

# C-reactive protein on postoperative day 3 as a predictor of infectious complications following gastric cancer resection

Yuji Shishido · Kazumasa Fujitani ·  
Kazuyoshi Yamamoto · Motohiro Hirao ·  
Toshimasa Tsujinaka · Mitsugu Sekimoto

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## Abstract

**Background** Postoperative infectious complications (PICs) after gastric cancer resection remain a clinically relevant problem. Early detection of PICs, before critical illness develops, may be of considerable clinical benefit. The aims of this study were to investigate the predictive factors for PICs and to define the clinical parameters for detecting them early in patients with gastric cancer resection.

**Methods** Clinical data for 417 consecutive patients undergoing elective gastrectomy for primary gastric cancer between 2009 and 2012 were retrospectively analyzed. Diagnostic accuracy was determined by the area under the receiver operating characteristic curve (AUC). Univariate and multivariate logistic regression analyses identified clinical factors predicting PICs of grade III or more according to the Clavien–Dindo classification.

**Results** Forty-four patients developed PICs of grade  $\geq$ III [10.6 %, 95 % confidence interval (CI) 7.6–13.5 %]. As a systemic inflammatory marker, C-reactive protein (CRP) on postoperative day (POD) 3 had superior diagnostic accuracy for PICs (AUC 0.802, 95 % CI 0.735–0.870) with a calculated cutoff value of 17.7 mg/dl, yielding a

sensitivity of 0.66 (95 % CI 0.524–0.774) and a specificity of 0.84 (95 % CI 0.821–0.850). Multivariate analysis identified CRP on POD 3 of 17.7 mg/dl or greater [odds ratio (OR) 8.094, 95 % CI 3.568–19.342] as well as clinical stage  $\geq$ II (OR 4.445, 95 % CI 1.478–15.881) and operation time  $\geq$ 250 min (OR 3.638, 95 % CI 1.449–10.137) as significant predictive factors for PICs after gastrectomy.

**Conclusions** Elevated CRP levels on POD 3 will help physicians predict the postoperative course and facilitate decision-making regarding prompt, comprehensive clinical searches and therapeutic approaches for PICs.

**Keywords** C-reactive protein · Postoperative infectious complications · Gastric cancer

## Introduction

Gastric cancer is the fourth most common malignancy worldwide, and the second leading cause of cancer-related death [1, 2]. Although surgical resection provides the only possibility of cure in patients with gastric cancer, postoperative complications remain a clinically relevant problem [3] despite improvements in surgical procedures and perioperative care after gastric cancer surgery. Following resection of gastric cancer, overall morbidity and mortality rates have been reported to be 17.4–24.5 % and 0.6–0.8 %, respectively, in East Asia [4–6], while higher overall morbidities of 13.6–46 % and mortalities of 0.6–13 % have been demonstrated after radical gastrectomy in the West [7–11]. In particular, infectious complications are the most common cause of postoperative morbidity and mortality [3, 12]. However, infectious complications are often diagnosed only after the patient develops clinical symptoms, thus requiring major clinical interventions such as reoperation

Y. Shishido · K. Yamamoto · M. Hirao · M. Sekimoto  
Department of Surgery, Osaka National Hospital, Osaka, Japan

K. Fujitani (✉)  
Department of Surgery, Osaka Prefectural General Medical  
Center, 3-1-56 Bandaihigashi, Sumiyoshi-ku, Osaka 558-8558,  
Japan  
e-mail: fujitani@gh.opho.jp

T. Tsujinaka  
Department of Surgery, Kaizuka City Hospital, Kaizuka, Osaka,  
Japan

and/or intensive care. Therefore, early detection of these complications through a prompt, intensive clinical search may be of considerable clinical benefit.

This retrospective analysis was conducted to investigate predictive factors for postoperative infectious complications, including systemic inflammatory markers such as C-reactive protein (CRP) and white blood cell (WBC) count, and to define relevant clinical parameters for early detection of these complications in patients who have undergone gastric cancer resection.

