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RESEARCH ARTICLE

Predictive Factors for the Development of Surgical Site Infection After Colorectal Cancer Surgery

Kolorektal Kanser Cerrahisi Sonrası Cerrahi Alan Enfeksiyonu Gelişimi için Prediktif Faktörler

Oğuz Uğur Aydın, Lütfi Soylu

Güven Hospital, Clinic of General Surgery, Ankara, Turkey

ABSTRACT

Aim: In this study, we aimed to determine the predisposing factors and cut-off values for surgical site infection in patients who were operated for colorectal cancer.

Method: We retrospectively analyzed data of 86 patients who were operated for colorectal cancer in our general surgery department in between 2015 and 2017. Age, gender, body mass index, American Society of Anesthesiologists (ASA) score, presence of chronic pulmonary disease, hematocrit (Hct) levels, albumin level, surgery duration, disease location (colon or rectum), presence or absence of ileostomy or colostomy in operation, presence of hyperglycemia, and surgeon volume were evaluated for associations with the development of superficial or deep surgical site infection.

Results: All parameters were found to be significant for the development surgical site infection except sex and body mass index. Cut-off values were 63.5 years for age, 167.5 minutes for surgery duration, 3.05 g/dL for albumin, and 33.15% for Hct.

Conclusion: We believe that the probability of surgical site infection after colorectal cancer surgery is high in patients who are older than 63.5 years, who had surgery longer than 167.5 minutes, and whose albumin level was below 3.05 g/dL and Hct was below 33.15% preoperatively. If patients operated for colorectal cancer are hyperglycemic, are in the ASA 3 risk group, undergo diverting ostomy during the surgery, have chronic lung diseases, or have rectal or classification stage 3 cancer, they should be evaluated in consideration of the above cut-off points, keeping in mind that these patients are at a high risk of developing superficial or deep surgical site infection, and they should monitored carefully for signs and symptoms of infection.

Keywords: Colorectal cancer, surgical site infection, predictive value

ÖZ

Amaç: Bu çalışmada kolorektal kanser nedeniyle opere edilen hastalarda cerrahi alan enfeksiyonu gelişmesine predispozisyon yaratan faktörler ve kesim değerleri ortaya konmak istenmiştir.

Yöntem: 2015-2017 yılları arasında hastanemiz genel cerrahi bölümünde kolorektal kanser nedeniyle acil ya da elektif olarak opere edilmiş 86 hastaya ait datalar retrospektif olarak incelendi. Hastalara ait; yaş, cinsiyet, vücut kitle indeksi, Amerikan Anestezistler Derneği (ASA) skoru, kronik akciğer hastalığı varlığı, hematokrit (Hct) seviyeleri, albümin düzeyi, operasyon süresi, hastalığın lokalizasyonu (kolon ya da rektum), operasyonda kolostomi ya da ileostomi açılıp açılmadığı, hiperglisemi varlığı, cerrah volümünün; yüzeyel ya da derin cerrahi alan enfeksiyonu gelişimini etkileyip etkilemediğinin değerlendirilmesi amaçlandı.

Bulgular: Cinsiyet ve vücut kitle indeksi dışında kalan tüm parametrelerin cerrahi alan enfeksiyonu gelişmesinde anlamlı olduğu tespit edildi. Yaş için; 63,5, operasyon süresi için; 167,5 dakika, albümin için; 3,05 ve Hct için de; 33,15 kesim değeri olarak bulundu.

Sonuç: Altmış üç buçuk yaşın üzerinde, ameliyatı 167,5 dakikadan daha uzun süren, ameliyat öncesi albümin değeri 3,05'in ve Hct değeri 33,15'in altında olan hastalarda ameliyat sonrası cerrahi alan enfeksiyonu gelişme ihtimalinin yüksek olduğunu düşünmekteyiz. Eğer kolorektal kanser nedeniyle opere edilecek hastalar; diyabetik, ASA 3 risk grubunda, ameliyat sırasında saptırıcı ileostomi ya da kolostomi açılmış, kronik akciğer hastalığına sahip, kanser rektumda yerleşmiş ve postop yapılan sınıflamada hastalığın evre 3 olduğu tespit edilmiş ise yukarıdaki kesim değerleri ile beraber değerlendirilerek hastada yüzeyel ya da derin cerrahi alan enfeksiyonu gelişme ihtimalinin yüksek olduğunu akılda tutmak ve enfeksiyona ait belirti ve bulguları iyi değerlendirmek gerektiğini düşünüyoruz.

