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C-Reactive Protein-based Prognostic Measures Are Superior at Predicting Survival Compared with Peripheral Blood Cell Count-based Ones in Patients After Curative Resection for Pancreatic Cancer

YUKI FUJIWARA, KOICHIRO HARUKI, HIROAKI SHIBA, RYOGA HAMURA, TAKASHI HORIUCHI, YOSHIHIRO SHIRAI, KENEI FURUKAWA, TAKESHI GOCHO and KATSUHIKO YANAGA

Department of Surgery, The Jikei University School of Medicine, Tokyo, Japan

Abstract. *Aim: Prognostic factors of recurrence and survival in various cancer types have been reported and include C-reactive protein (CRP)-based measures as evidenced by the Glasgow prognostic score (GPS), as well as peripheral blood cell-based prognostic values such as the prognostic index (PI), neutrophil–to–lymphocyte ratio (NLR), and platelet–to–lymphocyte ratio (PLR). The aim of this study was to identify significant prognostic values and compare them for suitability for use in patients after curative pancreatic resection for pancreatic cancer. Materials and Methods: Between 2000 and 2015, 188 patients were enrolled in this retrospective study. The relationship between clinicopathological variables including various prognostic values and disease-free (DFS) and overall (OS) survival was investigated by univariate analysis. The area under the receiver operating characteristics curve (AUC) was evaluated to compare the predictive ability of each of these scoring systems. Multivariate analysis was then performed to identify clinicopathological variables that associated DFS and OS. Results: In univariate analysis, GPS, modified GPS, CRP to albumin ratio and PI were significant risk factors for both DFS and OS. The AUC of CRP-based scores (GPS, modified GPS, and CRP to albumin ratio) were consistently larger in comparison with PI, which consists of both CRP and peripheral blood cell scores, at all time points for both DFS and OS. In multivariate analysis, GPS was the only independent risk factor of tumor recurrence and survival. Conclusion: CRP-based prognostic scores have an independent value for both tumor recurrence and prognosis in patients after curative resection for pancreatic cancer, and are superior to other peripheral blood cell count-based prognostic scores.*

Correspondence to: Yuki Fujiwara, MD, The Jikei University School of Medicine, 3-25-8, Nishi-Shinbashi, Minato-ku, Tokyo 105-8461, Japan. Tel: +81 334331111 ext. 2345, Fax: +81 334331230, e-mail: sheetan@jikei.ac.jp

Key Words: Pancreatic cancer, C-reactive protein, CRP-based prognostic values, Glasgow prognostic score.

Pancreatic carcinoma is one of the most fatal human malignant digestive cancers and the fourth leading cause of cancer-related death worldwide (1). Although elective surgical pancreatic resection is the curative treatment for pancreatic cancer, only 10-15% of patients with pancreatic cancer are able to undergo pancreatic resection (2). However, the overall survival rate of patients who undergo such curative surgical resection remains poor in spite of improvements in surgical techniques, instruments, and postoperative management (3, 4). Prognostic factors for long-term survival in patients undergoing resection of pancreatic cancer include small tumor size, absence of lymph node involvement, curative (R0) resection and the absence of adjuvant chemotherapy (5-7).

Recently, the prognostic outcomes of patients with cancer have been reported to be associated not only with tumor-related factors but also with host-related factors. Systemic inflammation-based values have been determined in patients with different resectable malignancies as independent factors of tumor recurrence and tumor-related prognosis. These values can generally be divided into three groups: I: The Glasgow prognostic score (GPS) (8-10), modified GPS (mGPS), and C-reactive protein (CRP) to albumin ratio (CRP/Alb ratio) (11, 12) are based on CRP; II: The neutrophil to lymphocyte ratio (NLR) (13) and platelet to lymphocyte ratio (PLR) (14) are based on counts of peripheral blood cell components; III: The prognostic index (PI) derived by combination of serum albumin and peripheral lymphocyte count (15), and the prognostic nutritional index score (PNI) derived by combination of serum CRP and white blood cell (WBC) count (16) are based on peripheral blood cell components.

The aim of this retrospective study was to determine the most clinically useful prognostic score by comparing these inflammation-based prognostic scores in patients after curative pancreatic resection for pancreatic cancer.

Materials and Methods

Patients. Between 2000 and 2015, 195 patients with primary pancreatic cancer underwent curative pancreatic resection with lymphadenectomy at the Department of Surgery, The Jikei University Hospital, Tokyo, Japan. Out of these, seven patients were subsequently excluded due to loss to follow-up in the early postoperative period, leaving the remaining 188 patients for this retrospective study.

