Journal of
Health Science and Alternative Medicine

Original Article   Open Access

Postoperative C-Reactive Protein as a Biomarker for Complications Following Gastrectomy in Gastric Cancer Patients

Yen Bi Ter[1], Wor Mi Thi[2*], Kyaw Min Htike[2], Ei Sandar U[3]

[1] *Yangon General Hospital, Myanmar*

[2] *Faculty of Public Health, Khon Kaen University, Thailand*

[3] *University of Medicine 1, Yangon, Myanmar*

ABSTRACT

Introduction: Globally, gastric cancer ranks as the fifth most prevalent malignancy and the third leading cause of mortality related to cancer, with surgical resection being merely a curative treatment option. Postoperative complications continue to pose major challenges that impact patient outcomes and require prompt detection and management. C-reactive protein (CRP) had the potential role in predicting postoperative complications, but the knowledge was limited in different healthcare settings. The study aimed to identify the predictive role of CRP levels tested on postoperative day 4 (POD4) on the occurrence of complications in gastric cancer patients following gastrectomy.

Methods: This was a single-center, cross-sectional study conducted in two hospitals in Myanmar. The study included 145 patients scheduled for gastrectomy. Data collection involved patient records, clinical examinations, and laboratory investigations. The association between CRP and post gastrectomy complication was analyzed by independent t-test and multiple logistic regression. The association was described using an Adjusted Odds Ratio (AOR), 95% Confidence Interval (CI), and p-value. The statistically significant level was considered at the p-value of < 0.05.

Results: The mean age of patients was 59.5 years, with a predominance of males (58.6%). Complications were identified in 12.4% of cases (95%CI=7.52-18.91). The mean CRP level for patients without complications was 107.98 mg/L, compared to 178.99 mg/L for those with complications (p-value<0.001). Specifically, patients with anastomotic leaks had a mean CRP level of 254 mg/L. Multiple logistic regression analysis indicated that elevated POD4 CRP levels were a significant predictor of complications, with an AOR of 1.38 (95%CI=1.12-1.71). The cut-off CRP value of 135.8mg/L demonstrated the best predictable level for complications with an Area Under ROC curve of 86.0%, a sensitivity of 72.2%, and a specificity of 99.2%.

Conclusion: This study highlighted CRP as a biomarker for complications in gastric cancer patients undergoing gastrectomy. Elevated CRP levels may assist clinicians in identifying at-risk patients, thereby enabling timely interventions and improved patient outcomes.

Keywords: CRP; Predictor; Gastric cancer; Post gastrectomy complications

Introduction

Gastric cancer is a significant global health concern and ranks as the fifth most prevalent malignancy as well as the third leading cause of mortality related to malignancy worldwide [1]. This disease poses a considerable burden [2], particularly as surgical resection is merely a curative treatment option available for patients diagnosed with gastric cancer [3]. Despite surgical techniques and perioperative care advancing, the incidence of postoperative complications continues to be a clinically relevant issue [4]. Among the various complications that can arise postoperatively, infectious complications represent the most common causes of morbidity and mortality [5]. These

complications are frequently diagnosed only after the patient presents with clinical symptoms, which can necessitate significant medical interventions such as reoperation or admission to intensive care units [6]. Therefore, early detection of postoperative complications is crucial, and proactive clinical surveillance could substantially enhance patient outcomes. Recent evidence has identified postoperative systemic inflammatory markers to be independent predictors of infectious complications following various surgical procedures [7].

C-reactive protein (CRP) has emerged as a significant inflammatory marker, known for its role as an opsonin as well as an activator of innate immune cells, particularly neutrophils, along with of having dual anti- and pro-inflammatory activities [8]. CRP levels typically begin to rise 4 to 6 hours after surgical injury, peaking around 48 hours and usually return to baseline within 72 to 168 hours after uncomplicated procedures [9]. Therefore, persistently elevated CRP levels after 72 hours indicate an ongoing inflammatory process, suggesting the possibility of postoperative complications after gastrointestinal surgeries [7, 10-13]. Evidence also suggested the potential role of CRP in the early detection of complications in patients with gastric cancer, particularly measuring it on a postoperative day 3 [13] and day 4 [12] after gastric cancer resection. Furthermore, a meta-analysis revealed that CRP levels were evaluated four days after surgery, demonstrating the most diagnostic accuracy for the concurrence complications following surgical operations [14].