## Patients and methods

### Study population

We retrospectively reviewed the records of 417 consecutive patients who underwent elective gastrectomy for primary gastric cancer between January 1, 2009 and December 31, 2012 at Osaka National Hospital. All the patients received perioperative management by clinical path, which routinely included antibiotic prophylaxis (1 g intravenous cefazolin 30 min before surgical incision, repeated every 3 h during surgery) and blood samplings on postoperative days (PODs) 1 and 3. Data were collected on the following variables: age, sex, preoperative body mass index (BMI), serum albumin (Alb) level, performance status (PS) based on the Eastern Cooperative Oncology Group (ECOG) scale, physical status based on the American Society of Anesthesiologists (ASA) classification, initial clinical stage, the presence of neoadjuvant chemotherapy, surgical procedures (mode of approach, type of resection, degree of lymph node dissection, and presence of combined splenectomy and/or distal pancreatectomy), operation time, intraoperative blood loss, serum CRP level and WBC count after surgery, and postoperative complications according to the Clavien–Dindo classification [13, 14].

### Outcome measures

Surgical and nonsurgical complications occurring from the start of surgery to hospital discharge were documented prospectively. The following postoperative infectious complications were analyzed: abdominal abscess (collection of pus confirmed by percutaneous drainage), pancreatic fistula (drain output of any measurable volume of fluid on or after POD 3 with an amylase content greater than three times the serum amylase level [15]), anastomotic leakage (positive-contrast swallow test), wound infection (purulent exudate in the wound with positive bacterial culture), and pneumonia (clinical signs of pneumonia with radiographic evidence and positive sputum culture or

bronchoalveolar lavage). Serum levels of CRP and WBC counts were measured on PODs 1 and 3.

### Statistical analysis

SPSS statistical software version 19.0 (IBM SPSS, Chicago, IL, USA) was used for all statistical analyses, and a two-sided *P* value <0.05 was considered significant. Continuous data are presented as mean  $\pm$  standard deviation (SD) or median with range, as indicated. The Mann–Whitney test and chi-square test were employed to evaluate differences in continuous and categorical variables, respectively. Diagnostic accuracy was determined by the area under the receiver operating characteristic (ROC) curve (AUC) [16–18]. An AUC >0.8 was considered to indicate high diagnostic accuracy, given that at least 80 % of the patients with the disease were classified correctly [19]. AUCs were computed using the nonparametric trapezoidal method, with their 95 % confidence intervals (CIs) obtained using the approach of DeLong et al. [20]. The optimal cutoff values were determined by maximizing Youden's index (sensitivity + specificity – 1). Univariate and multivariate logistic regression analyses were used to identify clinical risk factors for postoperative infectious complications of grade III or more according to the Clavien–Dindo classification.

## Results

### Patient characteristics

Patient characteristics are summarized in Table 1. The study population consisted of 140 women and 277 men with a mean age of  $66.1 \pm 11.3$  years. The preoperative mean BMI and Alb level of all patients were  $22.1 \pm 3.5$  kg/m<sup>2</sup> and  $4.1 \pm 0.5$  g/dl, respectively. Four hundred six patients had a PS of 0 or 1 on the ECOG scale, and 361 patients had an ASA-graded physical status of 1 or 2. Neoadjuvant chemotherapy was administered to 31 patients, and 212 patients had disease of clinical stage I. The majority of the patients underwent open gastrectomy, and 152 patients received total gastrectomy. Three hundred and ten patients underwent D2 or more lymphadenectomy, with combined splenectomy and distal pancreatectomy performed in 46 and 8 patients, respectively. The median operation time was 252 (range 124–668) minutes, with a median blood loss of 200 (range 10–1935) ml. Postoperative infectious complications of grade III or greater according to the Clavien–Dindo classification [13, 14] were observed in 44 patients (10.6 %, 95 % CI 7.6–13.5 %), involving anastomotic leakage in 19, pancreatic fistula in 6, abdominal abscess in 10, wound infection in 3, and

**Table 1** Patient characteristics ( $n = 417$ )

Characteristic	$n = 417$
Age (years)	$66.1 \pm 11.3$
Sex	
Male	277
Female	140
BMI ( $\text{kg}/\text{m}^2$ )	$22.1 \pm 3.5$
Preoperative serum albumin (g/dl)	$4.1 \pm 0.5$
ECOG-PS <sup>1</sup> 0/1/2/3	365/41/8/3
ASA-PS <sup>2</sup> 1/2/3	105/256/56
Clinical stage I/II/III/IV	212/73/85/47
Neoadjuvant chemotherapy	
Present	31
Absent	386
Mode of surgical approach	
Laparoscopic	50
Open	367
Type of resection	
Distal gastrectomy	233
Proximal gastrectomy	32
Total gastrectomy	152
Degree of lymph node dissection (D) 0/1/2/3	8/99/295/15
Combined resection	
Splenectomy	46
Distal pancreatectomy	8
Operation time (min)	252 (124–668)
Blood loss (ml)	200 (10–1935)
Postoperative infectious complications according to the Clavien-Dindo classification	
None or <grade III	373
$\geq$ grade III	44