Anahtar Kelimeler: Kolorektal kanser, cerrahi alan enfeksiyonu, prediktif değer

Address for Correspondence/Yazışma Adresi: Oğuz Uğur Aydın MD
Güven Hospital, Clinic of General Surgery, Ankara, Turkey
Phone: +90 545 546 84 87 **E-mail:** oguzuguraydin71@gmail.com **ORCID ID:** orcid.org/0000-0002-4458-9158
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Introduction

Surgical site infection (SSI) is the most common complication following respiratory, cardiovascular, and thromboembolic complications, and is the most important cause of increased morbidity and mortality.[1] The main sources are the normal skin, mucosal, and intestinal flora as well as surgical personnel, the operating room, and all equipment used during surgery. The incidence is about 1.9-3.4% in developed countries,[2] and slightly higher in Turkey (about 4.1%).[3] SSI is one of the complications that cause significant morbidity after colorectal surgery, and occurs postoperatively at rates as high as 20-30%.[4,5,6] Superficial and deep SSIs are the result of different pathogenesis and risk factors, and are directly related to surgical procedures.[2,7] Each technique employed in surgical procedures evokes a different inflammatory response.[8,9] Deep SSI has more serious consequences and may require reoperation, whereas superficial SSI generally leads to an extended hospital stay.[10,11] Numerous factors are shown to be associated with SSI development, including diabetes[12], smoking[13,14], systemic steroid use[15], obesity (being 20% heavier than ideal weight), age,[16,17,18] malnutrition,[19,20] and use of perioperative blood and blood products.[21,22] Furthermore, it has been proposed that the development of superficial SSI is linked to factors such as high body mass index (BMI) and the presence of ostomy,[23,24] while deep SSIs are related more to blood transfusion, history of abdominal surgery, and poor nutrition.[23,25] Other factors identified in the literature as associated with SSI are American Society of Anesthesiologists (ASA) score, wound class,[26] surgery duration[27], BMI[28], presence of chronic diseases,[28] video-assisted procedures,[28] smoking,[29] blood transfusion, and preoperative bathing.[30] Due to the severe consequences of SSIs, it is necessary to develop strategies for preventing these infections. These strategies facilitate the identification of risk factors and the implementation of interventions aimed at minimizing such postoperative complications. In this study, we aimed to determine whether factors such as age, gender, BMI, ASA score, presence of chronic lung disease, presence of hyperglycemia, hematocrit (Hct) and albumin levels, location of disease (colon or rectum), surgery duration, colostomy or ileostomy during the operation, and surgeon volume are associated with rates of SSI among patients who underwent colorectal surgery.

Materials and Methods

The data of 86 patients who underwent emergency or elective surgery for colorectal cancer in the general surgery unit of our hospital between 2015 and 2017 were analyzed retrospectively. We evaluated whether there were any associations between superficial and deep SSI development and gender, BMI, ASA score, presence of chronic lung disease, age, Hct levels, albumin level, surgery duration, location of disease (colon or rectum), whether colostomy or ileostomy was performed during the operation, presence of hyperglycemia, and surgeon volume. Patients who were under antibiotic therapy for any reason starting before surgery and continuing afterward were excluded from the study. Chronic lung disease was defined as the need for continuous treatment or medication use due to any lung disease. Hyperglycemia was defined as a preoperative fasting blood glucose level over 180 mg/dL. Surgeon volume was considered high for the surgeons performing only colorectal surgeries and low for general surgeons. Empiric preoperative antibiotics were administered as 2 g of second generation cephalosporin, combined with an agent effective against anaerobes if perforation was observed in laparotomy. Antibiotherapy continued for 24 hours after surgery. The preoperative antibiotic dose was administered following anesthesia induction and immediately before cutaneous incision. An additional dose of antibiotics was given in operations longer than 3 hours. SSI was presumed in patients who exhibited one of the following symptoms or findings in the skin, subcutaneous tissues, or abdomen within 30 days after surgery: purulent drainage, bacterial growth in tissue or fluid samples, and local symptoms of infection (pain, redness, sensitivity). Patient-related and surgery-related factors were identified for patients who developed SSI.

