



The Systemic Inflammation-Based Prognostic Score Predicts Postoperative Complications in Patients Undergoing Pancreaticoduodenectomy

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Guangzhen Qu 

Dong Wang

Weiyu Xu 

Kai Wu 

Wei Guo 

Department of General Surgery, Beijing Friendship Hospital, Capital Medical University, Beijing, 100050, People's Republic of China

Background: Although many studies have confirmed the correlation between inflammation-based or nutritional markers and postoperative complications in patients undergoing colorectal cancer surgery, their correlation after undergoing pancreaticoduodenectomy (PD) remains unclear.

Methods: We retrospectively reviewed the clinical data of patients who underwent PD in Beijing Friendship hospital between 2018 and 2020. Univariate analysis, multivariate analysis, and receiver operating characteristic curve (ROC) were performed. We assessed the preoperative modified Glasgow Prognostic Score (mGPS), C-reactive protein/albumin ratio (CAR), C-reactive protein (CRP), postoperative Glasgow Prognostic Score (poGPS), CRP on postoperative day 3 (POD3) and CAR on POD3. The optimal cut-off values were determined by performing logistic regression analysis.

Results: Of the 172 patients who underwent PD, 74 (43.0%) developed complications, of whom 27 (15.7%) had clinically relevant postoperative pancreatic fistulas (CR-POPF) and 36 (20.9%) had positive drainage fluid cultures. Elevated levels of preoperative mGPS ($P<0.001$), poGPS ($P<0.001$), CRP ($P<0.001$) and CAR on POD3 were associated with postoperative complications. CRP on POD3 (OR=1.028, 95% CI=1.017–1.039, $P<0.001$) was an independent risk factor associated with postoperative complications in both univariate and multivariate analyses. CAR on POD 3 showed the largest area under the curve (AUC=0.883, $P<0.001$). Compared with $CAR<4.86$, $CAR \geq 4.86$ on POD3 was associated with a higher probability of complications (85.5% vs 14.6%, $P<0.001$), especially CR-POPF (33.3% vs 4.9%, $P<0.001$), intra-abdominal infection (36.2% vs 10.7%, $P<0.001$) with a positive drainage fluid culture.

Conclusion: CAR, an inflammatory response-based marker, can effectively predict early postoperative complications in patients undergone PD.

Keywords: C-reactive protein, albumin, Glasgow Prognostic Score, pancreaticoduodenectomy, complications prediction

Introduction

Pancreatic cancer is a highly lethal malignancy that ranks fourth for cancer-related deaths in the United States and second for digestive system cancer-related deaths.¹ Surgical resection is the only potentially curative treatment for pancreatic tumors. Pancreaticoduodenectomy (PD), which was performed and refined by Whipple in 1935 based on the experience of his predecessors, was used to resect pancreatic neoplasms.² Large clinical centres use improved surgical techniques and critical care to treat patients with postoperative complications, which decreased the mortality rates

Correspondence: Wei Guo
Email guowei@cmmu.edu.cn

after PD to around 2–3%.³ Despite this reduction in mortality, postoperative complication rates of PD persist at 30–40%,^{4,5} even in some large centres. Common complications include bleeding, delayed gastric emptying, and fistula formation from any of the three enteric anastomoses: gastrojejunostomy, hepaticojejunostomy, and pancreaticojejunostomy.^{6–9} Postoperative pancreatic fistula (POPF), the most common complication, may prolong the stay and cause life-threatening secondary complications such as delayed abdominal bleeding.¹⁰ Timely management of these complications may reduce patient suffering and psychological burden. Inflammatory response-based prognostic scoring systems have gained increasing attention for predicting postoperative complications, and those systems include C-reactive protein/albumin ratio (CAR), modified Glasgow prognostic score (mGPS) and postoperative Glasgow prognostic score (poGPS). In a meta-analysis of 1832 patients undergoing colorectal surgery,¹¹ it concluded that C-reactive protein (CRP) on postoperative day (POD) 4 had an improved negative predictive value for infectious complications. A study¹² suggested that the decline in albumin level in the early postoperative period reflects the magnitude of surgical trauma and was associated with adverse postoperative outcomes. Another study reported¹³ that CAR on POD3 was an independent predictor of clinically relevant POPF. CRP and albumin alone may only reflect the extent of the inflammatory response and the nutritional condition. Based on this, we assess the postoperative inflammatory response and nutritional status of the patient in combination with CRP and albumin. We evaluated the significance of CAR, mGPS and poGPS for predicting early postoperative complications in patients who underwent PD.