BMI body mass index, ECOG Eastern Cooperative Oncology Group, PS<sup>1</sup> performance status, ASA American Society of Anesthesiologists, PS<sup>2</sup> physical status

pneumonia in 6. Five patients died during hospitalization, resulting in an in-hospital mortality rate of 1.2 % (95 % CI 0.15–2.57 %). Cause of death was anastomotic leakage in 2, pneumonia in 2, and abdominal abscess in 1.

#### Associations of postoperative CRP level and WBC count with infectious complications

Chronological changes in CRP and WBC values after gastrectomy are demonstrated in Fig. 1a and b. A sharp and persistent rise in CRP was observed until POD 3 in patients with postoperative infectious complications of grade  $\geq$ III, at which point the CRP level was significantly higher than for patients with postoperative infectious complications of grade <III. In contrast, WBC reached its highest level on POD 1 and declined thereafter, showing a similar tendency between patients with and without postoperative infectious complications of grade  $\geq$ III.

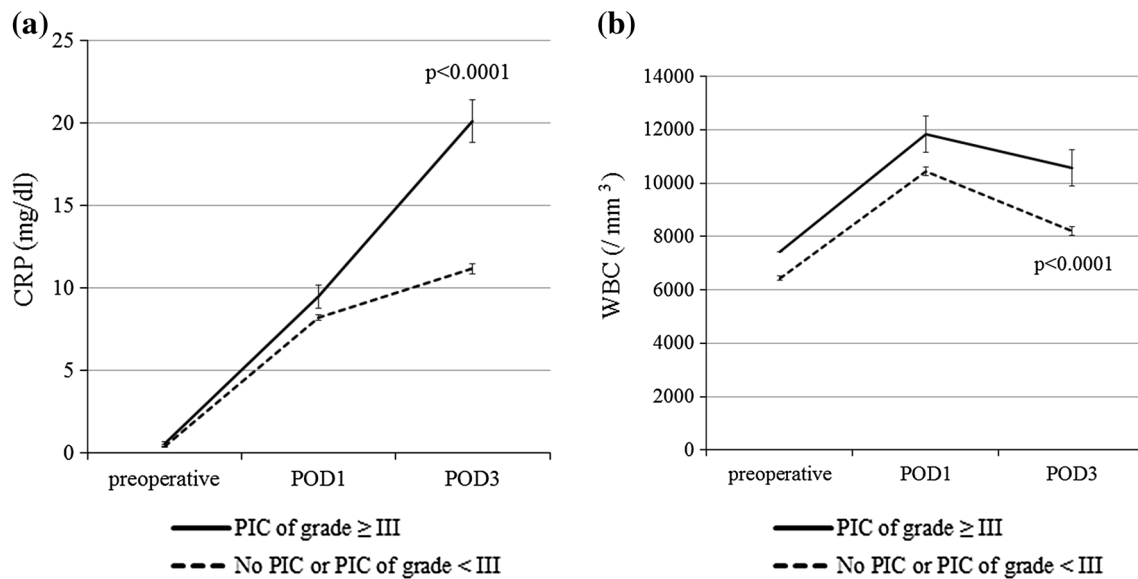
When following the CRP values from POD 3 through POD7, they were  $17.54 \pm 9.18$  mg/dl on POD 5 and  $11.51 \pm 7.06$  mg/dl on POD 7 in patients with postoperative

infectious complications of grade  $\geq$ III, and  $9.50 \pm 5.42$  mg/dl and  $4.34 \pm 4.63$  mg/dl on PODs 5 and 7, respectively, in patients with postoperative infectious complications of grade  $\leq$ III. There was a statistically significant difference in CRP levels on both PODs 5 ( $p \leq 0.001$ ) and 7 ( $p \leq 0.001$ ) between patients with and without postoperative infectious complications of grade  $\geq$ III.