Statistical Analysis

Chi-square analysis was used to evaluate associations between SSI development and categorical (qualitative) variables such as gender, ASA score, hyperglycemia, presence of stoma, chronic lung disease, surgeon volume, tumor-containing segment, having an emergency or elective surgery, and cancer stage. Independent Samples t test was used to analyze whether the means of continuous variables such as age, BMI, surgery duration, albumin level, and Hct level differed significantly according to infection status. Cut-off values for the quantitative variables were determined using receiver operating characteristic (ROC) curve analyses based on the infection status. The data were analysed using SPSS 20.0 software and the analyses were made at a confidence level of 95%.

Results

The incidence of SSI among patients who underwent surgery for colorectal cancer in our center was 24.41%. Of these patients, 61.9% were males and 38.1% were females. ASA score was 3 for 61.9% and 4 for 14.3% of the patients. Hyperglycemia was present in 76.2% and chronic lung disease in 71.4% of these patients. A diverting stoma (ileostomy/colostomy) was created during surgery in 76.2% of the cases. High-volume surgeons performed 71.4% and low-volume surgeons 28.6% of procedures that resulted in

SSI. The tumor was located in the rectum in 81% and in the colon in 19% of the patients. Tumor, node, metastasis (TNM) stage was stage 3 for 61.9% and stage 4 for 23.8% of the patients with SSI. The patients' demographical data are presented in Table 1. Mean age, surgery duration, and albumin and Hct levels differed significantly between patients with and without SSI ($p<0.05$), but there was no significant difference in mean BMI ($p>0.05$) (Table 1). The patients with SSI had higher mean age and surgery duration but significantly lower mean albumin and Hct levels than patients who did not develop infection ($p<0.05$). Patients who were over 63.5 years of age, underwent surgery longer than 167.5 minutes, and had preoperative albumin level below 3.05 g/dL and Hct level below 33.15% were at higher risk of developing SSI. Cut-off values for these parameters are shown in Table 2. ROC curve analyses for age, surgery duration, and hemoglobin and Hct levels are given in Figures 1, 2, 3, 4.

Table 1. Patient's demographic datas

		SSI				p
		No (n=65)		Yes (n=21)		
		n	%	n	%	
Gender	Male	35	53.8%	13	61.9%	0.349
	Female	30	46.2%	8	38.1%	
ASA score	1	3	4.6%	1	4.8%	**0.023***
	2	37	56.9%	4	19.0%	
	3	20	30.8%	13	61.9%	
	4	5	7.7%	3	14.3%	
Hyperglycemia	No	42	64.6%	5	23.8%	**0.001***
	Yes	23	35.4%	16	76.2%	
Ostomy	No	57	87.7%	5	23.8%	**0.000***
	Yes	8	12.3%	16	76.2%	
Chronic lung disease	No	56	86.2%	6	28.6%	**0.000***
	Yes	9	13.8%	15	71.4%	
Surgeon volume	Low	9	13.8%	15	71.4%	**0.000***
	High	56	86.2%	6	28.6%	
Tumor-containing segment	Rectum	6	9.2%	17	81.0%	**0.000***
	Colon	59	90.8%	4	19.0%	
Emergency surgery	No	57	87.7%	5	23.8%	**0.000***
	Yes	8	12.3%	16	76.2%	
Elective surgery	No	6	9.2%	16	76.2%	**0.000***
	Yes	59	90.8%	5	23.8%	
TNM Stage	1	18	27.7%	0	0.0%	**0.000***
	2	42	64.6%	3	14.3%	
	3	4	6.2%	13	61.9%	
	4	1	1.5%	5	23.8%	
		Mean ± SD		Mean ± SD		
Age (years)		55.2±10.2		68.9±12.2		**0.000***
Body mass index		27.8±3.9		29.4±3.2		0.098
Surgery duration (min)		154.3±29.2		184.3±35.7		**0.000***
Albumin (g/dL)		3.3±0.3		2.8±0.3		**0.000***
Hematocrit (%)		36±4.4		28.9±4		**0.000***

