Original Article

Prevalence, Microbiological Profile, and Risk Factors of Surgical Site Infections in Saudi Patients with Colorectal Cancer

Marwh Gassim Aldriwesh[1,2], Abrar Alnodley[1], Norah Almutairi[1], Mohammed Algarni[2,3,4], Ayyob Alqarni[2,4,5], Bayan Albdah[6], Mutaib Mashraqi[7]

[1]Department of Clinical Laboratory Sciences, College of Applied Medical Sciences, King Saud Bin Abdulaziz University for Health Sciences, [2]King Abdullah International Medical Research Center, Departments of [3]Oncology and [5]General Surgery, Ministry of National Guard–Health Affairs, [4]Department of Medicine, College of Medicine, King Saud Bin Abdulaziz University for Health Sciences, [6]Department of Biostatistics and Bioinformatics, King Abdullah International Medical Research Center, Riyadh, [7]Department of Clinical Laboratory Sciences, College of Applied Medical Sciences, Najran University, Najran, Saudi Arabia

Abstract

Background: Resection surgery in patients with colorectal cancer (CRC) patients is associated with potential complications, including surgical site infection (SSI).

Objectives: To estimate the prevalence rate of SSI, identify the common pathogens responsible for SSI, and determine potential risk factors for SSI development in a cohort from Saudi Arabia.

Materials and Methods: Patients with CRC who underwent bowel resection surgery at King Abdulaziz Medical City, Riyadh, between January 01, 2016, and December 31, 2019, were retrospectively included. Demographics, comorbidities, surgical procedure data, and the results of preoperative laboratory tests were retrospectively collected from medical records through the health information system. The study population was divided into two groups: those who developed SSI and those who did not.

Results: A total of 92 patients with CRC who underwent resection surgery were included, of which 54 (58.7%) were males. The median age was 65 (IQR 55.5–75.0) years. SSI was observed in 25 (27.2%) patients. The most frequently isolated organisms were *Escherichia coli* and *Pseudomonas aeruginosa*, followed by *Klebsiella pneumoniae*, vancomycin-sensitive *Enterococcus faecium*, and methicillin-resistant *Staphylococcus aureus*. Three *E. coli* isolates were producers of extended-spectrum beta-lactamases, and two *K. pneumoniae* isolates exhibited a multidrug resistance profile. Low preoperative serum albumin level was identified as a significant independent risk factor for developing SSI (AOR = 0.853, 95% CI = 0.748–0.973, $P = 0.0181$).

Conclusion: The study found a notable prevalence of SSI among the included patients. Gram-negative bacteria were more involved in SSI events and were also associated with drug-resistance patterns. Gut microbiota bacteria

Address for correspondence: Dr. Marwh Gassim Aldriwesh, Department of Clinical Laboratory Sciences, College of Applied Medical Sciences, King Saud Bin Abdulaziz University for Health Sciences, P. O. Box 3660, Riyadh 11481, Saudi Arabia.
E-mail: aldriweshm@ksau-hs.edu.sa

Submitted: 02-Jan-2023 **Revised:** 27-Mar-2023 **Accepted:** 11-Jun-2023 **Published:** 15-Jul-2023

Access this article online	
Quick Response Code:	Website: https://journals.lww.com/sjmm
	DOI: 10.4103/sjmms.sjmms_3_23

How to cite this article: Aldriwesh MG, Alnodley A, Almutairi N, Algarni M, Alqarni A, Albdah B, *et al*. Prevalence, microbiological profile, and risk factors of surgical site infections in Saudi patients with colorectal cancer. Saudi J Med Med Sci 2023;11:208-18.

were most commonly involved in SSIs. Low preoperative serum albumin levels predicted the development of postoperative SSI, and thus its close monitoring and management before surgery could reduce the SSIs.

Keywords: Antimicrobial resistance, colorectal surgery, hypoalbuminemia, risk factors, Saudi Arabia, surgical site infection

INTRODUCTION

In colorectal resection surgery, the prevalence of SSI is estimated to range from 2.4% to 21.6%, according to the National Nosocomial Infection System of the US Centers for Disease Control and Prevention (CDC).[1] Moreover, the incidence rate of SSI related to colorectal cancer (CRC) is four times higher than any other abdominal surgery.[2] The development of SSI in patients who have undergone colorectal resection surgery might have a negative impact on their overall health status and result in longer hospitalization and readmission, which all contribute negatively to their quality of life and increase healthcare cost.[3]

According to the CDC, the identification of SSI is based on both clinical and microbiology laboratory observations. SSI is an infection that develops within 30 days after a surgical operation and meets at least one of the following criteria: purulent drainage, pain or tenderness, local swelling, and redness or heat.[4] It is classified into three classes according to the infected anatomical site: (1) superficial incisional SSI (i.e. infection in the skin or subcutaneous tissue); (2) deep incisional SSI (i.e. infection in deep soft tissue: fascia and muscle); and (3) organ/space SSI (i.e. infection in the organ or space apart from the incised abdominal wall layers).[4]

Microorganisms associated with CRC-related SSI basically originate from the patient's endogenous normal microbiota or from exogenous sources such as the hospital environment, surgical tools, or surgical team members.[5] According to the literature, the most frequent pathogens responsible for SSI in patients with CRC originate from the patient's normal microbiota that reside in the colon and rectum,[6] specifically Gram-negative bacilli (*Escherichia coli* and *Klebsiella pneumoniae*) and Gram-positive cocci (mainly *Enterococcus* species).[7] The Gram-positive cocci *Staphylococcus aureus* (which is known to inhabit anterior nares, nasopharynx, and skin) has also commonly been isolated from SSIs and is associated with a resistance pattern against multiple antibiotics, including oxacillin.[8-11] In contrast, *Pseudomonas aeruginosa*, an opportunistic Gram-negative bacillus that commonly inhabits hospital environments, has been documented as a significant exogenous pathogen in SSIs.[8,11,12] The emergence of *P. aeruginosa* in clinical settings might be due to poor infection control practices, including a lack of hand hygiene among surgical team members, or due to increased resistance patterns of Gram-negative pathogens against disinfectants.[13] Critically ill or immunocompromised patients with CRC may develop SSI associated with multi-drug resistant (MDR) microorganisms, which worsens the patient's well-being and increases the burden of treatment cost.[10] Therefore, the World Health Organization guidelines emphasize the importance of the proper use of antimicrobial prophylaxis to minimize the risk of antimicrobial resistance development.[14] Antimicrobial use was reported as one of the key exogenous inducers responsible for alterations in gut microbiota in terms of composition and function (dysbiosis).[15] Previous studies indicated that gut microbiota dysbiosis increases the development of MDR bacteria.[16]