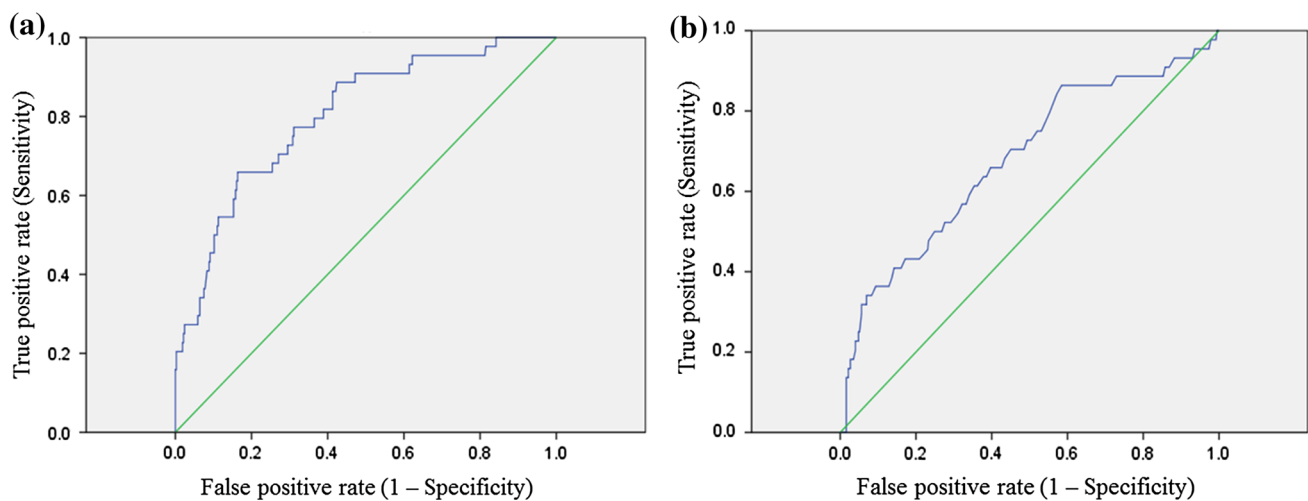
The diagnostic accuracy of CRP and WBC on POD 3 for the occurrence of postoperative infectious complications of grade  $\geq$ III was evaluated by the AUC, as shown in Fig. 2a and b, respectively. CRP on POD 3 had superior diagnostic accuracy (AUC 0.802, 95 % CI 0.735–0.870), with a calculated optimal cutoff value of 17.7 mg/dl, compared to WBC on POD 3 (AUC 0.680, 95 % CI 0.590–0.770).

#### Predictive factors for postoperative infectious complications of grade III or more

The results of univariate and multivariate analyses of various clinical factors, such as age, sex, preoperative BMI, Alb, ECOG-PS, ASA physical status, clinical stage,



**Fig. 1a–b** Postoperative chronological changes in CRP levels (a) and WBC counts (b). *PIC* postoperative infectious complication, *POD* postoperative day



**Fig. 2a–b** ROC curves for the diagnostic accuracy of CRP (a) and WBC (b) on POD 3 in predicting postoperative infectious complications of grade  $\geq$ III

presence of neoadjuvant chemotherapy, surgical procedures (mode of approach, type of resection, degree of lymph node dissection, and presence of combined splenectomy and/or distal pancreatectomy), operation time, intraoperative blood loss, and CRP on POD 3 for postoperative infectious complications of grade  $\geq$ III are summarized in Table 2. Among these, clinical stage of II or more [odds ratio (OR) 4.445, 95 % CI 1.478–15.881], operation time  $\geq$ 250 min (OR 3.638, 95 % CI 1.449–10.137), and CRP on POD 3 of 17.7 mg/dl or greater (OR 8.094, 95 % CI 3.568–19.342) were identified as significant independent predictive factors for infectious complications after gastrectomy.

## Discussion

Overall morbidity and mortality rates after gastric cancer resection were most recently reported to be 14.2 and 1.1 % for distal gastrectomy and 21.5 and 2.3 % for total gastrectomy, respectively, in a nationwide survey in Japan [21]. These results are consistent with the findings from previous East Asian reports [4–6] showing morbidity and mortality rates of 17.4–24.5 % and 0.6–0.8 %, respectively, while higher overall morbidity rates of 13.6–46 % and mortality rates of 0.6–13 % have been demonstrated after radical gastrectomy in the West [7–11]. Infectious complications such as pancreatic fistula, anastomotic

**Table 2** Univariate and multivariate analyses of clinical factors for postoperative infectious complications of grade  $\geq$ III