SSI: Surgical site infection, ASA: American Society of Anesthesiologists, TNM: Tumor, nod, metastasis, SD: Standard deviation

*p<0.05

Table 2. Cut-off values for age, surgery duration, albumin, and hematocrit

	Area	Standard error	p	95% Confidence interval		Cut-off value
				Lower limit	Upper limit	
Age	0.825	0.058	0.000*	0.711	0.938	63.5
Surgery duration	0.760	0.069	0.000*	0.625	0.896	167.5
Albumin	0.142	0.052	0.000*	0.041	0.243	3.05
Hematocrit	0.107	0.040	0.000*	0.029	0.186	33.15

*p<0.001

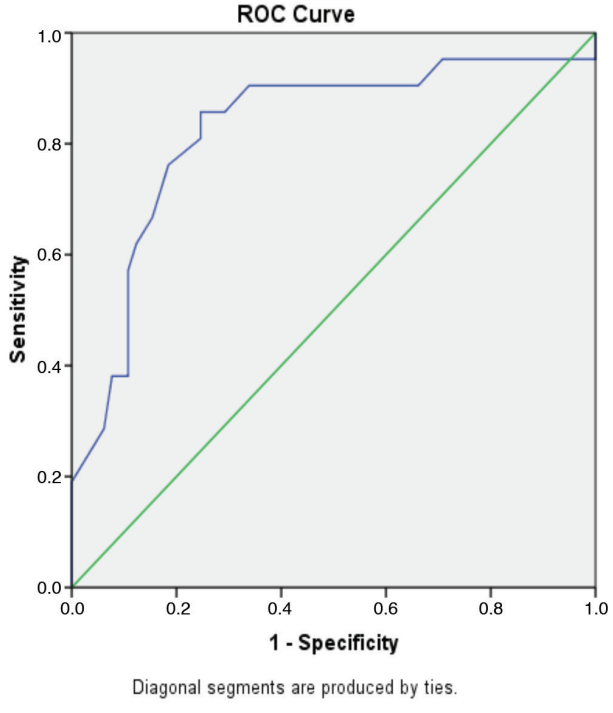


Figure 1. ROC analysis for age

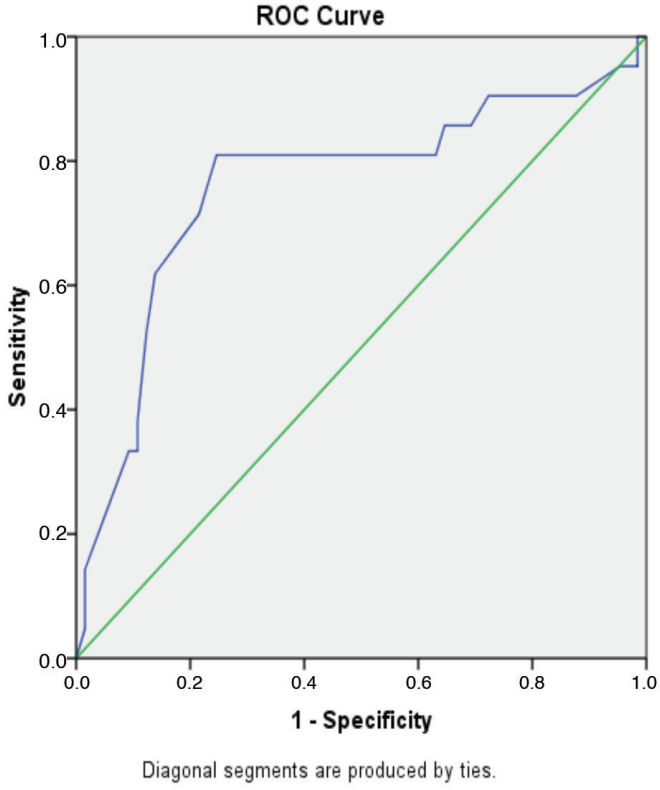


Figure 2. ROC analysis for operation time

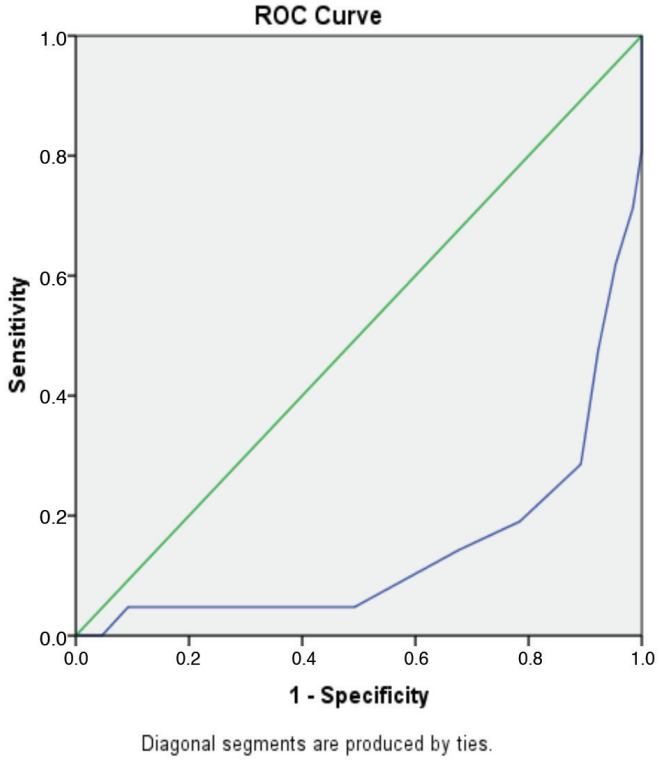


Figure 3. ROC analysis for albumin

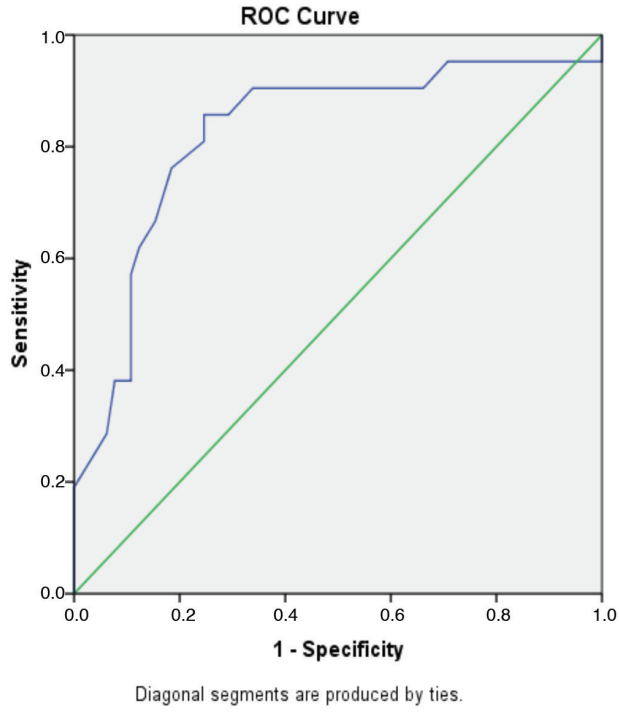


Figure 4. ROC analysis for hematocrit

Discussion

In this study we aimed to determine which factors were significantly related to SSI development among a group of patients who were operated for colorectal cancer and retrospectively identified as having developed superficial or deep SSI. With the exception of gender and BMI, we found that all investigated parameters were associated with SSI development after colorectal cancer. The general infection rate among patients we operated for colorectal cancer was 24.41%, consistent with the literature. The development of SSI after colorectal surgery is a common and expected complication. Bacterial contamination occurring during bowel resection may cause infection. The bacterial load is particularly high in the large intestine compared to the upper gastrointestinal system, and contamination of the surgical site may result in infection. Development of SSI is directly associated with the patient, the disease, and the surgical procedure.[30,31] Anatomic location of the cancer is one of the most important predictive factors. Konishi et al.[32] stated that the risk of superficial or SSI is higher in rectal cancer than in colon cancer. Diverting ostomy is more common in patients with rectal cancer than colon cancer, the tumor is closer to the anal verge, and the operation is generally longer. Therefore, bacterial contamination occurs more frequently in rectal cancer surgeries.[33,34] This was also true in our patients with SSI, 81% of whom were operated

