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Original Study

SURGICAL SITE INFECTION AFTER SURGERY FOR COLORECTAL CANCER

Kolorektal kanserlerin cerrahi tedavisi sonrasında görülen cerrahi enfeksiyonlar

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ABSTRACT

Surgical site infection (SSI) is one of the most common morbidities following colorectal surgery. We identify risk factors to predict the likelihood that a patient will develop a SSI after a colorectal resection for colorectal cancer.

This investigation was designed as a retrospective study of 67 patients who underwent colorectal resection for colorectal cancer. We evaluated influence of gender, age, nutritional status indicators, body mass index, ASA score, diabetes mellitus and local tumor stage.

A total of 14 (21%) incisional SSIs were identified. Patients who developed incisional SSI were mostly male, obese, they have higher ASA score, local more advanced tumor, and they were more often diabetics. But the difference was not statistically significant. Only hypoalbuminemia (P = 0.01) and hypoproteinemia (P = 0.02) proved to be statistically significant risk factors for SSI.

In conclusion, good preoperative nutritional status (based on albumin and total protein level) is the most important factor for preventing SSI in patients with colorectal cancer surgery.

Key words: Surgical site infection, colorectal surgery, risk factors, albumin, prealbumin, protein

ÖZET

Cerrahi yara enfeksiyonları kolorektal cerrahi sonrasındaki en önemli morbidite nedenlerinden birisidir. Kolorektal tümörler için yapılan cerrahi rezeksiyonları takiben gelişen cerrahi yara enfeksiyonlarının önceden tesbitini sağlayabilecek olan risk faktörlerini tanımladık.

Bu retrospektif çalışmaya 67 kolorektal kanser vakası dahil edildi. Çalışmada cinsiyet, yaş, beslenme durumu indikatörleri, vücut kitle indeksi, ASA skoru, diyabet ve tümörün evresi araştırıldı.

Vakaların 14'ünde (%21) Cerrahi yara enfeksiyonu saptandı. Enfekte vakaların çoğu erkek, şişman, ASA skoru yükselmiş ve sıklıkla diyabetli hastalardı. Ancak bu farklılık istatistiksel olarak anlamlı değildi. Bir risk faktörü olarak, hipoalbuminemi (P=0.01) ve hipoproteinemi (P=0.02) cerrahi yara enfeksiyonu için istatistiksel olarak anlamlıydı.

Sonuç olarak, kolorektal kanserlerin cerrahi tedavisine bağlı olarak ortaya çıkan cerrahi yara enfeksiyonlarından korunmak için, preoperatif dönemde yapılacak dengeli nutrisyonel desteğin önemli olduğu saptandı.

Anahtar kelimeler: Cerrahi yara enfeksiyonu, kolorektal cerrahi, risk faktörleri, albumin, prealbumin, protein.

INTRODUCTION

Surgical site infection (SSI) is an infection of the tissues, organs or spaces exposed by surgeons during performance of an invasive procedure. SSIs are the third most common hospital-acquired infection, account for 14% to 16% of all such infections. Among surgical patients SSI is the most frequent nosocomial infection, liable for up to 38% of all these infections (1,2). SSIs are consistently associated with significant morbidity and mortality, prolonged hospitalization,

increased intensive care unit admissions and more frequent readmissions. SSIs also increase medical expense. Total inpatient costs for a patient with a SSI are approximately twice that for patients without a SSI (1). The development of SSIs is related to four factors: 1. the degree and type of microbial contamination of the wound during surgery, 2. the duration of the procedure, 3. host factors such as age, diabetes, malnutrition, obesity, immune suppression, anemia, radiation, chronic skin disease, these factors can be approximately summarize under American Society of Anesthesiologists (ASA) preoperative assessment score 4. external factors such as skin preparation, contamination of instruments, inadequate antibiotic prophylaxis (1,2).

Surgical site infection in patients undergoing colorectal resection has been specifically studied because it is a frequent cause of morbidity with an incidence 3-30%. Contemplated and simultaneously influenceable risk factors for the development of SSI include improper administration of antimicrobial prophylaxis, intraoperative hypothermia, hyperglycemia, poor nutritional status, tobacco use and intraoperative hypotension (2).