Although previous studies, such as Kim et al. (2017) [12] and Shishido et al. (2016) [13], have examined the association of CRP with postoperative complications in gastric cancer surgery, the optimal threshold and ideal postoperative day for CRP measurement remain controversial. Furthermore, variations in patient populations and healthcare practices across countries may exhibit different results. This underscores the need for studies that consider these contextual differences and assess the potential role of CRP on less commonly studied days, such as postoperative day 4, in underrepresented populations like patients from Myanmar. Therefore, this study aimed to investigate the predictive role of CRP on postoperative complications in gastric cancer patients by measuring CRP levels on POD4. Understanding the role of CRP in this context may enhance clinical decision-making and improve patient outcomes in the postoperative setting, particularly in the population that has a similar context to Myanmar.

Methods

Study design

This was a single-center cross-sectional study that evaluated the role of CRP on postoperative complications following gastrectomy in gastric cancer patients. This study design was considered due to the short half-life nature of CRP [9]. The study was conducted over one year, from January 2019 to December 2019, in the surgical wards of Yangon General Hospital (YGH) and New Yangon General Hospital (NYGH). The reference population included gastric cancer patients admitted to these hospitals, and the study population comprised all patients scheduled for gastrectomy during the study period. The minimum required sample size was determined using sample size estimation for a single proportion population [15] based on previous hospital data of 2018, with an available population size of 222. Using Z alpha of 1.96 at 95% confidence interval (CI) and the estimated proportion of major complications after total gastrectomy was 0.10 [12], with adding 4.0% non-response rate to cover unforeseen missing data and maintain sufficient statistical power leading to a calculated minimum required sample size of 145 patients. Inclusion criteria encompassed all patients undergoing gastrectomy for gastric cancer, while exclusion criteria included pregnant patients, evidence of pre-existing inflammatory condition, and those with ongoing infections prior to surgery.

No drugs or chemicals were involved in this study. Data collection utilized patient records, operation theater records, laboratory records, and imaging reports. Informed consent was obtained from all patients after a thorough explanation of the study objectives. Detailed history taking, clinical examinations, and relevant investigations were performed, with results recorded in a designated proforma. Operative findings and surgical details were meticulously documented. CRP levels were measured on postoperative day 4 (POD4). The laboratories from the respective hospitals operate the blood sample collection and measurement procedure following the National Health Laboratory, Myanmar guidelines. The assay method used for the CRP measurement was an immunoturbidimetry assay. Postoperative complications were monitored throughout the hospital stay. At the conclusion of the study, results were analyzed based on the recorded data.

Definition of complications

Septic complications following elective gastrectomy surgery encompass the presence of various conditions that can occur during the hospital stay, including anastomotic leak, surgical site infection (SSI), duodenal stump leakage, pneumonia, and urinary tract infection (UTI) that arose 4 days after gastrectomy. Anastomotic leakage is defined by the presence of one of the following criteria: detection of pus or enteric contents within drainage systems, the presence of an abdominal or pelvic collection at the anastomosis site as identified on postoperative computed tomography (CT) scans or ultrasound (USG), or evident anastomotic dehiscence observed during reoperation for postoperative peritonitis. Duodenal stump leakage

refers to any diagnosed leak from the duodenal stump, regardless of clinical consequences or treatment approaches which was identified by the presence of bile in the surgical drain or abdominal scan using CT or USG. A urinary tract infection is characterized by a positive urine culture or increased bacterial count accompanied by pus cells in routine urine examinations. Pneumonia is diagnosed based on clinical symptoms, physical examinations, and radiological findings. Surgical site infection (SSI) is defined by the Centers for Disease Control and Prevention (CDC) as an infection occurring in a surgical wound within 30 days post-operation. SSIs could be incisional or organ/space infections [16].

