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Postoperative C-reactive protein concentrations to predict infective complications following gastrectomy for cancer

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Abstract

Background and Objectives: Gastrectomy for gastric cancer is associated with significant infective postoperative complications. C-reactive protein (CRP) is a useful biomarker in the early detection of infective complications following major abdominal surgery. This single-centre retrospective study aimed to determine the relationship between postoperative CRP levels and development of postoperative infective complications after gastrectomy.

Methods: Daily postoperative CRP levels were analyzed to determine a CRP threshold associated with infective complications. ROC curve analysis was used to determine which postoperative day (POD) gave the optimal cutoff. Multivariate analysis was performed to determine significant factors associated with complications.

Results: One hundred and forty-four patients were included. A total of 61 patients (42%) had at least one infective complication. A CRP level of 220 mg/L was associated with the highest AUC (0.765) with a sensitivity of 70% and specificity of 76% (positive predictive value, 67%; negative predictive value, 78%). More patients with a CRP > 220 mg/L on POD 3 developed infective complications (67% vs. 21%, $p < 0.001$).

Conclusions: A CRP of more than 220 mg/L on POD 3 may be useful to alert clinicians to the increased risk of a postoperative infective complication or enable earlier safe discharge from critical care for those with a lower value.

KEYWORDS
CRP, gastrectomy, gastric cancer, inflammation, morbidity

1 | INTRODUCTION

Gastric cancer is the third most common malignancy and the fourth most common cause of cancer-related mortality globally, posing a significant burden of disease worldwide.[1] Gastric cancers typically present at an advanced stage which portends an unfavourable prognosis. Although survival rates of most cancers have significantly increased over time, mortality associated with gastric cancer remains high[2] and subtotal or total gastrectomy in association with various chemotherapy regimens remains the only curative intervention to date.

Gastrectomy involves high-risk major abdominal surgery with clinically significant postoperative stress, complications, and sequelae.[3–5] Efforts to maximize and facilitate the successful outcome of these resections have increased over recent years, including minimally invasive surgical techniques, and Enhanced Recovery After Surgery (ERAS) programs.[6–8] Despite these efforts, significant morbidity follows gastric cancer resection, affecting 23%–46% of patients, directly related to perioperative risk factors and comorbidity.[9–11] Identification of patients at increased risk of morbidity would facilitate appropriate monitoring and early intervention. The modified Glasgow Prognostic Scale (mGPS), which considers C-reactive protein (CRP) and albumin levels, has gained increased attention as a prognostic marker for gastrointestinal malignant disease survival and postoperative short-term complications, particularly colorectal cancers, and could play a role in gastric cancer as well.[12]

Commonly reported infective complications following gastrectomy include intra-abdominal abscess, wound infection, dehiscence, sepsis and pneumonia.[13,14] One of the most serious complications, however, is anastomotic leakage with a reported incidence of 2.1%–14.6% and a mortality rate of up to 50%.[15,16] Postoperative complications are often only diagnosed after the patient develops clinical symptoms or signs, thus requiring further major interventions such as reoperation and unplanned intensive care unit (ICU) admission, prolonging hospital stay, and putting the patient at further risk of additional morbidity or indeed mortality. Such complications are also thought to be associated with disease recurrence and poorer long-term survival due to suppression of the anticancer adaptive immune system.[17,18]

CRP has increasingly been studied as an early marker for postoperative complications. Raised CRP in the postoperative period has been linked to poor outcomes in colorectal, prostate and oesophagogastric cancer.[19–25] Although numerous studies have suggested CRP concentration, particularly on postoperative days (POD) 3 and 4, may be helpful predictors for the Postoperative course the CRP concentration thresholds suggested vary.[26–29] In a study of patients following rectal cancer surgery, Welsch et al.[27] reported that a raised CRP concentration of 140 mg/L on POD 3 was associated with infectious complications. Within the context of oesophagogastric cancer surgery, Dutta et al.[25] found CRP to be useful in predicting infectious complications and identified a threshold of 180 mg/L to be significant on POD 3 and 4. Interestingly, Saito et al.[26] demonstrated that CRP was a more reliable indicator than the presence of postoperative complications for postgastrectomy survival in their population.