Recurrence of tumor was defined as newly detected local or distant metastatic tumors by imaging modalities consisting of ultrasonography, computed tomography, or magnetic resonance imaging with or without increase in serum carcinoembryonic antigen (CEA) or serum carbohydrate antigen 19-9 (CA19-9).

Blood samples were obtained before elective pancreatic resection and hemograms, including absolute WBC, neutrophil, lymphocyte, monocyte and platelet counts, as well as serum albumin and CRP were routinely measured for each patient.

Definition of prognostic values. In order to compare the prognostic variables, definitions of GPS, mGPS, NLR, PLR, CRP/Alb ratio, PI and PNI are listed in Table I.

Relationship between prognostic values and clinicopathological variables. The relationship between clinicopathological findings and disease-free (DFS) and overall (OS) survival was investigated in patients with primary pancreatic cancer after curative pancreatic resection by univariate analysis. The following 28 variables were evaluated: Age, gender, type of operation, reconstruction of portal vein, duration of operation, intraoperative blood loss, body mass index (BMI), postoperative pancreatic fistula, postoperative complication based on Clavien-Dindo classification (17), intraoperative red blood cell concentrate or fresh frozen plasma transfusion, postoperative hospital stay, diabetes mellitus, serum CEA, serum CA19-9, neutrophil count, lymphocyte count, monocyte count, tumor differentiation, type of tumor, TNM classification based on the Union for International Cancer Control (UICC) 8th edition (18), resected margin, GPS, mGPS, NLR, PLR, CRP/Alb ratio, PNI and PI.

Receiver operating characteristics (ROC) curves were constructed for DFS and OS to compare those which were significant factors in univariate analysis. Four timepoints were used: 6, 12, 18 and 24 months for DFS status; and 12, 24, 36 and 60 for OS status. The areas under the ROC curve (AUC) of these scores were statistically compared at all these time points for both DFS and OS to determine which value was superior in both CRP-based and peripheral blood cell-based prognostic values.

Next, we compared the most useful prognostic value with clinical variables, and determined the independent prognostic factors in both DFS and OS by multivariate analysis. The evaluated factors consisted of the following: reconstruction of the portal vein, preoperative serum CA19-9, tumor differentiation, type of tumor, TNM classification, resected margin and GPS for DFS; reconstruction of the portal vein, preoperative serum CEA, preoperative serum CA19-9, tumor differentiation, type of tumor, resected margin and GPS for OS.

Table I. *Prognostic scores based on serum or blood cellular components*.

Index		Score
GPS	CRP (≤1.0 mg/dl) + Alb (≥3.5 g/dl)	0
	CRP (≤1.0 mg/dl) + Alb (<3.5 g/dl)	1
	CRP (>1.0 mg/dl) + Alb (≥3.5 g/dl)	1
	CRP (>1.0 mg/dl) + Alb (<3.5 g/dl)	2
mGPS	CRP (≤1.0 mg/dl) + Alb (≥3.5 g/dl)	0
	CRP (≤1.0 mg/dl) + Alb (<3.5 g/dl)	0
	CRP (>1.0 mg/dl) + Alb (≥3.5 g/dl)	1
	CRP (>1.0 mg/dl) + Alb (<3.5 g/dl)	2
NLR	Neutrophil:lymphocyte count <5:1	0
	Neutrophil:lymphocyte count ≥5:1	1
PLR	Platelet/lymphocyte count <150	0
	Platelet count /lymphocyte count 150-<300	1
	Platelet count/lymphocyte count ≥300	2
CRP/Alb ratio	CRP/Alb ≤0.004	0
	CRP/Alb >0.004	1
PI	CRP (≤1.0 mg/dl) + WBC count (≤7.0×10^3/μl)	0
	CRP (>1.0 mg/dl) + WBC count (≤7.0×10^3/μl)	1
	CRP (≤1.0 mg/dl) + WBC count (>7.0×10^3/μl)	1
	CRP (>1.0 mg/dl) + WBC count (>7.0×10^3/μl)	2
PNI	[Alb (g/dl)×10] + [5×lymphocyte count (/10^3)] ≥45	0
	[Alb (g/dl)×10] + [5×lymphocyte count (/10^3)] <45	1

Alb: Serum albumin; CRP: serum C-reactive protein; GPS: Glasgow prognostic score; mGPS: modified Glasgow prognostic score; NLR: neutrophil lymphocyte ratio score; PI: Prognostic index; PLR: platelet to lymphocyte ratio score; PNI: prognostic nutritional index; WBC: white blood cell.

