

Surgical site infection predictive factors in colorectal surgery

Fatores preditores de infecção do local cirúrgico em cirurgia colorretal

PEDRO SOARES-MOREIRA¹, GABRIELA TEIXEIRA², CRISTINA SILVA¹, EDUARDA MATOS², MARISA D. SANTOS¹

RESUMO

Introdução: Apesar de todos os progressos técnicos e científicos observados nas últimas décadas em Cirurgia, a Infecção do Local Cirúrgico (ILC) permanece elevado e com implicações nos resultados clínicos e custos hospitalares.

Objetivos: análise e identificação de fatores preditores de ILC em cirurgia eletiva colorretal.

Métodos: Estudo prospetivo realizado em doentes submetidos consecutivamente a cirurgia eletiva intestinal, com ressecção e anastomose primária entre 01-08-2013 e 31-08-2014, com registo dos dados demográficos, das cirurgias realizadas, dos potenciais parâmetros clínicos e analíticos de ILC, da morbidade cirúrgica e do tempo de internamento.

Resultados: Foram incluídos 139 doentes (mediana 70 anos, 59% homens). A cirurgia realizada foi predominantemente oncológica (100 doentes, 71.9%). A abordagem laparoscópica foi realizada em 79 procedimentos (56.8%). A ILC ocorreu em 27 doentes (19.4%), com deiscência de anastomose em 5 (3.6%) e uma taxa de mortalidade aos 60 dias de 0.7%. A utilização de via aberta ou laparoscópica não teve diferenças quanto à taxa de ILC. Quando presente, a ILC levou a um aumento significativo do tempo de internamento ($p=0.01$). Foram fatores preditores de ILC a dor, leucocitose, neutrofilia, hipoalbuminemia e aumento da proteína C reativa (PCR). Na análise multivariada apenas se mostraram preditores de ILC a elevação da PCR no 1^o, 3^o e 5^o dia de pós-operatório (DPO) e a presença de neutrofilia no 5^o DPO. Foram encontrados como *cut-offs* ideais da PCR aos 1^o, 3^o e 5^o DPO os valores 71.99, 96.66 and 142.72 mg/L (AUC 0.65; 0.81; 0.81).

Conclusão: O aumento da PCR nos 1^o, 3^o e 5^o dias de pós-operatório são os principais preditores de ILC e apresentam uma boa acuidade.

Palavras-chave: Infecção do local cirúrgico; cirurgia colorretal; fatores preditivos

ABSTRACT

Background: Despite all the scientific and technical progress observed in surgery in the last decades, surgical site infection (SSI) in colorectal surgery remains high and leads to significant implications in clinical outcomes and hospital costs.

Aims: To assess the rate of SSI and identify predictive factors in elective colorectal surgery.

Methods: Patients submitted to elective intestinal resection with primary anastomosis between 01-08-2013 and 31-08-2014 were prospectively recruited. Patients demographic data, surgical procedure performed, potential clinical and analytic parameters of SSI, surgical morbidity, and hospital stay length were prospectively recorded.

Results: 139 patients (median age 70 years old, 59% male) were enrolled. The most common indication for surgery was colorectal malignant disease (100 patients, 71.9%). Seventy-nine (56.8%) procedures were performed with laparoscopy, SSI occurred in 27 patients (19.4%) with anastomotic leak diagnosed in 5 patients (3.6%) with a 60-day mortality rate of 0.7%. No difference was found in SSI rate between open and laparoscopic approaches. SSI led to a significant increase in the length of stay ($p=0.01$). Predictive parameters of SSI in the univariate analysis were pain, leukocytosis, neutrophilia, hypoalbuminemia and increased of C-reactive protein (CRP). In the multivariate analysis only CRP showed to be a significant predictor of SSI at the 1st and 3rd postoperative day (POD). At POD5, both increased neutrophil count and CRP were predictive of SSI. The optimal cut-offs for CRP at POD1, POD3 and POD5 were respectively 71.99, 96.66 and 142.72 mg/L (AUC 0.65; 0.81; 0.81).

Conclusion: Increased CRP in the postoperative days 1, 3 and 5 was the main predictor of SSI with a very good diagnostic accuracy.

