Risk Factors Affecting Surgical Site Infections in Colorectal Cancer Surgery: Analysis of National Multicenter Data

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ABSTRACT

Aim: Surgical site infections (SSIs) are a significant complication in colorectal cancer (CRC) surgery. This study investigates the risk factors affecting SSI in CRC using national data.

Method: Prospective data collected from the Turkish Colon and Rectum Surgery Association Colorectal Cancer Database were retrospectively analyzed. A total of 1,216 patients who underwent surgery between July 2018 and March 2022 were included in the study. Factors affecting SSI were evaluated using multivariate analysis.

Results: The total SSI rate was 13.98% (9.29% superficial, 2.06% deep, and 2.63% organ/space). In univariate analyses, the presence of SSI was associated with several factors, including high body mass index (BMI), advanced TNM stage, presence of coronary artery disease (CAD), presence of concurrent malignancy, high American Society of Anesthesiologists score, receiving neoadjuvant therapy, emergency operation, open surgery, hand anastomosis, anastomosis configuration, iatrogenic ureter injury, simultaneous prostate resection, postoperative blood transfusion, evisceration, prolonged ileus, anastomotic leak, urinary fistula, urinary retention, postoperative bleeding, postoperative pneumonia, postoperative renal failure, reoperation and need for readmission. In multivariate analysis, high BMI [odds ratio (OR): 1.51, 95% confidence interval (CI): 1.02-2.21, p=0.0354], advanced stage disease (OR: 2.06, 95% CI: 1.38-3.07, p=0.0004), CAD (OR: 1.85, 95% CI: 1.14-3.01, p=0.0120), concurrent malignancy (OR: 3.35, 95% CI: 1.64-6.84, p=0.0009), receiving neoadjuvant therapy (OR: 1.76, 95% CI: 1.18-2.61, p=0.0048), emergency operation (OR: 3.26, 95% CI: 1.84-5.78, p<0.0001), postoperative blood transfusion (OR: 2.44, 95% CI: 1.67-3.56, p<0.0001) were identified as independent risk factors.

Conclusion: SSI following CRC is still a problem in our country. In this study, risk factors similar to those reported in the literature were detected. **Keywords:** Surgical site infection, colorectal cancer, prevention

Introduction

Infection, bleeding, and even death were seen as common complications of surgery before the mid-19th century. Thanks to pioneers such as Ignaz Semmelweis and Joseph Lister, a breakthrough has been made in surgical site infections (SSIs) and the associated problems. The positive momentum of the development of disinfection and sterilization has been maintained with the technical developments that enable it and the increase in antibiotic therapy options.¹ Despite this

progress, SSIs continue to constitute more than a third of healthcare-associated infections today and continue to be a significant health problem.²

When all types of operations are considered, the overall pooled incidence of SSI is estimated to be 2.5%.³ However, when looking specifically at digestive system surgery, this rate can rise above 11%.⁴ Therefore, SSI is of particular importance in colorectal surgery. Furthermore, SSI brings a significant additional cost burden for health systems. In the United



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States, the annual cost of SSI is estimated to be between 3.5 and 10 billion dollars.⁵ It has been reported that cases of SSI developing following colorectal operations can double the costs of index hospitalization and increase the 30-day costs by six times due to increased hospital stay.⁶ A study conducted in Turkey showed that the index hospitalization cost increases by 1.6 times in patients who develop an SSI.⁷

In addition to all these negative effects, there are studies reporting that SSI developed following colorectal cancer (CRC) surgery also negatively affects oncological outcomes.^{8,9} The Centers for Disease Control and Prevention (CDC) declared that no positive improvement was recorded in the rate of SSI following colon surgery in its last two reports, the 2021 and 2022 National and State Healthcare-Associated Infections Progress Reports.^{10,11} Thus, factors affecting SSI following colorectal surgery continue to be an important topic of research today in view of improving outcomes. This study aims to identify the factors affecting SSI in CRC surgery using a national database.

Materials and Methods

Patient Selection

The study protocol was approved by a Uludağ University Faculty of Medicine Clinical Research Ethics Committee (approval no: 2023-17/44, date: 19.09.2023).