The aim of the present study was to establish a CRP cutoff for predicting infective complications following gastrectomy in particular. Identifying a CRP threshold based on a large cohort provides a prognostic indicator that could prompt early investigations and close monitoring for patients who are high-risk for postoperative complications, while simultaneously aiding safer critical care step-down and discharge for those less likely to develop complications.

2 | MATERIALS AND METHODS

2.1 | Patients and methods

This study was a single-centre retrospective analysis of available patient records from an Upper GI tertiary referral University teaching hospital (Glasgow Royal Infirmary). All patients admitted to the ICU or Surgical High Dependency Unit (SHDU) following open surgical resection of a primary gastric cancer with curative intent, were identified over a 5-year period from September 2011 to July 2016. Patients were excluded if the resection was palliative or for secondary cancer, when disease progression made the resection impossible or if the resected tumour was benign.

Data were retrieved from a prospectively collected upper GI surgical clinical database pertaining to age, body mass index, gender, smoking status, pathology, tumour location, tumour depth, lymph node grading, metastatic disease, neoadjuvant therapy, prechemotherapy anaerobic threshold, and disease recurrence. The clinical electronic hospital records were interrogated for hospital length of stay and outcomes including complications.

Patients were categorized as either a subtotal or total resection of the stomach as per surgical operation note. Following the resection, all patients were initially admitted to either ICU or SHDU. Patients were kept nil-by-mouth until the integrity of the anastomosis was confirmed radiologically, typically between POD 5 and 9 for patients undergoing total gastrectomy.

All patients had daily blood tests including CRP, white cell count and albumin following their operation. Identification and management of complications were at the discretion of the treating clinicians who were not blind to these results.

The classification of postoperative complications was formed by the information available on electronic medical records both for patients who recovered in ICU and SHDU. This was then cross-checked against the separate surgical clinical database of complications.

2.2 | Definition of postoperative complications

Infective complications were defined as per European Perioperative Clinical Outcome (EPCO) definitions and included: Lower respiratory

tract infection, superficial wound infection, bacteraemia, urinary tract infection, and anastomotic breakdown.[30] In addition, we describe central line infections which were classified by a positive microbiology result alongside signs of inflammation around the device. The severity of these complications was also classified according to the Clavien–Dindo grade.[31]

2.3 | Statistical considerations

Categorical variable data were analyzed using the χ^2 test (or Fisher's exact test when necessary). Continuous variables were compared using an independent sample t test or Mann–Whitney U test.

A CRP cutoff value was determined using receiver operator characteristic (ROC) analysis. Youden's index was used to interpret the results of these ROC curves to determine the optimal cutoff values for a predictive test based on sensitivity and specificity. The area under the curve (AUC) was considered for each POD to determine which had the greatest. In light of this being a retrospective study, randomization was not possible.

Univariate and multivariate binary logistic regression was performed to assess the impact of covariables on the development of complications. Backward stepwise regression was used to create the model, including values with a p value of less than 0.05. A p value of less than 0.05 was considered statistically significant. Statistical analyses were carried out using SPSS Statistics for Windows, Version 25 (IBM).

3 | RESULTS

3.1 | Patient demographics

Of the total 144 patients, 89 were male, whereas 55 were female. The mean age was 66.7 years. Among these patients with gastric cancer, 75 (52.1%) underwent subtotal gastrectomy and 69 (47.9%) underwent total gastrectomy. The majority of patients had gastric adenocarcinoma (91.7%). Neo-adjuvant chemotherapy was administered to 76.4% of the total cohort. Detailed clinicopathologic characteristics of all patients are shown in Table 1.

Postoperative complications affected 79 patients (54.9%). Of those, 61 patients (42.4%) had at least one of the predefined infective complications; of these, 18 (12.5%) had an anastomotic leak in particular. Of all complications, 36 (45.6%) were Clavien–Dindo grade 3–5. Postoperatively, four patients died in ICU (2.8%)—all from multiorgan failure resulting from sepsis not related to anastomotic leaks. Some patients suffered multiple complications. Infective complications affected 36 patients (52.2%) following total gastrectomy (with an anastomotic leak rate of 15.9%), and 25 patients (33.3%) following subtotal gastrectomy (with an anastomotic leak rate of 5.3%). Ten patients (6.9%) required reoperation

and 28 patients (19.4%) had a recurrence of their disease. The mean hospital stay was 13 days with a 1-year mortality rate of 12.5%.