Methods

Patient Cohort and Data Collection

Data from 172 patients who underwent PD between June 2018 and October 2020 at Beijing Friendship hospital were obtained and retrospectively reviewed. All the surgeries were performed by three experienced hepatobiliary pancreatic surgeons. The following preoperative clinical data of the patients were recorded: age, gender, body mass index (BMI), proportion of patients with hypertension and diabetes mellitus, the American Society of Anaesthesiologists (ASA) status, preoperative serum CRP (mg/L) and serum albumin (g/L), preoperative CAR and patients with preoperative mGPS \geq 1. The upper CRP limit was 8 mg/L and the lower albumin limit was 35 g/L. Intraoperative data included

operative methods, operative time (mins), blood loss (mL), intraoperative blood transfusion (mL). Postoperative outcomes, such as CRP (mg/L), albumin (g/L), CAR on POD3, poGPS score \geq 1, hospitalization days, reoperation, mortality and tumour types, were assessed. Among the malignancies, in addition to pancreatic cancer, periampullary carcinoma malignancy was commonly observed, with 36 cases of ampullary carcinoma, 14 cases of duodenal carcinoma and 45 cases of distal bile duct carcinoma (Table 1). The preoperative and postoperative inflammatory response indexes were based on mGPS and poGPS (Table 2). POPF was defined according to the latest International Study Group of Pancreatic Surgery (ISGPS).¹⁴ Clinical relevant POPF referred to grade B/C fistula. The postoperative complications were classified according to the Clavien-Dindo classification system.¹⁵ Intra-abdominal infection with the positive bacterial culture of drainage fluid is defined as an infection of pathogenic bacteria cultured in peritoneal drainage fluid. Hospitalization days refer to the time from operation to discharge. Reoperation is defined as surgery performed because of life-threatening postoperative complications. Postoperative mortality included death before discharge and within 30 days after surgery. All the information of patients was confidential, all patients signed informed consent, and this retrospective study was conducted in accordance with the Declaration of Helsinki.

Surgical Technique and Perioperative Management

The surgical techniques included open pancreaticoduodenectomy (OPD), laparoscopic pancreatoduodenectomy (LPD) and laparoscopic conversion to open surgery. After the patient was given general anaesthesia, the upper abdominal incision was taken, the pancreatic head was dissected at a distance of 1–2 cm from tumour. A stent tube with a diameter matching with the pancreatic duct was inserted into the pancreatic duct to around 8–9 cm distance. The pancreatic stump was then closed together with the jejunum, and 5–0 Vicryl thread was used to make pancreaticojejunal mucosa anastomosis, the other end of the pancreatic fluid drainage tube was put into the distal jejunum, and then six needles were sutured. After suturing, the posterior wall was intermittently suture using 3–0 prolene, and the suture was tightened and knotted. Another 3–0 prolene thread was used to make continuous suture through the anterior wall of the pancreas with the plasma muscle layer of the jejunum, and the knot was pulled and tied. Biliary and gastrointestinal

Table I Univariate Analysis of Risk Factors Associated with Postoperative Complications