Factors that might be associated with SSI development in patients with CRC are patient-related factors, intraoperative factors, and postoperative surgical site management.[17] For instance, the patient's status before surgery, such as age, comorbidities (diabetes, heart, or renal diseases), cancer stage, and nutritional status might influence the patient's immunity and susceptibility to develop SSI.[2,7,17] Intraoperative factors, which include the duration and type of surgery (emergency vs elective, open, or laparoscopic colectomy) and the surgeon's experience may also affect the patient's risk for SSI development.[6,7] Further, inadequate postoperative surgical management, including poor hand hygiene when changing dressings or use of unsterile dressings, might increase host susceptibility to SSI development.[10]

A recent study conducted in Greece in 2021 reported that significant risk factors for SSI development in patients with CRC were old age (>70 years), diabetes, American Society of Anesthesiologists (ASA) scores >2, and history of chronic steroid use.[7] Meanwhile, a study conducted in Japan found that independent risk factors for SSI development after laparoscopic CRC surgery were preoperative serum albumin levels ≤2.5 g/dL, use of functional end-to-end

anastomosis, and non-polydioxanone sutures-plus.[18] Therefore, risk factors could vary across countries and across settings, and thus studies are required to determine the local risk factors.

In Saudi Arabia, CRC is the first and third most frequently diagnosed malignant tumor among males and females, respectively;[19] however, there is limited data on the prevalence, associated pathogens, and the potential risk factors of SSI development in patients with CRC. Therefore, the objectives of the present study were to estimate the prevalence rate of SSI in a cohort of Saudi Arabian patients with CRC, identify the most common pathogens responsible for SSI and demonstrate their antimicrobial resistance pattern, and determine potential risk factors for SSI development.

MATERIALS AND METHODS

Study design, setting, and participants

In this retrospective cohort study, non-probability convenience sampling was applied. The study was conducted at King Abdulaziz Medical City–Riyadh and King Abdullah International Medical Research Centre, which are part of the Ministry of National Guard–Health Affairs (MNGHA), Saudi Arabia. MNGHA hospitals are tertiary healthcare hospitals and implement infection prevention and control program to prevent postoperative SSIs.

All accessible records of patients who met the inclusion criteria from January 01, 2016, to December 31, 2019, were accessed. The inclusion criteria consisted of adult patients with a confirmed diagnosis of CRC who underwent curative surgical resection, with or without SSI development.

Variables

Data were retrieved from admission, readmission, CRC surgery follow-up notes, and emergency visit records. The patients' demographics, comorbidities, CRC clinical and diagnostic data of CRC, surgical procedure, preoperative biochemistry test results, and hematology laboratory analysis findings were collected.

Procedures

The clinical specimens collected from suspected patients were sent to the Division of Microbiology, Department of Pathology and Laboratory Medicine, for pathogen identification. Exudate from the infected surgical incision site was collected using two cotton-tipped swabs and transported to the laboratory in a transport medium. If an anaerobic infection was anticipated, an anaerobic transport medium was used. Upon receipt of the surgical incision (wound) swab at the laboratory, the Gram staining was performed, and bacterial culture was prepared using MacConkey agar, chocolate agar, blood agar, and phenylethyl alcohol agar. Then, the inoculated agar plates were incubated at 35–37°C for at least 24 h. If an anaerobic infection was predicted, anaerobic media, including anaerobic brucella modified blood agar, brucella laked blood agar with kanamycin and vancomycin, Bacteroides bile esculin agar and thioglycolate broth, were used and the samples were immediately incubated under anaerobic conditions. The resultant culture might show the growth of a single microorganism or a mixture of two microorganisms or more: the dominating two microbes were then cultured and tested for antimicrobial susceptibility. A beta-lactamase test was performed for Gram-negative bacteria. In cases where *Enterococcus* spp. was noted, the presence of vancomycin-resistant *Enterococcus* (VRE) was investigated.

Sterile body fluid specimens, including abdominal fluid, were collected by aseptic aspiration using a sterile needle and then expelled into a sterile container and transported directly to the laboratory, with immediate processing. Upon receipt, the fluid specimen was centrifuged, and the sediment was used to prepare two Gram-stained smears and to inoculate directly to a Bact/Alert vial and then incubated in a Bact/Alert Microbial Detection System (BioMérieux, Inc., Durham, North Carolina, USA) for 5 days. The culture was examined daily, and if positive, the pathogen was identified and tested for antimicrobial susceptibility.

The peripheral blood specimens collected from the suspected patients were inoculated in a Bact/Alert vial and incubated in the Bact/Alert Microbial Detection System (BioMérieux, Inc., Durham, North Carolina, USA) for 5 days. Positive blood cultures were Gram stained, and the attending physician was notified directly of the results. From a positive aerobic blood culture, an inoculation was made into MacConkey agar, chocolate agar, and blood agar, and incubated at 37°C for at least 24 h. For positive anaerobic blood cultures, anaerobic media including Brucella agars were used and then incubated in a blood culture anaerobic jar at 37°C for at least 72 h. Antimicrobial susceptibility testing (AST) of coagulase-negative staphylococci and *Viridans streptococci* identified from the positive blood cultures was only performed on request.

AST of the isolated pathogens was performed with the automated Vitek 2 system (BioMérieux, Inc., Durham, North Carolina, USA), which is based on the broth microdilution method.[5] The minimum inhibitory concentration results were interpreted and categorized mainly into susceptible, intermediate, or resistance within 6 to 8 h.[5] Genotyping methods

were also performed to detect antimicrobial resistance genes described in methicillin-resistant *Staphylococcus aureus* (MRSA), VRE, carbapenem-resistant *Enterobacteriaceae* (CRE), and extended spectrum β-lactamase (ESBL) producers. MDR Gram-negative bacteria were identified as bacteria with resistance or intermediate susceptibility to a minimum of one antimicrobial agent in at least three of five antimicrobial classes: (1) beta-lactams (piperacillin or piperacillin/tazobactam), (2) aminoglycosides (amikacin or gentamicin), (3) fluoroquinolones (ciprofloxacin or levofloxacin), (4) cephalosporins (ceftazidime, cefotaxime, ceftriaxone, or cefepime), and (5) carbapenems (imipenem or meropenem).[20]

Outcomes

The primary outcomes were determining the prevalence rate of SSIs and the causative microorganisms and their antimicrobial susceptibility profile. The secondary outcome was the prediction of the independent risk factor for postoperative SSI development.

Statistical analysis

The included patients were divided into two groups for the analysis: those who developed SSI and those who did not develop SSI. Data analysis was performed using the statistical program SAS version 9.4. (SAS Institute Inc., North Carolina, USA). The patients' data were expressed as a percentage for categorical variables and as a median with the interquartile range (IQR) for continuous variables with non-normal data distribution. The association between the categorical variables was assessed using the Fisher exact test. The Wilcoxon two-sample test was applied to test the association between the continuous variables with non-normal data distribution. Statistical significance was defined as a P value of < 0.05.

