



Original Article

Systemic Inflammatory Biomarkers, Especially Fibrinogen to Albumin Ratio, Predict Prognosis in Patients with Pancreatic Cancer

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Purpose Systemic inflammatory response is a critical factor that promotes the initiation and metastasis of malignancies including pancreatic cancer (PC). This study was designed to determine and compare the prognostic value of neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio (MLR), and fibrinogen-to-albumin ratio (FAR) in resectable PC and locally advanced or metastatic PC.

Materials and Methods Three hundred fifty-three patients with resectable PC and 807 patients with locally advanced or metastatic PC were recruited in this study. These patients were classified into a training set (n=758) and a validation set (n=402). Kaplan-Meier survival plots and Cox proportional hazards regression models were used to analyze prognosis.

Results Overall survival (OS) was significantly better for patients with resectable PC with low preoperative PLR (p=0.048) and MLR (p=0.027). Low FAR, MLR, NLR (p < 0.001), and PLR (p=0.003) were significantly associated with decreased risk of death for locally advanced or metastatic PC patients. FAR (hazard ratio [HR], 1.522; 95% confidential interval [CI], 1.261 to 1.837; p < 0.001) and MLR (HR, 1.248; 95% CI, 1.017 to 1.532; p=0.034) were independent prognostic factors for locally advanced or metastatic PC.

Conclusion The prognostic roles of FAR, MLR, NLR, and PLR in resectable PC and locally advanced or metastatic PC were different. FAR showed the most prognostic power in locally advanced or metastatic PC. Low FAR was positively correlated with OS in locally advanced or metastatic PC, which could be used to predict the prognosis.

Key words Pancreatic neoplasms, Systemic inflammatory markers, Fibrinogen-to-albumin ratio, Prognosis, Survival

Introduction

Pancreatic cancer (PC) has the worst prognosis of all malignant tumors, and shows similar rates for mortality and morbidity [1]. Worldwide, it is the fourth leading cause of cancer-related mortality [2]. Typically, 77% PC patients will be diagnosed with locally advanced or metastatic disease [3]. Although the comprehensive treatment of PC has improved significantly in recent years, its prognosis is still poor, with the 5-year survival rate being < 5% [1]. Therefore, developing appropriate treatment strategies for each patient based on indicators that could predict the prognosis of PC patients remains of clinical significance.

It is established that systemic inflammatory response mediated by circulating inflammatory biomarkers including C-reactive protein [4], neutrophils [5], lymphocytes, platelets [6], monocytes [7], and fibrinogen [8] play an important role

in the oncogenesis and development of malignant tumors. Studies have been conducted to evaluate the correlation of popular inflammatory biomarker ratios such as neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and monocyte-to-lymphocyte ratio (MLR) on overall survival (OS) in PC patients [9,10]. However, very few studies had reported the differences in the prognostic value of NLR, PLR, and MLR in PC patients.

Recently, accumulating evidence has confirmed that the fibrinogen-to-albumin ratio (FAR) is the vital predictor in various malignancies such as esophageal squamous cell carcinoma and chronic lymphocytic leukemia [11,12]. However, association between FAR and the prognosis of PC patients has not been explored to date. Moreover, no literature has discussed the group of resectable PC patients and the group of locally or metastatic PC patients separately when studying association between inflammation and PC prognosis.

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We therefore conducted this retrospective analysis to compare the prognostic significance of NLR, PLR, and MLR, FAR in patients with resectable PC and those with locally advanced or metastatic PC, aiming to estimate the independent prognostic factors to predict the biological characteristics and guide individualized comprehensive treatments in PC patients.

Materials and Methods

1. Patients

We enrolled patients with PC who were admitted to the Harbin Medical University Cancer Hospital from 2008 to 2018 based on strict inclusion and exclusion criteria. The inclusion criteria were as follows: (1) patients voluntarily agreed to participate in the study and signed the informed consent; (2) patients were aged > 18 years; (3) patients had histologically or cytologically confirmed resectable PC or were diagnosed with locally advanced or metastatic PC by clinical data; (4) patients did not receive any other treatments before enrollment; and (5) patients with complete clinicopathologic information and reasonable follow-up time. Patients with infection, inflammation-related diseases, hematological diseases, liver diseases, or other malignant tumors, and incomplete clinicopathologic data were excluded. Finally, 205 patients with resectable PC and 434 with locally advanced or metastatic PC were excluded (S1 Fig.). All included patients (n=1,160) were assigned to either a training set (n=758) or a validation set (n=402). The training set (from 2008 to 2014) included 224 cases of resectable PC and 534 cases of locally advanced or metastatic PC; whereas the validation set (from 2015 to 2018) included 129 cases of resectable PC and 273 cases of locally advanced or metastatic PC.