Keywords: Surgical site infection; colorectal surgery; predictive factors

BACKGROUND

Surgical site infection (SSI) are among the most frequent postoperative colorectal surgery complications.¹ SSI are also the most common type of healthcare-associated infections representing 21.8% of all infections, along with pneumonia.² They entail significant morbidity, high costs, readmission, absence from work and mortality. Despite scientific and technical progress and institutional efforts were successful in reducing SSI, namely

on colonic and rectal surgery, these consequences remain high.³ Several organizations (governmental and non-governmental) expend considerable time and resources in epidemiologic surveillance and clinical research regarding this issue.

Studies and interventions had appropriately focused mainly how to reduce the factors that cause infection. However, this may be difficult to achieve, particularly in colorectal surgery.⁴ Another way to approach this issue, in order to reduce associated

¹Department of Surgery, Digestive Surgery Service, Hospital de Santo António, Centro Hospitalar do Porto.

²Department of Surgery- Vascular Surgery Service, Hospital de Santo António, Centro Hospitalar do Porto

³Department of Community Health, Instituto de Ciências Biomédicas Abel Salazar

Correspondência: Marisa D. Santos • E-mail: marisadsantos@gmail.com • Morada: Largo Abel Salazar, 4099-003 Porto, Portugal • Telemóvel: 9917610718

TABLE 1

Patients' characteristics

	All patients (n=139)	SSI (n=27; 19.4%)	No-SSI (n=112; 80.6%)	p-value
Male sex, n (%)	82 (59.0)	18 (66.7)	64 (57.1)	0.37
Age (years), median (IQR)	70 (58-78)	75 (55-78)	69 (58-78)	0.92
ASA-class, n (%)				
I	5 (3.6)	1 (3.7)	4 (3.6)	0.71
II	89 (64.0)	16 (59.3)	73 (65.2)	
III	43 (30.9)	9 (33.3)	34 (30.4)	
IV	2 (1.4)	1 (3.7)	1 (0.9)	
Previous abdominal surgeries, n (%)	53 (38.1)	9 (33.3)	44 (39.3)	0.57
Indication for surgery				
Malignant disease	100 (71.9)	19 (70.4)	81 (72.3)	0.97
Benign lesions	30 (21.6)	6 (22.2)	24 (21.4)	
Inflammatory bowel disease	9 (6.5)	2 (7.4)	7 (6.2)	
Surgical approach				
Open	60 (43.2)	15 (55.6)	45 (40.2)	0.15
Laparoscopic	79 (56.8)	12 (44.4)	67 (59.8)	
Procedure				
Ileocecal resection	8 (5.76)	2 (7.71)	6 (5.4)	0.63
Right colectomy	38 (27.3)	7(25.9)	31 (27.7)	
Left colectomy	11 (7.9)	0	11 (9.8)	
Segmental colectomy	10 (7.2)	2 (7.4)	8 (7.1)	
Total colectomy	10 (7.2)	4 (14.8)	6 (5.4)	
Sigmoid colectomy	18 (13.0)	3 (11.1)	15 (13.4)	
Anterior resection of rectum	33 (23.7)	6 (22.)	27 (24.1)	
Abdomino-perineal resection	4 (2.9)	1 (3.7)	3 (2.7)	
Entero-colonic anastomosis	7 (5.0)	2 (7.4)	5 (4.5)	
Operation time (minutes), median (IQR)	180 (150-214)	193 (150-232)	180 (150-210)	
Length of Stay (days), median (IQR)	7 (6-11)	14.5 (10-18)	7 (5-8)	<0.001

morbidity and mortality, is the identification of predictive risk factors, mainly the early signs. Early diagnosis and treatment of infectious complications has proven to establish a significant impact on clinical and economical outcomes.⁵

Significant efforts have been made in order to identify risk factors of SSI in colorectal surgery.⁶ Previously described risk factors include:

