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ORIGINAL ARTICLE – COLORECTAL CANCER

A Postoperative Systemic Inflammation Score Predicts Short- and Long-Term Outcomes in Patients Undergoing Surgery for Colorectal Cancer

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ABSTRACT

Background. Following surgery, a significant proportion of patients develop postoperative complications that are associated with poorer long-term survival. Stereotypical markers of the systemic inflammatory response (SIR) have been shown to identify patients at increased risk of developing such complications. The aim of the present study was to examine the prognostic value of a postoperative systemic inflammation-based score in patients undergoing potentially curative surgery for colorectal cancer.

Methods. Patients with histologically proven colorectal cancer undergoing resection between 1999 and 2013 ($n = 813$) were grouped into two cohorts—a retrospective test cohort ($n = 402$) and a prospective validation cohort ($n = 411$). Patients were assessed for postoperative complications and had routine blood samples taken daily. The relationship between markers of the postoperative SIR and survival was examined using Cox regression analysis.

Results. In the test cohort, 87 patients developed an infective complication, while in the validation cohort, 106 patients developed an infective complication. In both cohorts, the postoperative SIR (C-reactive protein and albumin thresholds of >150 mg/L and <25 g/L, respectively) were associated with the development of infective complications (all $p < 0.01$). Using these thresholds, a scoring system [postoperative Glasgow prognostic score (poGPS)] was created, and on days 3 and 4 was associated with an incremental increase in the infective complication rate (all $p < 0.001$) and complication severity ($p < 0.001$). In the overall cohort, there were 175 cancer and 139 non-cancer deaths. The poGPS was also significantly associated with overall survival ($p < 0.05$).

Conclusions. The postoperative SIR, evidenced by the poGPS, was associated with increased complication rates and severity and a reduction in survival.

Colorectal cancer is the fourth most common cancer in the UK and the second most common cause of cancer death.[1] Despite death rates from colorectal cancer falling by approximately 14% over the last decade, approximately 40% of those diagnosed with colorectal cancer will die from their disease.[2]

In those deemed to have non-metastatic disease, surgery is the primary modality of cure; however, there has been a long-standing concern that although surgery provides the means of a potential cure for patients with colorectal cancer, the injury associated with surgery may stimulate tumor growth and dissemination.[3–7] Despite various infection control measures and the use of preoperative antibiotic prophylaxis following surgery, a significant proportion of patients develop postoperative complications, with the majority of these being infective in nature. Recently, it has become apparent that these complications, as well as having an adverse effect on patients quality of life,[8] are associated with both increased risk of cancer recurrence and poorer long-term survival.[6,9–12]

Therefore, there has been considerable interest in objectively identifying, early in the postoperative phase,

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which patients are at increased risk of developing infective complications in order to facilitate prompt investigation, treatment or, alternatively, safe discharge. In particular, the stereotypical marker of the systemic inflammatory response (SIR), C-reactive protein (CRP) has been extensively examined and concentrations greater than approximately 150 mg/L on days 3–5 have been shown to be useful.[13] In particular, it has been proposed that, in patients undergoing resection for colorectal cancer, CRP concentrations of ≤150 mg/L on postoperative days 3–5 are unlikely to develop infective complications, facilitating safe early discharge.[14]

McSorley et al. recently reported, in 377 patients, that the postoperative SIR, evidenced by CRP concentrations >150 mg/L, were associated with both complication severity and long-term outcome;[15] however, whether this observation provides the basis for a postoperative scoring system to predict both short- and long-term outcomes is not clear.

Therefore, the aim of the present study was to examine whether the combination of postoperative markers of the SIR, namely CRP and albumin, are useful in predicting the development of postoperative infective complications and long-term survival in a large cohort of patients undergoing potentially curative surgery for colorectal cancer.