Pancreatic fistula was defined by the guideline of the International Study Group on Pancreatic Fistula (ISGPF) (19). Pancreatic fistula was classified into three categories by ISGPF as follows: Transient pancreatic fistula (no clinical impact) (grade A); fistula requiring a change in management or adjustment in the clinical pathway (grade B); and fistula requiring a major change in clinical management or deviation from the normal clinical pathway (grade C). In the current study, grade B and C were defined as postoperative pancreatic fistula (POPF). Postoperative complications were defined by Clavien-Dindo classification and divided into two groups: grade II or less; and grade IIIa or more. Use of blood products and dose were determined by the preference of attending surgeons based on guidelines for administration of blood products by the Japanese Ministry of Health and Welfare (20), as well as intraoperative blood loss, postoperative hemoglobin, serum albumin, and prothrombin time.

This retrospective study was approved by the Ethics Committee of the Jikei University School of Medicine (no. 21-121).

Statistical analysis. Data are expressed as a mean±standard deviation (SD), or frequency. Univariate analysis of patient characteristics was performed using Mann–Whitney's *U*-test or chi-square test. Both univariate and multivariate analysis of DFS and OS were performed using Cox proportional regression models with backward elimination stepwise approach. The software package SPSS (version 20; IBM SPSS statistics®, Tokyo, Japan) was used for statistical analyses. All *p*-values were considered statistically significant when the probability of association was less than 0.05.

Table II. *Patient characteristics*.

Characteristic		Value
Age, years	Mean±SD (range)	67.0±9.87 (27-84)
Gender, n	Male: female	115:73
Disease-free survival, years	Median (95% CI)	1.07 (0.90-1.38)
Overall survival, years	Median (95% CI)	2.14 (1.92-2.90)
Duration of operation, min	Mean±SD (range)	497.6±144.6 (140-992)
Intraoperative blood loss, ml	Mean±SD (range)	1,183.2±1,457.6 (0-12,320)
Postoperative hospital stay, days	Mean±SD (range)	30.6±42.6 (8-419)
Preoperative serum CEA, ng/ml	Mean±SD (range)	7.86±22.6 (4-286)
Preoperative serum CA19-9, U/ml	Mean±SD (range)	277.2±601.9 (1-5,750)
Preoperative neutrophil count, $\times 10^3/\mu l$	Mean±SD (range)	3.65±2.0 (0.9-18.3)
Preoperative lymphocyte count, $\times 10^3/\mu l$	Mean±SD (range)	1.51±0.53 (0.6-4.0)
Preoperative serum Alb, g/dl	Mean±SD (range)	3.84±0.49 (2.7-4.9)
Preoperative serum CRP, mg/dl	Mean±SD (range)	0.789±1.8 (0.04-14.7)
TNM classification, n*	0: I: II: III: IV	4:53:96:31:4

Alb: Albumin; CA19-9, carbohydrate antigen 19-9; CEA, carcinoembryonic antigen; CI: confidence interval; CRP, C-reactive protein. *Based on 8th edition Union for International Cancer Control (18).

Results

Patient characteristics. Table II shows the patient characteristics. The mean age was 67.0 years (range=27-84 years). The operative procedures consisted of pancreaticoduodenectomy in 125, distal pancreatectomy in 57, central pancreatectomy in two and total pancreatectomy in four patients. The median of DFS and OS were 1.14 and 2.41 years, respectively. The 1-, 3-and 5-year DFS and OS rates were 56.1%, 27.0% and 18.3%, and 80.2%, 43.5% and 29.0%, respectively.

Univariate analysis of clinicopathological variables in relation to survival in patients after curative resection for pancreatic cancer. Table III lists the univariate analysis of the relationship between clinicopathological variables and DFS as well as OS after curative pancreatic resection. In univariate analysis of DFS, reconstruction of portal vein (p=0.002); preoperative serum CA19-9 ≥200 U/ml (p<0.001); not well-differentiated tumor (p<0.001); infiltrative tumor type (p=0.002); advanced TNM stage (p<0.001); positive resected margin (p=0.011); GPS score 1 or 2 (Figure 1A; p=0.008 and p<0.001, respectively); mGPS score 1 or 2 (Figure 1B; both p<0.001); CRP/Alb ratio score 1 (Figure 1C; p=0.003); and PI score 2 (Figure 1D; p=0.006) were significant factors for cancer recurrence. For OS, reconstruction of portal vein (p=0.017); preoperative serum CEA ≥10 ng/ml (p=0.044); preoperative serum CA19-9≥200 U/ml (p=0.003); not well-differentiated tumor (p=0.001); infiltrative tumor type (p=0.025); advanced TNM stage (p=0.002); positive resected margin (p=0.027); GPS score 1 or 2 (Figure 1E; p=0.002 and p<0.001 respectively); mGPS score 1 or 2 (Figure 1F; p<0.001); CRP/Alb ratio score 1 (Figure 1G; p<0.001); PI score 1 or 2 (Figure 1H; p=0.002 and p<0.006, respectively) were significantly associated with poor outcome.