Univariate and multivariate analyses were performed using the binary logit model to predict risk factors for SSI development in patients with CRC. The dependent variable was SSI, while the independent variables tested were diabetes, CRC stage, surgical procedure, preoperative blood transfusion, preoperative cancer treatment, serum albumin, white blood cells (WBCs), monocytes, neutrophils, hemoglobin, platelets, prothrombin time (PT), and international normalized ratio (INR). Multivariate analyses were adjusted for the following variables: diabetes, CRC stage, surgical procedure, perioperative blood transfusion, preoperative cancer treatment, potassium, serum albumin, glucose, WBCs, monocytes, neutrophils, hemoglobin, platelets, INR, and PT. A P value < 0.05 in the multivariate analysis indicated a statistically significant and independent risk factor for postoperative SSI development.

RESULTS

Clinical characteristics and laboratory parameters

The study included 92 patients with CRC who underwent curative surgical resection via laparoscopic colectomy or open colectomy. Of these, 38 were females (41.3%) and 54 were males (58.7%). The patient's median age was 65 years (IQR: 55.5–75.0 years). The details of their demographics, comorbidities, CRC diagnostic data, and preoperative biochemistry, and hematology laboratory findings are provided in Table 1.

A total of 25 (27.2%) patients developed SSI, of whom 22 (88.0%) had incisional SSI (superficial = 15, 60.0%; deep: 7, 28.0%) and 3 (12.0%) had organ/space SSI. The prevalence rate of SSI was significantly higher in males (n = 20; 80.0%) than in females (n = 5; 20.0%) (P = 0.0165). The highest prevalence of SSI (60.0%, n = 15) was in the patients with CRC who had an ASA score of III (i.e. severe systemic disease).[21] Moreover, the patients diagnosed with CRC stage III and with cancer in the left-side colon had the highest prevalence rates of SSI at 40.0% (n = 10) and 72.0% (n = 18), respectively.

Preoperative biochemistry and hematology blood analyses for a wide range of laboratory parameters showed generally normal values, as detailed in Table 1. However, the preoperative hemoglobin level of all CRC patients was low, equivalent to 112.0 g/L (IQR: 130.0–98.0 g/L), with no significant difference between the patients who developed SSI and those who did not. Furthermore, the patients' preoperative blood coagulation profiles revealed a significant difference in PT and INR between the patients who developed SSI and those who did not (P = 0.0031 and P = 0.0447, respectively).

Microbiological findings

For the 25 patients who developed postoperative SSI, the microbiology laboratory results showed different bacterial species, including Gram-positive and Gram-negative bacteria [Table 2]. The most frequent bacteria isolated from the clinical specimens were *E. coli* and *P. aeruginosa*, each identified in four SSI cases (32.0%). *K. pneumoniae*, *E. faecium*, and *S. aureus* were also identified as causative pathogens of SSI. Furthermore, 6 of the 25 SSI cases (24.0%) were due to polymicrobial infection. From the microbiological findings, four culture-negative SSI cases (16.0%) were identified; no anaerobic bacteria were isolated.

The results of the AST of Gram-negative bacteria indicated that neither the *E. coli* nor the *P. aeruginosa* isolates expressed a MDR phenotype. However, three

Table 1: Clinical characteristics and laboratory parameters of the included patients (*N*=92)