Data were obtained from the national Colorectal Cancer Database (CCD) of the Turkish Society of Colon and Rectal Surgery (TSCRS). Preoperative, operative and short-term (30 days) postoperative data of patients who underwent curative colon or rectal resection due to CRC are prospectively entered into this database. In total, 1,216 consecutive cases from 18 centers involving surgery due to colon or rectal cancer between July 2018 and March 2022 were included in the study.

Variables Examined

In the TSCRS-CCD, the data entry process is performed by the responsible colorectal surgeons from each data-providing center, and the entered data are then verified by the CCD working study group. Here, SSIs are defined according to the CDC classification.¹² The factors examined for their effect on SSI were grouped as patient- or disease-related, operationrelated, and postoperative factors. Patients were divided into two groups: those who developed SSI and those who did not. The main patient-related factors examined were age, gender, body mass index (BMI), hypertension (HT), diabetes mellitus (DM), coronary artery disease (CAD), chronic obstructive pulmonary disease (COPD), chronic kidney failure (CKF), smoking, accompanying malignancy status, past surgical history, and American Society of Anesthesiologists (ASA) score. The main disease-related factors were tumor localization, TNM stage, and neoadjuvant treatment status. The American Joint Committee on Cancer staging manual (8th edition)¹³ was used for TNM staging.

Operative setting (emergency/elective), operation time, operator, open or minimally invasive operation, anastomosis type (hand/stapler), anastomosis configuration (end-to-end, end-to-side, side-to-end, side-to side, j pouch), stoma formation, perioperative blood transfusion, iatrogenic organ injury, and simultaneous organ resections were the operation-related factors.

Postoperative factors examined for their effect on SSI were postoperative blood transfusion, wound evisceration, prolonged ileus, anastomotic leak, urinary retention, urinary fistula, postoperative bleeding, postoperative acute kidney failure, reoperation, and readmission.

Statistical Analysis

Continuous variables are expressed as mean ± standard deviation, time variables as percentile, and categorical variables as number (%). The significance between categorical variables was analyzed using Fisher's exact test or the chi-square test, and the significance between continuous variables was analyzed using the t-test or Wilcoxon rank-sum test. Independent risk factors were determined using logistic regression analysis and expressed by odds ratio (OR). Data were transferred to the JMP[®] (version 17.0. SAS Institute Inc., Cary, NC, 1989-2023) statistical package program, and statistical analyses were performed.

Results

The overall SSI rate was 13.98% (9.29% superficial incisional, 2.06% deep incisional, and 2.63% organ/space). Patient and disease-related factors, such as age, gender, DM, HT, COPD, CKF, smoking, past surgical history, and tumor localization, did not show a significant relationship with the presence of SSI in univariate analyses. The presence of SSI was found to be associated with factors such as high BMI, presence of CAD, presence of accompanying malignancy, high ASA score, receiving neoadjuvant treatment, and locally advanced clinical TNM stage. The patient-related factors are summarized in Table 1.

When the relationship between operation-related factors and the presence of SSI was examined, operation time (being above the 75th percentile), the operator being an assistant/ specialist, stoma formation status, and preoperative blood transfusion did not show a significant relationship. Emergency operation, open surgery, anastomotic technique, anastomosis configuration, iatrogenic ureter injury, simultaneous partial prostatectomy, and postoperative blood transfusion were found to be associated with the presence of SSI. The operationrelated factors are presented in Table 2. Among postoperative factors, evisceration, prolonged ileus, anastomotic leak, urinary fistula, urinary retention, postoperative bleeding, postoperative pneumonia, postoperative kidney failure, increased reoperation, and need for readmission were associated with the presence of SSI. The postoperative factors are detailed in Table 3. Factors showing a significant relationship with the presence of SSI were included in the multivariate analysis. Accordingly, BMI, advanced stage disease, CAD, accompanying malignancy, receiving neoadjuvant treatment, emergency operation, and postoperative blood transfusion were determined to be independent risk factors. The results of the multivariate analysis are summarized in Table 4.