Characteristics	Univariate analysis			Multivariate analysis		
	No. of patients	No. of patients with PICs of grade $\geq$ III	<i>P</i> value	Odds ratio	95 % CI	<i>P</i> value
Age (years)						
<75	322	28	0.023	1	0.784–4.929	0.146
$\geq$ 75	95	16		1.979		
Sex						
Female	140	9	0.051	1	0.463–3.175	0.737
Male	277	35		1.176		
BMI (kg/m <sup>2</sup> )						
<25	341	32	0.100	1	0.404–2.878	0.839
$\geq$ 25	76	12		1.106		
Preoperative serum albumin (g/dl)						
$\geq$ 3.5	366	37	0.431	1	0.263–2.555	0.817
<3.5	51	7		0.877		
ECOG-PS <sup>1</sup>						
0, 1	406	40	0.020	1	0.488–15.062	0.236
2, 3	11	4		2.822		
ASA-PS <sup>2</sup>						
1, 2	361	37	0.610	1	0.178–1.682	0.326
3	56	7		0.581		
Clinical stage						
I	212	7	<0.001	1	1.478–15.881	0.006
II, III, IV	205	37		4.445		
Neoadjuvant chemotherapy						
Absent	386	39	0.293	1	0.246–3.175	0.920
Present	31	5		0.937		
Mode of surgical approach						
Laparoscopic	50	2	0.108	1	0.198–12.171	0.766
Open	367	42		1.347		
Type of resection						
Partial	265	18	0.001	1	0.455–3.134	0.702
Total	152	26		1.205		
Degree of lymph node dissection (D)						
0, 1	107	7	0.117	1	0.289–3.162	0.878
2, 3	310	37		0.911		
Combined splenectomy and/or distal pancreatectomy						
Absent	363	29	<0.001	1	0.681–5.815	0.211
Present	54	15		1.963		
Operation time (min)						
<250	204	7	<0.001	1	1.449–10.137	0.005
$\geq$ 250	213	37		3.638		
Blood loss (ml)						
<200	209	10	<0.001	1	0.597–3.960	0.393
$\geq$ 200	208	34		1.497		
CRP on POD3 (mg/dL)						
<17.7	327	15	<0.001	1	3.568–19.342	<0.001
$\geq$ 17.7	90	29		8.094		

BMI body mass index, ECOG Eastern Cooperative Oncology Group, PS<sup>1</sup> performance status, ASA American Society of Anesthesiologists, PS<sup>2</sup> physical status, PICs postoperative infectious complications, CI confidence interval

leakage, and abdominal abscess represent major causes of postoperative morbidity and mortality. Postoperative infectious complications worsen early surgical outcomes, leading to longer hospital stays and higher medical costs. Therefore, early identification of patients at risk for infectious complications is undoubtedly of high clinical value, as it allows clinicians to initiate therapeutic surgical or medical interventions in potentially septic patients to avert life-threatening conditions. In addition, postoperative intra-abdominal infectious complications have been shown to adversely affect overall and relapse-free survival in patients undergoing curative gastrectomy for gastric cancer [22–24]. Thus, postoperative infectious complications can be catastrophic in patients undergoing gastric cancer resection, in terms of both short- and long-term outcomes.

There is presently no reliable diagnostic test with sufficient accuracy to detect postoperative infectious complications at an early stage. There are several biochemical markers of the acute systemic inflammatory response, including CRP and WBC, and several recent studies have suggested a possible role for CRP in predicting the likelihood of infectious complications after gastrointestinal cancer surgery [19, 25–31], as shown in Table 3. These studies have proposed that an abnormally elevated CRP level on POD 3 or 4 or persistent elevation of CRP may be a useful predictor of infectious complications. Of note, ROC analysis with an AUC  $\geq 0.8$  indicated that relatively similar CRP levels ranging from 12.3 to 19.0 mg/dl provided the best cutoff to balance sensitivity and specificity in a variety of gastrointestinal cancer surgeries. Our CRP cutoff of 17.7 mg/dl on POD 3 corresponds well with the cutoff values of the aforementioned studies, although it was not identical to all of them. The differences are likely to be due to different types of cancer, wide-ranging sample sizes, and varying criteria for the diagnosis of infectious complications. These findings suggest the universality of CRP as an early indicator of postoperative infectious complications.