- Patient-specific: age;^{6,7} functional status before surgery;⁶ American Society of Anesthesiologists (ASA) class;^{6,8} increased body mass index (BMI);^{6, 8-11} sarcopenia;⁷ history of chronic obstructive pulmonary disease,⁸ smoking,^{6, 8} alcohol consumption;⁶ wound class 3/4,⁸ sepsis,⁸ corticosteroid administration;⁸ disseminated cancer;¹² higher

glucose level;¹² underlying disease;¹³

- Preoperative: neoadjuvant chemoradiotherapy;¹⁴ hematocrit;⁶
- Per-operative: open surgery in some studies^{6,8,10} and laparoscopic in others;¹⁵ duration of surgical procedure;^{8,11,15} ileostomy at the beginning of the operation;¹² patient temperature < 36°C for greater than 60 minutes;¹² initial diagnosis of inflammatory bowel disease (IBD);¹⁵ presence of an abscess at surgery;¹¹ surgical procedure length;^{15,16} surgeon's case volume;¹² intraoperative contamination;¹⁰ stoma creation;¹⁷ blood transfusion;^{12, 18} length of antimicrobial administration;¹⁹ not using wound protection.¹⁰ Nomograms for SSI risk prediction have been

■ TABLE 2

Characterization of SSI cases

Patient ID	Clavien-Dindo	Clavien-Dindo 3/4/5	SSI Classification	Anastomotic leak	Surgical reintervention	Percutaneous drainage	Readmission <30 days - reason	Death
1	3a	Yes	O/S	-	-	Yes	-	-
8	2	-	O/S	-	-	-	-	-
10	3a	Yes	O/S	-	-	Yes	-	-
13	2	-	I	-	-	-	-	-
19	2	-	O/S	-	-	-	Intestinal obstruction	-
35	2	-	O/S	-	-	-	-	-
36	2	-	O/S	-	-	-	-	-
45	2	-	I	-	-	-	-	-
51	2	-	O/S	-	-	-	-	-
62	3b	Yes	O/S	Yes	Yes	-	-	-
63	4	Yes	O/S	Yes	Yes	-	-	-
69	2	-	O/S	-	-	-	-	-
75	5	Yes	O/S	-	-	Yes	SSI - O/S	Yes
77	3a	Yes	O/S	-	-	Yes	-	-
81	2	-	I	-	-	-	-	-
90	2	-	O/S	-	-	-	-	-
91	2	-	O/S	-	-	-	-	-
101	2	-	I	-	-	-	-	-
106	2	-	I	-	-	-	-	-
119	2	-	I	-	-	-	-	-
120	2	-	I	-	-	-	-	-
124	2	-	O/S	-	-	-	-	-
135	3b	Yes	O/S	Yes	Yes	-	-	-
140	3b	Yes	O/S	Yes	Yes	-	-	-
141	2	-	I	-	-	-	-	-
143	3b	Yes	O/S	Yes	Yes	-	-	-
149	2	-	I	-	-	-	-	-

Abbreviations: I - incisional (superficial or deep); O/S - organ/space.

proposed including highly statistically significant predictors of infection: age, alcohol abuse, ASA classification, stoma closure, open approach, BMI, and hematocrit.⁶

The complication signs are the aim of several studies, searching for the most sensitive and specific, including those associated with sepsis:

- Clinical: pain, tachycardia and hypotension;

- Analytic: white blood cell count (WBC); elevated C-reactive protein (CRP).^{11, 20}

AIMS

The aim of this study was to evaluate the rate of SSI in elective colorectal surgery with primary anastomosis and its impact in terms of morbidity and length of stay (LoS), and to identify clini-

■ TABLE 3

Surgical site infection according to surgical approach

SSI (27/139; 19.4%)	Laparoscopy (n=79; 56.8%)	Laparotomy (n=60; 43.2%)	p
Incisional infections	4; 5.1%	5; 8.3%	0.683
Organ/space infection	11; 13.9%	7; 11.7%	0.397
Organ/space infection + anastomotic leak	3; 3.8%	2; 3.3%	0.12
TOTAL	15; 19.0%	12; 20.0%	0.15

cal and laboratorial parameters with predictive value for the diagnosis of these infections. Early identification of signs of SSI may enable earlier interventions and better results.