2. Data collection

The detailed personal basic information and clinicopathologic data of the enrolled patients were obtained by consulting the medical records. The age of the patient was taken as the age at diagnosis. All patients with surgically treated resectable PC underwent TNM staging based on postoperative pathology. The TNM stage referenced was based on the American Joint Committee on Cancer (8th edition). The definition of resectable PC and locally advanced or metastatic PC refers to the criteria defining resectability status per the National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology (3rd edition 2019). Follow-up was conducted every three months after the patient's last hospitalization. The primary endpoint OS was defined as the initial diagnosis date to the last follow-up date; the latter was defined as the date of death or the last live follow-up during

this study (cut-off May 2019).

3. Blood sample collection and measurements

Routine hematology tests included counts of neutrophils, lymphocytes, monocytes, platelets, plasma fibrinogens and serum albumins. Two milliliters of ethylenediaminetetraacetic acid anticoagulated peripheral blood and 2 mL plasma anticoagulated by sodium citrate as well as serum samples were collected before breakfast within 7 days before diagnosis or treatment. The median value of duration between the date of diagnosis and start date of treatment of resectable PC patients was 3 days (range, 2 to 7 days; average, 3.6 days); this value was 2 days (range, 1 to 5 days, average, 2.11 days) in patients with locally advanced or metastatic PC. The samples were promptly centrifuged and processed within two hours. Peripheral blood cell counts were performed using the SYSMEX XN-9000 full-automated hematology analyzer (Sysmex, Tokyo, Japan). Plasma fibrinogen was detected using the Clauss method by the SYSMEX CS-5100 full-automatic coagulation analyzer (Sysmex) and the bromocresol green method by the BECKMAN COULTER Chemistry Analyzer AU5800 (Beckman Coulter Corporation, Tokyo, Japan) was selected to detect the level of albumin.

4. Statistical analysis

SPSS ver. 20.0 statistical software package (IBM Corp., Armonk, NY) and R project ver. 3.6.1 were utilized to establish a database to process clinical data. The "survival ROC" R packages was used to estimate time-dependent receiver operating characteristic (t-ROC) curves.

The maximum Youden index based on t-ROC analysis was used to calculate the optimal cut-off value, and areas under the t-ROC curves (AUCs) were used to evaluate the ability of each inflammatory biomarker to predict the prognosis. Survival curves were drawn according to the Kaplan-Meier method, survival comparison was performed by the log-rank test, and chi-square test was used for comparison between groups. To determine independent prognostic factors, Cox proportional hazards regression models were used for univariate and multivariate analyses. Furthermore, hazard ratio (HR) and 95% confidential interval (CI) were used to measure the power between them. All statistical tests were two-sided, and $p < 0.05$ was considered statistically significant.

Results

1. Patient characteristics

The detailed baseline characteristics of the resectable PC patients were shown in Table 1. The median follow-up time was 410 days, and 178 patients died during the follow-up

Table 1. Clinical and pathological characteristics of 224 resectable PC patients in training set

Characteristic	No. (%)
Sex	
Male	138 (61.6)
Female	86 (38.4)
Age (yr)	
≤ 65	113 (50.4)
> 65	111 (49.6)
Tumor location	
Head	165 (73.7)
Neck, body, and tail	59 (26.3)
Maximum tumor diameter (cm)	
≤ 2.9	123 (54.9)
> 2.9	101 (45.1)
Degree of differentiation	
Well-moderate	168 (75.0)
Poor	59 (25.0)
T category	
1	7 (3.1)
2	64 (28.6)
3	152 (67.9)
4	1 (0.4)
N category	
0	132 (58.9)
1	92 (41.1)
TNM	
I	31 (13.8)
II	191 (85.3)
III	2 (0.9)
CEA (ng/mL)	
≤ 4.42	87 (38.8)
> 4.42	137 (61.2)
CA 19-9 (U/mL)	
≤ 49.77	130 (58.0)
> 49.77	94 (42.0)
NLR	
≤ 3.09	14 (6.3)
> 3.09	210 (93.8)
PLR	
≤ 139.63	117 (52.2)
> 139.63	108 (47.8)
MLR	
≤ 0.45	165 (73.7)
> 0.45	59 (26.3)
FAR	
≤ 0.09	79 (35.3)
> 0.09	145 (64.7)

CA 19-9, serum carbohydrate antigen 19-9; CEA, carcinoembryonic antigen; FAR, fibrinogen-to-albumin ratio; MLR, monocyte-to-lymphocyte ratio; NLR, neutrophil-to-lymphocyte ratio; PC, pancreatic cancer; PLR, platelet-to-lymphocyte ratio.