Comparison of AUC for prognostic value. Figure 2 shows the ROC curves for DFS at 6,12, 18 and 24 months and for OS at 12, 24, 36 and 60 months using scores for GPS, mGPS, CRP/Alb ratio score and PI score, which were significantly associated with both DFS and OS in the univariate analysis. The comparison of AUC to assess the discriminatory ability of each scoring system is shown in Table IV. The AUC for scores for CRP-based measures GPS, mGPS and CRP/Alb ratio were consistently larger in comparison with the peripheral blood cell count-based PI score at all time points for both DFS and OS. This showed that CRP-based prognostic measures such as GPS score, mGPS score and CRP/Alb ratio were superior to other prognostic scores for PI, PNI, NLR and PLR at predicting tumor recurrence as well as prognosis in patients with pancreatic cancer.

Multivariate analysis of clinicopathological variables in relation to survival in patients after curative resection for pancreatic cancer. Table V lists multivariate analysis of the relationship of the clinicopathological variables with GPS score and DFS as well as OS after curative pancreatic resection. In multivariate analysis of DFS, preoperative serum CA19-9 ≥200 U/ml (p=0.016), not well-differentiated tumor (p=0.001), advanced TNM stage (p=0.027), GPS score 1 (p=0.015) and GPS score 2 (p=0.001) were independent risk factors of cancer recurrence. In OS, preoperative serum CEA ≥10 ng/ml of (p=0.008), not well-differentiated tumor (p=0.006), advanced

Table III. *Univariate analysis of disease-free and overall survival in patients with pancreatic cancer after pancreatic resection.*

		N	Disease-free survival		Overall survival	
Factor	Subgroup		Hazard ratio (95% CI)	*p*-Value	Hazard ratio (95% CI)	*p*-Value
Age	<70 Years	102	Ref		Ref	
	≥70 Years	86	0.744 (0.535-1.036)	0.080	0.831 (0.581-1.188)	0.309
Gender	Male	115	Ref		Ref	
	Female	73	0.909 (0.650-1.272)	0.909	0.846 (0.588-1.217)	0.367
Type of operation	PD	125	Ref		Ref	
	Other	63	0.767 (0.539-1.090)	0.139	0.735 (0.503-1.073)	0.111
Portal vein reconstruction	No	155	Ref		Ref	
	Yes	33	1.899 (1.274-2.830)	0.002	1.698 (1.098-2624)	0.017
Duration of operation	<500 min	94	Ref		Ref	
	≥500 min	94	1.064 (0.767-1.475)	0.710	1.036 (0.729-1.472)	0.844
Intraoperative blood loss	<800 ml	96	Ref		Ref	
	≥800 ml	92	1.013 (0.731-1.403)	0.938	1.220 (0.859-1.735)	0.267
BMI	<25 kg/m^2	158	Ref		Ref	
	≥25 kg/m^2	30	0.720 (0.453-1.144)	0.165	0.740 (0.454-1.208)	0.229
POPF (grade B or C)	No	159	Ref		Ref	
	Yes	29	1.001 (0.635-1.576)	0.998	1.188 (0.743-1.900)	0.471
Postoperative complications*	≤Grade II	146	Ref		Ref	
	≥Grade IIIa	42	1.298 (0.879-1.915)	0.190	1.210 (0.789-1.856)	0.383
Intraoperative RCC or FFP transfusion	No	133	Ref		Ref	
	Yes	55	1.153 (0.809-1.644)	0.430	1.375 (0.946-1.999)	0.095
Postoperative hospital stay	<30 Days	131	Ref		Ref	
	≥30 Days	57	1.233 (0.867-1.754)	0.243	1.149 (0.787-1.678)	0.473
Diabete mellitus	No	119	Ref		Ref	
	Yes	69	0.915 (0.650-1.287)	0.609	0.901 (0.622-1.304)	0.581
Preoperative serum CEA	<10 ng/ml	163	Ref		Ref	
	≥10 ng/ml	25	1.440 (0.888-2.335)	0.139	1.654 (1.013-2.699)	0.044
Preoperative serum CA19-9	<200 U/ml	131	Ref		Ref	
	≥200 U/ml	57	1.993 (1.408-2.823)	<0.001	1.762 (1.217-2.551)	0.003
Preoperative neutrophil count	<3.0×10^3/μl	80	Ref		Ref	
	≥3.0×10^3/μl	108	0.790 (0.569-1.097)	0.159	0.809 (0.568-1.151)	0.239
Preoperative lymphocyte count	<2.0×10^3/μl	29	Ref		Ref	
	≥2.0×10^3/μl	159	1.430 (0.891-2.294)	0.139	1.470 (0.890-2.427)	0.132
Preoperative monocyte count	<300/μl	80	Ref		Ref	
	≥300/μl	108	0.953 (0.686-1.323)	0.772	0.854 (0.601-1.213)	0.378
Tumor differentiation	Well-differentiated	73	Ref		Ref	
	Other	115	2.110 (1.481-3.005)	<0.001	1.870 (1.284-2.724)	0.001
Type of tumor	Other	64	Ref		Ref	
	Infiltrative type	124	1.751 (1.221-2.511)	0.002	1.550 (1.058-2.272)	0.025
TNM Stage**	0, I or II	153	Ref		Ref	
	III or IV	35	1.885 (1.345-2.641)	<0.001	1.976 (1.290-3.027)	0.002
Resected margin	R0	133	Ref		Ref	
	R1 or R2	55	1.574 (1.110-2.232)	0.011	1.535 (1.051-2.243)	0.027
GPS	0	123	Ref		Ref	
	1	38	1.717 (1.151-2.562)	0.008	1.976 (1.282-3.047)	0.002
	2	27	3.071 (1.925-4.900)	<0.001	4.082 (2.564-6.498)	<0.001
mGPS	0	140	Ref		Ref	
	1	21	2.498 (1.541-4.049)	<0.001	2.463 (1.436-4.224)	0.001
	2	27	3.043 (1.918-4.826)	<0.001	3.880 (2.460-6.121)	<0.001
NLR	0	171	Ref		Ref	
	1	17	0.799 (0.431-1.479)	0.475	0.993 (0.534-1.845)	0.982
PLR	0	90	Ref		Ref	
	1	87	1.136 (0.521-2.475)	0.749	0.815 (0.371-1.791)	0.611
	2	11	1.510 (0.693-3.289)	0.299	1.184 (0.541-2.587)	0.673
CRP/Alb ratio score	0	100	Ref		Ref	
	1	88	1.655 (1.193-2.294)	0.003	1.928 (1.355-2.744)	<0.001