PATIENTS AND METHODS

Patients with histologically proven colorectal cancer who, on the basis of intraoperative findings and preoperative computed tomography, were considered to have undergone potentially curative resection at a single center between March 1999 and May 2013 were included in the analyses ($n = 813$). All patient data were anonymized and all tumors were staged according to conventional tumor, node, metastasis (TNM5) classification, as per the Royal College of Pathologists guidelines[16] and additional pathological data obtained from the pathology reports issued at the time of the resection. Patients were grouped into two cohorts and, in both cohorts, patient characteristics were collected in a prospective manner. In the test cohort (surgery from March 1999 to November 2007; $n = 402$) postoperative complication data were collected retrospectively from electronic records. In the validation cohort (surgery from January 2008 to May 2013; $n = 411$) postoperative complication data were prospectively collected from patient records following discharge. Due to the prospective method of data collection, the Clavien–Dindo classification of complications was also recorded for this validation cohort.

Preoperatively, all patients received thromboembolism prophylaxis and antibiotic prophylaxis as per local protocols. Blood samples were taken for routine laboratory analysis pre and postoperatively. The preoperative SIR was assessed using the modified Glasgow prognostic score[17] (mGPS; electronic supplementary Table 1).

The postoperative SIR was assessed using the postoperative Glasgow prognostic score (poGPS; electronic supplementary Table 1). In essence, a postoperative CRP concentration below 150 mg/L, regardless of albumin concentration, scored 0, a CRP concentration ≥ 150 mg/L and albumin >25 g/L scored 1, and CRP ≥ 150 mg/L and albumin <25 g/L scored 2. The creation of this score was initially performed in the retrospective test cohort, and an attempt to subsequently validate this in the prospective validation cohort was then performed.

Postoperatively, all patients underwent daily clinical assessment. Clinicians were not blinded to these daily blood results and additional investigations and management were instigated at the surgical team's discretion based on the relevant clinical findings.

Patients were assessed for both non-infective (ileus, acute coronary syndrome, acute myocardial infarction, pulmonary embolism and arrhythmias) and infective complications (wound, intra-abdominal abscess, anastomotic leak, urinary tract infection, and pneumonia). The criteria used to define these complications were the same as has been previously described[18,19]. In short, a wound infection included the presence of pus that discharged spontaneously or required drainage; an intra-abdominal abscess was confirmed by imaging and required either conservative therapy with antibiotics or drainage; an anastomotic leak was defined as a fistula to the bowel anastomosis that was confirmed radiologically or diagnosed at relaparotomy; and pneumonia was diagnosed as the presence of X-ray changes and fever that required antibiotic therapy and urinary tract infection as positive urine culture in the presence of symptoms that required antibiotic therapy. Patients were routinely followed up for 5 years following resection, as per national guidelines. The date and cause of death were cross-checked with the cancer registration system and the Registrar General (Scotland). The West of Scotland Research Ethics Committee approved this study.

Statistical Analysis

The comparison of categorical and continuous variables was performed using the Chi square test and Mann–Whitney U test, respectively. Univariate survival analysis was performed using Cox proportional hazards regression in order to calculate hazard ratios (HR) and 95% confidence intervals (95% CI). A two-sided p value of <0.05 was considered statistically significant. Statistical analysis was performed using SPSS version 22.0 for Windows (IBM Corporation, Armonk, NY, USA).

RESULTS

In both the test ($n = 402$) and validation cohorts ($n = 411$), the majority of patients were aged >65 years, were male, had a colonic tumor, and had an elective operation. Comparison of the clinicopathological characteristics in both cohorts is shown in Table 1. There were significantly fewer emergency procedures ($p < 0.05$), more T1 tumors and less T3 tumors ($p < 0.005$), a greater overall complication rate ($p < 0.001$), and a greater infective complication rate ($p < 0.001$) in the validation cohort. Median follow-up of survivors in the test cohort was 116 months (range 76–180), and 31 months (range 10–71) in the validation cohort.