Characteristics	Overall, *n* (%)	Postoperative SSI		*P*
		No (*n*=67), *n* (%)	Yes (*n*=25), *n* (%)	
Age	65.0 (75.0–55.5)	64.0 (74.0–54.0)	69.0 (76.0–60.0)	0.1892
Gender				
Female	38.0 (41.3)	33.0 (49.2)	5.0 (20.0)	0.0165
Male	54.0 (58.7)	34.0 (50.7)	20.0 (80.0)	
BMI (18.5–24.9 kg/m^2)	28.1 (30.3–23.2)	28.6 (30.4–23.1)	26.6 (30.2–23.3)	0.4663
Previous abdominal surgery	13.0 (14.1)	8.0 (11.9)	5.0 (20.0)	0.3296
Heart disease	15.0 (16.3)	12.0 (17.9)	3.0 (12.0)	0.7519
Chronic kidney disease	7.0 (7.6)	5.0 (7.4)	2.0 (8.0)	1.0000
Diabetes	47.0 (51.1)	33.0 (49.2)	14.0 (56.0)	0.6425
ASA score				
I	2.0 (2.2)	2.0 (2.9)	0	0.7218
II	29.0 (31.5)	23.0 (34.3)	6.0 (24.0)	
III	50.0 (54.3)	35.0 (52.2)	15.0 (60.0)	
IV	7.0 (7.6)	4.0 (5.9)	3.0 (12.0)	
CRC stage				
I	10.0 (10.8)	8.0 (11.9)	2.0 (8.0)	0.7911
II	27.0 (29.3)	19.0 (28.3)	8.0 (32.0)	
III	41.0 (44.5)	31.0 (46.2)	10.0 (40.0)	
IV	14.0 (15.2)	9.0 (13.4)	5.0 (20.0)	
Surgical procedure				
Laparoscopic colectomy	45.0 (48.9)	34.0 (50.7)	11.0 (44.0)	0.4935
Open colectomy	35.0 (38.0)	23.0 (34.3)	12.0 (48.0)	
Switched from laparoscopic colectomy to open colectomy	12.0 (13.0)	10.0 (14.9)	2.0 (8.0)	
CRC location				
Right colon	6.0 (6.5)	4.0 (5.9)	2.0 (8.0)	0.7409
Left colon	72.0 (78.2)	54.0 (80.6)	18.0 (72.0)	
Transverse colon	7.0 (7.6)	4.0 (5.9)	3.0 (12.0)	
Right and left colon	2.0 (2.1)	1.0 (1.5)	1.0 (4.0)	
Total colon	4.0 (4.3)	3.0 (4.5)	1.0 (4.0)	
Subtotal colon	1.0 (1.1)	1.0 (1.5)	0	
Preoperative anemia	70.0 (76.1)	51.0 (76.1)	19.0 (76.0)	1.0000
Perioperative blood transfusion	5.0 (5.4)	3.0 (4.5)	2.0 (8.0)	0.6103
Preoperative cancer treatment	29.0 (31.5)	18.0 (26.9)	11.0 (44.0)	0.1350
Preoperative biochemistry				
Estimated glomerular filtration rate (>60 mg/mmol)	101.0 (119.5–86.0)	102.0 (120.0–87.0)	99.0 (114.0–81.0)	0.4043
Serum creatinine†	67.0 (75.5–59.5)	66.0 (75.0–57.0)	68.0 (76.0–65.0)	0.1139
Blood urea nitrogen‡	3.8 (5.8–2.8)	3.5 (5.3–2.7)	4.5 (6.0–3.4)	0.1459
Uric acid§	278.5 (364.0–232.0)	279.5 (361.0–228.0)	274.5 (371.5–238.0)	0.5967
Bilirubin (3.4–20.5 μmol/L)	7.2 (10.6–5.7)	7.3 (11.0–5.8)	7.1 (9.8–5.7)	0.5997
Phosphorus (0.74–1.52 mmol/L)	1.1 (1.3–1.0)	1.1 (1.3–1.0)	1.2 (1.3–1.1)	0.3948
Calcium (2.1–2.55 mmol/L)	2.2 (2.3–2.1)	2.2 (2.3–2.1)	2.2 (2.3–2.1)	0.3974
Potassium (3.5–5.1 mmol/L)	4.2 (4.5–3.9)	4.3 (4.6–3.9)	4.0 (4.3–3.8)	0.0738
Sodium (136–145 mmol/L)	138.0 (140.0–136.0)	138.0 (140.0–136.0)	138.0 (140.0–137.0)	0.7471
Chloride (98–107 mmol/L)	106.0 (108.0–103.0)	106.0 (108.0–103.0)	105.0 (107.0–103.0)	0.4329
CO_2 (22–29 mmol/L)	22.0 (24.0–20.0)	22.0 (24.0–20.0)	24.0 (24.0–21.0)	0.1884
Total protein (64–83 g/L)	65.5 (70.0–61.5)	66.0 (71.0–62.0)	65.0 (68.0–60.0)	0.2313
Serum albumin (35–50 g/L)	37.0 (40.0–33.0)	37.0 (40.0–33.0)	36.0 (38.0–34.0)	0.4120
Glucose (2.9–7.8 mmol/L)	6.2 (8.5–5.0)	6.1 (7.8–4.9)	7.5 (11.1–5.5)	0.1104
Alkaline phosphatase (40–150 U/L)	81.0 (103.0–66.0)	80.5 (99.0–66.0)	87.5 (134.5–66.0)	0.2599
Alanine aminotransferase (5–55 U/L)	15.0 (20.0–11.0)	15.0 (20.0–12.0)	14.0 (18.5–10.0)	0.3681
Aspartate aminotransferase (5–34 U/L)	16.0 (21.0–13.0)	16.0 (21.0–13.0)	16.0 (21.0–12.5)	0.6086
Preoperative hematology laboratory analysis				
White blood cells (4–11×10^9/L)	7.4 (9.3–5.4)	7.5 (9.5–5.7)	6.9 (8.8–5.1)	0.2378
Basophils (0.0–0.1×10^9/L)	0.0 (0.1–0.0)	0.0 (0.1–0.0)	0.0 (0.1–0.0)	0.3332
Monocytes (0.1–1.1×10^9/L)	0.5 (0.6–0.4)	0.5 (0.7–0.4)	0.4 (0.6–0.3)	0.0964
Eosinophils (0.1–0.7×10^9/L)	0.2 (0.3–0.1)	0.2 (0.3–0.1)	0.2 (0.4–0.1)	0.2067
Neutrophils (2.0–7.5×10^9/L)	4.1 (6.2–3.1)	4.2 (6.1–3.4)	4.0 (8.2–2.4)	0.5339
Lymphocytes (1.0–4.4×10^9/L)	2.0 (2.5–1.4)	2.0 (2.4–1.6)	1.9 (3.2–1.4)	0.9545
Hemoglobin‖	112.0 (130.0–98.0)	111.0 (130.0–99.0)	116.0 (129.0–98.0)	0.9930
Red blood cell¶	4.4 (4.8–4.1)	4.4 (4.8–4.0)	4.4 (4.7–4.2)	0.6799
Hematocrit**	0.4 (0.4–0.3)	0.3 (0.4–0.3)	0.4 (0.4–0.3)	0.8160
Platelet (150–400×10^9/L)	302.5 (431.0–226.0)	303.0 (434.0–247.0)	283.0 (351.0–217.0)	0.3065
Preoperative blood coagulation profile††				

Contd...

Table 1: Contd...

Characteristics	Overall, *n* (%)	Postoperative SSI		*P*
		No (*n*=67), *n* (%)	Yes (*n*=25), *n* (%)	
PT (11–13.5 s)	11.3 (11.9–10.9)	11.2 (11.7–10.9)	11.9 (13.0–11.2)	0.0031
INR (0.8–1.2)	1.0 (1.1–1.0)	1.0 (1.1–1.0)	1.1 (1.1–1.0)	0.0447
Partial thromboplastin time (24.8–32.9 s)	27.3 (29.1–25.9)	27.3 (29.1–26.0)	27.2 (30.3–25.6)	0.5882

**Hematocrit: 0.42–0.54 and 0.36–0.54 for male and female, respectively. Normal ranges: †Serum creatinine: 64.0–110.0 μmol/L and 50.0–98.0 μmol/L for male and female, respectively, ‡Blood urea nitrogen: 3.0–9.2 mmol/L and 3.5–7.2 mmol for male and female, respectively, §Uric acid: 220.0–450.0 μmol/L and 150.0–370.0 μmol/L for male and female, respectively, ‖Hemoglobin: 135.0–180.0 g/L and 120–160 g/L for male and female, respectively, ¶Red blood cell: 4.5–6.1×10^{12}/L and 4.0–5.4×10^{12}/L for male and female, respectively, ††Three patients out of 92 were on warfarin before surgery (3.3%) and one patient out of 25 (of those who developed SSI) was on warfarin before surgery (4.0%). ASA – American Society of Anesthesiologists; BMI – Body mass index; CRC – Colorectal cancer; SSI – Surgical site infection; PT – Prothrombin time; INR – International normalized ratio

E. coli isolates were identified as ESBL producers. Two *K. pneumoniae* isolates resulted in a MDR resistance profile: one isolate was resistant to all the antimicrobial agents tested, including carbapenem, and the other isolate was cephalosporine-resistant *K. pneumoniae* [Table 2]. The Gram-positive bacterium *E. faecium* isolated from two SSI cases demonstrated a sensitivity pattern against vancomycin. However, the *S. aureus* isolate was resistant to oxacillin and was identified as MRSA.

Risk factors for surgical site infection development

In the univariate analysis, none of the variables were found to be significant risk factors related to SSI development in patients with CRC. However, in the multivariate logistic regression analysis, preoperative serum albumin level was identified as an independent risk factor for SSI development in patients with CRC (adjusted odds ratio [AOR]: 0.853; 95% confidence interval [CI]: 0.748–0.973; $P = 0.0181$) [Table 3].