Data analysis

Data was collected using a structured proforma and subsequently entered into Excel 2013 software for analysis. To maintain data quality, a thorough cleaning process was conducted to check for errors, incompleteness, and duplication. Any data that did not meet these quality standards was excluded from the study. The recorded data were then statistically analyzed in accordance with the study objectives using Stata software, version 18. Continuous variables were presented using their mean with standard deviation for the data with normal distribution, median, minimum, and maximum values for the skewed data, while categorical data were presented as proportions and percentages. The outcome variable was described using frequency, percentage, and 95% confidence intervals (CIs). Logistic regression was employed to identify factors associated with postoperative complications in patients undergoing gastrectomy. Subsequently, multiple logistic regression was conducted after controlling for potential confounders. The factors with p-value resulting from the bivariate analysis provided less than 0.25, including sex, duration of stay at the hospital, and type of anastomosis, to refine the analysis and ensure robust results. Appropriate graphical representations were utilized to enhance the clarity and interpretability of the findings.

Ethical considerations

The research protocol was submitted to the Academic Board and the Ethical Review Committee of the University of Medicine 1, Yangon. The study was carried out following approval from the Ethical Review Committee [Reference no. Ethical (128/2018)]. Informed consent was obtained from all patients undergoing gastrectomy in the Surgical Wards of New Yangon General Hospital and Yangon General Hospital, ensuring ethical standards were met during data collection.

Results

A total of 145 patients with gastric cancer who had undergone gastrectomy were included in the study, with a mean age of 59.5 years (SD ± 12.10), ranging from 28 to 91 years. Most patients were between 50-69 years old, accounting for 54.4%, while 24.2% were aged 70 or older. More than half of the participants were male (58.6%). The average duration of hospital stay was 19.6 days (SD ± 7.57). Postoperative hospital stays were predominantly 10 days or more. The mean operation time was 3.2 hours. Among the approaching methods in doing surgery, laparotomy was the most common method (94.5%), while laparoscopy and laparoscopic assistance were less frequently used. The mean C-reactive protein (CRP) level on postoperative day 4 was 116.79 mg/L (SD ± 31.32), indicating varying degrees of inflammation among patients. Most patients (77.9%) underwent partial gastrectomy, and lymph node dissection was predominantly D1+ (96.5%). Most anastomoses were hand-sewn (75.2%), while mechanical anastomoses accounted for 24.1% (Table 1).

Table 1 Baseline characteristics and clinical profile of patients with gastric cancer undergoing gastrectomy (n=145)

Characteristics	n	%
Age (Completed age in years)		
< 50	31	21.4
50-59	39	26.9
60-69	40	27.5
≥70	35	24.2
Mean (SD)	*59.5±12.10*	
Min: Max	*28:91*	
Sex		
Male	85	58.6
Female	60	41.4
Duration of stay at hospital		
<18 days	59	40.6
≥18 days	86	59.4
Mean (SD)	*19.6±7.57*	
Min: Max	*10:77*	

Characteristics	n	%
Hospital stays after operation		
<10 days	56	38.6
≥10 days	89	61.4
Mean (±SD)	*11.4±7.22*	
Median (Min: Max)	*10 (7:68)*	
Operation time		
≤3 hours	63	43.4
>3 hours	82	56.6
Mean (±SD)	*3.2±1.09*	
Min: Max	*1.33:7.83*	
Surgical approach		
Laparotomy	137	94.5
Laparoscopy	6	4.1
Laparoscopic Assistant	2	1.4
Post-operation Day 4 CRP (mg/L)		
Mean (±SD)	*116.7±31.32*	
Min: Max	*51.1:254*	
Gastrectomy level		
Partial	113	77.9
Total	23	15.8
Subtotal	9	6.3
Lymph node dissection		
D1+	140	96.5
D1	4	2.8
D2	1	0.7
Type of anastomosis		
Hand-sewn	109	75.2
Mechanical	35	24.1
None	1	0.7

Postoperative Complications in Gastric Cancer Patients Following Gastrectomy

In this study, complications following gastrectomy in gastric cancer patients were observed in 12.4% of cases (95%CI=7.52-18.91) (Table 2). The majority of complications were surgical site infections (SSI), posing 83.2% of total complications, followed by anastomotic leakage, SSI and anastomotic leakage, and duodenal stamp leakage (Figure 1).