Table 1. Patient-related factors

Variable		SSI (+), n (%)	SSI (-), n (%)	p value
Age		63.69±0.95	62.68±0.38	0.32
Gender	Female	56 (11.76)	420 (88.24)	0.07
	Male	114 (15.41)	626 (84.59)	
BMI		27.46±0.34	26.28±0.13	0.0015
НТ	Yes	67 (14.47)	396 (85.53)	0.69
HI	No	103 (13.68)	650 (86.32)	
DM	Yes	42 (16.54)	212 (83.46)	0.10
	No	128 (13.31)	834 (86.69)	0.10
CAD	Yes	32 (20.25)	126 (79.75)	0.0148
CAD	No	138 (13.04)	920 (86.96)	0.0110
COPD	Yes	8 (15.38)	44 (84.62)	0.76
	No	162 (13.92)	1,002 (86.08)	0.70
CKE	Yes	5 (27.78)	13 (72.22)	0.08
	No	165 (13.77)	1,033 (86.23)	0.00
Malignancy	Yes	13 (24.53)	40 (75.47)	0.0236
Manghaney	No	157 (13.5)	1,006 (86.5)	
Smoking	Yes	21 (13.91)	130 (86.09)	0.97
Smoking	No	149 (13.99)	916 (86.01)	
Tumor localization	Colon	100 (12.71)	687 (87.29)	0.07
	Rectum	70 (16.36)	358 (83.64)	
	1	14 (7.87)	164 (92.13)	
TNM stage	2	31 (10.51)	264 (89.49)	<0.0001
	3	83 (20.34)	325 (79.66)	
	4	26 (19.7)	106 (80.3)	
ASA score	1	28 (9.86)	256 (90.14)	
	2	97 (14.1)	591 (85.9)	
	3	41 (17.83)	189 (82.17)	0.0369
	4	3 (25)	9 (75)	
	5	1 (50)	1 (50)	
Neoadiuvant therapy	Yes	72 (19.2)	303 (80.8)	0.0005
	No	98 (11.68)	741 (88.32)	0.0005
Previous surgery	Yes	47 (16.49)	238 (83.51)	0.15
	No	122 (13.15)	806 (86.85)	

Variables reported in ^{*}median (minimum-maximum) or [#]mean ± standard deviation. N: Number of studies reporting the variable, SSI: Surgical site infection, BMI: Body mass index, HT: Hypertension, DM: Diabetes mellitus, CAD: Coronary artery disease, COPD: Chronic obstructive pulmonary disease, CKF: Chronic kidney failure, ASA: American Society of Anesthesiologists

Discussion

SSI is a significant clinical problem that negatively affects morbidity, mortality, and cost, and potentially worsens oncological outcomes. There are complex and numerous factors related to the patient, surgeon, operation, and postoperative care that affect the risk of SSI. The CDC reports that around half of SSIs can be reduced if a focus is placed on correctable factors. In the present study, points that could be effective in reducing SSI are highlighted beyond the commonly reported measures.

In addition to providing an idea about the general medical condition of the patients, the ASA score can show a significant relationship with the presence of SSI. In fact, SSI is significantly common in patients with a high ASA score (>2).¹⁴ In previously conducted studies, a high ASA score is reported as a risk factor for SSI following CRC surgery.^{15,16} In a study examining the risk factors for SSI following laparoscopic colon cancer surgery, Nakamura et al.¹⁷ did not find the ASA score to be a significant variable. However, in the present study, patients with an ASA score of >1 were evaluated as high ASA

score. In the literature, when a high ASA score is taken as >2, it is mostly considered as a significant variable in terms of SSI. However, although a significant relationship was found in univariate analyses in the present study, the ASA score was not determined to be an independent variable.

In this study, obesity and the presence of CAD were determined to be independent risk factors for the development of SSI. On the contrary, the presence of HT, DM, and COPD were found not to be independent risk factors for the development of SSI. Studies on the risk posed by the presence of DM and HT in terms of SSI present complex results. While some publications emphasize that DM is an independent risk factor,^{18,19} in a prospective study examining risk factors for SSI following colorectal resection, it was stated that DM and HT were not independent variables.²⁰ When combined with the results of the present study, it becomes important whether factors such as DM and HT cause microcirculatory damage that can result in SSI development in the patient beyond their presence. When CAD is considered as vasculopathy developing in the organism with the effect of DM, HT, hyperlipidemia, smoking,