Malnutrition is a common problem in cancer patients; simultaneously it adversely affects surgical outcomes. Serum albumin, prealbumin or total protein are simple tools to assess patients' nutritional status. Albumin is used most often. Hypoalbuminemia has been shown to be associated with increased mortality and morbidity rates in both hospitalized patients and community-dwelling elderly persons. Albumin also has been found to predict postoperative mortality and morbidity for patients undergoing elective surgery (3).

The goal of this retrospective study was to prove significance of risk factors for SSI in patients undergoing colorectal resection for colorectal cancer. We evaluated influence of gender, age, nutritional status indicators (preoperative serum protein, albumin and prealbumin levels), body mass index, ASA score, diabetes mellitus and local tumor stage.

MATERIAL AND METHOD

This is a single-center, retrospective study. Patients who underwent acute or elective colorectal resection (laparoscopic assisted right or left hemicolectomy, laparoscopic assisted rectum or sigmoid resection, Hartmann's procedure) for colorectal cancer between January 2010 and June 2013 were identified for inclusion in the study. Patients with abdominoperineal resection, partial and total pelvic exenteration were excluded, as well as those who underwent simple colostomy closure with associated wedge or segmental resection. According to fast track protocol, our patients do not receive any oral mechanical bowel preparation. Each patient is preoperatively routinely shaven. Cefuroxim is given 30minutes prior the incision. Repeated dose of a prophylactic antibiotic was administered during an operation of long duration (more than 2 hours) and then stopped within 24 hours after the operation. For site preparation, 2-propanol with benzalkoniumchlorid (Cutasept® G, USA) scrub is used.

Patients' hospital records were reviewed for demographic and clinical data. We were interested in age, gender, height, weight, diagnosis, history of diabetes, preoperative protein, albumin and prealbumin level, ASA score as determined by the anesthesiologist. Local tumor stage (T) according to TNM classification was defined by the pathologist.

Patients´ age was evaluated as a continuous variable. Body mass index (BMI) in kg/m^2 (calculated from height and weight at the time of admission), preoperative serum protein, prealbumin and albumin level were evaluated as continuous variables as well. Gender, ASA score, diabetes mellitus and primary tumor extent (T) was assessed as a categorical variable.

The postoperative course was evaluated according to development of an incisional SSI. The length of postoperative stay was counted. The criteria for incisional SSI were an infection that occurred at the incision site involving the skin and subcutaneous tissue or even muscle and facial layers. At least one of the following condition occurred: purulent drainage from the incision; an organism isolated from a culture of fluid from the incision; incisional pain, tenderness, localized swelling, redness, or heat, and opening of the wound. We did not distinguish between superficial and deep incisional SSI.

The data were evaluated using descriptive statistical methods. To determine the risk factors for incisional SSI statistical analyses were performed using Statatistica six sigma version 7 software. Continuous variables were compared using the Mann-Whitney U test, while categorical data were compared using the two-tailed Fisher exact test. A value of $p<0.05$ was considered statistically significant.

RESULTS

A total of 67 patients underwent acute or elective colorectal resections and were included to our study (consisting of 8 Hartmann resections, 3 right hemicolectomies, 3 left hemicolectomies, 51 rectosigmoid resections, 1 transversum resection and 1 colectom) (Table 1).

The mean patient age was 65 ± 12 years (34-92 years); male/female ratio was 26 / 41. Mean ASA score was 2,5±0,7; mean T (TNM classification) tumor stage 2,8±0,8.

Physiological levels of prealbumin are 0,2-0,4 g/l. 48% of our patients had preoperative levels lower, average value was 0,2±0,07 g/l. Normal range of albumin serum level is 35 - 53g/l, in our group the mean value was 41±6 g/l, 16% of the patients had hypoalbuminemia. The reference range for total protein is typically 65-82g/l, mean level of our patients was 68±9 g/l, and hypoproteinemic were 21% of the patients.