Variables	All (n=172)	Postoperative Complications		P
		Yes (n=74)	No (n=98)	
Age (years)	60.1±9.5	62.2±7.1	58.5±10.8	0.007
Gender (n,%)				0.002
Male	105 (61%)	55 (74%)	50 (51%)	
Female	67 (39%)	19 (25.7%)	48 (49.0%)	
BMI, kg/m ²	23.87±3.00	4.16±2.77	3.65±3.15	0.271
Hypertension (n,%)	67 (39%)	29 (39.19%)	38 (38.78%)	0.956
Diabetes (n,%)	44 (25.6%)	22 (29.73%)	22 (22.45%)	0.279
ASA (n,%)				0.483
I	2 (1.2%)	0	2 (2.04%)	
II	100 (58.1%)	41 (55.41%)	59 (60.20%)	
III	69 (40.1%)	33 (44.59%)	36 (36.73%)	
IV	1 (0.6%)	0	1 (1.02%)	
Pre CRP, mg/L	13.39±5.81	19.02±33.98	8.75±15.07	0.033
Pre albumin, g/L	36.54± 4.29	35.59±4.40	37.26±4.08	0.011
Pre CAR	0.38±0.74	0.55±0.94	0.21±0.4	0.008
Pre mGPS≥I, n (%)	68 (39.53%)	40 (54.05%)	28 (28.57%)	<0.001
Surgical approach, n (%)				0.385
OPD	94 (54.7%)	36 (48.65%)	58 (59.18%)	
LPD	59 (34.3%)	29 (39.19%)	30 (30.61%)	
LPD convert to OPD	19 (11%)	9 (12.16%)	10 (10.20%)	
Surgery time, min	262.50±108.57	313.24±114.80	281.58±102.11	0.058
Blood loss, mL	459.49±481.77	552.11±625.90	383.91±303.32	0.041
Blood transfusion, mL	165.58±304.93	191.08±329.58	146.33±285.13	0.342
Tumor character, n (%)				0.449
Malignant	136 (79.07%)	61 (82.43%)	75 (76.53%)	
PDAC	19	15	4	
Ampullary carcinoma	36	18	18	
Distal bile duct carcinoma	45	23	22	
Duodenal carcinoma	14	2	12	
Other	22	3	19	
Non-malignant	36 (20.93%)	13 (17.57%)	23 (23.47%)	
CRP on POD3, mg/L	142.78±74.72	191.08±329.58	146.33±285.13	<0.001
Albumin on POD3, g/L	31.52±4.15	30.32±3.19	32.42±4.56	0.001
CAR on POD3	4.67±2.64	6.58±2.38	3.15±1.67	<0.001
poGPS≥I on POD3, n (%)	76 (44.18)	57 (77.03%)	19 (19.39%)	<0.001
Postoperative stay (days)	18.00±18.33	31.69±23.42	8.43±10.16	<0.001
Reoperation, n	6	5	1	0.086
Mortality, n	2	1	1	1.0

Note: P<0.05 was significant.

Abbreviations: BMI, body mass index; Pre, preoperative; CRP, C-reactive protein; CAR, C-reactive protein/albumin ratio; mGPS, modified Glasgow Prognostic Score; OPD, open pancreaticoduodenectomy; LPD, laparoscopic pancreaticoduodenectomy; POD3, postoperative day 3; poGPS, postoperative Glasgow Prognostic Score.

anastomosis was performed after the completion of the pancreaticojejunostomy. Finally, two silicone drainage tubes were placed near pancreaticoenteric and bilioenteric anastomosis.

Statistical Analysis

Statistical analysis was performed using SPSS version 23.0 (IBM Corp., Armonk, NY: IBM Corp.) and MedCalc version 19.6 (MedCalc Software bvba, Ostend,

Table 2 The Composition and Contents of Modified Glasgow Prognostic Score (mGPS) and Postoperative Glasgow Prognostic Score (poGPS)

Modified Glasgow Prognostic Score (mGPS)	mGPS
C-reactive protein < 10 mg/l and albumin >35 g/L	0
C-reactive protein ≥10 mg/L	1
C-reactive protein ≥ 10 mg/l and albumin <35 g/L	2
Postoperative Glasgow Prognostic Score (poGPS)	poGPS
C-reactive protein ≤150 mg/L albumin<25g/L or ≥ 25g/L	0
C-reactive protein >150 mg/L and albumin ≥25 g/L	1
C-reactive protein >150 mg/L and albumin <25 g/L	2