Table 2.	. Operation-related factor	rs
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Variable		SSI (+), n (%)	SSI (-), n (%)	p-value	
Operative condition	Emergent	23 (26.14)	65 (73.86)	0.0006	
	Elective	147 (13.03)	981 (86.97)	0.0006	
Operation time (>75 percentile)				0.56	
Operator	Specialist	161 (14.07)	983 (85.93)	0.7	
	Resident	9 (12.5)	63 (87.5)	0.7	
Or anotice annual ab	Open	120 (19.11)	508 (80.89)	<0.0001	
Operative approach	Minimally invasive	50 (8.5)	538 (91.5)		
	Hand sewn	12 (13.33)	78 (86.67)		
Anastomosis	Staple	119 (12.04)	869 (87.96)	0.0036	
	None	17 (26.56)	47 (73.44)		
	J pouch	2 (28.57)	5 (71.43)		
	End-end	56 (9.33)	544 (90.67)		
Anastomosis configuration	End-side	5 (10.2)	44 (89.8)	0.0132	
	Side-end	25 (16.45)	127 (83.55)		
	Side-side	43 (15.93)	227 (84.07)		
Stome	+	56 (14.78)	323 (85.22)	0.21	
Stoma	-	93 (12.14)	673 (87.86)	0.21	
Dari amanativa bland tu	+	8 (12.5)	56 (87.5)	0.71	
Peri-operative blood tx	-	162 (14.1)	987 (85.9)	0.71	
Tatua gania suntan inismu	+	3 (50)	3 (50)	0.0390	
latrogenic ureter injury	-	167 (13.8)	1,043 (86.2)	0.0309	
Cimultan acus prostato reception	+	3 (75)	1 (25)	0.0007	
Simultaneous prostate resection	-	167 (13.78)	1,045 (86.22)	0.0097	

Variables reported in 'median (minimum-maximum) or #mean ± standard deviation. SSI: Surgical site infection, N: number of studies reporting the variable

and many other factors, the fact that, unlike DM and HT, the disease was found to be an independent risk factor for SSI in the present study provides some resolution to the contradictory results in the literature.

Similarly, obesity (BMI >30) was found to be an independent variable in terms of SSI. Obesity is a commonly reported

risk factor for SSI.²¹ In a study conducted on a large-scale CRC surgery series, Shariq et al.²² reported that there was a significant risk increase for SSI and other wound complications in patients exhibiting metabolic syndrome criteria. Taking a holistic view in terms of CAD and obesity, these results are consistent with those obtained in the present study.

Table 3. Postoperative factors

Variable		SSI (+), n (%)	SSI (-), n (%)	p value
Postoperative blood tx	Yes	69 (22.19)	242 (77.81)	<0.0001
	No	101 (11.17)	803 (88.83)	
Evisceration	Yes	12 (60)	8 (40)	-0.0001
	No	158 (13.21)	1,038 (86.79)	<0.0001
	Yes	21 (22.83)	71 (77.17)	0.0100
Prototiged lieus	No	149 (13.26)	975 (86.74)	0.0109
Amost on atia lack	Yes	20 (33.9)	39 (66.1)	.0.0001
Anastomotic leak	No	111 (10.89)	908 (89.11)	<0.0001
I Luin and not on tion	Yes	8 (30.77)	18 (69.23)	0.126
Offinary retention	No	162 (13.61)	1,028 (86.39)	0.120
Luin and fistula	Yes	3 (60)	2 (40)	0.0217
Urinary fistula	No	167 (13.79)	1,044 (86.21)	
Postoperative bleeding	Yes	5 (38.46)	165 (13.72)	0.0252
	No	8 (61.54)	1,038 (86.28)	0.0232
Postoperative pneumonia	Yes	4 (44.44)	5 (55.56)	0.0262
	No	166 (13.75)	1,041 (86.25)	0.0203
Postoperative AKF	Yes	5 (33.33)	10 (66.67)	0.0465
	No	165 (13.74)	1,036 (86.26)	0.0403
Reoperation	Yes	34 (42.5)	46 (57.5)	<0.00001
	No	136 (11.98)	999 (88.02)	
Readmission	Yes	40 (37.38)	67 (62.62)	-0.0001
	No	130 (11.72)	979 (88.28)	<0.0001

Variables reported in ^{*}median (minimum-maximum) or [#]mean ± standard deviation. N: number of studies reporting the variable, SSI: Surgical site infection, AKF: Acute kidney failure