Table 2 Postoperative complications in gastric cancer patients following gastrectomy (n=145)

| Complications (Any one of complication)	n	%	95%CI
No	127	87.6	81.09-92.47
Yes	18	12.4	7.52-18.91
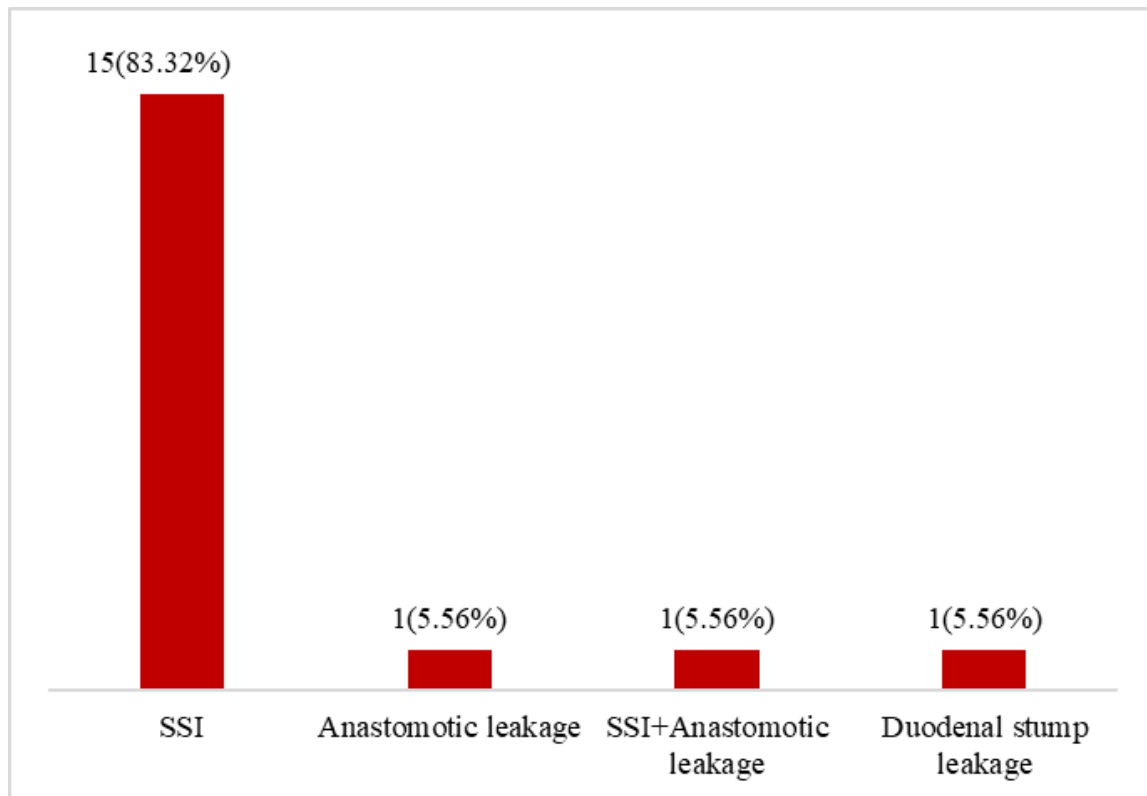
Figure 1 Distribution of types of infectious complication among the study population

*Mean Post Operative Day 4 CRP level by complications after gastrectomy*

The analysis reveals a significant association between elevated CRP levels and the occurrence of complications (Figure 2-3). The mean CRP level was significantly higher in the patients with complications than in those who did not have complications. The highest mean CRP values were seen in the group with anastomotic leakage with or without SSI followed by duodenal stump leakage (and SSI alone) (Table 3).