Belgium) software. Continuous variables are expressed as mean ± standard deviation, while categorical variables are presented as proportion. The statistical significance of quantitative variables between groups was determined using independent sample student's *t* test, whereas that of qualitative variables was determined using chi-square test or Fisher's exact test. To determine the independent risk factors of postoperative complications, variables showing a certain degree of correlation ($P < 0.05$) with postoperative outcomes in univariate analysis were selected for multivariate logistic regression analysis. Receiver operating characteristics (ROC) curve analysis was performed for preoperative mGPS, preoperative CAR and CRP on POD3 and poGPS and CAR on POD3. Youden's index was calculated to select the optimal cut-off value of the CAR and patients were categorized into two groups for comparison. The area under the curve (AUC) values along with corresponding 95% confidence intervals (CI) were used to calculate the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy at the optimal cut-off value of these indicators for predicting postoperative complications.

Results

Patient Characteristics

Out of 172 patients who underwent PD, 74 (43.0%) developed postoperative complications, whereas 98 (57.0%) did not. As shown in Table 2, the mean age of the patients was 60.1 ± 9.5 years. A total of 105 (61.0%) patients were males and 67 (39.0%) were females. Out of the 74 patients who developed postoperative complications, two died because of postoperative complications.

Univariate and Multivariate Analysis of Possible Risk Factors for Postoperative Complications

We categorised patients into two groups: complication and without complication. The average age of patients with postoperative complications was higher than that of patients without complications (62.2 ± 7.1 vs 58.5 ± 10.8 , $P = 0.007$). The sex ratio between the two groups was significantly different (74% male vs 51% male, $P = 0.002$). Univariate analysis showed that preoperative CRP level (19.02 ± 33.98 vs 8.75 ± 15.07 , $p = 0.033$), preoperative albumin level (35.59 ± 4.40 vs 37.26 ± 4.08 , $p = 0.011$) preoperative CAR (0.55 ± 0.94 vs 0.21 ± 0.4 , $p = 0.008$), the number of people with $mGPS \geq 1$ (40, 54.05% vs 28, 28.57%, $p < 0.001$) and blood loss were statistically different between the two groups (Table 1). The postoperative serum biochemical indexes such as CRP and albumin levels, CAR and poGPS were significantly associated with postoperative complications ($p < 0.01$) (Table 1). The mGPS, which incorporates serum albumin and CRP levels, reflects systemic inflammation and nutritional status. Similarly, CAR and poGPS are dependent on CRP and albumin levels; therefore, we did not include mGPS, CAR and poGPS in multivariate analysis. In multivariate analysis, independent factors related to postoperative complications such as gender (male/female, OR = 0.012; 95% CI = 0.051–0.694, $P = 0.012$), age (OR = 1.083; 95% CI = 1.009–1.162, $P = 0.027$) and POD3 CRP level (OR = 1.028, 95% CI = 1.017–1.039, $P < 0.001$) were included (Table 3). Although there was a significant correlation between preoperative CRP level and postoperative complications in univariate analysis, it was not statistically significant in multivariate analysis ($P = 0.072$). For CRP on

Table 3 Multivariate Analysis of Factors Associated with Postoperative Complications

Variables	OR	95% CI	P
Age, years	1.083	1.009–1.162	0.027
Gender (male)	0.188	0.051–0.694	0.012
Preoperative CRP, mg/L	1.027	0.998–1.057	0.072
Preoperative albumin, g/L	0.864	0.740–1.009	0.065
Blood loss, mL	1.001	0.999–1.002	0.324
CRP on POD3, mg/L	1.028	1.017–1.039	<0.001
Albumin on POD3, g/L	0.956	0.842–1.085	0.482

Abbreviations: OR, odds ratio; CI, confidence interval; CRP, C-reactive protein; POD3, postoperative day 3.