Table 2. Clinical and pathological characteristics of 534 locally and metastatic PC patients in training set

Characteristic	No. (%)
Sex	
Male	317 (59.4)
Female	217 (40.6)
Age (yr)	
≤ 52	107 (20.0)
> 52	427 (80.0)
Tumor location	
Head	232 (43.4)
Neck, body, and tail	302 (56.6)
Distant metastasis	
Yes	416 (77.9)
Locally advanced	118 (22.1)
Aggressive treatments	
Yes	239 (44.8)
No	295 (55.2)
CEA (ng/mL)	
≤ 25.98	417 (78.1)
> 25.98	117 (21.9)
CA 19-9 (U/mL)	
≤ 582.9	280 (52.4)
> 582.9	254 (47.6)
NLR	
≤ 2.61	175 (32.8)
> 2.61	359 (67.2)
PLR	
≤ 170.73	372 (69.7)
> 170.73	162 (30.3)
MLR	
≤ 0.36	295 (55.2)
> 0.36	239 (44.8)
FAR	
≤ 0.079	238 (44.6)
> 0.079	296 (55.4)

CA 19-9, serum carbohydrate antigen 19-9; CEA, carcinoembryonic antigen; FAR, fibrinogen-to-albumin ratio; MLR, monocyte-to-lymphocyte ratio; NLR, neutrophil-to-lymphocyte ratio; PC, pancreatic cancer; PLR, platelet-to-lymphocyte ratio.

period. Among the 224 resectable PC patients enrolled in this study, 138 (61.6%) were male. In 165 patients (73.7%), the tumor was located in the head of the pancreas, and in the remaining 59 patients (26.3%), it was located in the neck, body, or tail of the pancreas. According to the TNM stage, the majority of patients (85.3%) were classified as stage II. The clinicopathological features of resectable PC patients in the validation set are shown in S2 Table.

As shown in Table 2, a total of 534 patients with locally advanced or metastatic PC were selected based on strict

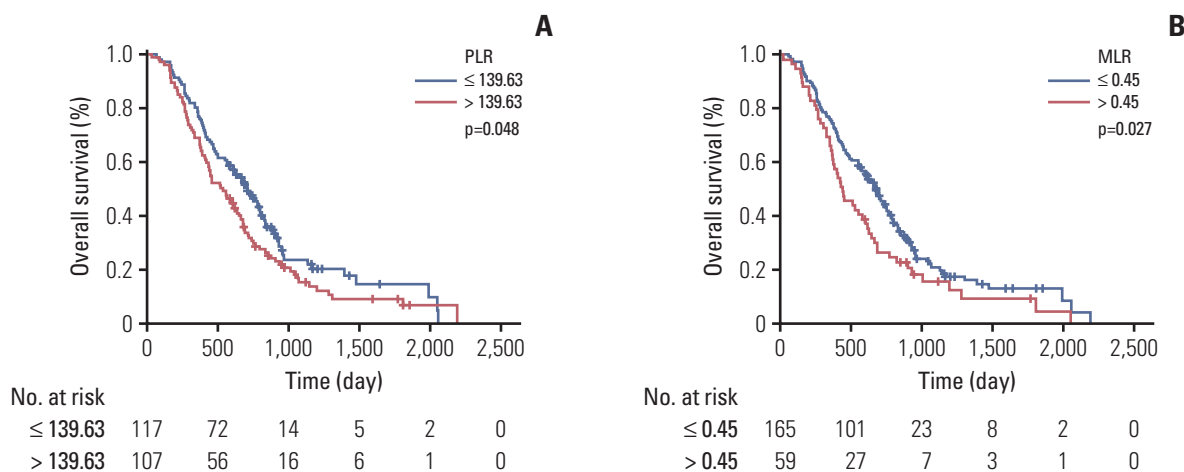


Fig. 1. Kaplan-Meier survival curves of resectable pancreatic cancer (PC) patients in training set based on platelet-to-lymphocyte ratio (PLR) and monocyte-to-lymphocyte ratio (MLR). (A) Data in training set compares PLR ≤ 139.63 vs. > 139.63 ($p < 0.05$). (B) Data in training set compares MLR ≤ 0.45 vs. > 0.45 ($p < 0.05$).

inclusion and exclusion criteria. The median follow-up time was 212 days, and 453 patients died during follow-up. Aggressive treatments in 239 patients (44.8%) included first-line chemotherapy, chemoradiotherapy, chemotherapy combined with targeted therapy and participate in clinical trials. The aggressive treatment modalities administered to patients are summarized in S3 Table. The detailed baseline characteristics of locally advanced or metastatic PC patients in the validation set are shown in S4 Table.