for rectal cancer and 19% for colon cancer. We noted a significant correlation between SSI development and the tumor containing segment. Poor blood glucose control has been associated with negative perioperative results such as metabolic dysfunction, infection, insufficient wound healing, and higher mortality. The American Diabetes Association suggests a perioperative blood glucose level between 80 and 180 mg/dL.[35] Hyperglycemia affects blood flow and tissue oxygenation, leading to endothelial dysfunction and prolonged inflammatory response and disrupting normal wound healing,[36] and is associated with SSI.[37] We observed that a large proportion (76.2%) of patients with SSI had perioperative blood glucose higher than 180 mg/dL. Therefore, we believe there is significant correlation between infection development and hyperglycemia.

Studies indicate that patients with advanced colorectal cancer (TNM stage 3 or 4) have an independent risk factor for SSI development.[38,39] This may be related to the extent of lymph node dissection. Although disease stage was reportedly not a risk factor for SSI in some studies[40], we found that 61.9% of patients with SSI were at TNM stage 3 and 23.8% were at TNM stage 4 in our study. Therefore, we believe there is significant correlation between infection development and advanced disease. Some authors have argued that surgeon volume is inversely correlated with SSI development.[41] This means that the incidence of SSI is higher after operations performed by surgeons with less experience in colorectal cancer operations, or in other words, by surgeons who do not perform colorectal cancer surgery exclusively. This may be attributed to less experienced surgeons requiring longer to perform the same procedures or deviating from the standard techniques during surgery. Consistent with the literature, we found that a large proportion (71.4%) of the patients who developed SSI were operated by surgeons with a lower volume of such cases compared to those who were operated by surgeons performing only colorectal surgeries (28.6%). Therefore, we believe surgeon volume is significantly associated with infection development. Lower serum albumin, ASA scores of 3 or 4, and chronic lung diseases are patient-related factors that increase the risk of SSI. These factors lead to poor tissue perfusion in the skin or deep tissues and thereby to SSI development.[42,43] Serum albumin is one of the best indicators of nutritional status and is directly related to postoperative complications.[44] Hypoalbuminemia delays wound healing by inhibiting collagen synthesis and causing granuloma formation.[45] In our study group, we determined an albumin cut-off value of 3.05 g/dL for patients who developed SSI. Our results suggest that patients with albumin levels below this point have significantly higher risk of developing SSI. The ASA classification is a useful evaluation system in which patients are preoperatively classified, and anesthesia approaches and monitoring methods in particular are determined accordingly. Higher ASA score corresponds to an increase in comorbid diseases and is directly related to the complications in the early postoperative period.[44,46,47,48] ASA 3 corresponds to patients with compensated systemic disease, meaning diseases that limit patients' activities but are not debilitating, such as hypovolemia, latent cardiac insufficiency, history of myocardial infarction, advanced diabetes, and limited pulmonary function. In our patient group, the risk of developing SSI was significantly higher among those with ASA 3. Chronic lung diseases reflect conditions with chronic hypoxemia. Chronic obstructive pulmonary disease (COPD) is characterized by chronic inflammation of the airways, parenchyma, and pulmonary vasculature. In advanced COPD, peripheral airway obstruction, parenchymal destruction, and pulmonary vessel abnormalities reduce the gas exchange capacity of the lungs, causing hypoxemia and later hypercapnia. These physiopathologic mechanisms result in delayed wound healing and SSI. We noted that patients with SSI had a significantly higher rate of chronic lung diseases. Obesity is known to play a role in the etiology of colon cancer.[49,50] The World Health Organization classifies BMI as underweight (BMI below 18.5), normal weight (BMI 18.5-24.9), overweight/preobesity (25-29.9), and obesity grade 1 (30-34.99), 2 (35-39.99), and 3 (above 40).[51] BMI below 20 and above 30 is believed to be a risk factor for SSI development. Amri et al.[52] have stated that BMI does not cause an increase in parameters such as complication rates after colorectal surgery, length of hospital stay, and reoperation and may only increase wound-related complications. However, in the present study we found that mean BMI was not significant associated with development of infection ($p>0.05$).