METHODS

This prospective study was performed at a tertiary care hospital. Selected patients include those who were submitted to elective intestinal resection with primary anastomosis between 01-08-2013 and 31-08-2014 in our tertiary referral center. Patients demographic data, surgical procedure performed, operative findings, clinical evaluations and laboratorial results, pathological report, morbidity and duration of hospital stay were prospectively entered into a computerized database. Laboratory values were analyzed based on the laboratory range of normality. Clinical and laboratorial parameters were recorded in four main time moments: pre-operative; 1st, 3rd and 5th postoperative day (POD).

Surgical procedures were performed by board certified surgeons or by residents under their direct supervision. Standard preoperative antibiotic prophylaxis and postoperative thromboembolism prophylaxis was performed. Anastomosis were performed both manually or stapled accordingly the usual clinical practice or personal choice of the surgeon. Patients whose surgery was converted were considered as having an open procedure. Complications were graded according to the Dindo–Clavien classification.²¹ SSI were defined according to the Centers of Disease Control guidelines.²² When clinical or subclinical anastomotic leaks were suspected, the diagnosis were confirmed by imaging study (CT scan or WS contrast) or by reoperation.

For this study we defined two subset of lower GI leak:

clinical minor – presence of luminal contents through the drain or wound site causing local inflammation, e.g. fever (temperature >38° C), leukocytosis (white cell count > 12.000/litre), fecal discharge from wound or drain or abscess. Leak may also be detected on imaging studies. In those cases, prolonged hospital stay were required but without surgical intervention.

Clinical major – the signals and symptoms may be similar to clinical minor but the presence of a severe disruption to anastomosis required surgical intervention.

The primary endpoint of this study was to determine the most accurate and earliest clinical signs and laboratory parameters for the detection of SSI. Secondary endpoints were to determine SSI rate and its impact in LoS and to compare laparoscopic and open approaches relative to SSI. The present study was approved by the hospital Ethics Committee.

STATISTICAL ANALYSIS

Continuous variables are presented as mean (standard deviation) if non-normally distributed or; median (interquartile range) if non-normally distributed. Categorical variables are presented as counts and proportions. Comparison between SSI vs. no-SSI groups was performed using χ^2 test for categorical variables, independent samples t-test for normally distributed continuous variables and Mann-Whitney U test when the distribution was skewed. Friedman test was used to analyze the differences in each predictor parameter across the various time points after surgery – POD 1, 3 and 5.

A univariate analysis was performed for variables potentially associated with SSI. Then, the predictors of SSI were assessed using a multivariate logistic regression with backward variable selection for each POD.

■ TABLE 4

Univariate analysis of each clinical and analytic potential predictor of SSI for each time point after surgery (Mann-Whitney U test) and across time points (Friedman test)

Variables	P-value (Mann-Whitney U)	P-value (Friedman)
Pain		
POD1	0.02	
POD3	0.03	<0.001
POD5	0.10	
Temperature		
POD1	0.61	
POD3	0.26	0.13
POD5	0.48	
Heart Rate		
POD1	0.94	
POD3	0.03	0.03
POD5	0.06	
Systolic Blood Pressure		
POD1	0.30	
POD3	0.19	<0.001
POD5	0.21	
White Blood Cell Count		
POD1	0.12	
POD3	0.01	<0.001
POD5	0.001	
Neutrophil Count		
POD1	0.06	
POD3	0.003	<0.001
POD5	<0.001	
Hemoglobin		
POD1	0.31	
POD3	0.06	0.73
POD5	0.07	
Albumin		
POD1	0.62	
POD3	0.004	0.053
POD5	0.014	
C-Reactive Protein		
POD1	0.021	
POD3	<0.001	<0.001
POD5	<0.001	

The ability of CRP to discriminate SSI from no-SSI patients was evaluated by the receiver operating characteristic (ROC) curve and the area under the curve (AUC). The optimal CRP cut-off value for SSI prediction was estimated using the Youden Index.

Statistical analysis was performed using STATA 12.1 (StataCorp LP) and IBM SPSS Statistics for Windows 22.0 (IBM Corp) softwares. Statistical

significance was set for p values of less than 0.05.