2. The optimal cut-off value of NLR, PLR, MLR, and PLR for survival analysis

The t-ROC curves were used to calculate the best cut-off values of NLR, PLR, MLR, and FAR. The optimum cut-off value of preoperative NLR, PLR, MLR, and FAR of resectable PC patients in the training set were 3.09, 139.63, 0.45, and 0.09, respectively. According to the optimum cut-off value, 224 patients with resectable PC were divided into low-value group and high-value group (Table 1). According to the ROC curve analysis of FAR, MLR, NLR, and PLR, 534 patients with locally advanced or metastatic PC were divided into two groups, in which the optimal cut-off value was 0.079, 0.36, 2.61, and 170.73, respectively (Table 2). The detailed data of ROC curve analysis are shown in S5 and S6 Tables.

3. PLR and MLR were associated with prognosis of resectable PC

Survival curves showed that patients in the low PLR (≤ 139.63) and low MLR (≤ 0.45) groups had longer OS than those in the high PLR (> 139.63) ($p=0.048$) and high MLR (> 0.45) ($p=0.027$) groups (Fig. 1A and B). However, there were no significant associations between NLR and FAR and

prognosis. To test the predictive value of PLR and MLR for OS, we further conducted survival analysis in the validation set. The low PLR ($p=0.007$) and low MLR ($p=0.002$) groups had better OS (S7A and S7B Fig.).

Multivariate analysis of the Cox regression model revealed that all inflammatory biomarkers in this study were not independent predictors of OS in resectable PC (S8 Table).

4. FAR, MLR, NLR, and PLR were associated with prognosis of locally advanced or metastatic PC patients

The Kaplan-Meier survival curves indicated that patients in low FAR ($p < 0.001$), low MLR ($p < 0.001$), low NLR ($p < 0.001$), and low PLR ($p=0.003$) groups had longer OS than those in the respective high-value groups (Fig. 2A-D). We verified this conclusion in the validation set as well. Low FAR ($p < 0.001$), MLR ($p=0.003$), NLR ($p=0.002$), and PLR ($p=0.025$) were associated with greater OS (S9A-S9D Fig.).

Next, we performed Kaplan-Meier analysis of patients stratified according to treatment modalities. As shown in S10A-S10F Fig., low FAR ($p=0.001$, $p < 0.001$), low MLR ($p < 0.001$, $p=0.015$), and low NLR ($p < 0.001$, $p=0.044$) significantly predicted better OS in patients who did or did not receive aggressive treatments, respectively; whereas, low PLR ($p < 0.001$) significantly predicted better OS in patients who received aggressive treatments (S10G Fig.). In the group that did not receive aggressive treatments, decreasing PLR was not associated with increased OS ($p > 0.05$) (S10H Fig.).

Univariate analysis revealed that carcinoembryonic antigen (CEA) (HR, 1.466; 95% CI, 1.185 to 1.813; $p < 0.001$), carbohydrate antigen 19-9 (CA 19-9; HR, 1.299; 95% CI, 1.085 to 1.557; $p=0.004$), NLR (HR, 1.453; 95% CI, 1.197 to 1.765; $p < 0.001$), PLR (HR, 1.338; 95% CI, 1.100 to