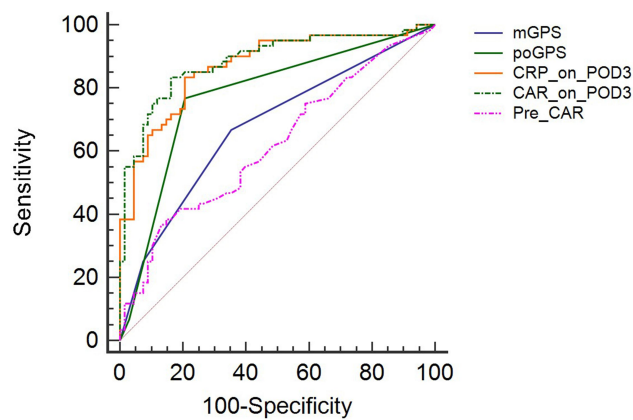


Figure 1 Receiver operating characteristic (ROC) curve of inflammation response-based indicators associated with postoperative complications.

Abbreviations: mGPS, modified Glasgow Prognostic Score; CAR, C-reactive protein/albumin; poGPS, postoperative Glasgow Prognostic Score; CRP, C-reactive protein; POD3, postoperative day 3.

POD3 was an independent risk factor for predicting complications, We speculated that CAR and poGPS calculated by CRP and albumin would be more sensitive than preoperative CRP and mGPS in predicting postoperative complications.

Significance of CRP, CAR, mGPS and poGPS in Predicting Postoperative Complications

We analysed the receiver operating characteristic curve of all five indicators (preoperative mGPS and CAR, CRP, CAR, and poGPS on POD3) representing inflammatory response (Figure 1) (Table 4). The AUC of the five

inflammatory response indexes was more than 0.6, with the smallest value for preoperative CRP (0.606, $P = 0.033$) and 0.883 ($P < 0.001$) for CAR on POD3. For the preoperative CAR, when the optimal cut-off value was 10.98, the AUC was 0.606 ($P = 0.033$), the sensitivity was 40%, the specificity was 83.56%, the PPV was 66.70%, the NPV was 62.90%, and the accuracy was 54.90%. For preoperative mGPS, the AUC was 0.667 ($P < 0.001$) and accuracy was 64.70%. The preoperative mGPS score was divided into three grades (0, 1 and 2). When the optimal cut-off value was 0, its corresponding sensitivity, specificity, PPV and NPV were 66.67%, 63.01%, 59.70% and 69.70%. For poGPS, AUC was 0.780 ($P < 0.001$) and the accuracy was 78.40%. It was divided into 3 levels by its score (0, 1 and 2 points), with the optimal cut-off value at 0 point (sensitivity, 77.03%; specificity, 79.57%; PPV, 75.00%; NPV, 81.30%), 1 point (sensitivity, 5.41%; specificity, 97.85%; PPV, 56.50%; NPV, 56.50%) and 2 point (sensitivity, 0; specificity, 100%; PPV, 55.70%). For CRP on POD3, AUC was 0.870 ($P < 0.001$), and at an optimal cut-off value of 142 mg/L, sensitivity, specificity, PPV, NPV and accuracy were 82.43%, 79.57%, 85.10%, 76.20% and 77.80%, respectively. For CAR on POD3, AUC was 0.883 ($P < 0.001$), and at an optimal cut-off value of 4.86, sensitivity, specificity, PPV, NPV and accuracy were 79.73%, 86.02%, 84.20%, 81.90% and 82%, respectively. The CAR value on POD3 was the highest positive predictive value and was shown to be more effective in distinguishing the patients in complication and without complication groups. As CAR value on POD3 was calculated by taking the ratio of CRP and albumin values that reflect the

Table 4 Accuracy of Risk Factors in Predicting Postoperative Complications

Variable	AUC	P	Cut-off Value	Sensitivity	Specificity	NPV	PPV	Accuracy
Preoperative CAR	0.606	0.033	10.98	40.00%	83.56%	62.90%	66.70%	54.90%
Preoperative mGPS	0.667	<0.001	0	66.67%	63.01%	69.70%	59.70%	64.70%
			1	25%	91.78%	59.80	71.40%	
			2	0%	100%	54.90%	–	
CRP on POD3	0.870	<0.001	142	82.43%	79.57%	85.10%	76.20%	77.80%
CAR on POD3	0.883	<0.001	4.86	79.73%	86.02%	84.20%	81.90%	82%
poGPS on POD3	0.780	<0.001	0	77.03%	79.57%	81.30%	75.00%	78.40%
			1	5.41%	97.85%	56.50%	66.70%	
			2	0%	100%	–	55.70%	

Abbreviations: CAR, C-reactive protein/albumin ratio; CRP, C-reactive protein; mGPS, modified Glasgow Prognostic Score; poGPS, postoperative Glasgow Prognostic Score; POD3, postoperative day 3.

dynamic change in the degree of the inflammatory response and nutritional status in the early postoperative period, we will further analyse its significance in predicting postoperative complications.