Table III. *Continued*

Table III. *Continued*

Factor	Subgroup	N	Disease-free survival		Overall survival	
			Hazard ratio (95% CI)	*p*-Value	Hazard ratio (95% CI)	*p*-Value
PNI	0	63	Ref		Ref	
	1	125	1.165 (0.818-1.658)	0.397	0.983 (0.675-1.429)	0.927
PI	0	132	Ref		Ref	
	1	39	1.441 (0.953-2.180)	0.083	1.981 (1.293-3.033)	0.002
	2	17	2.190 (1.248-3.841)	0.006	2.798 (1.581-4.953)	<0.001

Alb: Serum albumin; BMI: body mass index; CA19-9: carbohydrate antigen 19-9; CEA: carcinoembryonic antigen; CRP: serum C-reactive protein; FFP: fresh frozen plasma; GPS: Glasgow prognostic score; mGPS: modified Glasgow prognostic score; NLR: neutrophil lymphocyte ratio score; PI: Prognostic index; PLR: platelet to lymphocyte ratio score; PNI: prognostic nutritional index; PD: pancreaticoduodenectomy; POPF: postoperative pancreatic fistula; RCC: red blood cell concentrate. *Clavien-Dindo classification (17). **Based on 8th edition Union for International Cancer Control (18).