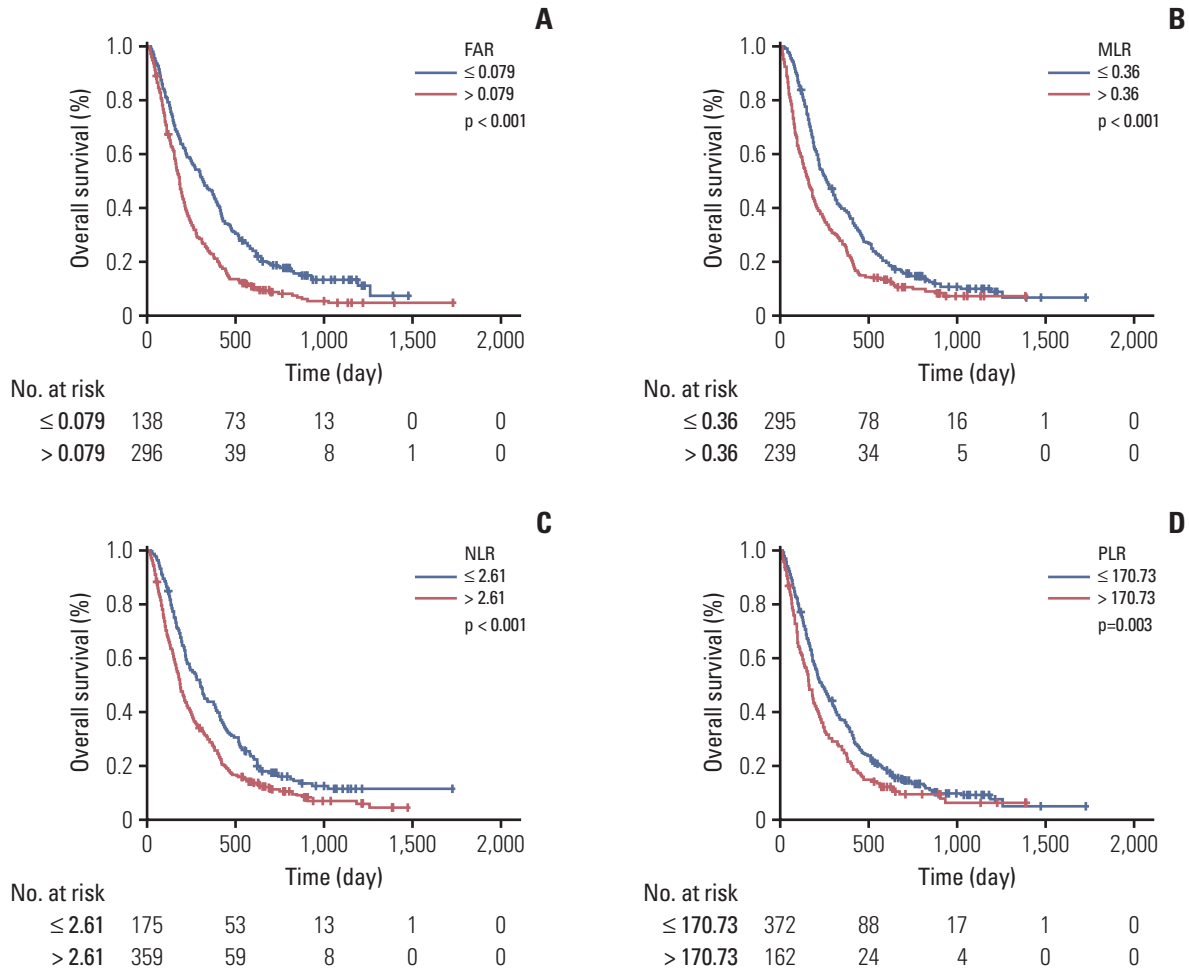


Fig. 2. Kaplan-Meier survival curves of locally advanced or metastatic pancreatic cancer (PC) patients in training set based on fibrinogen-to-albumin ratio (FAR), monocyte-to-lymphocyte ratio (MLR), neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR). (A) Data in training set compares FAR ≤ 0.079 vs. > 0.079 ($p < 0.001$). (B) Data in training set compares MLR ≤ 0.36 vs. > 0.36 ($p < 0.001$). (C) Data in training set compares NLR ≤ 2.61 vs. > 2.61 ($p < 0.001$). (D) Data in training set compares PLR ≤ 170.73 vs. > 170.73 ($p < 0.05$).

1.627; $p=0.004$), MLR (HR, 1.502; 95% CI, 1.253 to 1.800; $p < 0.001$), and FAR (HR, 1.634; 95% CI, 1.359 to 1.964; $p < 0.001$) were significantly prognostic factors for locally advanced or metastatic PC. In addition, multivariate analyses showed CEA (HR, 1.336; 95% CI, 1.067 to 1.673; $p=0.012$), MLR (HR, 1.248; 95% CI, 1.017 to 1.532; $p=0.034$), and FAR (HR, 1.522; 95% CI, 1.261 to 1.837; $p < 0.001$) were independent prognostic factors for locally advanced or metastatic PC (Table 3).