3.2 | Biomarkers against time

There was a significant rise in CRP from POD 0 (day of the operation) to POD 2 and 3 in all patients (Figure 1). Median CRP was significantly higher from POD 2 onwards in patients with complications (all $p < 0.001$).

3.3 | Determining a diagnostic CRP cutoff and utility for prediction of postoperative complications

A ROC analysis curve was created to determine the point at which CRP levels had the highest combined sensitivity and specificity (Figure 2) in relation to infective complications. Analysis of cutoffs taken from each POD is shown in Table 2. The area under the curve (AUC) was greatest on Day 3 (0.765).

The optimal cutoff of CRP was 220 mg/L, which gave a sensitivity and specificity of 70% and 76% respectively. On the basis of the high prevalence of infective complications, this gave a positive predictive value (PPV) of 67%, and a negative predictive value (NPV) of 78%. Of note, POD3 CRP of above 200 was also associated with a higher Clavien–Dindo grade ($p < 0.001$). The complication rates for patients with a POD3 CRP above and below this threshold are described in Table 3. The significance of the type of surgical procedure was considered here as well, as a total gastrectomy is generally considered a riskier procedure than a subtotal gastrectomy and, therefore, may play a role in the development of postoperative complications.

3.4 | Predictors of complication

Multivariate analysis was performed for the clinicopathologic characteristics to determine the influence of other factors on the development of postoperative complications (Table 4). Although unadjusted analysis found a CRP cutoff of 220 mg/L, smoking status, mGPS and surgical procedure type to be significantly associated with infective complications, only the CRP cutoff remained statistically significant (OR: 10.3, 95% CI: 4.12–25.68, $p < 0.001$) in the multivariate model.

4 | DISCUSSION

This study of patients following elective resection for gastric cancer demonstrates a significant association between postoperative CRP concentration and infective complications. A CRP threshold concentration of 220 mg/L on POD 3 may be useful to predict the

TABLE 1 Characteristics of patients who underwent either subtotal or total gastrectomy

	All gastrectomies (n = 144)	Subtotal gastrectomies (n = 75)	Total gastrectomies (n = 69)
Patient characteristics			
Demographics			
Mean age (years)	66.7	66.8	66.1
Body mass index, n (%)			
<19.9	6 (4.2)	6 (8.0)	0
20–24.9	54 (37.5)	30 (40.0)	24 (34.8)
25–29.9	57 (39.6)	28 (37.3)	29 (42.0)
>30	27 (18.7)	11 (14.7)	16 (23.2)
Sex			
Male	89 (61.8)	43 (57.3)	46 (66.7)
Female	55 (38.2)	32 (42.7)	23 (33.3)
Comorbidities, n (%)			
Any comorbidity	81 (56.3)	41 (54.7)	40 (58.0)
Type 2 diabetes mellitus	22 (15.3)	9 (12.0)	13 (18.8)
COPD	8 (5.6)	4 (5.3)	4 (5.8)
Ischaemic heart disease	22 (15.3)	12 (16.0)	10 (14.5)
Anaemia	38 (26.4)	19 (25.3)	19 (27.5)
Smoking status			
Nonsmoker	59 (41.0)	31 (41.3)	28 (40.6)
Smoker	27 (18.7)	15 (20.0)	12 (17.4)
Ex-smoker	58 (40.3)	29 (38.7)	29 (42.0)
Cancer characteristics			
Cancer type, n (%)			
Adenocarcinoma	132 (91.7)	73 (97.3)	59 (85.5)
Gastrointestinal stromal tumour	10 (6.9)	2 (2.7)	8 (11.6)
Neuroendocrine	2 (1.4)	0	2 (2.9)
Cancer location			
Proximal stomach	75 (52.1)	22 (29.3)	53 (76.8)
Distal stomach	69 (47.9)	53 (70.7)	16 (23.2)
Tumour depth			
T1	42 (29.1)	18 (24.0)	24 (34.8)
T2	23 (16.0)	15 (20.0)	8 (11.6)
T3	56 (38.9)	29 (38.7)	27 (39.1)
T4	23 (16.0)	13 (17.3)	10 (14.5)
Nodal involvement, n (%)			
N0	85 (59.0)	42 (56.0)	43 (62.3)
N1	28 (19.4)	17 (22.7)	11 (16.0)
N2	22 (15.3)	10 (13.3)	12 (17.4)
N3	9 (6.3)	6 (8.0%)	3 (4.3%)
Metastasis	0	0	0