Colorectal cancers are common among the elderly population. The incidence increases dramatically after the age of 50. Some studies have indicated that older patients undergo colorectal cancer surgery more frequently than younger patients.[53] Conversely, some studies report that superficial or deep SSI risk is lower in older patients. This has been attributed to patient awareness.[54] However, the results of our study showed that SSI development risk was higher in patients over a cut-off point of 63.5 years of age compared to those who were younger. This may be related to the more frequent need for emergency surgery in patients over this age. Longer surgery time means more surgical trauma and higher chance of intestinal contamination. There are studies reporting that operations lasting longer than 180 minutes pose an independent risk factor for the development of superficial and deep SSI.[55,56] In our study, the cut-off value for surgery duration was similar, at 167.5

minutes, and superficial and deep SSIs were significantly more common following operations that lasted longer than this time.

Stomas protect distal colonic anastomosis. Stoma-related complications may emerge when opening or closing the stoma. Various studies have indicated that diverting ostomy is a risk factor for morbidity, mortality, and SSI development.[57] In a study by Ricciardi et al.[58] including 79.775 patients, SSI developed in 10.2% of the patients with stoma and was significantly more common among patients with stoma than those without. Studies comparing ileostomy and colostomy have shown significantly higher infection rates among patients with colostomy;[59] however, we did not compare ileostomy and colostomy in our group of patients. In our study group, it was found that 76.2% of the SSI patients required a diverting stoma. Therefore, we believe that there is a significant association between infection development and the opening of diverting stoma. Bayar et al.[60] reported that postoperative SSI occurred at a significantly higher rate among patients who underwent emergency colorectal cancer surgery. In the present study, 12.3% of patients without infection underwent emergency surgery versus 76.2% of those who developed infection. There was a significant relationship between colorectal surgeries performed as emergency procedures and rate of infection ($p<0.05$). In a prospective study by Itatsu et al.[61] including 1980 patients, the SSI rate after elective colorectal surgery was 11.7%. In a study by Tang et al.[62], this rate was 10%. In our series, 76.2% of the patients who developed infection had undergone emergency surgery, which was consistent with numerous other studies in the literature. In recent years, laparoscopic surgery has been providing better results in terms of cosmesis and patient satisfaction, and it is reasonable to anticipate that this approach will also reduce rates of postoperative SSI. In one study comparing laparoscopic and open procedures, the incidence of SSI was about 6%.[40] A limitation of our study is that we analyzed only SSIs in the colorectal cancer patients who had open surgeries, and therefore no comparison could be made with SSI rates after laparoscopic surgery. Our results suggest that patients who are older than 63.5 years of age, have a preoperative albumin value below 3.05 g/dL, have and a preoperative Hct value below 33.15%, and are operated for longer than 167.5 minutes have a higher risk of developing postoperative SSI. If patients operated for colorectal cancer are hyperglycemic, are in the ASA 3 risk group, undergo diverting ostomy during the surgery, have chronic lung diseases, or have rectal or TNM stage 3 cancer, they should be evaluated in consideration of the above cut-off points, keeping in mind that these patients are at a high risk of developing superficial or deep SSI, and they should monitored carefully for signs of infection. The study was retrospective, nonrandomized, and based on a single center.

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Ethics

Ethics Committee Approval: Retrospective study.

Informed Consent: Retrospective study.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: O.U.A., L.S., Concept: O.U.A., Design: O.U.A., L.S., Data Collection or Processing: O.U.A., Analysis or Interpretation: O.U.A., L.S., Literature Search: O.U.A., Writing: O.U.A.

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