5. The predictive effect of FAR on prognosis was greater than that of MLR, NLR, and PLR

Although the multivariate analysis showed that both FAR and MLR were independent prognostic factors for locally advanced or metastatic PC, the AUC of FAR (0.641) was

greater than that of MLR (0.569), NLR (0.558), and PLR (0.548) (Fig. 3B-E). Therefore, the prognostic role of FAR was greater than that of MLR, NLR, and PLR. In addition, we confirmed that the predictive effect of FAR on prognosis was more powerful than that of the fibrinogen and albumin levels (S11 Fig.). Correlation analysis showed that FAR was associated with NLR, PLR, and MLR ($p < 0.001$) (S12 Table).

However, when we stratified patients based on FAR levels and performed subgroup analysis of prognosis, FAR level was not associated with response to therapy (S13 Fig.).

Table 3. Univariate and multivariate analyzes of locally advanced or metastatic PC patients in training set

Characteristic	Univariate analysis		Multivariate analysis		
	HR (95% CI)	p-value	HR (95% CI)	Wald	p-value
Sex (male vs. female)	1.025 (0.853-1.231)	0.792	-	-	-
Age (≤ 52 yr vs. > 52 yr)	1.080 (0.803-1.353)	0.501	-	-	-
Tumor location (head vs. neck, body, and tail)	1.007 (0.839-1.207)	0.943	-	-	-
Distant metastasis (yes vs. locally advanced)	0.964 (0.918-1.013)	0.147	-	-	-
Aggressive treatment (yes vs. no)	0.889 (0.742-1.065)	0.210	-	-	-
CEA (≤ 25.98 ng/mL vs. > 25.98 ng/mL)	1.466 (1.185-1.813)	< 0.001	1.336 (1.067-1.673)	6.364	0.012
CA 19-9 (≤ 582.9 U/mL vs. > 582.9 U/mL)	1.299 (1.085-1.557)	0.004	1.160 (0.959-1.404)	2.338	0.126
NLR (≤ 2.61 vs. > 2.61)	1.453 (1.197-1.765)	< 0.001	1.137 (0.909-1.424)	1.262	0.261
PLR (≤ 170.73 vs. > 170.73)	1.338 (1.100-1.627)	0.004	1.121 (0.903-1.391)	1.065	0.302
MLR (≤ 0.36 vs. > 0.36)	1.502 (1.253-1.800)	< 0.001	1.248 (1.017-1.532)	4.505	0.034
FAR (≤ 0.079 vs. > 0.079)	1.634 (1.359-1.964)	< 0.001	1.522 (1.261-1.837)	19.171	< 0.001

CA 19-9, serum carbohydrate antigen 19-9; CEA, carcinoembryonic antigen; CI, confidence interval; FAR, fibrinogen-to-albumin ratio; HR, hazard ratio; MLR, monocyte-to-lymphocyte ratio; NLR, neutrophil-to-lymphocyte ratio; PC, pancreatic cancer; PLR, platelet-to-lymphocyte ratio.

Discussion

In this study, we provided confirmation that the prognostic value of the same inflammatory marker was different in patients with resectable PC and those with locally advanced or metastatic PC. For instance, low FAR and low NLR were positively associated with locally advanced or metastatic PC but had no significant associations with resectable PC. Thus far, many studies have confirmed that systemic inflammatory markers such as NLR, PLR, and MLR were associated with the prognosis of PC patients. Liu et al. [13] confirmed that low derived NLR was positively correlated with the prognosis of PC patients. Stotz et al. [14] reported that decreased MLR was a significant factor for better cancer-specific survival in PC patients. However, when discussing the relationship between inflammatory markers and prognosis in PC patients, the aforementioned parameters have hardly addressed separately in patients with resectable PC and those with locally advanced or metastatic PC. Nevertheless, our study suggested that the biological behaviors of resectable PC and locally advanced or metastatic PC may be very diverse. When discussing the prognostic factors, different stages of the disease should be discussed discretely.

Recently, studies have shown that tumor-associated inflammation, which is the seventh feature of cancer, is involved in every step of tumorigenesis and cancer progression [15,16]. Inflammatory biomarkers can reflect the severity of systemic inflammation [17]. Mei et al. [9] demonstrated that elevated NLR and MLR were associated with significantly shorter median survival in patients with resectable PC. Qi et

al. [18] concluded that high NLR, PLR, and MLR were significantly associated with decreased OS in locally advanced or metastatic PC. However, these studies did not compare the prognostic role of inflammatory biomarkers involved in the study. By performing this study, we demonstrated that the effect on prognostic prediction of FAR was more powerful than MLR, followed by NLR and PLR for locally advanced or metastatic PC patients. To our knowledge, this is the first study to assess the differences in the prognostic role of NLR, PLR, MLR, and FAR between PC patients.