TABLE 1 (Continued)

	All gastrectomies (n = 144)	Subtotal gastrectomies (n = 75)	Total gastrectomies (n = 69)
Operative features, n (%)			
Received neoadjuvant therapy	110 (76.4)	60 (80.0)	50 (72.5)
Preoperative anaerobic threshold			
<11	33 (22.9)	17 (22.7)	16 (23.2)
>11	48 (33.3)	20 (26.7)	28 (40.6)
Pre-op mGPS 1–2	41 (28.5)	19 (25.3)	22 (31.9)

Abbreviations: COPD, chronic obstructive pulmonary disease; Pre-op mGPS, preoperative modified Glasgow Prognostic Scale.
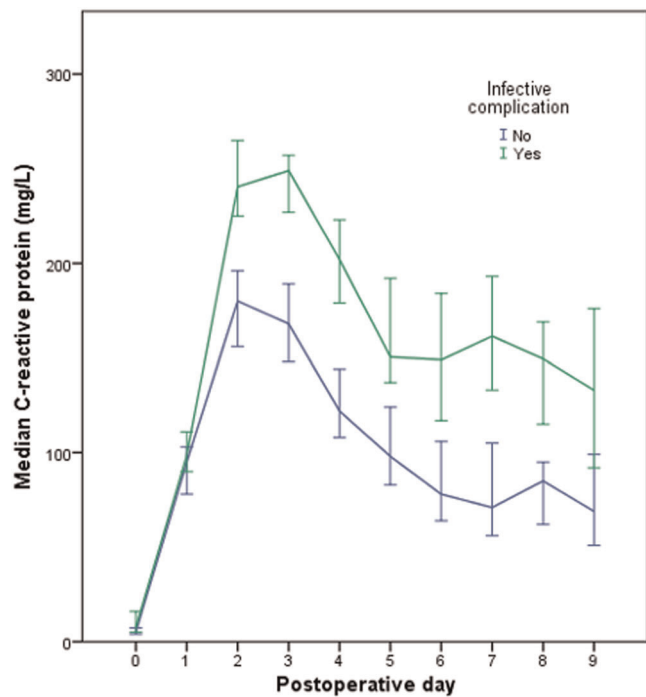
FIGURE 1 Median C-reactive protein (mg/L) trends from the day of operation (Day 0) to postoperative day 9
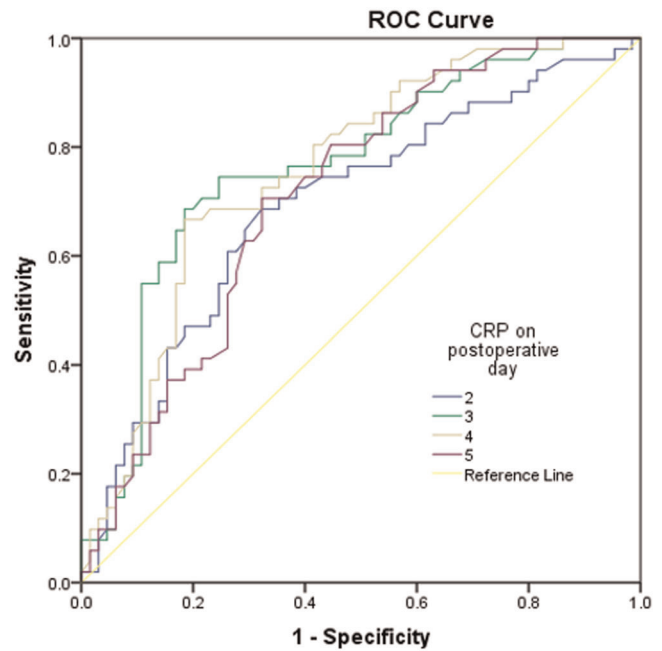
FIGURE 2 Receiver operative curves (ROC) for the gastrectomy group for postoperative Day 2 till Day 5—C-reactive protein (CRP) to predict infective complication