Table 3 Mean CRP level by complication

Complications	n	CRP		p-value
		Mean	SD	
Any one of complication				
No	127	107.9	15.34	
Yes	18	178.9	43.49	
Mean CRP of complications by subgroup				
SSI	15	170.3	40.84	
Duodenal stump leakage	1	189.8	N/A	<0.001
Anastomotic leakage	1	254.0	N/A	
SSI and anastomotic leakage	1	223.0	N/A	
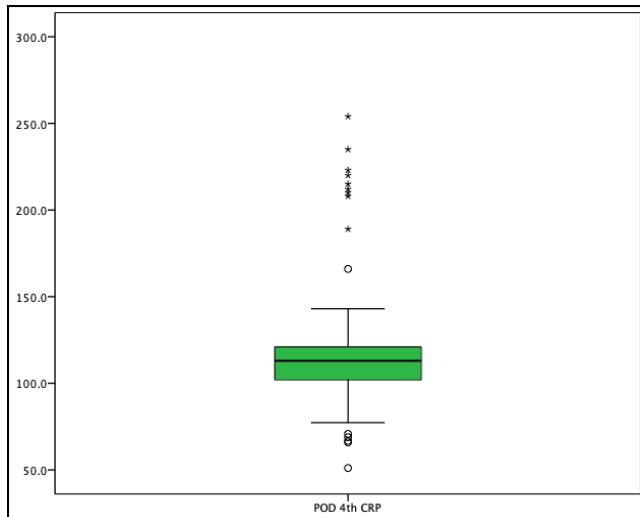
Figure 2 Distribution of CRP level at POD 4th day
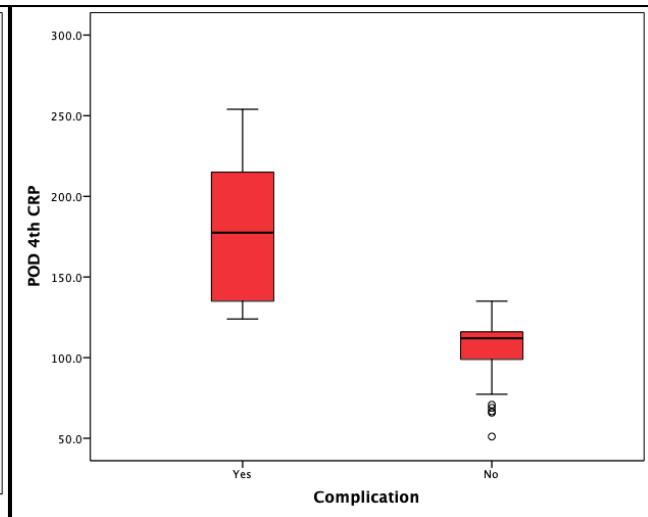
Figure 3 Association between infectious complication and CRP level

Factors associated with postoperative complications in patients undergoing gastrectomy

Patients with longer hospital stays had an increased risk of complications, with a crude odds ratio (OR) of 1.07 (95%CI=1.02-1.14) for total hospital stay and an OR of 1.06 (95%CI=1.01-1.12) for postoperative stay. Patients with elevated CRP levels were more likely to develop complications, with an OR of 1.41 (95%CI=1.14-1.74). This underscores the importance of monitoring CRP levels as an early indicator of postoperative issues, allowing for timely interventions. Other factors, such as age, sex, operation time, gastrectomy level, and the type of anastomosis, did not show statistically significant associations with complications. While female patients and those with mechanical anastomosis appeared to have higher complication rates, these differences were not significant. Overall, the study highlights that both prolonged hospital stays and elevated CRP levels are key predictors of postoperative complications, with CRP being a particularly valuable marker for the early identification of at-risk patients (Table 4).

Table 4 Factors associated with postoperative complications in patients undergoing gastrectomy

Characteristics	Total	Complications n (%)	Crude OR	95% CI	p-value
Age	145	N/A	1.26	0.79-2.02	0.324
Sex					
Male	85	8 (9.4)	1.00		0.196
Female	60	10 (16.6)	1.93	0.71-5.21	
Duration of stay at hospital	145	N/A	1.07	1.02-1.14	0.007**
Hospital stays after operation	145	N/A	1.06	1.01-1.12	0.019*
Operation time	145	N/A	1.01	0.64-1.58	0.971
Gastrectomy level					
Partial	113	13 (11.5)	1.00		0.542
Total/subtotal	32	5 (15.6)	1.42	0.47-4.35	
Post-operation Day 4 CRP	145	N/A	1.41	1.14-1.74	<0.001**
Type of anastomosis					
Hand-sewn	110	11 (10.0)	1.00		0.135
Mechanical	35	7 (20.0)	2.25	0.80-6.34	

*Note: n= Number of samples, N/A= Not Applicable, *significant at p-value < 0.05, **significant at p-value <0.01, ***significant at p-value <0.001*

C-reactive protein as a predictor of post-operative complications

After adjusting sex, duration of stay at the hospital, and type of anastomosis, CRP remained significantly associated with postoperative complications; the likelihood of complications increased with every unit of CRP increase by 38.0% (Adjusted Odds Ratio (AOR) = 1.38, 95% CI= 1.12-1.71). In summary, after controlling for other covariates, postoperative day 4 CRP levels emerged as the significant predictor of post-gastrectomy complications, highlighting the value of CRP as an early indicator in clinical monitoring.