Evidence has shown that systemic inflammation could promote the release of fibrinogen, which can be synthesized by hepatocytes and hepatic malignant cells [19,20]. Many studies have suggested that fibrinogen could promote the proliferation and metastasis of tumor cells by the following mechanisms: involving in the formation of extracellular matrix and inducing epithelial-mesenchymal transition and interleukin (IL)-6 synthesis [21-23]. Albumin not only reflects the nutritional status of cancer patients but also shows association with systemic inflammation [24]. For instance, tumor necrosis factor- α and IL-6 inhibit the synthesis of albumin, causing hypoalbuminemia [25]. Present studies have indicated that hyperfibrinogenemia was significantly correlated with shorter OS in patients with advanced PC and hypoalbuminemia is negatively correlated with prognosis in patients with hepatocellular carcinoma and diffuse large B-cell lymphoma [26-28]. Based on the above studies, researchers were keen to explore whether FAR was also associated with prognosis. A study by Li et al. [29] which showed the cut-off value of FAR as 0.09 proved that low FAR was significantly

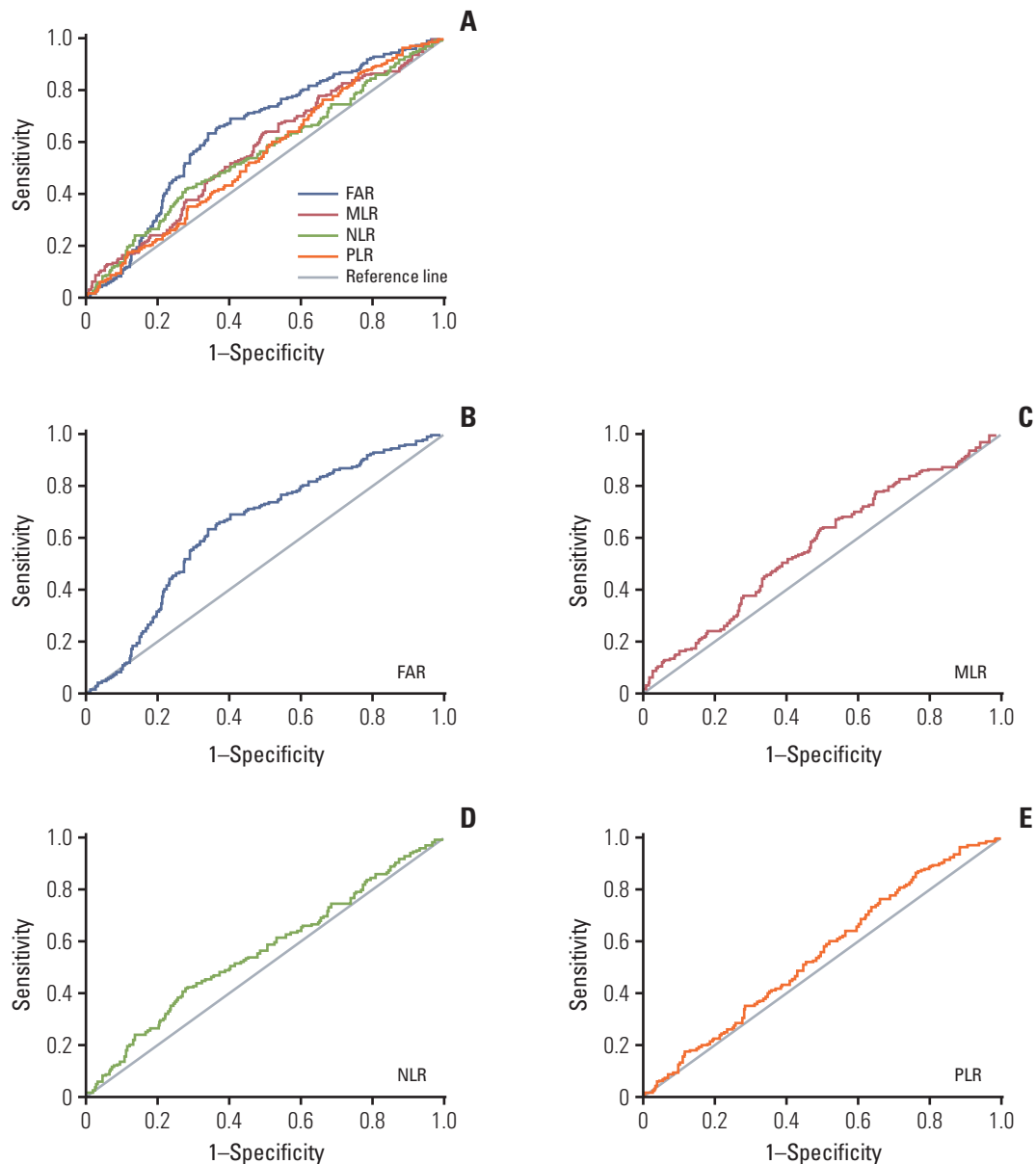


Fig. 3. Receiver operating characteristic (ROC) analysis based on fibrinogen-to-albumin ratio (FAR) (B), monocyte-to-lymphocyte ratio (MLR) (C), neutrophil-to-lymphocyte ratio (NLR) (D), platelet-to-lymphocyte ratio (PLR) (E) of locally advanced or metastatic pancreatic cancer patients in training set. (A) The area under the ROC curve (AUC) indicates the diagnostic power of FAR was the most powerful. (B) The AUC indicates the diagnostic power of FAR. In this model, the best cut-off point for FAR was 0.079, AUC was 0.641 (95% confidence interval [CI], 0.594 to 0.689), the sensitivity of the Yoden index was 0.635, and the specificity was 0.656. (C) The AUC indicates the diagnostic power of MLR. In this model, the optimal cut-off point for MLR was 0.36, AUC was 0.569 (95% CI, 0.519 to 0.619), the sensitivity of the Yoden index was 0.635, and the specificity was 0.504. (D) The AUC indicates the diagnostic power of NLR. In this model, the optimal cut-off point for NLR was 2.61, AUC was 0.558 (95% CI, 0.507 to 0.609), the sensitivity of the Yoden index was 0.416, and the specificity was 0.721. (E) The AUC indicates the diagnostic power of PLR. In this model, the best cut-off point for PLR was 170.73, AUC was 0.548 (95% CI, 0.498 to 0.598), the sensitivity of the Yoden index was 0.761, and the specificity was 0.341.