TABLE 2 Area under the curve (AUC), C-reactive protein cutoffs (mg/L), sensitivity (%), specificity (%), positive predictive value (PPV), and negative predictive value (NPV) for optimum cutoffs for infective complications in the gastrectomy group

Postoperative day	AUC	CRP cutoff (mg/L)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Gastrectomy						
Day 2	0.693	215	71	65	63	72
Day 3	0.765	220	70	76	67	78
Day 4	0.759	160	71	68	65	73
Day 5	0.714	130	69	69	65	72

development or exclude the likelihood of such infective complications in this group of patients before clinical signs (PPV 67%, NPV 78%). This may prompt early investigation and intervention, or prevent inappropriate early discharge from critical care, with the hope of improving postoperative outcomes.

In this study, CRP concentration was not significantly associated with the development of anastomotic leaks alone (7% in patients with CRP < 220 mg/L vs. 20% for patients with CRP 220 mg/L, $p = 0.060$) although this may be due to the low numbers involved with only 18 patients experiencing an anastomotic leak.

TABLE 3 Outcomes among patients for all patients, those with POD3 CRP < 220 mg/L and >220 mg/L

	All patients n = 144	CRP < 220 mg/L n = 84	CRP > 220 mg/L n = 60	p Value
Outcome, n (%)				
Any complication	79 (54.9)	33 (37.1)	46 (76.7)	**<0.001**
Infective complications, n (%)				
At least one infective complication	61 (42.4)	21 (25.0)	40 (66.7)	**<0.001**
Lower respiratory tract infections	35 (24.3)	11 (13.1)	24 (40.0)	**0.001**
Wound Infections	9 (6.3)	1 (1.2)	8 (13.3)	**0.048**
Bacteraemia	9 (6.3)	1 (1.2)	4 (6.7)	0.129
Other infections (UTI, line infection)	13 (9.0)	5 (6.0)	13 (21.7)	0.449
Anastomotic leaks	18 (12.5)	6 (7.1)	12 (20.0)	0.060
Among subtotal gastrectomy	–	2 (2.4)	3 (5.0)	0.151
Among total gastrectomy	–	4 (4.8)	9 (15.0)	0.335
Subtotal gastrectomy	–	9 (10.7)	16 (26.7)	**<0.001**
Total gastrectomy	–	12 (14.3)	24 (40.0)	**0.002**
Reoperation, n (%)	10 (6.9)	4 (4.8)	6 (10.0)	0.273
Hospital stay, median (IQR) (days)	13 (11.3–17)	13 (11–16)	14 (12–20.5)	
Disease recurrence, n (%)	28 (19.4)	16 (19.0)	12 (20.0)	0.732
Mortality, n (%)				
In-hospital	4 (2.8)	2 (2.4)	2 (3.3)	0.845
1-year mortality	18 (12.5)	9 (10.7)	9 (15.0)	0.558
Clavien–Dindo grade, n (%)				
1–2/3–4/5	45(31.3)/30 (20.1)/4(2.8)	29(34.5)/53 (63.1)/2(2.4)	23(38.3)/35(58.3)/2(3.3)	**<0.001**

Note: Bold values are the statistically significant.

Abbreviations: CRP, C-reactive protein; IQR, interquartile range; POD, postoperative day; UTI, urinary tract infection.

Previous work from this same centre by Dutta et al.[25] found that a CRP threshold of 180 mg/L on POD 3 was significantly associated with the development of anastomotic leaks in patients undergoing oesophagectomy (n = 79) and gastrectomy (n = 57). Anastomotic leak incidence is estimated to be 0%–17% for gastrectomy versus 0%–40% for oesophagectomy.[32] Considering the current study examined solely gastrectomy this may explain this particular discrepancy. The present study confirms the findings by Dutta et al. who established an association between CRP on POD 3 and the development of infective complications. They provided a sensitivity of 71% and specificity of 65% (compared to 70% and 76%, respectively in the present study).