DISCUSSION

This study found that in a cohort from Saudi Arabia, the prevalence of SSI in CRC patients is 27.2%, which is relatively higher than that reported in recent studies from China (3.7%), Spain (12.3%), and Greece (21.8%),[1,7,22] and relatively lower than that reported from Japan (32.1%).[23] The percentage of emergency surgery can influence the rate of SSIs in CRC; however, given that only 20% of the patients who developed SSI in the current study underwent emergency surgery, this may not be a plausible explanation for the noted differences in SSIs. Another potential explanation for these differences in SSI rates is the patient population: in the current study, about 54% of all included CRC patients had an ASA score of 3, whereas larger proportions of the population in the other studies with lower SSI rates had ASA scores of ≤2.0.[1,7,22] Therefore, this may indicate that CRC patients with severe systemic disease (ASA score ≥3.0) have a higher risk of developing SSI than patients with ASA ≤2.0.

The study found that the rate of SSI was significantly higher among males than females and also more common among those with CRC diagnosed on the left side of the colon than in other anatomical sites of the colon. However, these findings may be skewed by the fact that overall, the population of males was higher than females (58.7% vs. 41.3%, respectively), which is unsurprising given that CRC is more common in males,[24] and that most of the study population had left-sided CRC (78.2%).

In terms of the microbiological findings, the Gram-negative bacilli *E. coli* and *P. aeruginosa* were the most common pathogens isolated from the clinical specimens. *E. coli* is a facultative anaerobic bacterium belonging to the *Enterobacteriaceae* family and is considered part of the normal gut microbiota. It can be spread from one patient to another, especially in a hospital environment, or transmitted from its original location (gastrointestinal tract) to a normally sterile body site.[5] In contrast, *P. aeruginosa* is an aerobic bacterium belonging to the *Pseudomonadaceae* family. This bacterium is known to inhabit hospital environments, such as respiratory equipment, sinks, and showers.[5] The second most common pathogens isolated from SSI were *K. pneumoniae* (Gram-negative bacillus bacterium and a member of gut normal microbiota) and *E. faecium* (Gram-positive coccus bacterium that colonizes the human gut and is known to commonly cause nosocomial infections).[5]

Few studies on SSIs among CRC surgery patients have focused on the causative microorganisms. The predominance of *E. coli* observed in the current study is consistent with the findings of previous studies.[7,25] However, in a study published by Nakamura *et al*., who reported only five clinical cases of SSI in CRC patients, *Bacteroides spp.* (anaerobic bacterium and member of gut normal microbiota) were the most prevalent pathogens isolated.[26] However, none of the SSIs in the current study were caused by *Bacteroides spp.* In this context, and regardless of the specific genus and species type of isolated pathogens from SSIs, the results of the current and previous studies[7,25,26] indicate that gut microbiota bacteria are most commonly involved in SSI events.

Table 2: Microbiology profile of the patients who developed surgical site infection

Specimen	Gram staining	Causative microbe	Antimicrobial susceptibility test	
			Susceptible	Resistant
Wound swab*	Moderate WBCs and Gram-negative bacilli	*P. aeruginosa*	Ceftazidime, piperacillin-tazobactam, ciprofloxacin, gentamicin	None
Wound swab	Few WBCs and Gram-negative bacilli	*P. aeruginosa*	Ceftazidime, piperacillin-tazobactam, ciprofloxacin, gentamicin	None
Wound swab	Moderate WBCs and Gram-negative bacilli	*P. aeruginosa*	Ceftazidime, piperacillin-tazobactam, ciprofloxacin, gentamicin	None
Wound discharge*	Rare WBCs and Gram-negative bacilli	*P. aeruginosa*	Ceftazidime, piperacillin-tazobactam, ciprofloxacin, gentamicin	None
Wound swab	Moderate WBCs and Gram-negative bacilli	*E. coli*, ESBL	Ciprofloxacin, gentamicin Imipenem, meropenem, piperacillin-tazobactam, trimethoprim-sulfamethoxazole	Ampicillin, ceftriaxone
Wound swab	Moderate WBCs and Gram-negative bacilli	*E. coli*, ESBL	Gentamicin, imipenem, meropenem, piperacillin-tazobactam	Ampicillin, ceftriaxone, ciprofloxacin, trimethoprim-sulfamethoxazole
Wound swab	Rare WBCs and no organisms seen	*E. faecium*	Vancomycin	Ampicillin, gentamicin synergy
Wound swab	Rare WBCs and Gram-positive cocci	MRSA	Vancomycin, trimethoprim-sulfamethoxazole	Oxacillin, cefazolin, clindamycin, erythromycin
Wound swab	Few WBCs and no organisms seen	Skin flora	NA§	
Wound swab	Rare WBCs, Gram-positive bacilli and Gram-positive cocci	Skin flora	NA	
Wound swab	Rare WBCs, Gram-negative bacilli, Gram-positive cocci, and Gram-positive bacilli	Mixed Gram-positive and Gram-negative bacteria	NA	
Wound swab	Moderate WBCs and Gram-negative bacilli	Mixed Gram-positive and Gram-negative bacteria	NA	
Wound swab	Few WBCs and Gram-negative bacilli	Mixed Gram-positive and Gram-negative bacteria	NA	
Wound swab	Rare WBCs and no organisms seen	No growth	NA	
Wound discharge	Rare WBCs and no organisms seen	No growth	NA	
Abdominal aspiration‖	No WBCs and Gram-negative bacilli	Carbapenem resistant and cephalosporine resistant *K. pneumoniae*	None	Ampicillin, ceftriaxone, gentamicin, amikacin, trimethoprim-sulfamethoxazole, ciprofloxacin, imipenem, meropenem, piperacillin-tazobactam, colistin, tigecycline
Abdominal drain‖	Few WBCs, Gram-negative bacilli, and Gram-positive cocci	*E. coli*, ESBL	Imipenem, meropenem, piperacillin-tazobactam, ciprofloxacin, amikacin, trimethoprim-sulfamethoxazole	Ampicillin, ceftriaxone, gentamicin
		E. faecium	Vancomycin	Ampicillin
Abdominal aspiration	Many WBCs and Gram-positive cocci	*S. anginosus*	Not performed¶	
Abdominal aspiration	Moderate WBCs and no organisms	Mixed Gram-positive bacteria	NA	
Abdominal aspiration	Rare WBCs and no organisms seen	Mixed Gram-positive bacteria	NA	
Abdominal aspiration	Rare WBCs and no organisms seen	No growth	NA	
Abdominal aspiration	Few WBCs and no organisms seen	No growth	NA	
Peripheral blood**	Gram-negative bacilli	*E. coli*	Ceftriaxone, ciprofloxacin, gentamicin	Ampicillin, piperacillin-tazobactam, trimethoprim-sulfamethoxazole
Peripheral blood	Gram-negative bacilli	Cephalosporine, β-lactam and β-lactam/β-lactamase inhibitor combination resistant *K. pneumoniae*	Ciprofloxacin, amikacin, imipenem, meropenem, piperacillin-tazobactam	Ampicillin, ceftriaxone, trimethoprim-sulfamethoxazole, gentamicin

Contd...