Test Cohort

With regard to short-term outcomes, 87 patients (22%) developed an infective complication. Of the preoperative factors in this cohort, emergency presentation ($p < 0.01$) and raised preoperative CRP concentrations ($p < 0.05$) were associated with the development of infective complications. Moreover, rectal surgery ($p < 0.01$), exceeding the postoperative thresholds for CRP on days 3 and 4 (both $p < 0.001$) and albumin on days 3 and 4 (both $p < 0.001$), and the days 3 and 4 poGPS (both $p < 0.001$) were also associated with the development of infective complications (Table 2).

In patients undergoing surgery for colon cancer ($n = 259$), 46 (18%) developed an infective complication. In these patients, emergency presentation ($p < 0.001$), exceeding the postoperative days 3 and 4 thresholds of CRP ($p < 0.001$) and albumin ($p < 0.005$), and the days 3 and 4 poGPS (both $p < 0.001$) were associated with the development of infective complications (electronic supplementary Table 2).

When using the postoperative scoring system (poGPS) (Table 4), an incremental increase in the day 3 poGPS from 0 to 1 to 2 resulted in an increase in the infective complication rate from 10.3 to 31.0 to 56.6% ($p < 0.001$), and, using the day 4 poGPS, from 17.0 to 50.0 to 73.9% ($p < 0.001$).

TABLE 1 Comparison of clinicopathological characteristics in both the test and validation cohorts

Characteristic	Test cohort ($n = 402$)	Validation cohort ($n = 411$)	p Value
Age, years			0.153
<65	131 (33)	137 (33)	
65–74	131 (33)	155 (38)	
>74	140 (34)	119 (29)	
Sex			0.828
Female	184 (46)	185 (45)	
Male	218 (54)	226 (55)	
Emergency presentation			0.047
No	354 (88)	379 (92)	
Yes	48 (12)	32 (8)	
Tumor site			0.933
Colon	261 (65)	268 (65)	
Rectum	141 (35)	143 (35)	
TNM stage			0.002
0	1 (1)	10 (2)	
I	52 (13)	80 (20)	
II	179 (44)	177 (43)	
III	170 (42)	144 (35)	
All complications			<0.001
No	298 (74)	254 (62)	
Yes	100 (25)	156 (38)	
Infective complications			<0.001
No	298 (74)	254 (62)	
Yes	87 (22)	106 (26)	

Data are expressed as n (%)

TNM tumor node metastasis

TABLE 2 Clinical characteristics and preoperative systemic inflammation of patients undergoing resection for colorectal cancer, and their postoperative complications in the test cohort ($n = 402$)

Characteristic	No complication ($n = 298$)	Infective complications ($n = 87$)	*P* Value
Age, years			0.359
<65	102 (79)	27 (21)	
65–74	89 (73)	33 (21)	
>74	107 (80)	27 (20)	
Sex			0.356
Female	140 (79)	36 (21)	
Male	158 (76)	51 (24)	
Emergency presentation			0.006
No	269 (80)	69 (20)	
Yes	29 (62)	18 (38)	
Tumor site			0.007
Colon	204 (82)	46 (18)	
Rectum	94 (70)	41 (30)	
TNM stage			0.255
0	0 (0)	1 (100)	
I	39 (75)	13 (25)	
II	131 (77)	40 (23)	
III	128 (79)	33 (21)	
Preoperative CRP, mg/L			0.040
≤10	174 (81)	40 (19)	
>10	124 (72)	47 (28)	
Preoperative albumin, g/L			0.677
≥35	239 (78)	68 (22)	
<35	59 (76)	19 (24)	
Preoperative mGPS			0.119
0	174 (81)	40 (19)	
1	84 (73)	31 (27)	
2	40 (71)	16 (29)	
Postoperative day 3, mg/L			<0.001
CRP ≤ 150	165 (89)	20 (11)	
CRP > 150	99 (60)	66 (40)	
Postoperative day 3, g/L			<0.001
Albumin ≥ 25	183 (82)	41 (18)	
Albumin <25	68 (60)	45 (40)	
Day 3 poGPS			<0.001
0	165 (89)	20 (11)	
1	74 (67)	36 (33)	
2	22 (42)	30 (58)	
Postoperative day 4, mg/L			<0.001
CRP ≤ 150	202 (82)	44 (18)	
CRP > 150	23 (40)	35 (60)	
Postoperative day 4, g/L			<0.001
Alb ≥ 25	176 (82)	38 (18)	
Alb <25	42 (52)	39 (48)	
Day 4 poGPS			<0.001
0	202 (82)	44 (18)	
1	15 (45)	18 (55)	