The utility of CRP as a marker of postoperative infective complications demonstrated in this study is consistent with findings from a meta-analysis by Adamina et al.,[33] who compared the predictive value of CRP for complications following various types of abdominal surgery. They found the AUC to be 0.86 for gastrectomy compared with the AUC of 0.77 in our study. Although validity would need to be assessed for this particular population, tests with an AUC greater than 0.70 are typically deemed to be of clinical

value. The CRP threshold established in the present study of 220 mg/L on POD 3 is slightly higher than cutoffs suggested by other studies, such as 177 mg/L quoted by Shishido et al.,[34] 149 mg/L quoted by Obama et al.,[35] and 180 mg/L quoted by Dutta et al.[25] These discrepancies may be attributed to a number of factors such as the criteria used to define complications, whether the surgical procedure was laparoscopic or open, and the patient demographic.[36,37] It is also worth noting here that in the current literature CRP cutoffs have been identified for a single type of operation and one universal POD3 CRP may not be appropriate.

The study confirms the utility of CRP as a helpful guide in clinical practice. Although patient demographic, preoperative state, comorbidity and a multitude of other factors affect patient outcomes, POD3 CRP, which has a high NPV, may be a useful risk factor that can be taken into account when considering the safe stepdown of patients to ward-level-based care. Furthermore, it may be a helpful tool in alerting clinicians to patients at higher risk of postoperative infective complications and may aid in early detection, treatment and management adjustments in the intensive care and high dependency setting, since clinical signs are often insensitive. Consequently, CRP

TABLE 4 Gross odds ratio and adjusted odds ratio of clinicopathological variables and its association with developing an infective complication

		Gross odds ratio	95% CI	p Value	Adjusted OR	CI at 95%	p Value
Patient characteristics							
Demographics	Mean age (years)	66.7	–	–	–	–	–
	Body mass index						
	<19.9	0.81	0.13–4.86	0.813	–	–	–
	20–24.9	1.00	–	–	–	–	–
	25–29.9	1.10	0.49–2.40	0.831	–	–	–
	>30	2.34	0.89–6.16	0.084	–	–	–
	Sex						
	Male	0.58	0.30–1.18	0.137	–	–	–
	Female	1	–	–	–	–	–
Comorbidities	Any comorbidity	0.77	0.39–1.49	0.432	–	–	–
	Type 2 diabetes mellitus	0.46	0.17–1.25	0.126	–	–	–
	COPD	2.38	0.55–10.37	0.248	–		
	Ischaemic heart disease	1.7	0.65–4.47	0.281	–	–	–
	Anaemia	0.76	0.36–1.60	0.467	–	–	–
	Smoking status						
	Nonsmoker	1	–	–	–	–	–
	Smoker	2.46	1.16–5.21	**0.019**	–	–	–
	Ex-smoker	1.86	0.74–4.86	0.184	1.10	0.35–3.41	0.879
Cancer characteristics	Cancer type						
	Adenocarcinoma	1	–	–	–	–	–
	Gastrointestinal stromal tumour	0.74	0.05–12.04	0.830	–	–	–
	Neuroendocrine	0.67	0.03–14.03	0.794	–	–	–
	Cancer location						
	Proximal stomach	1	–	–	–	–	–
	Distal stomach	1.14	0.58–2.25	0.707	–	–	–
	Tumour depth						
	T1	0.78	0.06–9.89	0.846	–	–	–
	T2	1.64	0.58–4.66	0.356	–	–	–
	T3	1.00	0.31–3.27	1.000	–	–	–
	T4	1.01	0.37–2.72	0.990	–	–	–
	Nodal involvement						
	N0	1	–	–	–	–	–
	N1	1.07	0.24–4.84	0.926	–	–	–
	N2	1.92	0.38–9.65	0.427	–	–	–
	N3	1.25	0.24–6.65	0.794	–	–	–
	Metastasis	–	–	–	–	–	–
Operative features	Procedure type						
	Subtotal gastrectomy	–	–	–	–	–	–

TABLE 4 (Continued)

		Gross odds ratio	95% CI	p Value	Adjusted OR	CI at 95%	p Value
	Total gastrectomy	2.46	1.25–4.84	**0.009**	2.41	0.98–5.93	0.055
	Received neoadjuvant therapy	1.50	0.69–3.25	0.304	–	–	–
	Preoperative anaerobic threshold						
	<11	0.65	0.27–1.60	0.347	–	–	–
	>11	1.00	–	–	–	–	–
	Pre-op mGPS 1–2	2.28	1.06–4.93	**0.036**	2.24	0.89–5.64	0.087
Postoperative features	CRP						
	≤220	1.00	–	–	–	–	–
	>220	7.29	3.42–15.5	**<0.001**	10.30	4.12–25.68	**<0.001**

Note: Bold values are the statistically significant.