Table 1: Types of surgery and SSI complications			
Type of operation	**SSI**	**No SSI**	**Total**
Hartmann resection	4	4	8
Hemicolectomy l. sin	2	1	3
Hemicolectomy l. dx	1	2	3
Rectum/sigma resection	7	44	51
Colectomy	0	1	1
Transversum resection	0	1	1

Thirty day postoperative mortality was 7% (5 patients died; 1 decompensation of chronic pulmonary disease, 1 decompensation of chronic cardiac failure, 1 massive pulmonary embolism and 2 anastomotic leakage with sepsis and respiratory failure).

A total of 14 (21%) incisional SSIs were identified. Patients were divided into 2 groups, with or without incisional SSI, and compared. There was no difference in age. Patients who developed incisional SSI were mostly male (86%). They were more likely to have a higher BMI, higher ASA score given pre-operatively, local more advanced tumor (higher T), and they were more often diabetics. But the difference was not statistically significant.

Twentyfive percent of patients with prealbumin lower than 0,2 g/l, 44% of patients with albumin lower than 35g/l a 36% of patients with total serum protein lower than 64g/l developed SSI. Hypoalbuminemia (P=0.01) and hypoproteinemia (P=0.02) proved to be statistically significant risk factors for SSI. Table 2 summarizes the patient characteristics and SSI incidence.

Length of hospital stay of patients with SSI was significantly longer than the stay of no SSI patients; 21days (9-34) vs. 11 days (5-30), P = 0.0002. Patients who underwent extensive operations (Miles abdominoperineal amputation and pelvic exenteration) have much higher rate of SSI, as documented in Table 3, just for illustration.

Table 2: Patients´ characteristics and SSI.			
Patients´ characteristics	**Incisional SSI**	**No SSI**	**p -value**
Total	14	53	
Age (years)	64 +/-16	65 +/-11	0,8
Gender			0,06
Female	14% (2)	45% (24)	
Male	86% (12)	55% (29)	
Diabetes mellitus	36% (5)	23% (12)	0,3
ASA	2,7 +/-0,7	2,5 +/-0,6	0,4
BMI (kg/m^2)	29 +/-5	26 +/-4	0,1
Prealbumin (g/l)	0,15 +/-0,07	0,20 +/-0,07	0,08
Albumin (g/l)	34 +/-6	40 +/-6	**0,01**
Total protein (g/l)	60 +/-10	70 +/-8	**0,02**
T stage	3 +/-0,7	2,7 +/-0,8	0,2
Hospitalization (days)	21+/-8	11 +/-5	**0,0002**

Table 3: SSI in the extensive operated group.		
Operation	**Incisional SSI**	**No SSI**
Abdominoperineal amputation	4 (45%)	5 (55%)
Pelvic exenteration	3 (75%)	1 (25%)

DISCUSSION

Our rate of incisional SSI for colorectal resections (21%) is within the range mentioned in the literature (3% to 30%). Quite high number can be justified by inclusion of acute operated patients. On the other hand, we must admit, that we excluded patients with extensive surgery (abdominoperineal amputation, pelvic exenteration).

The objective of this study was to identify potential risk factors that independently predict

development of incisional SSI. We showed, that patients with SSI tend to be male, tend to have diabetes, higher BMI, ASA and T score, lower prealbumin level. But all these factors were not statistically significant. Probably due to relatively small group. The most important risk factors for SSI development were hypoproteinemia and hypoalbuminemia.

Male sex is not often mentioned as a potential risk factor, but in Tang´s et al. study, men have higher probability to acquire SSI after colorectal surgery (Odds Ratio 1,5) (3).

More studies identified obesity as a risk factor for SSI development in patients undergoing colorectal resections (4-7).The growing epidemic of obesity in Western world may be responsible for increasing the overall morbidity of elective colorectal resection, due to increasing rates of SSI in this group of patients. According to some studies, obese patients have also higher probability to acquire colorectal cancer (8).

Diabetes is an important risk factor according to some studies too. A deficiency in the defense mechanisms of patients with diabetes is well documented. According to a recent study from USA, especially higher than normal glucose control at postoperative time is associated with SSI (9). We followed-up the postoperative glucose levels of diabetic patients too, but we refrained from evaluation because of small diabetic group.

Higher ASA status is according to some authors (3,10) significant risk factor for postoperative complications following rectal cancer surgery too.