Table 4. Multivariate analysis

Variable	OR	CI (95%)	p value
High BMI (>30)	1.51	1.02-2.21	0.0354
Advanced stage disease (TNM 3 and 4)	2.06	1.38-3.07	0.0004
CAD	1.85	1.14-3.01	0.0120
Accompanying malignancy	3.35	1.64-6.84	0.0009
Received neoadjuvant treatment	1.76	1.18-2.61	0.0048
Emergency operation	3.26	1.84-5.78	<0.0001
Postoperative blood transfusion	2.44	1.67-3.56	<0.0001

Variables reported in median (minimum-maximum) or mean \pm standard deviation. N: number of studies reporting the variable. OR: Odds ratio, CI: Confidence interval, BMI: Body mass index, CAD: Coronary artery disease

It is known that malignancies weaken immunity by disrupting the balances of cellular and humoral immune responses and weaken defense against infectious complications.²³ This effect arises from cytokine release resulting from a warning mechanism caused by tumor cells, and in studies based on the fact that this mechanism may be more pronounced in advanced stage tumors, it is reported that the presence of advanced stage and metastatic tumors is a risk factor for SSI.²⁴⁻²⁶ In the present study, both advanced stage disease (TNM stage 3 and 4) and the presence of accompanying malignancy were determined to be independent risk factors for SSI.

Neoadjuvant chemoradiotherapy (NCRT) has been reported to cause an increase in SSI and other complications due to its negative effects on local microvascular structure in the pelvic region in rectum surgery and systemic effects in colon surgery.^{27,28} In the present study, having received NCRT was found to be a significant risk factor for SSI. This result may be significant in terms of tumor stage and localization and multivariate analysis.

Emergency operative setting potentiates many factors related to the patient, operation, and operator, posing an additional risk of mortality and morbidity. In a previous study, it was stated that emergency resections in CRC surgery could be associated with high morbidity, mortality, and even poor oncological outcomes.²⁹ In the present study, the risk of developing SSI following CRC surgery performed under emergency conditions was found to be 3.26 times higher compared with elective cases.

It is well known that allogeneic blood transfusion leads to an increase in pro-inflammatory cytokines, causing an immunocompromised picture. In this regard, many studies examining the relationship between perioperative blood transfusion and SSI have reported significant results.30 Some studies aimed to specify a threshold value for the amount of transfusion that causes a significant risk increase, whereas others examined the direct effect of the presence of transfusion.³¹ Even meta-analyses report conflicting results on blood transfusion as a risk factor for SSI.32,33 In the present study, the relationship between preoperative blood transfusion and postoperative blood transfusion with the presence of SSI was examined separately, and the latter was determined to be an independent risk factor. The significance of blood transfusion in the postoperative period in this regard may be associated with the addition of factors such as transfusionrelated immune modulation, transfusion reactions, and agents coming through the transfused blood product to induce immune weakness brought about by surgical stress.

Study Limitations

The major limitation of this study is its retrospective design. As such, data entry errors may be present, despite all patient data entered into the TSCRS-CCD being cross-checked by CCD study group members. Data were obtained from a database including certain variables, and investigating other potential risk factors was not possible since patient chart review was not feasible. However, studying prospectively maintained, multicentric, and national data gives this study its clinical value.

Conclusion

The SSI rate determined in the present study is consistent with the data in the existing literature. According to our results, selective postoperative blood transfusion, avoiding unnecessary neoadjuvant therapy, optimizing prehabilitation, and expanding CRC screening may help reducing SSI rate following CRC surgery. SSI will continue to be a significant issue in surgical practice, and there is a need for the continuity of more extensive studies on this subject.

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Ethics

Ethics Committee Approval: The study protocol was approved by a Uludağ University Faculty of Medicine Clinical Research Ethics Committee (approval no: 2023-17/44, date: 19.09.2023).

Informed Consent: Retrospective study.

Authorship Contributions

Surgical and Medical Practices: A.A.A., B.G., Ö.I., Concept: B.G., Ö.I., Design: B.G., Ö.I., Data Collection or Processing: Ö.I., Analysis or Interpretation: Ö.I., Literature Search: A.A.A., B.G., Ö.I., Writing: A.A.A., B.G., Ö.I.

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