RESULTS

A total of 139 consecutive patients submitted to an elective colorectal surgery with primary anastomosis between 01-08-2013 and 31-08-2014 were identified from a dedicated prospective database and enrolled in the present study. Patients cha-

TABLE 5

Predictors of SSI at POD5 – Multivariate analysis

Variable	OR (95%CI)	p-value
CRP (per 10mg/L increase)	1.18 (1.08-1.30)	<0.001
Neutrophil Count (per 1.0x10 ⁹ /L)	1.36 (1.01-1.82)	0.042

TABLE 6

Diagnostic accuracy of CRP at POD1, POD3 and POD5 for SSI diagnosis

CRP	Optimal Cut-off (mg/L)	Sensitivity	Specificity	AUC (95%CI)	p-value
POD1	71.19	0.84	0.44	0.65 (0.53 -0.76)	0.021
POD3	96.66	0.85	0.58	0.81 (0.71-0.92)	<0.001
POD5	142.73	0.65	0.92	0.81 (0.70-0.92)	<0.001

racteristics and perioperative course as well as the analysis of their relation with the occurrence of SSI are presented in Table 1. Most patients were male (59%); median age was 70 years old; the ASA-class most represented were II followed by III (representing together 92.6% of patients); over 1/3 had previous abdominal surgeries; the most frequent indication for surgery was malignant disease followed by benign disease and lastly by IBD for which a specific group was created to reflect the specificities associated with these diseases. No statistically significant differences were found between SSI and no-SSI groups regarding gender, age, ASA-class, history of previous abdominal surgery or indication for surgery.

Regarding the surgical procedure, right colectomy was the most performed surgery followed by anterior resection of rectum and sigmoid colectomy. The preferred approach was laparoscopic and the overall median operative time was 180 minutes. There were no statistically significant differences between SSI and no-SSI groups regarding these variables. Applying Clavien-Dindo classification of complications we found: Grade II (n=18); Grade III (n=7); IV (n=1); V (n=1). This means that 9/27 (grades III/IV and V), i.e. 1/3 of complications implied significant morbidity.

SSI occurred in 27 patients (19.4%), of whom 1 died (0.7%) within 60 days. Most infections were organ/space (2/3) rather than incisional (1/3) (Table 2). There was no difference in the rate of SSI between surgical approaches (19.0% in

laparoscopy vs. 20.0% in laparotomy) (Table 3). Anastomotic leak occurred in 5 (3.6%) patients that needed surgical reintervention. Four cases of organ/space SSI were drained by percutaneous approach, without need for reoperation, even though one needed a second drainage due to recurrence after discharge. There was one case of mortality due to severe sepsis with consequent multiorgan dysfunction in a patient that was admitted in the UCI with concurring intra-abdominal abscess, pneumonia and urinary tract infection. LoS was significantly higher in the SSI group (p<0.001). LoS was significantly shorter for the laparoscopic approach [median (IQR) 7 (5-9) days for laparoscopy vs. 7 (6-14) for open surgery, p=0.01]. Two early (<30 days) readmissions occurred due to early intestinal obstruction and one recurrence of O/S SSI.

Predictive parameters of SSI in the univariate analysis for each time point after surgery and across time points are shown in Table 4. At POD1, only pain and CRP were significant predictors of SSI. At POD3, pain, heart rate, WBC count, neutrophil count, albumin and CRP were all predictors of SSI in univariate analysis. At POD5 clinical parameters lost their significance and only laboratory variables such as WBC count, neutrophils, albumin and CRP were predictors of SSI in the univariate analysis. CRP in SSI and no-SSI groups on POD 1, 3 and 5 are shown in Figure 1.

In the multivariate analysis only CRP showed to be a significant predictor of SSI at POD1 (OR 1.11 per 10mg/L increase, 95%CI 1.01-1.22,

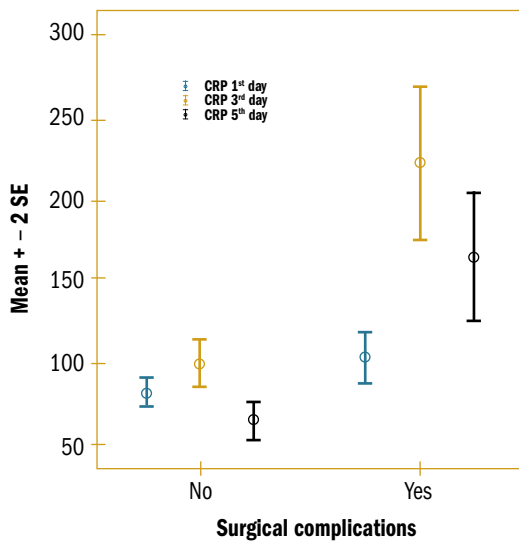


FIGURE 1. CRP range in SSI and no-SSI groups on POD 1,3 and 5

$p=0.036$) and POD3 (OR 1.15 per 10mg/L increase, 95%CI 1.09-1.22, $p<0.001$). At day 5, both increased neutrophil count and CRP were predictive of SSI (Table 5).