correlated with favorable OS in patients with non-small cell lung cancer. Liang et al. [30] confirmed that patients with operable soft tissue sarcoma with a decreased FAR had

a longer median survival time and a lower 5-year OS rate than those with high FAR, and the cut-off value of FAR in this study was 0.0726. To our best knowledge, the reported

FAR cut-off value of 0.079 has been used for the first time to investigate its prognostic power in patients with PC. We also showed that low FAR was positively correlated with OS in patients with locally advanced or metastatic PC. The existing research studies indicate that the best cut-off value varies in different malignancies even with respect to different stages of the disease. Although the specific reason and potential mechanism of these differences remain unclear, they remind us that different tumors and diseases at different stages have their own unique biological behaviors. Therefore, more studies are needed to further verify these conclusions.

Our study has some limitations. First is the study design including retrospective data collection. Second, the relatively small sample size may have lead to a reporting bias. Moreover, single-center data analysis cannot represent the overall population. However, despite these limitations, we have confirmed that FAR can be used to predict locally advanced or metastatic PC. A multi-center, large-sample, prospective study is needed to further validate these conclusions.

In conclusion, when discussing the relationship between prognostic factors and PC, different stages of the disease should be discussed separately. FAR might be a potential indicator to predict poor prognosis in locally advanced or metastatic PC patients, and the predictive power of FAR is greater than that of MLR, NLR, and PLR.

Electronic Supplementary Material

Supplementary materials are available at Cancer Research and Treatment website (<https://www.e-crt.org>).

Ethical Statement

The study was approved by the Ethics Committee of Harbin Medical University Cancer Hospital (2018-118-IIT). All patient signed the informed consent before recruitment.

Author Contributions

Conceived and designed the analysis: Fang L, Zhang YQ, Li ZW, Zhang CH, Lou CJ.

Collected the data: Fang L, Yan FH, Liu C, Chen J, Wang D, Lian J, Yao Y, Wang BJ, Li RY, Han SL, Bai YB, Yang JN.

Performed the analysis: Fang L, Yan FH, Liu C, Chen J, Wang D, Lian J, Yao Y, Wang BJ, Li RY, Han SL, Bai YB, Yang JN.

Wrote the paper: Fang L, Zhang YQ, Li ZW, Zhang CH, Lou CJ.

Conflicts of Interest

Conflicts of interest relevant to this article was not reported.

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