Table 2: Contd...

Specimen	Gram staining	Causative microbe	Antimicrobial susceptibility test	
			Susceptible	Resistant
Peripheral blood	Gram-positive cocci	*S. viridans* group	Not performed	

*Wound swab and wound discharge were processed as wound culture; §NA – The antimicrobial susceptibility test was NA as per laboratory guidelines; ‖Abdominal aspiration and abdominal drain were processed as sterile body fluid culture; ¶The AST was performed if only was requested by attending physician; **Peripheral blood was processed as blood culture. AST – Antimicrobial susceptibility testing, MRSA – Methicillin-resistant *S. aureus; P. aeruginosa – Pseudomonas aeruginosa;* WBCs – White blood cells; *E. coli – Escherichia coli;* NA – Not applicable; *E. faecium – Enterococcus faecium; S. anginosus – Streptococcus anginosus; K. pneumonia – Klebsiella pneumonia; S. viridans – Streptococcus viridans; Staphylococcus aureus – S. aureus;* ESBL – Extended spectrum β-lactamase (the isolate was resistant to all β-lactam and β-lactam/β-lactamase inhibitor combination except carbapenems)

Table 3: Predictors of postoperative surgical site infection in patients with colorectal cancer who underwent curative surgical resection

Variable	Univariate analysis			Multivariate analysis*		
	OR	95% CI	*P*	AOR	95% CI	*P*
Diabetes	1.311	0.521–3.302	0.5652	0.642	0.157–2.618	0.5364
CRC stage						
II	1.684	0.291–9.744	0.5609	0.476	0.038–5.915	0.5637
III	1.290	0.234–7.098	0.7699	0.398	0.036–4.341	0.4496
IV	2.222	0.334–14.796	0.4093	0.288	0.019–4.482	0.3745
Surgical procedure						
Open colectomy	1.613	0.609–4.273	0.3364	0.498	0.115–2.152	0.3506
Switched from laparoscopic colectomy to open colectomy	0.618	0.117–3.262	0.5709	0.460	0.049–4.341	0.4979
Preoperative blood transfusion	1.856	0.291–11.82	0.5128	2.669	0.22–32.39	0.4408
Preoperative cancer treatment	2.139	0.822–5.568	0.1194	3.076	0.828–11.428	0.0933
Serum albumin	0.953	0.886–1.026	0.1984	0.853	0.748–0.973	0.0181
White blood cell	0.921	0.776–1.093	0.3475	0.935	0.628–1.393	0.7416
Monocyte	0.188	0.017–2.02	0.1675	0.090	0.001–6.199	0.2652
Neutrophil	1.017	0.978–1.057	0.4103	1.087	0.893–1.323	0.4041
Hemoglobin	1.005	0.983–1.027	0.6723	1.023	0.985–1.063	0.2299
Platelet	0.999	0.995–1.002	0.4271	1.001	0.995–1.007	0.7111
PT	0.998	0.986–1.009	0.6816	0.998	0.984–1.012	0.7643
INR	0.846	0.467–1.533	0.5811	0.813	0.306–2.161	0.6784

*Multivariate analyses were adjusted for the following variables – Diabetes, CRC stage, surgical procedure, perioperative blood transfusion, preoperative cancer treatment, serum albumin, white blood cells, monocytes, neutrophils, hemoglobin, platelets, INR and PT. INR – International normalized ratio; PT – Prothrombin time; CRC – Colorectal cancer; OR – Odds ratio; AOR – Adjusted OR; CI – Confidence interval

There is an increasing trend in the incidence rate of SSIs caused by antimicrobial-resistant pathogens. This might reflect a higher proportion of severely ill, immunocompromised patients or improper use of antimicrobial prophylaxis.[10] However, the AST of isolated pathogens from SSIs, specifically after CRC surgery, has scarcely been investigated. Previous studies that reported the microbiology profile of SSIs in CRC patients did not examine antimicrobial susceptibility and resistance patterns of isolated pathogens,[7,25,26] which makes comparisons with such studies difficult. The presence of antimicrobial resistance negatively impacts patients' health due to the need for prolonged hospitalization, extended antimicrobial therapy duration, increased morbidity and mortality, and requirement of a new antimicrobial therapy, which could increase the risk of toxicity, such as renal injury and *Clostridium difficile* infection.[15,27] A previous prospective, global, multicenter cohort study conducted to investigate SSIs after abdominal surgery reported that patients in low- and middle-income countries (LMICs) were at higher risk of developing SSIs than patients in high-income countries and that these countries might have greater rates of antimicrobial resistance.[28] In a more recent review, the authors highlighted the burden of SSIs as the most frequent hospital-acquired infection, particularly in LMICs.[29] The higher SSI rates observed in LMICs might result from inadequate compliance with the surgical antibiotic prophylaxis guidelines (in terms of administration time and duration) to prevent SSI or due to the unavailability of antibiotics guidelines in some healthcare institutions.[29]

The variables included in our univariate and multivariate analyses to determine the risk factors for SSI development in CRC patients have previously been reported to be independent risk factors. For instance, patient-associated factors, including diabetes, CRC stage, preoperative serum albumin and hemoglobin levels, and WBC count, have been reported as independent risk factors for SSI development.[18,30-35] Similarly, surgery-associated factors, such as blood loss and blood transfusion, and the type of surgical procedures (open colectomy versus laparoscopic colectomy) were highlighted as independent risk factors for SSI development.[26,36-38]

Preoperative chemotherapy and radiotherapy have also been shown to be independent risk factors for SSI development.[3,39] However, no variable in the current study was found to be a significant risk factor in the univariate analysis.

While the median value of preoperative serum albumin levels between patients who developed SSIs (median: 36.0 g/L [IQR 38.0–34.0]) and those who did not (median: 37.0 g/L [IQR 40.0–33.0]) was not determined to be a significant risk factor in the univariate analysis, in the multivariate analysis,[40] a lower preoperative serum albumin level was found to be a significant independent risk factor for SSI development in CRC patients. This finding was consistent with those reported previously.[18,30,33] Serum albumin is a key nourishment indicator, a low level of which reflects a malnourishment state.[41] A previous review discussed the negative impact of low albumin levels on postoperative recovery, including low collagen synthesis, low tissue healing and granuloma development in surgical wounds which eventually leads to a delay in the healing process.[42] Further, malignancy is associated with inadequate oral intake, intestinal blockage, intestinal fistula, poor absorption, and loss of large volumes from the gastrointestinal tract, which results in the malnourished state frequently observed in colorectal surgery patients.[41] From a biological point of view, the nourishment status of a patient plays a primary role in the immune system.[43] Therefore, immunity alterations induced by malnutrition might increase the risk of SSI and the duration of hospitalization, mortality, morbidity, readmission, and, consequently, the economic burden.[44] Therefore, more emphasis is being placed on preoperative nutritional status and nutritional support for patients by recommending the use of formulas rich in amino acids, anti-inflammatory factors, and antioxidants.[45]

The current study examined the preoperative blood coagulation profiles and indicated a significant difference in median values of PT and INR between the patients who developed SSIs and those who did not ($P = 0.0031$ and $P = 0.0447$, respectively). In the multivariate analysis, neither PT nor INR were identified as predictors for SSI. The higher PT and INR median values observed in patients with CRC who developed SSI might be mediated by differential effects of proinflammatory cytokines.[46]

Strengths and Limitations

CRC is one of the most common cancers in Saudi Arabia, yet this is the first study from the country to provide the SSI rates in patients who have undergone CRC surgery as well as to present the microbiological profile of the associated pathogens and the potential risk factors of the SSIs in these patients.