In predicting complications, diagnostic accuracy was performed with different CRP cut-off values at 124 mg/L, 135.8 mg/L, 168 mg/L, and 178.99 mg/L. While considering both to detection of the complications reliably and the reduction of false positives, the cut-off CRP value of 135.8mg/L revealed the most appropriate diagnostic accuracy in predicting complications with an Area Under Receiver Operation Curve (AUC) of 86.0%, sensitivity of 72.2% (95%CI=46.5-90.3), specificity of 99.2% (95%CI= 95.7-100), high positive predictive value (PPV) of 92.9% (95%CI=66.1-99.8) and high negative predictive value (NPV) of 96.2% (95%CI=91.3-98.7). Although the cut-off value of 124mg/L yielded the best AUC values and NPV, it has more opportunity to be false positives due to the lower specificity and lower PPV (Table 5).

Table 5 CRP cut-off analysis at different CRP levels

Metrics	CRP cut-off			
	124mg/L	135.8 mg/L	168 mg/L	178.99 mg/L
Sensitivity (95%CI)	100.0% (81.5-100)	72.2% (46.5-90.3)	50.0% (26.0-74.0)	50.0% (26.0-74.0)
Specificity (95%CI)	89.8% (83.1-94.4)	99.2% (95.7-100)	100.0% (97.1-100.0)	100.0% (97.1-100.0)
Positive predictive value (PPV) (95%CI)	58.1% (39.1-75.5)	92.9% (66.1-99.8)	100.0% (66.4-100.0)	100.0% (66.4-100.0)
Negative predictive value (NPV) (95%CI)	100.0% (96.8-100.0)	96.2% (91.3-98.7)	93.4% (87.8-96.9)	93.4% (87.8-96.9)
ROC area	95.0 %	86.0%	75.0%	75.0%
Likelihood Ratio (+) (95 % CI)	9.7 (5.84-16.3)	91.7 (12.7-659.7)	-	-
Likelihood Ratio (-) (95% CI)	-	0.2 (0.1-0.5)	0.5 (0.3-0.7)	0.5 (0.3-0.7)

Discussion

This study explored the association between C-reactive protein (CRP) levels and postoperative complications in gastric cancer patients who underwent gastrectomy. The patient cohort consisted of 145 individuals with a mean age of 59.5 years, predominantly comprising middle-aged and elderly individuals, which aligned with the demographic profile typical of gastric cancer patients. The higher prevalence of male patients reflected known trends in gastric cancer epidemiology, underscoring the necessity for targeted screening and preventive measures, especially among older males with a family history of the disease. Furthermore, the study reported a complication rate of 12.4%, highlighting the overall efficacy of the surgical interventions employed. Notably, the absence of major complications such as urinary tract infections and pneumonia suggested effective perioperative management practices.

The mean CRP levels indicated a significant inflammatory response in patients with complications, further substantiating previous research findings. The findings demonstrated that elevated CRP levels measured on postoperative day 4 were significantly associated with various complications, particularly surgical site infections (SSIs) and anastomotic leaks. As anastomotic leaks could have severe inflammation, CRP response might be exaggerated than any other conditions. This response could come from tissue injury, inflammation, or infections due to leakage of bowel contents into the peritoneal cavity, which stimulates hepatic CRP production [17]. Furthermore, findings regarding SSIs indicated that patients with these infections had a mean CRP level of 170.33mg/L, which is consistent with the previous evidence [13].

Moreover, statistical analysis from this study also revealed a strong correlation between elevated CRP levels and the presence of postoperative complications, yielding 38% higher odds of having complications with a 1mg/L rise of CRP. CRP is synthesized as part of the acute phase response, stimulated by IL-6, a-TNF, and IL-1b originating at the site of inflammation. This protein acts at the endothelial cells and on complement, thereby participating in the inflammatory cascade. Its short half-life makes CRP a valuable marker for

detecting disease activity, inflammatory response, and postoperative recovery or the appearance of postoperative complications [17]. Provided that, our finding emphasizing CRP's potential as a distinguishing factor in clinical assessments underscores the significance of monitoring complications and the role of CRP in enhancing clinical decision-making among gastric cancer patients as other studies did [11, 18].