With regard to the diagnostic value of postoperative CRP concentrations in predicting infectious complications, particularly after gastric cancer resection, there has been no report focusing on patients after gastric cancer resection, though there are limited reports with relatively small sample sizes of 136–210 patients [19, 31] relating to gastroesophageal junction cancer as well as gastric cancer. Additionally, the sample size of the present study, at 417 patients, is currently the largest in the literature on esophagogastric cancer surgery [19, 31], as shown in Table 3.

Although D2 gastrectomy is now recommended as the standard surgical procedure for patients with resectable gastric cancer in Europe [32, 33] and the United States [34], as well as in East Asia [35], various degrees of lymphadenectomy were performed in previous Western studies [19, 31] investigating CRP values following esophagogastric cancer surgery. Interestingly, however, those two studies [19, 31] were similar to our own in terms of the CRP cutoff value identified as the best predictor of postoperative infectious complications, which suggests that optimal predictive value of CRP was only minimally affected by differing amounts of surgical stress and varying incidences of postoperative morbidity in relation to the specific lesions being treated.

As for the impact of initial surgical stress on CRP values on POD 3, there were no significant differences between laparoscopic and open surgery ( $p = 0.2801$ ), distal and total gastrectomy ( $p = 0.5597$ ), and D1 and D2 lymph node dissection ( $p = 0.3336$ ) in our patients. Furthermore, when analyzing the predictive factors for postoperative infectious complications of grade  $\geq III$  according to the type of resection, only CRP on POD 3 of 17.7 mg/dl or greater (OR 6.333, 95 % CI 1.567–29.336) was identified as a significant predictive factor after distal gastrectomy with D2 dissection ( $n = 161$ ), while operation time  $\geq 250$  min (OR 5.484, 95 % CI 1.215–39.933) and CRP on

**Table 3** Literature examining the value of CRP for predicting postoperative infectious complications following gastrointestinal cancer surgery

Study	Type of cancer	Patients ( <i>n</i> )	POD	CRP cutoff (mg/dL)	Sensitivity (%)	Specificity (%)	AUC
Welsch et al. [25]	R	48	3	14.0	80	81	0.88
Welsch et al. [26]	P	688	4	14.0	70	87	0.86
Korner et al. [27]	CR	231	3	19.0	82	73	0.82
Mackay et al. [28]	CR	160	4	14.5	85	86	0.87
Warschkow et al. [29]	CR	1187	4	12.3	66	77	0.76
Plat et al. [30]	CR	454	3	17.0	74	75	0.80
Dutta et al. [19]	OG	136	3	18.0	52	64	0.81
Warschkow et al. [31]	OG	210	4	14.1	78	70	0.77
This study	G	417	3	17.7	66	84	0.80

R rectal, P pancreatic, CR colorectal, OG esophagogastric, POD postoperative day, CRP C-reactive protein, AUC area under the receiver operating characteristic curve



POD 3 of 17.7 mg/dl or greater (OR 7.518, 95 % CI 2.015–31.840) were identified as significant predictive factors for postoperative infectious complications of grade  $\geq$  III after D2 total gastrectomy ( $n = 134$ ).

In our cohort, postoperative infectious complications of grade III or greater occurred in 44 patients (10.6 %, 95 % CI 7.6–13.5 %). Recent East Asian studies have demonstrated similar  $\geq$  grade 3 infectious complication rates of 8.2–9.9 % [36, 37] after gastrectomy, suggesting that our patients were not exceptional in this regard. Therefore, we believe that our findings could be highly relevant for, and might be generalizable to, patients undergoing gastrectomy for gastric cancer. Additionally, in these 44 patients, the median day of diagnosis of postoperative infectious complications was POD 6, with anastomotic leakage ( $n = 19$ ) being detected on POD 7 at median, pancreatic fistula ( $n = 6$ ) on POD 3, abdominal abscess ( $n = 10$ ) on POD 7, wound infection ( $n = 3$ ) on POD 7, and pneumonia ( $n = 6$ ) on POD 6. These findings suggest that elevated CRP levels on POD 3 preceded the development of infectious complications by 3 days. During these 3 days, preemptive antibiotic use or surgical intervention through further diagnostic measures such as thoracic X-rays, upper gastrointestinal series, or CT scans could improve patient outcomes. However, the impact on morbidity and mortality of early intervention based on postoperative monitoring of CRP concentrations should be further investigated in a prospective study.