However, the study has some limitations. The high prevalence of SSI reported herein might be due to the small sample size obtained from the single-center CRC patient cohort. The small sample size might also influence the univariate and multivariate analysis results. However, our findings are compatible with those reported previously. Nonetheless, large-scale prospective studies are needed to obtain results that can be validated and generalized.

CONCLUSION

The study found that about one-fourth of the CRC patients who underwent resection surgery developed SSIs. Gram-negative bacteria were more involved in SSI events and were also associated with drug-resistance patterns. In addition, gut microbiota bacteria were found to be most commonly involved in SSI events. The preoperative serum albumin level was identified as an independent and significant risk factor for SSI development, highlighting the need for careful nutritional status evaluation and management before surgery.

Ethical consideration

The study received ethical approval from the Institutional Review Board of King Abdullah International Medical Research Centre (KAIMRC), Ministry of National Guard Health Affairs (MNGHA), Riyadh, Saudi Arabia (Protocol Approval No.: RYD-22-417780-1495; date: February 3, 2022). The requirement for patient consent was waived owing to the study's retrospective design. In addition, the procedures followed were in accordance with the Declaration of Helsinki, 2013.

Data availability statement

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

Peer review

This article was peer-reviewed by three independent and anonymous reviewers.

Author contributions

Conceptualization: M.G.A. and M.M.; Methodology: M.G.A., M.A., A.A., A.Alnodley, N.A., and M.M.; Data analysis, B.A.; Writing – original draft preparation: M.G.A.; Writing – review and editing: M.G.A., A.A., M.A., M.M., B.A.; Supervision: M.G.A.

All authors have read and agreed to the published version of the manuscript.

Acknowledgement

We thank Ms. Raghad Alaqeel, Ms. Dina Alsaidalani and Ms. Sarah Albawardi at the Department of Clinical Laboratory Sciences, College of Applied Medical Sciences, King Saud bin Abdulaziz University for Health Sciences for their contribution in data collection.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Hou TY, Gan HQ, Zhou JF, Gong YJ, Li LY, Zhang XQ, *et al.* Incidence of and risk factors for surgical site infection after colorectal surgery: A multiple-center prospective study of 3,663 consecutive patients in China. Int J Infect Dis 2020;96:676-81.
2. Pak H, Maghsoudi LH, Soltanian A, Gholami F. Surgical complications in colorectal cancer patients. Ann Med Surg 2020;55:13-8.
3. Ikeda A, Fukunaga Y, Akiyoshi T, Nagayama S, Nagasaki T, Yamaguchi T, *et al.* Wound infection in colorectal cancer resections through a laparoscopic approach: A single-center prospective observational study of over 3000 cases. Discov Oncol 2021;12:2.
4. Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR, Committee THICPA. Guideline for prevention of surgical site infection, 1999. Infect Control Hosp Epidemiol 1999;20:247-80. Available from: https://www.cambridge.org/core/journals/infection-control-and-hospital-epidemiology/article/abs/guideline-for-prevention-of-surgical-site-infection-1999/31585A523649826D6497F019D0907A60. [Last accessed on 2022 Jul 29].
5. Tille P. Bailey & Scott's Diagnostic Microbiology-e-Book; Amsterdam, The Netherlands: Elsevier Health Sciences; 2015.
6. Pochhammer J, Köhler J, Schäffer M. Colorectal surgical site infections and their causative pathogens: Differences between left- and right-side resections. Surg Infect (Larchmt) 2019;20:62-70.
7. Panos G, Mulita F, Akinosoglou K, Liolis E, Kaplanis C, Tchabashvili L, *et al.* Risk of surgical site infections after colorectal surgery and the most frequent pathogens isolated: A prospective single-Centre observational study. Med Glas (Zenica) 2021;18:438-43.
8. Călina D, Docea AO, Rosu L, Zlatian O, Rosu AF, Anghelina F, *et al.* Antimicrobial resistance development following surgical site infections. Mol Med Rep 2017;15:681-8.
9. Hassan RS, Osman SO, Aabdeen MA, Mohamed WE, Hassan RS, Mohamed SO. Incidence and root causes of surgical site infections after gastrointestinal surgery at a public teaching hospital in Sudan. Patient Saf Surg 2020;14:45.
10. Owens CD, Stoessel K. Surgical site infections: Epidemiology, microbiology and prevention. J Hosp Infect 2008;70 Suppl 2:3-10.
11. Misha G, Chelkeba L, Melaku T. Bacterial profile and antimicrobial susceptibility patterns of isolates among patients diagnosed with surgical site infection at a tertiary teaching hospital in Ethiopia: A prospective cohort study. Ann Clin Microbiol Antimicrob 2021;20:33.
12. Oguntibeju OO, Rau N. Occurrence of Pseudomonas Aeruginosa in Post-Operative Wound Infection; 2004. Available from: www.pjms.com.pk. Last accessed date 26 June 2023.
13. McDonnell G, Russell AD. Antiseptics and disinfectants: Activity, action, and resistance. Clin Microbiol Rev 1999;12:147-79.
14. Allegranzi B, Zayed B, Bischoff P, Kubilay NZ, de Jonge S, de Vries F, *et al.* New WHO recommendations on intraoperative and postoperative measures for surgical site infection prevention: An evidence-based global perspective. Lancet Infect Dis 2016;16:e288-303.
15. Menz BD, Charani E, Gordon DL, Leather AJ, Moonesinghe SR, Phillips CJ. Surgical antibiotic prophylaxis in an era of antibiotic resistance: Common resistant bacteria and wider considerations for practice. Infect Drug Resist 2021;14:5235-52.
16. Matzaras R, Nikopoulou A, Protonotariou E, Christaki E. Gut microbiota modulation and prevention of dysbiosis as an alternative approach to antimicrobial resistance: A narrative review. Yale J Biol Med 2022;95:479-94.
17. Banaszkiewicz Z, Cierzniakowska K, Tojek K, Kozłowska E, Jawień A. Surgical site infection among patients after colorectal cancer surgery. Pol Przegl Chir 2017;89:9-15.
18. Nakamura T, Takayama Y, Sato T, Watanabe M. Risk factors for wound infection after laparoscopic surgery for colon cancer. Surg Laparosc Endosc Percutan Tech 2020;30:45-8.
19. Alyabsi M, Algarni M, Alshammari K. Trends in colorectal cancer incidence rates in Saudi Arabia (2001-2016) using Saudi national registry: Early versus late-onset disease. Front Oncol 2021;11:730689.
20. Weiner LM, Webb AK, Limbago B, Dudeck MA, Patel J, Kallen AJ, *et al.* Antimicrobial-resistant pathogens associated with healthcare-associated infections: Summary of data reported to the national healthcare safety network at the centers for disease control and prevention, 2011-2014. Infect Control Hosp Epidemiol 2016;37:1288-301.
21. Daabiss M. American Society of Anaesthesiologists physical status classification. Indian J Anaesth 2011;55:111-5.
22. Páramo-Zunzunegui J, Alonso-García M, Rodríguez-Villar D, Drewniak-Jakubowska J, Calvo-Espino P, Cuberes-Montserrat R, *et al.* Incidence of surgical infection and risk factors in colorectal surgery – A prospective cohort study. Cir Cir 2021;89:156-62.
23. Watanabe M, Suzuki H, Nomura S, Maejima K, Chihara N, Komine O, *et al.* Risk factors for surgical site infection in emergency colorectal surgery: A retrospective analysis. Surg Infect (Larchmt) 2014;15:256-61.
24. Wong MC, Ding H, Wang J, Chan PS, Huang J. Prevalence and risk factors of colorectal cancer in Asia. Intest Res 2019;17:317-29.
25. Du M, Liu B, Li M, Cao J, Liu D, Wang Z, *et al.* Multicenter surveillance study of surgical site infection and its risk factors in radical resection of colon or rectal carcinoma. BMC Infect Dis 2019;19:411.
26. Nakamura T, Mitomi H, Ihara A, Onozato W, Sato T, Ozawa H, *et al.* Risk factors for wound infection after surgery for colorectal cancer. World J Surg 2008;32:1138-41.
27. Branch-Elliman W, O'Brien W, Strymish J, Itani K, Wyatt C, Gupta K. Association of duration and type of surgical prophylaxis with antimicrobial-associated adverse events. JAMA Surg 2019;154:590-8.
28. Bhangu A, Ademuyiwa AO, Aguilera ML, Alexander P, Al-Saqqa SW, Borda-Luque G, *et al.* Surgical site infection after gastrointestinal surgery in high-income, middle-income, and low-income countries: A prospective, international, multicentre cohort study. Lancet Infect Dis 2018;18:516-25.
29. Mwita JC, Ogunleye OO, Olalekan A, Kalungia AC, Kurdi A, Saleem Z, *et al.* Key issues surrounding appropriate antibiotic use for prevention of surgical site infections in low- and middle-income countries: A narrative review and the implications. Int J Gen Med 2021;14:515-30.
30. Dominioni L, Imperatori A, Rotolo N, Rovera F. Risk factors for surgical infections. Surg Infect (Larchmt) 2006;7 Suppl 2:S9-12.
31. Silvestri M, Dobrinja C, Scomersi S, Giudici F, Turoldo A, Princic E, *et al.* Modifiable and non-modifiable risk factors for surgical site infection after colorectal surgery: A single-center experience. Surg Today 2018;48:338-45.
32. Kamboj M, Childers T, Sugalski J, Antonelli D, Bingener-Casey J, Cannon J, *et al.* Risk of surgical site infection (SSI) following colorectal resection is higher in patients with disseminated cancer: An NCCN member cohort study. Infect Control Hosp Epidemiol 2018;39:555-62.
33. Tanaka T, Sato T, Yamashita K, Hosoda K, Nakamura T, Watanabe M. Effect of preoperative nutritional status on surgical site infection in