TABLE 2 continued

Characteristic	No complication ($n = 298$)	Infective complications ($n = 87$)	*P* Value
2	5 (23)	17 (77)	

Data are expressed as *n* (%)

mGPS modified Glasgow prognostic score, *TNM* tumor node metastasis, *CRP* C-reactive protein, *poGPS* postoperative Glasgow prognostic score

Validation Cohort

In this cohort, findings similar to those in the test cohort were observed. With regard to short-term outcomes, 106 patients (26%) developed an infective complication. Male sex ($p < 0.005$), exceeding the postoperative thresholds for CRP on days 3 and 4 (both $p < 0.001$) and albumin on days 3 and 4 (both $p < 0.005$), and the days 3 and 4 poGPS (both $p < 0.001$) were also associated with the development of infective complications (Table 3).

When using the postoperative scoring system (Table 4), an incremental increase in the day 3 poGPS resulted in an increase in the infective complication rate from 14.4 to 28.9 to 41.9% ($p < 0.001$), and, using the day 4 poGPS, from 17.9 to 32.2 to 53.7% ($p < 0.001$). An increase in the day 3 poGPS score resulted in an increase in severity of Clavien–Dindo Scores ($p < 0.001$), as did an increase in the day 4 poGPS ($p < 0.001$).

Overall Cohort (n = 813)

With regard to long-term outcomes, univariate survival analysis between the clinicopathological characteristics, the pre- and postoperative SIR, is shown in Table 5. There were 175 cancer deaths and 139 non-cancer deaths. Age ($p < 0.001$), TNM stage ($p < 0.001$), venous invasion ($p < 0.005$), margin involvement ($p < 0.001$), peritoneal involvement ($p < 0.001$), adjuvant therapy ($p < 0.05$), and mGPS ($p < 0.001$), as well as exceeding the postoperative days 3 and 4 threshold for CRP (both $p < 0.05$) and albumin (both $p < 0.05$), and the days 3 and 4 poGPS ($p < 0.05$), were associated with OS.

Furthermore, in patients undergoing resection of colon cancer (electronic supplementary Table 3), age ($p < 0.01$), emergency presentation ($p < 0.05$), TNM stage ($p < 0.001$), venous invasion ($p < 0.05$), margin involvement ($p < 0.001$), and adjuvant therapy ($p < 0.05$), as well as the mGPS ($p < 0.001$), exceeding the days 3 and 4 threshold for CRP ($p < 0.05$) and albumin ($p < 0.001$), and the days 3 and 4 poGPS ($p < 0.005$) were associated with overall survival.

DISCUSSION

The results of the present study confirm that the development of postoperative complications, particularly infective complications, was associated with the postoperative SIR in patients undergoing surgery for colorectal cancer. Furthermore, an objective postoperative scoring approach (poGPS) was capable of stratifying the risk of developing postoperative infective complications, ranging from approximately 12% with a score of 0 to approximately 30% with a score of 1, and approximately 50% with a score of 2. These results have been demonstrated in a retrospective 'test cohort' and subsequently validated in the prospective 'validation' cohort. Moreover, the postoperative SIR, evidenced by the poGPS, was associated with survival in patients undergoing surgery for colorectal cancer.