As shown in Fig. 2a, CRP on POD 3 had superior diagnostic accuracy for postoperative infectious complications (AUC 0.802, 95 % CI 0.735–0.870), with a calculated optimal cutoff value of 17.7 mg/dl. Using this cutoff value, the sensitivity was 0.66 (95 % CI 0.524–0.774), and the specificity was 0.84 (95 % CI 0.821–0.850), which corresponded well with the results of previous studies as shown in Table 3. These results suggest a moderate diagnostic accuracy of CRP for detecting postoperative infectious complications. In addition, in this study, the estimated optimal cutoff value of 17.7 mg/dl for CRP on POD 3 yielded a positive predictive value (PPV) of 0.32 (95 % CI 0.256–0.378) and a negative predictive value (NPV) of 0.95 (95 % CI 0.936–0.970), which were in accordance with the PPV of 0.50 (95 % CI 0.37–0.63) and the NPV of 0.89 (95 % CI 0.77–0.95) reported by Warschkow et al. [31] following gastroesophageal cancer surgery. The high NPV of 0.95 suggests that the development of postoperative infectious complications can be ruled out when the CRP value on POD 3 is 17.7 mg/dl or less, whereas the PPV of 0.32 is too low to rule in postoperative infectious complications. Due to this moderate diagnostic performance, CRP should not be used as a “black-and-white” criterion with sufficiently high performance to correctly predict infectious complications in clinical

practice. CRP levels must be interpreted in the context of the whole clinical picture. Thus, elevated CRP levels  $\geq$  17.7 mg/dl on POD 3 should raise the degree of suspicion for infectious complications after gastrectomy. The reliable ability to predict an uncomplicated postoperative course would certainly be of significant value to clinicians when incorporated into early discharge criteria.

Despite its moderate accuracy, CRP of 17.7 mg/dl or greater on POD 3 (OR 8.094, 95 % CI 3.568–19.342) was identified as a significant independent predictive factor for postoperative infectious complications after gastrectomy, as shown in Table 2. To the best of our knowledge, this is the first study proving that CRP level in the early postoperative period is an independent predictor for postoperative infectious complications, at least in the field of gastric cancer surgery, since examinations of the relationship of CRP level with postoperative infectious complications are scarce [19, 31], as shown in Table 3. Patients with elevated CRP levels  $\geq$  17.7 mg/dl on POD 3 should be screened for potential infectious processes, though the discriminatory performance is insufficient to precisely predict infectious complications in clinical practice. As a consequence, CRP is nonspecific but helpful and relevant to clinical assessment in the postoperative setting after gastric cancer resection.

Other systemic inflammatory markers such as WBC count and body temperature have been reported to have poor diagnostic accuracy for detecting postoperative infectious complications, as they do not differ significantly from uneventful courses until later stages [26, 27]. This is in contrast to CRP, which demonstrated consistent increases on PODs 2–4. In addition, both WBC count and body temperature failed to predict unfavorable outcomes as precisely as increases in CRP did [19, 25, 26, 29, 30]. The results of the present study are consistent with previous studies that highlighted the superiority of elevated CRP level over WBC count and body temperature in predicting the development of postoperative infectious complications. Although the reasons for this discrepancy in relative predictive value between CRP and WBC count remain unclear, it might be speculated that CRP is more sensitive to the presence of infection because it plays an important direct role in innate immunity as an early defense against infection, assisting complement binding to foreign and damaged cells and enhancing phagocytosis by macrophages [19]. In addition, the short CRP half-life of 19 h makes it an optimal marker to detect the inflammatory response during postoperative recovery.

In conclusion, we investigated predictive factors for postoperative infectious complications and identified an elevated CRP level  $\geq$  17.7 mg/dl on POD 3 as a significant predictor for infectious complications after gastrectomy. To the best of our knowledge, this is the first Asian study

examining the relationship of CRP values with postoperative infectious complications, and our sample size of 417 patients was the largest thus far in the literature on esophagogastric cancer [19, 31], as shown in Table 3. However, the limitations of this study, which include its retrospective and single-institution nature, need to be taken into account before generalizing its results to daily clinical practice until prospective, multicenter validation is available. Furthermore, prospective studies should investigate whether early diagnostic or therapeutic approaches based on elevated CRP level on POD 3 actually lead to earlier detection of postoperative infectious complications, improved outcomes, and reduced morbidity after gastrectomy. Nonetheless, we believe that our findings will help physicians predict patients' postoperative courses and facilitate decision-making regarding prompt, comprehensive clinical searches for postoperative infectious complications.

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