The optimal cut-offs for CRP at POD1, POD3 and POD5 were respectively 71.99, 96.66 and 142.72 mg/L, with an AUC respectively of 0.65, 0.81 and 0.81 (Table 6). CRP cutoffs had the highest sensitivity at POD3 (85%) and the highest specificity at POD5 (92%). At POD1, the OR of SSI for patients with CRP above the optimal cut-off of 71.19mg/L was 4.06 (95%CI 1.31-12.63) compared to patients with lower levels. At POD3, the OR of SSI rose to 7.65 (95%CI 2.45-23.87) for patients with CRP above 96.66mg/L. At POD5, patients with CRP values above 142.73mg/L had a risk of developing SSI 22.67 times higher than patients with lower CRP levels (OR 22.67, 95%CI 6.70-76.67).

DISCUSSION

Colorectal surgery complications are common and responsible for the most of morbidity, mortality and excess length of stay (LoS) in general surgery practice.^{11, 23} This is supported by our study that demonstrated significant morbidity due to SSI and increase of LoS. Increased CRP in the postoperative days 1, 3 and 5 was the main predictor of SSI with a very good diagnostic accuracy.

Regarding the absence of patients with Grade I complications of the Clavien-Dindo classification,

we can admit the possibility of under-reporting these complications because of the occasional difficulty of differentiating them from normal postoperative course. There were also some few cases of wound infections that were opened at the bedside, that could be classified as Grade I; however the need for additional interventions, namely pharmacological, may have upgraded them to higher levels of Clavien-Dindo classification. Most infections were organ/space (2/3) rather than incisional (1/3). This may reflect an under registry of simpler complications without need for intervention other than bedside drainage. The recognition of this bias is actually the basis of the principle of grading complications based on the therapy used to treat them, as has been previously stated in the widely used Clavien-Dindo classification.²¹ If invasive techniques are usually extensively reported, daily bedside gestures may not be taken notice and registered. However since Clavien-Dindo grade 1 complications entail minimal morbidity and need for intervention this would have little impact on the overall picture.

SSI did not significantly differ with the approach (laparoscopic vs. open), as could be expected, in neither incisional or organ/space infection. This may be due to reduced sample power or to the use of wound protector in open surgery. The anastomotic leak rate was also not significantly different between surgical approaches supporting the safety of laparoscopy.

Even though in univariate analysis clinical parameters seem to play a role as potential predictors of SSI, when analyzed in a multivariate analysis their predictive strength was lost and only analytic parameters showed relevance, namely: CRP on POD 1, 3 and 5; and neutrophil count on POD 5.

WBC and CRP are the most commonly used markers of postoperative infectious complications.¹¹ Some previous studies have shown that CRP had a high diagnostic accuracy for the early detection of inflammatory complications and the accuracy of WBC was significantly lower.²⁴ Monitoring CRP level in laparoscopic colorectal surgery demonstrated a high diagnostic accuracy for infectious complications, thus allowing for safe and early discharge.¹¹ CRP accuracy has been demonstrated both in open²⁵ and laparoscopic surgery¹¹ with different cutoffs having been suggested.