This study appears to finally tie the SIR to outcomes following surgery for colorectal cancer. Specifically, the present study builds on work by McSorley et al. who, in a cohort of 377 patients, reported that the magnitude of the postoperative SIR was significantly associated with long-term outcomes, independent of complications and tumor stage[15]. These findings, along with the present study, would appear to suggest that the mechanisms behind the development of postoperative complications and poor long-term survival are linked by the SIR. Therefore, a plausible hypothesis is that the cancer itself elicits an SIR in a significant proportion of patients, while the added surgical injury produces an immunological hit in all patients that leads to homeostatic decompensation in some. The nature and consequences of that decompensation may be the same as seen in patients with untreated or metastatic disease, perhaps even stimulating the growth of residual cancer cells (micrometastatic disease). Moreover, it would appear that the SIR involves both a dimension of magnitude and duration, both of which affect the prognosis. Consistent with this hypothesis, it has recently been reported that serum and peritoneal fluid samples from patients undergoing colorectal cancer surgery who had postoperative peritoneal infection increased the in vitro invasiveness

TABLE 3 Clinical characteristics and preoperative systemic inflammation of patients undergoing resection for colorectal cancer and their postoperative complications in the validation cohort ($n = 411$)

Characteristic	No complication ($n = 254$)	Infective complications ($n = 106$)	p Value
Age, years			0.853
<65	88 (69)	39 (31)	
65–74	99 (72)	38 (28)	
>74	67 (70)	29 (30)	
Sex			0.003
Female	132 (78)	37 (22)	
Male	122 (64)	69 (36)	
Emergency presentation			0.135
No	239 (72)	95 (28)	
Yes	15 (58)	11 (42)	
Tumor site			0.055
Colon	173 (74)	61 (26)	
Rectum	81 (64)	45 (36)	
TNM stage			0.221
0	8 (80)	2 (20)	
I	54 (76)	17 (24)	
II	112 (73)	42 (27)	
III	80 (64)	45 (36)	
Preoperative CRP, mg/L			0.688
≤10	185 (71)	75 (29)	
>10	69 (69)	31 (31)	
Preoperative albumin, g/L			0.594
≥35	168 (71)	67 (29)	
<35	86 (69)	39 (31)	
Preoperative mGPS			0.902
0	185 (71)	75 (29)	
1	26 (70)	11 (30)	
2	43 (68)	20 (32)	
Postoperative day 3, mg/L			<0.001
CRP ≤ 150	131 (83)	26 (17)	
CRP > 150	108 (59)	75 (41)	
Postoperative day 3, g/L			0.003
Albumin ≥ 25	142 (77)	42 (23)	
Albumin <25	97 (62)	59 (38)	
Day 3 poGPS			<0.001
0	131 (83)	26 (17)	
1	54 (67)	26 (33)	
2	53 (52)	49 (48)	
Postoperative day 4, mg/L			<0.001
CRP ≤ 150	142 (79)	38 (21)	
CRP > 150	63 (50)	64 (50)	
Postoperative day 4, g/L			<0.001
Albumin ≥ 25	130 (78)	37 (22)	
Albumin <25	75 (54)	64 (46)	
Day 4 poGPS			<0.001
0	142 (79)	38 (21)	
1	36 (65)	19 (35)	

TABLE 3 continued

Characteristic	No complication ($n = 254$)	Infective complications ($n = 106$)	p Value
2	26 (37)	44 (63)	

Data are expressed as n (%)

mGPS modified Glasgow prognostic score, *TNM* tumor node metastasis, *CRP* C-reactive protein, *poGPS* postoperative Glasgow prognostic score

TABLE 4 Days 3 and 4 poGPS and the development of postoperative complications in patients undergoing potentially curative resection for colorectal cancer in both the test and validation cohorts