Abbreviations: CI, confidence interval; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; mGPS, modified Glasgow Prognostic Score; OR, odds ratio.

can be used to monitor the subsequent effectiveness of treatment. According to several studies, increased serum CRP levels precede radiologic and clinical diagnosis of complications such as anastomotic leakage. They reported that the detection of sustained serum CRP elevation may decrease the time for indicating reoperation, which could lead to lower mortality rates and hospital costs.[38,39]

The rate of all-cause complications in this study was higher than that of prior studies at 54.2%. This may be because of the inclusion of a wide range of complications in the criteria. The in-hospital mortality rate of 2.1% was slightly lower than that reported in other studies, where 30-day mortality is reported to be between 2% and 13%.[10,40] Despite these discrepancies it is interesting that the values are similar and most often CRP concentration at POD 3 or 4 is shown to be significant. This implies that daily CRP monitoring can provide warning of a postoperative infection. Moreover, this is a particularly early stage in recovery following major surgery and is, therefore, clinically valuable.

Total gastrectomy is in general a more complicated procedure involving high-risk anastomosis between oesophagus and jejunum and is more often associated with the extension of surgery to the spleen and neighbouring organs in cases of locally advanced tumours than subtotal gastrectomy.[41] Those undergoing total gastrectomy are generally a higher risk population. Furthermore, subtotal gastrectomy has been linked with significantly fewer anastomotic fistula and lower mortality.[42] Although there was a higher rate of anastomotic leak noted among those having had a total gastrectomy (4% among subtotal vs. 15% among total gastrectomy), in this study surgical procedure was not associated with all-cause infective complications on multivariate analysis after correcting for smoking status, CRP cutoff, and mGPS.

Finally, the question remains as to whether the postoperative systemic inflammatory response merely reflects the evolving complication, or whether it also plays a role in causing the complication. The postoperative systemic inflammatory response is primarily an innate immune response, and there appears to be a relative suppression of the adaptive immune system. There is evidence that attenuation of the postoperative systemic inflammatory response is associated with fewer complications and improved survival after both colorectal and pancreatic cancer surgery.[43–45] Another potential explanation is that postoperative complications arise in patients that suffer a disproportionate inflammatory response to the initial surgery. In this case, the elevated CRP may indicate patients who are at risk of complications rather than a marker of an early stage of an infective complication. A meta-analysis has reported that preoperative administration of corticosteroids is associated with a reduction in the postoperative systemic inflammatory response (SIR), measured by CRP, which in turn has been shown to decrease the rate of complications following surgery for gastrointestinal cancers.[46] This suggests that the magnitude of the postoperative SIR and postoperative complications may be causally related. However, prospective research to confirm this is limited in both quantity and quality and further work in this is needed.

One of the main limitations of this study is its retrospective nature, in particular the study's reliance on the accuracy and quality of notes and patient records. The time of diagnosis of infective complications was not taken into consideration in the analysis. The relative timing of the CRP concentration and complication will interact with their association. In this instance, where CRP concentrations were not hidden from diagnosing clinicians, this means there is a higher risk of false-positive diagnoses of complications with high CRP concentrations and false-negative complications with low CRP concentration. Thus, measurements of CRP concentration on later PODs will be preceded by more complications than CRP measured on earlier PODs. Furthermore, the study only included information from a single centre which limits the study's generalizability. During data collection, it was noted that 11.7% of the total number of CRP blood values (POD 0–9) were missing, particularly in those patients who had a relatively uncomplicated recovery. Multiple imputations were used to assess the impact of this and in assessing the imputation model in ROC analysis no significant difference was found compared to the original data set.

5 | CONCLUSIONS

In summary, the results of this study are consistent with the current literature of CRP's utility as an early predictor of infective postoperative complications in gastrectomy for cancer. A CRP threshold of 220 mg/L on POD could be used to alert clinicians of patients who may require monitoring and early investigation and intervention for the development of a possible infective complication while providing some reassurance in stepping down patients to ward level care in those at lower risk.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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