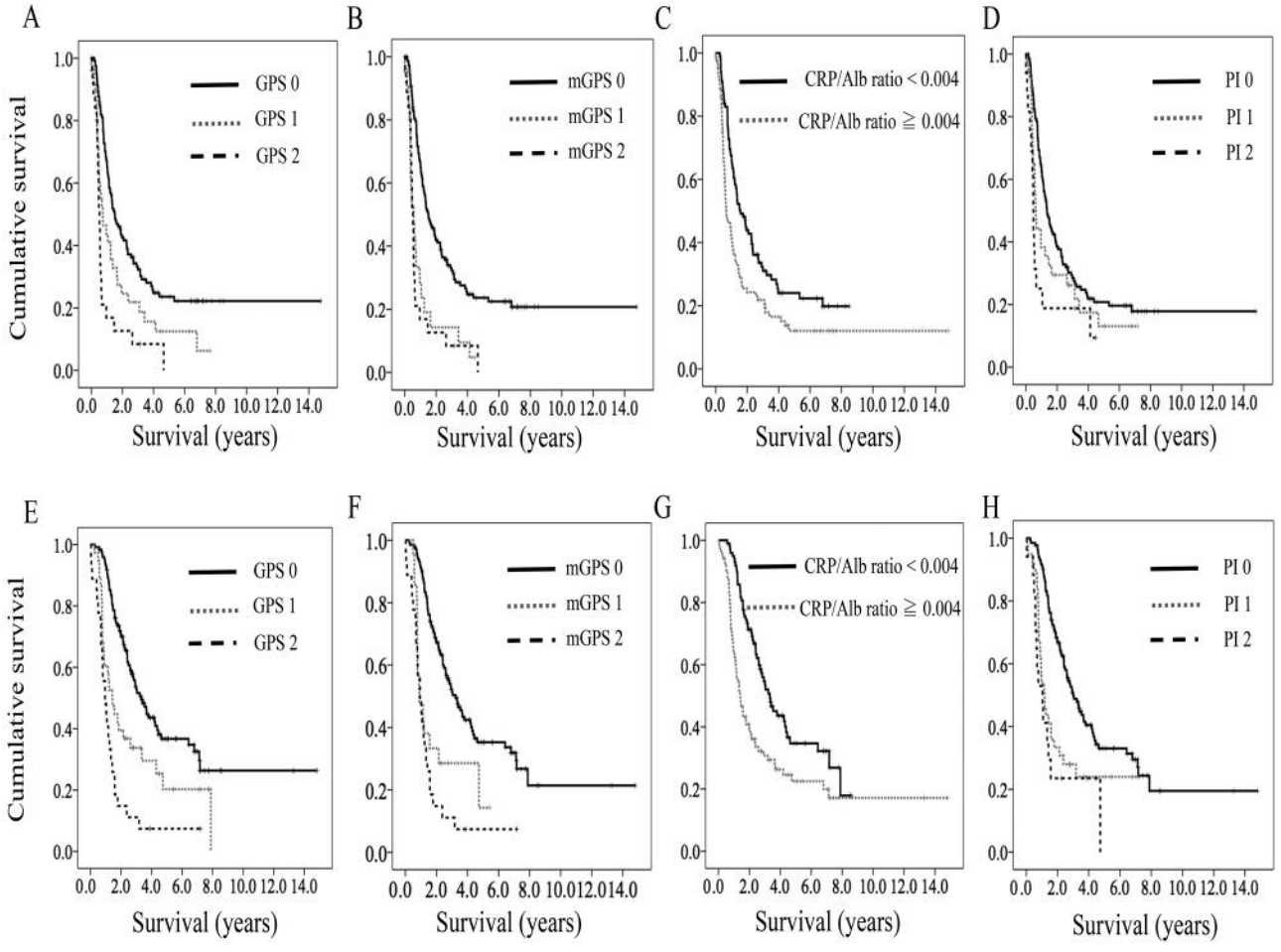

Figure 1. *Disease-free (A-D) and overall survival (E-H) in patients with pancreatic cancer according to prognostic measures: Glasgow prognostic score (GPS) (A, E), modified GPS (B, F), serum C-reactive protein (CRP)/serum albumin (Alb) ratio (C, G) and prognostic index (PI) (D, H).*