These differences depend on the POD studied and desired accuracy, i.e., sensibility/specificity and positive predictive value (PPV) / negative predictive value (NPV). One study describes that even though the magnitude of the systemic inflammatory response (SIR), as evidenced by CRP, following colon surgery had been shown to be greater in open than in laparoscopic resection, the threshold concentrations of C-reactive protein for the development of postoperative infective complications were remarkably similar on POD 3 and 4 in both approaches.²⁰ CRP value on POD 4 revealed a NPV for infectious complications of 89% and allowed safe and early discharge of selected patients after colorectal surgery.²⁵ This has been later confirmed in one meta-analysis that found a NPV of 84.3(80.8-87.3)% but, however, a PPV of 50.4(46.0-54.8)%.²⁶ The CRP cutoff suggested for open surgery was amazingly similar, ranging from 123-125mg/l, on two different studies.^{24, 27} Regarding laparoscopic surgery one study suggested a cutoff of 56mg/l for a diagnostic accuracy of 78%.¹¹

In this study CRP optimal cutoff value increased with time and this was accompanied by increasing odds ratio. By POD 5 the OR peaked and reached 22.67 what is in accordance with the expected lowering of CRP after 48h of the surgical insult if no infectious complication is associated.

LoS was significantly shorter for the laparoscopic approach. Since the groups proved comparable, this is probably related to other well-known benefits of laparoscopy such as pain control time to first defecation, resumption of diet.²⁸

As expected, need for surgical reintervention was more prevalent in the SSI group. Hospital Length of Stay (LoS) was also significantly longer in the SSI group.

CONCLUSIONS

The rate of SSI in colorectal surgery remains high and implies a significant increase in the LoS in these patients as well as in the need for reintervention. The main predictor of SSI in this study was the elevated CRP as early as at POD1, supporting the routine use for early detection of complications. ■

REFERENCES

- Alves A, Panis Y, Mathieu P, et al. Postoperative mortality and morbidity in french patients undergoing colorectal surgery: Results of a prospective multicenter study. *Archives of Surgery*. 2005;140(3):278-83.
- Magill SS, Edwards JR, Bamberg W, Beldavs ZG, Dumyati G, Kainer MA, et al.