CAR for Predicting Postoperative Complications and Infection

A total of 103 patients with low CAR (CAR <4.86) and 69 patients with high CAR (CAR ≥4.86) were recorded. Out of 103 patients, 15 patients (14.6%) developed postoperative complications (Table 5). Out of 69 patients, 59 patients (85.5%) developed postoperative complications. Significant differences were observed between complication and without complication groups, and the complications were graded as Grade I, II, IIIa, IIIb and IVa. (P ≤0.01). However, for Grade IVb and V complications, no difference was observed between the two groups, probably because of the small number of patients (two, each) who developed Grade IVb and V complications. Out of the two patients who developed grade V complications, one died because of abdominal haemorrhage and the other died because of decreased immune function caused by infection and poor nutritional status. In patients who developed

complications of grade III or greater, there were distinct differences between the two groups (7, 6.8% vs 23, 33.3% P<0.001). In patients who developed grade III or higher grade complications, distinct differences were observed between the two groups (7, 6.8% vs 23, 33.3% P <0.001). To predict clinically relevant POPF, statistical significance was observed in pancreatic duct diameters between the two groups (median 5 vs 3, P = 0.023), whereas no significant statistical difference was observed in pancreatic texture between the two groups (8.74% vs 17.39%, P = 0.095). This can be because of the fact that pancreatic texture assessment depends on the subjective judgment of the surgeon (Table 5). Prediction of postoperative drain culture-positive intra-abdominal infection showed that intra-abdominal infection was significantly different between the two groups (10.7% vs 36.2%, P <0.001). From the peritoneal drainage fluid culture, we found that common pathogenic species in postoperative abdominal infection were *Enterococcus faecium*, *Pseudomonas aeruginosa* and *Escherichia coli* (Table 6). The AUC was 0.671 (95% CI=0.572–0.77, P<0.001)

Table 5 Incidence of Postoperative Complications Between Two Groups According to Postoperative C-Reactive Protein/Albumin Ratio (CAR)

Variables	CAR<4.86 (n=103)	CAR≥4.86 (n=69)	P
All	15 (14.6%)	59 (85.5%)	< 0.001
Grade I	3 (2.9%)	8 (11.6%)	< 0.001
Grade II	5 (4.9%)	28 (40.6%)	<0.001
Grade IIIa	3 (2.9%)	9 (13.0%)	< 0.001
Grade IIIb	2 (1.9%)	5 (7.2%)	0.001
Grade IVa	1 (1.0%)	6 (8.7%)	<0.001
Grade IVb	0	2 (1.9%)	–
Grade V	1 (1.0%)	1 (1.0%)	0.134
Grade III or great	7 (6.8%)	23 (33.3%)	<0.001
Pancreatic fistula (grade B/C)	5 (4.9%)	22 (33.3%)	0.001
Diameter	5 (3–6)	3 (3–4)	0.023
Pancreatic texture (soft texture,%)	9 (8.74%)	12 (17.39%)	0.095

Note: Clavien-Dindo complications grade.