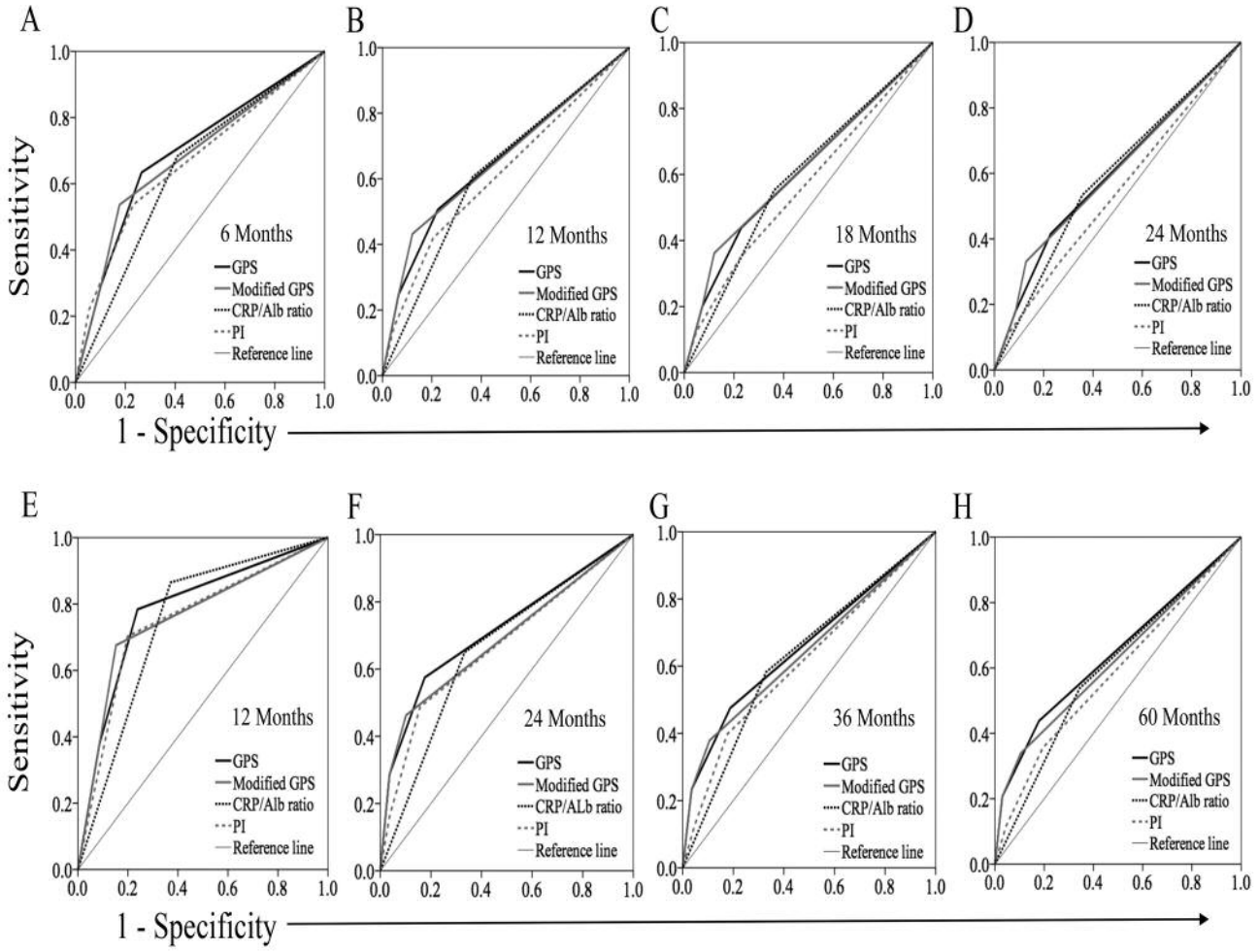

Figure 2. *Receiver operating characteristics curve according to prognostic measures for disease-free outcome prediction at 6 (A), 12 (B), 18 (C) and 24 (D) months and for overall mortality at 12 (E), 24 (F), 36 (G) and 60 (H) months.*

TNM stage (p=0.024), and GPS (p=0.002) or 2 (p<0.001) were independent risk factors of poor prognosis.

Discussion

The antitumor host immune response has an important role in progression and prognosis of a tumor. The intimate interaction of inflammation and tumor biology has been well-recognized (21-23). Cancer-related inflammation promotes proliferation of tumor cells, tumor angiogenesis, and invasion and metastasis of cancer cells because of activation by interleukin-1, interleukin-6 as well as tumor necrosis factor α, and an increase in the number of regulatory T-lymphocytes (24, 25). In fact, some types of pro-inflammatory cytokines such as interleukin-1 and interleukin-6 are increased in patients with pancreatic cancer (26).

GPS was first reported as an independent prognostic factor for patients with inoperable lung cancer in 2003 (27). Some studies reported that GPS predicted tumor-related prognosis not only in patients with various advanced and unresectable gastrointestinal cancer with poor performance status and severe body weight loss (28-30), but also in those with various types of resectable digestive cancer (8-10). The peripheral blood cell component-based values as represented by NLR and PLR have already been reported as prognostic factors of tumor-related outcome (13, 14, 31). A high neutrophil count in peripheral blood contributes to tumor angiogenesis due to their acting as important compartments for circulating vascular endothelial growth factor (32). Platelets are often activated by tumor cells and release several types of cytokines that promote angiogenesis (33). Moreover, immune response against tumors depends on the number of

Table IV. *Comparison of area under the curve (AUC) for survival of patients after pancreatic resection using serum C-reactive protein-based prognostic scores.*