- Multistate point-prevalence survey of health care-associated infections. *The New England journal of medicine*. 2014;370(13):1198-208.
- Centers for Disease Control and Prevention. 2013 National and State Healthcare-Associated Infections Progress Report. Published January 14, 2015. Available at www.cdc.gov/hai/progress-report/index.html.
- Ghuman A, Chan T, Karimuddin AA, Brown CJ, Raval MJ, Phang PT. Surgical Site Infection Rates Following Implementation of a Colorectal Closure Bundle in Elective Colorectal Surgeries. *Diseases of the colon and rectum*. 2015;58(11):1078-82.
- Law WL, Choi HK, Lee YM, Ho JW. The impact of postoperative complications on long-term outcomes following curative resection for colorectal cancer. *Annals of surgical oncology*. 2007;14(9):2559-66.
- Hedrick TL, Sawyer RG, Friel CM, Stukenborg GJ. A method for estimating the risk of surgical site infection in patients with abdominal colorectal procedures. *Diseases of the colon and rectum*. 2013;56(5):627-37.
- Lieffers JR, Bathe OF, Fassbender K, Winget M, Baracos VE. Sarcopenia is associated with postoperative infection and delayed recovery from colorectal cancer resection surgery. *British journal of cancer*. 2012;107(6):931-6.
- Kohut AY, Liu JJ, Stein DE, Sensenig R, Poggio JL. Patient-specific risk factors are predictive for postoperative adverse events in colorectal surgery: an American College of Surgeons National Surgical Quality Improvement Program-based analysis. *American journal of surgery*. 2015;209(2):219-29.
- Watanabe J, Tatsumi K, Ota M, Suwa Y, Suzuki S, Watanabe A, et al. The impact of visceral obesity on surgical outcomes of laparoscopic surgery for colon cancer. *International journal of colorectal disease*. 2014;29(3):343-51.
- Han J, Wang Z, Wei G, Yi B, Ma H, Gao Z, et al. [Risk factors associated with incisional surgical site infection in colorectal cancer surgery with primary anastomosis]. *Zhonghua wai ke za zhi [Chinese journal of surgery]*. 2014;52(6):415-9.
- Adamina M, Warschkow R, Naf F, Hummel B, Rduch T, Lange J, et al. Monitoring c-reactive protein after laparoscopic colorectal surgery excludes infectious complications and allows for safe and early discharge. *Surgical endoscopy*. 2014;28(10):2939-48.
- Shaffer VO, Baptiste CD, Liu Y, Srinivasan JK, Galloway JR, Sullivan PS, et al. Improving quality of surgical care and outcomes: factors impacting surgical site infection after colorectal resection. *The American surgeon*. 2014;80(8):759-63.
- Pendlimari R, Cima RR, Wolff BG, Pemberton JH, Huebner M. Diagnoses influence surgical site infections (SSI) in colorectal surgery: a must consideration for SSI reporting programs? *Journal of the American College of Surgeons*. 2012;214(4):574-80; discussion 80-1.
- Francis NK, Mason J, Salib E, Allanby L, Messenger D, Allison AS, et al. Factors predicting 30-day readmission after laparoscopic colorectal cancer surgery within an enhanced recovery programme. *Colorectal disease : the official journal of the Association of Coloproctology of Great Britain and Ireland*. 2015;17(7):O148-54.
- Turina M, Remzi FH, Dietz DW, Kiran RP, Seyidova-Khosknabi D, Hammel JP, et al. Quantification of risk for early unplanned readmission after rectal resection: a single-center study. *Journal of the American College of Surgeons*. 2013;217(2):200-8.
- Baucom RB, Phillips SE, Ehrenfeld JM, Holzman MD, Nealon WH, Sharp KW, et al. Defining intraoperative hypothermia in ventral hernia repair. *The Journal of surgical research*. 2014;190(1):385-90.
- Yamamoto S, Fujita S, Akasu T, Ishiguro S, Kobayashi Y, Moriya Y. Wound infection after elective laparoscopic surgery for colorectal carcinoma. *Surgical endoscopy*. 2007;21(12):2248-52.
- Halabi WJ, Jafari MD, Nguyen VQ, Carmichael JC, Mills S, Pigazzi A, et al. Blood transfusions in colorectal cancer surgery: incidence, outcomes, and predictive factors: an American College of Surgeons National Surgical Quality Improvement Program analysis. *American journal of surgery*. 2013;206(6):1024-32; discussion 32-3.
- Hagihara M, Suwa M, Ito Y, Muramatsu Y, Kato Y, Yamagishi Y, et al. Preventing surgical-site infections after colorectal surgery. *Journal of infection and chemotherapy : official journal of the Japan Society of Chemotherapy*. 2012;18(1):83-9.
- Ramanathan ML, MacKay G, Platt J, Horgan PG, McMillan DC. The impact of open versus laparoscopic resection for colon cancer on C-reactive protein concentrations as a predictor of postoperative infective complications. *Annals of surgical oncology*. 2015;22(3):938-43.
- Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Annals of surgery*. 2004;240(2):205-13.
- Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for Prevention of Surgical Site Infection, 1999. Centers for Disease Control and Prevention (CDC) Hospital Infection Control Practices Advisory Committee. *American journal of infection control*. 1999;27(2):97-132; quiz 3-4; discussion 96.
- Schilling PL, Dimick JB, Birkmeyer JD. Prioritizing quality improvement in general surgery. *Journal of the American College of Surgeons*. 2008;207(5):698-704.
- Warschkow R, Tarantino I, Torzewski M, Naf F, Lange J, Steffen T. Diagnostic accuracy of C-reactive protein and white blood cell counts in the early detection of inflammatory complications after open resection of colorectal cancer: a retrospective study of 1,187 patients. *International journal of colorectal disease*. 2011;26(11):1405-13.
- Warschkow R, Beutner U, Steffen T, Muller SA, Schmied BM, Guller U, et al. Safe and early discharge after colorectal surgery due to C-reactive protein: a diagnostic meta-analysis of 1832 patients. *Annals of surgery*. 2012;256(2):245-50.
- 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. *The British journal of surgery*. 2015;102(6):590-8.
- Ortega-Deballon P, Radais F, Facy O, d'Athis P, Masson D, Charles PE, et al. C-reactive protein is an early predictor of septic complications after elective colorectal surgery. *World journal of surgery*. 2010;34(4):808-14.
- Vennix S, Pelzers L, Bouvy N, Beets GL, Pierie JP, Wiggers T, et al. Laparoscopic versus open total mesorectal excision for rectal cancer. *The Cochrane database of systematic reviews*. 2014;4:Cd005200.