Table 6 CAR of Two Groups in Predicting Intra-Abdominal Infection

Bacterials	CAR<4.86 (n=103)	CAR≥4.86 (n=69)	P
		11 (10.7%)	25 (36.2%)
<i>Enterococcus faecium</i>	4	12	
<i>Candida albicans</i>	2	2	
<i>Pseudomonas aeruginosa</i>	2	2	
<i>Escherichia coli</i>	1	6	
<i>Staphylococcus haemolyticus</i>	1	3	
<i>Enterobacter cloacae</i>	1	2	
<i>Aerogenes</i>	1	0	
<i>Enterococcus faecalis</i>	0	4	
<i>Klebsiella pneumoniae</i>	0	2	
<i>Citrobacter freundii</i>	0	2	
<i>Candida glabrata</i>	0	1	
<i>Proteus mirabilis</i>	0	1	
<i>Pseudomonas fluorescens</i>	0	1	
<i>Stenotrophomonas maltophilia</i>	0	1	

Abbreviation: CAR, C-reactive protein/albumin ratio.

(Figure 2). The CAR value on POD3 was closely related to clinically relevant POPF occurrence (AUC = 0.732, 95% CI = 0.633–0.830, $P < 0.001$) (Figure 3).

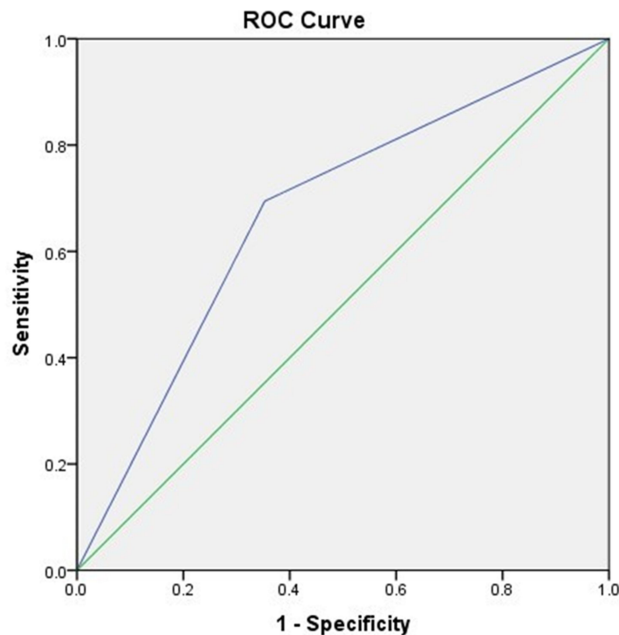


Figure 2 The receiver operating characteristic curve of CAR predicting abdominal infection on postoperative day 3 AUC=0.671, 95% CI=0.572–0.770, $P=0.002$.

Abbreviations: CAR, C-reactive protein/albumin; AUC, area under the curve; CI, confidence interval.

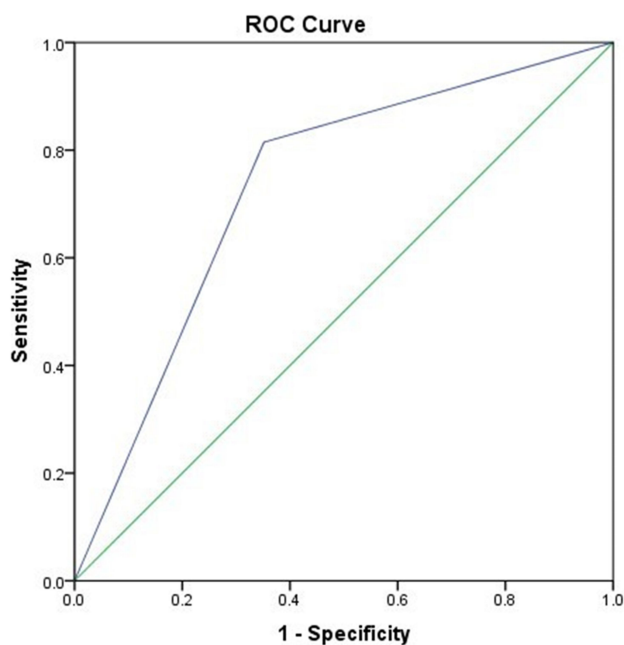


Figure 3 Receiver operating characteristic curve of CAR in predict of CR-POPF on postoperative day 3 AUC=0.732, 95% CI=0.633–0.830, $P < 0.001$.

Abbreviations: CAR, C-reactive protein/albumin ratio; CR-POPF, clinical relevant postoperative pancreatic fistula; AUC, area under the curve; CI, confidence interval.