colorectal cancer resection. Dig Surg 2017;34:68-77.
34. Liu L, Liu L, Liang LC, Zhu ZQ, Wan X, Dai HB, *et al*. Impact of preoperative anemia on perioperative outcomes in patients undergoing elective colorectal surgery. Gastroenterol Res Pract 2018;2018:2417028.
35. Moyes LH, Leitch EF, McKee RF, Anderson JH, Horgan PG, McMillan DC. Preoperative systemic inflammation predicts postoperative infectious complications in patients undergoing curative resection for colorectal cancer. Br J Cancer 2009;100:1236-9.
36. Tang R, Chen HH, Wang YL, Changchien CR, Chen JS, Hsu KC, *et al*. Risk factors for surgical site infection after elective resection of the colon and rectum: A single-center prospective study of 2,809 consecutive patients. Ann Surg 2001;234:181-9.
37. Boni L, Benevento A, Rovera F, Dionigi G, Di Giuseppe M, Bertoglio C, *et al*. Infective complications in laparoscopic surgery. Surg Infect (Larchmt) 2006;7 Suppl 2:S109-11.
38. Kirchhoff P, Clavien PA, Hahnloser D. Complications in colorectal surgery: Risk factors and preventive strategies. Patient Saf Surg 2010;4:5.
39. Konishi T, Watanabe T, Kishimoto J, Nagawa H. Elective colon and rectal surgery differ in risk factors for wound infection: Results of prospective surveillance. Ann Surg 2006;244:758-63.
40. Mengual-Macenlle N, Marcos PJ, Golpe R, González-Rivas D. Multivariate analysis in thoracic research. J Thorac Dis 2015;7:E2-6.
41. Maykel JA. Perioperative nutrition support in colorectal surgery. In: Complexities in Colorectal Surgery: Decision-Making and Management. New York: Springer; 2014. p. 29-44.
42. Truong A, Hanna MH, Moghadamyeghaneh Z, Stamos MJ. Implications of preoperative hypoalbuminemia in colorectal surgery. World J Gastrointest Surg 2016;8:353-62.
43. Mainous MR, Deitch EA. Nutrition and infection. Surg Clin North Am 1994;74:659-76.
44. Culebras JM. Malnutrition in the twenty-first century: An epidemic affecting surgical outcome. Surg Infect (Larchmt) 2013;14:237-43.
45. Mazaki T, Ishii Y, Murai I. Immunoenhancing enteral and parenteral nutrition for gastrointestinal surgery: A multiple-treatments meta-analysis. Ann Surg 2015;261:662-9.
46. Levi M, Keller TT, van Gorp E, ten Cate H. Infection and inflammation and the coagulation system. Cardiovasc Res 2003;60:26-39.