Postoperative day	CRP (mg/L)	Albumin (g/L)	poGPS	No. of patients	No complications/infective complications (n)	Infective complication rate (%)	Clavien–Dindo grade (0/1–2/3–5)[a]
Test cohort ($n = 402$)							
3							
	≤150	<25 or ≥ 25	0	194	165/20	10.3	–
	>150	≥25	1	116	74/36	31.0	–
	>150	<25	2	53	22/30	56.6	–
4							
	≤150	<25 or ≥ 25	0	259	202/44	17.0	–
	>150	≥25	1	36	15/18	50	–
	>150	<25	2	23	5/17	73.9	–
Validation cohort ($n = 411$)							
3							
	≤150	<25 or ≥ 25	0	180	131/26	14.4	72/22/6
	>150	≥25	1	90	54/26	28.9	61/30/9
	>150	<25	2	117	53/49	41.9	45/41/14
4							
	≤150	<25 or ≥ 25	0	212	142/38	17.9	67/25/8
	>150	≥25	1	59	36/19	32.2	61/34/5
	>150	<25	2	82	26/44	53.7	32/47/21

CRP C-reactive protein, *poGPS* postoperative Glasgow prognostic score

[a] Only available in the validation cohort

capacity of cancer cell lines, causing increased tumor dissemination and tumor cell survival[20]. If this were to prove to be the case, then it may be that colorectal cancer surgery should be practiced in such a way to minimize the postoperative SIR. This study lays the foundation for further work in this field.

In the present study, it was of interest that elevated poGPS scores were significantly associated with emergency presentation and the presence of a SIR preoperatively. It has now been established that patients who present as an emergency for surgery for colorectal cancer have poorer 5 year survival[21–23]. In the present study, when only patients who had elective surgery and an mGPS of 0 were examined, the poGPS stratified the postoperative infective complication rate on both day 3 (poGPS0 rate was 13.7%, poGPS1 rate was 32.8%, and poGPS2 rate was 50.7%; $p < 0.001$) and day 4 (poGPS0 rate was 17.3, poGPS1 rate was 43.1%, and poGPS2 rate was 71.4%; $p < 0.001$). In addition, the poGPS stratified the 5 year survival rates on day 3 (poGPS0 rate was 74%, poGPS1 rate was 67%, and poGPS2 rate was 60%; $p = 0.039$). Therefore, the results of the present study

TABLE 5 Relationships between clinicopathological factors, pre- and postoperative systemic inflammatory response in patients undergoing potentially curative resection for colorectal cancer ($n = 813$)

Clinicopathological characteristic	Cancer-specific survival		Overall survival	
	Univariate analysis (95% CI)	*p* Value	Univariate analysis (95% CI)	*p* Value
Age, years (<65/65–74/>74)	1.20 (1.00–1.44)	0.056	1.57 (1.36–1.81)	<0.001
Sex (female/male)	1.32 (0.98–1.79)	0.071	1.21 (0.96–1.51)	0.100
Site (colon/rectum)	1.06 (0.78–1.44)	0.712	0.89 (0.70–1.13)	0.332
Emergency (no/yes)	1.75 (1.16–2.63)	0.008	1.33 (0.95–1.86)	0.094
TNM stage (0/I/II/III)	2.26 (1.77–2.89)	<0.001	1.53 (1.30–1.80)	<0.001
Venous invasion (no/yes)	1.75 (1.29–2.39)	<0.001	1.44 (1.15–1.80)	0.002
Margin involvement (no/yes)	4.85 (3.34–7.03)	<0.001	3.13 (2.25–4.35)	<0.001
Peritoneal involvement (no/yes)	2.22 (1.63–3.01)	<0.001	1.68 (1.32–2.14)	<0.001
Tumor perforation (no/yes)	2.21 (1.09–4.50)	0.028	1.51 (0.80–2.83)	0.201
Adjuvant therapy (no/yes)	1.07 (0.76–1.50)	0.695	0.75 (0.57–0.99)	0.045
Preoperative systemic inflammation				
mGPS (0/1/2)	1.36 (1.13–1.65)	0.001	1.36 (1.18–1.57)	<0.001
Postoperative systemic inflammation				
Day 3 CRP > 150 mg/L (no/yes)	1.31 (0.96–1.79)	0.088	1.41 (1.12–1.78)	0.004
Day 3 albumin <25 g/L (no/yes)	1.38 (1.00–1.90)	0.047	1.42 (1.11–1.81)	0.005
Day 3 poGPS (0/1/2)	1.20 (0.99–1.46)	0.059	1.27 (1.10–1.47)	0.001
Day 4 CRP > 150 mg/L (no/yes)	1.31 (0.93–1.84)	0.129	1.33 (1.02–1.74)	0.035
Day 4 albumin <25 g/L (no/yes)	1.36 (0.98–1.90)	0.068	1.48 (1.15–1.91)	0.002
Day 4 poGPS (0/1/2)	1.22 (0.99–1.50)	0.065	1.21 (1.03–1.42)	0.024