Our study identified a CRP cutoff value of 135.8 mg/L on POD4, demonstrating high diagnostic accuracy (AUC = 86.0%, sensitivity = 72.2%, specificity = 99.2%). This threshold aligns with prior research identifying CRP as a predictor of complications but is lower than the 168 mg/L reported in other studies [12]. This variability may reflect differences in patient populations, surgical techniques, or assay methods. Future studies should standardize CRP measurement protocols and explore population-specific thresholds to enhance clinical applicability.

Consequently, this study also identified prolonged hospital stays was associated with postoperative complications. The association between longer hospitalizations and increased complication rates suggested that these patients may have experienced more complex clinical scenarios or slower recovery trajectories, warranting closer surveillance. The presence of postoperative complications itself could also significantly extend the recovery process, leading to increased treatment courses as well as medical expenditure, resulting in longer hospital stays [19]. Therefore, attention needs to be drawn to the improvement in the quality of perioperative management, including patients' nutrition, body constitution, preoperative inflammation, and clinical care to reduce complications after gastric resection as well as to shorten the hospital duration in gastric cancer patients [20].

In fact, this study unlocked not only the potential role of CRP in assessing complications during the postoperative period but also the potential applicability of CRP in reducing healthcare-related costs and unnecessary usage of healthcare resources. As it could serve as an early warning for complications, prompt management may, in turn, help mitigate the consequences, such as prolonged hospital stays, higher economic costs, and the need for intensive care unit (ICU) admission, making it a more cost-effective option [21].

However, as our study covered two hospitals, there could be potential for inter-hospital variability in CRP measurements, surgical practices, and standard of care. Moreover, due to the single-center study design, the generalizability of the result is limited. Similarly, due to the variability in the population itself, such as pre-existing behavior practices, cultural influence, and regional differences in health care practices, the study's findings could not reflect the population with better

health care settings or geographical settings. Therefore, we suggested multi-center studies with bigger cohorts considering individual factors, behavioral factors, clinical factors, and other biomarkers, which could help refine CRP cut-off values, setting its threshold to use as an early predictor of complications while minimizing the potential inter-rater and intra-rater bias. Furthermore, longitudinal studies can help determine whether the rise in CRP is indirectly associated with long-term outcomes such as recurrence risk, patient survival, or quality of life, even though CRP itself diminishes over time. Such insights could inform strategies for long-term management. Nevertheless, our findings highlight the significant role of CRP in predicting post-gastrectomy complications, supporting its potential to improve routine clinical practice by enabling earlier detection and better management of postoperative issues, especially in a similar context as Myanmar.

Conclusion

In conclusion, this study reinforced the significance of CRP as a predictor of postoperative complications in gastric cancer patients undergoing gastrectomy. Elevated CRP levels on postoperative day 4 were found to be a strong indicator of complications, particularly SSIs and anastomotic leaks. CRP cut-off of 135.5mg/L could serve as a better predictor for complications. Therefore, it is recommended to add routine CRP monitoring into postoperative care protocols to facilitate early identification of at-risk patients, ultimately enhancing patient outcomes and clinical management strategies. Future studies emphasizing standardizing CRP measurement protocols, establishing population-specific thresholds, and conducting longitudinal studies to assess the association of CRP with long-term outcomes are suggested to enhance its applicability in clinical practice.

Competing Interests

The authors declare no competing interests exist.

Acknowledgments

References

[1] Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. CA: A Cancer Journal for Clinicians. 2015;65(1):5-29.

[2] Morgan E, Arnold M, Camargo MC, Gini A, Kunzmann AT, Matsuda T, et al. The current and future incidence and mortality of gastric cancer in 185 countries, 2020-40: a population-based modelling study. EClinicalMedicine. 2022; 47: 101404.