	Disease free survival				Overall survival		
Time point	AUC	95% CI	*p*-Value	Time point	AUC	95% CI	*p*-Value
6 Months							
GPS	0.691	0.595-0.787	<0.001	12 Months	0.784	0.697-0.871	<0.001
mGPS	0.678	0.579-0.778	<0.001		0.761	0.666-0.856	<0.001
CRP/Alb ratio	0.637	0.543-0.732	0.007		0.747	0.665-0.829	<0.001
PI	0.663	0.563-0.764	0.001		0.753	0.659-0.846	<0.001
12 Months							
GPS	0.652	0.571-0.733	<0.001	24 Months	0.714	0.637-0.791	<0.001
mGPS	0.656	0.575-0.737	<0.001		0.686	0.606-0.766	<0.001
CRP/Alb ratio	0.620	0.539-0.701	0.005		0.658	0.579-0.738	<0.001
PI	0.612	0.530-0.695	0.008		0.669	0.588-0.749	<0.001
18 Months							
GPS	0.612	0.532-0.692	0.009	36 Months	0.657	0.580-0.735	<0.001
mGPS	0.620	0.540-0.699	0.005		0.642	0.564-0.720	0.001
CRP/Alb ratio	0.595	0.514-0.677	0.025		0.627	0.546-0.707	0.003
PI	0.567	0.486-0.649	0.113		0.613	0.532-0.693	0.008
24 Months							
GPS	0.595	0.514-0.678	0.028	60 Months	0.641	0.563-0.720	0.001
mGPS	0.598	0.516-0.680	0.024		0.623	0.543-0.702	0.005
CRP/Alb ratio	0.588	0.505-0.672	0.043		0.597	0.513-0.681	0.028
PI	0.537	0.453-0.622	0.392		0.584	0.501-0.667	0.057

Alb: Serum albumin; CI: confidence interval; CRP: serum C-reactive protein; GPS: Glasgow prognostic score; mGPS: modified Glasgow prognostic score; PI: prognostic index.

lymphocytes in peripheral blood (21). In our previous study, PLR (≥150) was an independent risk factor for both DFS and OS in patients with resectable pancreatic cancer (14). However, in the current study, PLR was not found to be a significant factor of DFS nor OS in univariate analysis. This is because the PLR score was divided into three groups using cut-off values of 150 and 300 to compare with the original PLR scoring system (34). The difference of sample sizes and follow-up duration compared with our previous study may be also one reason to explain this discrepancy.

Analysis and comparison of prognostic variables among the same patient group is very important in order to identify clinically useful scores predicting tumor recurrence and outcome in patients with cancer. In addition, it is also important to analyze prognostic factors in patients with cancer while distinguishing between operable and inoperable cases. A single study showed a comparison of these inflammation-based prognostic values in patients with pancreatic cancer, in which NLR (>5) was superior to the mGPS, PI, PLR and PNI for prognostication (31). Therefore, to the best of our knowledge, the current study is the first report to identify and compare several inflammation-based prognostic values in patients with pancreatic cancer after pancreatic resection.

Conclusion

CRP-based prognostic scores have an independent value for both tumor recurrence and prognosis in patients after curative pancreatic resection for pancreatic cancer, and are superior to other peripheral blood cell count-based prognostic scores.

Conflicts of Interests

All Authors declare no conflict of interests in regard to this study.

Ethics approval

This study was approved by the Ethics Committee of the Jikei University School of Medicine (21-121).

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Table V. *Multivariate analysis of disease-free and overall survival in patients with pancreatic cancer after pancreatic resection.*

	N	Disease-free survival		Overall survival	
Factor		Hazard ratio (95% CI)	*p*-Value	Hazard ratio (95% CI)	*p*-Value
Portal vein reconstruction					
No	155	Ref		Ref	
Yes	33	1.260 (0.817-1.945)	0.296	1.137 (0.703-1.839)	0.600
Preoperative serum CEA					
<10 ng/ml	163	-		Ref	
≥10 ng/ml	25	-	-	2.001 (1.196-3.349)	0.008
Preoperative serum CA19-9					
<200 U/ml	131	Ref		Ref	
≥200 U/ml	57	1.570 (1.089-2.261)	0.016	1.419 (0.961-2.095)	0.078
Tumor differentiation					
WelI-differentiated	73	Ref		Ref	
Other	115	1.816 (1.259-2.619)	0.001	1.736 (1.170-2.576)	0.006
Type of tumor					
Other	64	Ref		Ref	
Infiltrative type	124	1.279 (0.873-1.874)	0.207	1.223 (0.812-1.842)	0.318
TNM stage*					
0, I or II	153	Ref		Ref	
III or IV	35	1.594 (1.053-2.411)	0.027	1.684 (1.070-2.650)	0.024
Resected margin					
R0	133	Ref		Ref	
R1 or R2	55	1.290 (0.895-1.857)	0.172	1.224 (0.823-1.820)	0.318
GPS					
0	123	Ref		Ref	
1	38	1.667 (1.104-2.516)	0.015	2.053 (1.310-3.217)	0.002
2	27	2.396 (1.463-3.926)	0.001	3.642 (2.216-5.987)	<0.001

CA19-9: Carbohydrate antigen 19-9; CEA: carcinoembryonic antigen; CI: confidence intervaI; GPS: Glasgow prognostic score. *Based on 8th edition Union for International Cancer Control (18).

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