Discussion

To our knowledge, no previous study has implicated postoperative CAR in the prognoses of patients who underwent pancreaticoduodenectomy. For patients with pancreatic head cancer, PD is the only treatment that can cure the cancer. In recent years, the mortality rate after PD has decreased to about 5%; however, the incidence of postoperative complications is 50–60%.^{16–18} Surgical tissue cutting injury, leakage of digestive fluid during operation and hypothermia caused by prolonged anaesthesia can initiate an inflammatory response in the body. CRP is a positive acute-phase inflammatory reactant synthesized by the liver and a marker of systemic inflammation and a widely used serum marker.¹⁹ Albumin is a negative acute phase reactant, its content in the blood decreases with increasing degrees of inflammation. Hypoalbuminemia correlates with the severity of inflammation, prognosis of the disease and mortality.^{20,21} Therefore, CRP and albumin levels are the two markers that represent a balance between inflammation and nutritional status. Mutillo²² reported that CRP and albumin levels were not associated with 1, 3, and 5-year survival after PD. They represent only recent inflammation and nutritional status after PD. An increase in CRP level and a decrease in albumin level before surgery may indicate a higher risk of developing postoperative complications. Therefore, experienced surgeons may administer hypoalbuminemia or control inflammation in patients before PD.

Sakamoto¹³ reported that serum CRP level on POD 3 in patients with clinical relevant POPF was significantly higher than levels in patients with non-clinical relevant POPF. A significant association was observed between the regulation of serum CRP levels and the polymorphisms in interleukin-6 promoter.²³ Hubner¹² reported that early postoperative albumin drop reflects the magnitude of surgical trauma and is correlated with adverse clinical outcomes. To accurately predict the postoperative complications, we determined the ratio of CRP and albumin values as an ideal indicator. Postoperative CAR and poGPS were based on CRP and albumin levels and were highly potential for determining postoperative complications. Among them, CAR on POD3 beyond preoperative or postoperative CRP alone as well as preoperative mGPS offers the best possibility to distinguish patients with complications from those without complications.

In patients who underwent PD, clinicians mainly focus on POPF as it is the most common complication after PD.²⁴

However, POPF merely represents a fatal complication after PD. Therefore, the focus should be moved from POPF to other major complications such as infection and bleeding. Xiaolong Ge²⁵ reported that $CAR \geq 2.2$ on POD3 could predict the postoperative complications of colorectal cancer. Our study also showed that CAR on POD3 is closely associated with postoperative complications after PD. When the CAR value is ≥ 4.86 on POD3, the patient has a higher risk of developing POPF and infection. Therefore, antibiotics can be used to treat abdominal infection and POPF injury can be cured by adjusting the position and placement time of the drainage tube. The results of drainage fluid bacterial culture could help select targeted antibiotics, as well as avoid the increased resistance associated with long-time usage of antibiotics.

Purvi²⁶ suggested that postoperative complications and mortality were increased in females and in patients older than 74 years, which is consistent with our study. Both univariate and multivariate analyses indicated that age and gender were associated with postoperative complications. The limitations of our study include the small sample size, high proportion of male patients. Apart from these, a retrospective study has its own limitations. We did not perform subgroup analyses for OPD, LPD and conversion of laparoscopy to open PD.

Conclusion

Our study shows that CAR level has an accurate predictive value for postoperative complications in the early days of PD. Early and effective prediction of postoperative complications and related interventions could help reduce the hospitalization of patients, reduce the economic burden, and enable the smooth transition of the perioperative period in patients who underwent PD.

Ethics Statement and Consent to Participate

All the patients have signed written informed consent forms for their data to be used in the study and the data were kept confidential. The ethics of this study was authorized by the Beijing Friendship Hospital Affiliated to Capital Medical University and followed the guidelines outlined in the Declaration of Helsinki.

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Author Contributions

All authors contributed to data analysis, drafting or revising the article, have agreed on the journal to which the article will be submitted, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Disclosure

All authors declare that they have no conflicts of interest.

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