[3] Menon G, El-Nakeep S, Babiker HM. Gastric Cancer. [Updated 2024 Oct 28]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK459142/.
Menon G, El-Nakeep S, Babiker HM. Gastric Cancer. [Updated 2024 Oct 28]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK459142/

[4] Javed H, Olanrewaju OA, Owusu FA, Saleem A, Pavani P, Tariq H, et al. Challenges and solutions in postoperative complications: a narrative review in general surgery. Cureus. 2023;15(12): e50942.

[5]. Zabaglo M, Leslie SW, Sharman T. Postoperative Wound Infections. [Updated 2024 Mar 5]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK560533/.

[6] Montravers P, Augustin P, Zappella N, Dufour G, Arapis K, Chosidow D, et al. Diagnosis and management of the postoperative surgical and medical complications of bariatric surgery. Anaesthesia Critical Care & Pain Medicine. 2015; 34(1): 45-52.

[7] Van Daele E, Vanommeslaeghe H, Peirsman L, Van Nieuwenhove Y, Ceelen W, Pattyn P. Early postoperative systemic inflammatory response as predictor of anastomotic leakage after esophagectomy: a systematic review and meta-analysis. Journal of Gastrointestinal Surgery. 2024; 28(5): 757-65.

[8] Mouliou DS. C-reactive protein: pathophysiology, diagnosis, false test results and a novel diagnostic algorithm for clinicians. Diseases. 2023;11(4):132.

[9] Maniar RN, Navaneedhan G, Ranvir S, Maniar AR, Dhiman A, Agrawal A. What is the normal trajectory of interleukin-6 and C-reactive protein in the hours and days immediately after TKA? Clinical Orthopaedics and Related Research. 2019; 477(1): 41-6.

[10] McSorley ST, Ramanathan ML, Horgan PG, McMillan DC. Postoperative C-reactive protein measurement predicts the severity of complications following surgery for colorectal cancer. International Journal of Colorectal Disease. 2015; 30(7): 913-7.

[11] Straatman J, Harmsen AM, Cuesta MA, Berkhof J, Jansma EP, van der Peet DL. Predictive value of C-reactive protein for major complications after major abdominal surgery: a systematic review and pooled-analysis. PLoS One. 2015; 10(7): e0132995.

[12] Kim EY, Yim HW, Park CH, Song KY. C-reactive protein can be an early predictor of postoperative complications after gastrectomy for gastric cancer. Surgical Endoscopy. 2017; 31: 445-54.

[13] Shishido Y, Fujitani K, Yamamoto K, Hirao M, Tsujinaka T, Sekimoto M. C-reactive protein on postoperative day 3 as a predictor of infectious complications following gastric cancer resection. Gastric Cancer. 2016; 19: 293-301.

[14] Adamina M, Steffen T, Tarantino I, Beutner U, Schmied BM, Warschkow R. Meta-analysis of the predictive value of C-reactive protein for infectious complications in abdominal surgery. Journal of British Surgery. 2015; 102(6): 590-8.

[15] Hahn GJ, Meeker WQ. Statistical intervals: a guide for practitioners: John Wiley & Sons; 2011.

[16] Berríos-Torres SI, Umscheid CA, Bratzler DW, Leas B, Stone EC, Kelz RR, et al. Centers for disease control and prevention guideline for the prevention of surgical site infection, 2017. JAMA Surgery. 2017; 152(8): 784-91.

[17] Sproston NR, Ashworth JJ. Role of C-reactive protein at sites of inflammation and infection. Front Immunol. 2018; 9: 754.

[18] Tokunaga M, Tanizawa Y, Bando E, Kawamura T, Terashima M. Poor survival rate in patients with postoperative intra-abdominal infectious complications following curative gastrectomy for gastric cancer. Annals of Surgical Oncology. 2013; 20: 1575-83.

[19] Yu Z, Liang C, Xu Q, Li R, Gao J, Gao Y, et al. Analysis of postoperative complications and long-term survival following radical gastrectomy for patients with gastric cancer. Scientific Reports. 2024; 14(1): 23869.

[20] Kanda M. Preoperative predictors of postoperative complications after gastric cancer resection. Surgery Today. 2020; 50(1): 3-11.

[21] Gomez-Rosado J-C, Salas-Turrens J, Olry-de-Labry-Lima A. Economic cost analysis related to complications in general and digestive surgery. Cirugía Española (English Edition). 2018; 96(5): 292-9.