CI confidence interval, *mGPS* modified Glasgow prognostic score, *poGPS* postoperative Glasgow prognostic score, *TNM* tumor node metastasis, *CRP* C-reactive protein

would indicate a role for a postoperative SIR scoring system in predicting both short- and long-term outcomes in patients undergoing surgery for colorectal cancer.

It was recently reported that the depletion of skeletal muscle mass following surgery for colorectal cancer was greater with older age, female sex, open surgery, and an elevated preoperative SIR, as evidenced by the neutrophil lymphocyte ratio[24]. Therefore, consistent with the present results, it may be hypothesized that this was related to a greater postoperative SIR. Given the above, it would be of interest to examine whether approaches to minimize the poGPS, other than laparoscopic surgery, such as perioperative steroids[25], would reduce the loss of skeletal muscle mass following surgery for colorectal cancer.

This study has several potential clinical benefits. In those with a low score, it may provide the clinician with reassurance regarding the development of infective complications, and allow prompt discharge, particularly in an enhanced recovery setting. In contrast, in those with a high score, it may provide an early warning to the clinician and prompt reassessment and management of the patient. In addition, by enabling objective comparison of the impact of different surgical approaches and techniques on the magnitude of the postoperative SIR following surgery, it may be possible to identify individuals or techniques that minimize the poGPS score[26]. Finally, by acting as a therapeutic target, the use of postoperative anti-inflammatory agents has the potential to improve short-term outcomes. The use of anti-inflammatory agents in the postoperative period, particularly following colorectal surgery, continues to be a subject of intense debate, with studies reporting conflicting outcomes[27–29]. Cautious use in the postoperative period may provide benefit to patients with an exaggerated postoperative SIR, but more work is required to test this.

The magnitude of surgical injury in different colorectal procedures may be different, e.g. for colonic resections and rectal resections. This may also vary across surgical centers, with differences in patient cohorts and operative expertise. Therefore, the present results require external validation. However, given the simplicity of the measurement of postoperative SIR developed, such validation can be readily tested.

In the present study, thresholds for CRP and albumin were examined using receiver operating curve analysis and

postoperative infective complications as an endpoint. On day 3, these were 153 mg/L and 26 g/L, respectively, and 125 mg/L and 27 g/L, respectively, on day 4. These were similar to those established from previous meta-analysis (CRP > 150 mg/L and albumin <25 g/L) and therefore the latter thresholds were used in the analysis. A limitation of the present study was that there are intrinsic and extrinsic factors not accounted for that may potentially affect the relationship between the postoperative SIR and long- and short-term outcomes in patients undergoing surgery for colorectal cancer. For example, comorbidities, the quality and type of anesthesia/surgery, blood loss, and blood transfusion may all affect this relationship. Nevertheless, the poGPS provides an objective framework against which such factors are to be investigated.

CONCLUSIONS

The magnitude of the postoperative SIR, as evidenced by the poGPS, was associated with an incremental increase in the postoperative infective complication rates and a reduction in survival. Elevated systemic inflammation, whether prior to or following surgery, is associated with poor outcome in patients with colorectal cancer.

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