantly higher in patientswho had NLR >2.05 (p<0.001).

Our study found that WBCs, platelets count, and PLR were significantly higher in cases who had NLR >2.05 compared to cases who had NLR ≤2.05. Whereasalbumin, AG ratio, Duration of 1st chemotherapy, and progression-free survival were significantly lower in patients with NLR >2.05 compared to cases who had NLR ≤2.05.Our results were consistent withXue et al. [20],who reported that platelet count and Platelets lymphocyte ratio were significantly higher in cases who had NLR >5 than those who had NLR ≤ 5.

The present study had some limitations, includingthe sample size, since we included 80 cases. It was a single-centerretrospective study. A large-scalemulticentric study would be valuable to support our findings.

CONCLUSIONS

Our findings suggest that NLR may serve as a valuable prognostic and predictive biomarker in the context of advanced pancreatic cancer, aiding in treatment decision-making and patient management

Conflict of Interest: Nothing to declare.

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