Bot et al. showed that advanced tumor stage increases the risk of postoperative infectious complications at both the resection site ($p < 0.001$) and distant to the resection site ($p = 0.015$) (11).

We are in agreement with all these results, but we can not verify them statistically. Our results indicate, that the most important role for surgical site infection is nutritional status. Patients with colorectal cancer are at risk of malnutrition due to cancer-induced higher metabolism, dietary intake reduction and cancer cachexia. Tumor necrosis factor-alpha is considered to be the main mediator of cancer cachexia as it is responsible for different metabolic alterations and leads to impairment of hepatic protein synthesis. Cancer patients also have increased whole protein turnover. Total protein half-life is 80 days, albumin has a half-life of 18 days, and their lower concentrations reflect prolonged malnourishment, unlike prealbumin which ´s half-life is 2 days. Hypoalbuminemia is widely accepted to be a good indicator for malnutrition in many studies (10). It is associated with poor tissue healing, decreased collagen synthesis in the surgical wounds or at the anastomosis, and impairment of immune responses, delayed recovery of bowel function (12,13). The stress of surgery can further deplete protein reserves and lead to multiple organ dysfunctions and greater susceptibility to nosocomial infections.

The use of total serum protein levels as markers of nutritional status is not so often. Our findings are pointing on the correlation of low total serum protein and SSI (p=0,02). In a study concerning bariatric surgery, patients with serum total protein concentration <53 g/l have higher risk of SSI; odds ratio 13; p=0.003(14).

However, an association between hypoalbuminemia and adverse surgery outcome has been recognized for many years. Seltzer et al. reviewed 500 consecutive medical-surgical admissions and found a fourfold increase in complications and a sixfold increase in mortality in patients with a serum albumin level < 35 g/l (15). Reinhardt et al. described hospital mortality of 24% of patients with depressed serum albumin (16). He found an inverse linear relationship between serum albumin level and hospital mortality. In 50 patients with albumin levels < 20 g/l, the mortality rate was 62%. Rich et al. claims, that patients undergoing cardiac surgery who had hypoalbuminemia, tend to have higher postoperative mortality and morbidity rates; that albumin less than 35 g/l is powerful predictor of postoperative renal dysfunction, increased length of stay and gastrointestinal disorders (17). Similar results brought the study evaluating 54.215 major non cardiac-surgical patients. A decrease in serum albumin from 46g/l to less than 21g/l was associated with an exponential increase in mortality rates from less than 1% to 29% and in morbidity rates from 10% to 65% (18).

Importance of hypoalbuminemia in colorectal surgery was brought to mind by Lohsirivat et al.´s study, where 244 patients undergoing elective oncological resection for rectal adenocarcinoma were encompassed. Hypoalbuminemia was the only significant risk factor (odds ratio 2.22, $P < 0.015$) for postoperative complications (surgical site infections, anastomotic leakage, distant infections) (10).

We have focused just on relationship between hypoalbuminemia and SSI and came to similar results, preoperative hypoalbuminemia has been associated with increased postoperative SSI (p=0,01). Simultaneously, patients with SSIs have prolonged hospitalization (p=0,0002).

The role of prealbumin as a predictor of clinical outcomes in patients undergoing colorectal surgery was less studied . We did not prove significant relationship between lower prealbumin level and SSIs. Lin MY et al. consider serum prealbumin level less important for estimation of postoperative course than albumin level, because prealbumin level correlated only with increased overall and infectious morbidity but not non-infectious morbidity or mortality, whereas albumin level was a significant predictor of overall postoperative morbidity, infectious and non-infectious complications, and mortality (19).

Prealbumin has gained the interest of clinicians because of its short half-life which allows not only detecting short-term impairment in energy balance but also monitoring the potential effectiveness

of nutritional support (20). In our institution's clinical laboratory, the cost for measurement of serum albumin and protein is 2€ per test compared with 13€ per test for serum prealbumin, a nearly 7 times difference. Thus, routine inclusion of prealbumin level in preoperative testing for the purpose of risk assessment is not clinically advisable or cost-effective. However, if severe clinical malnutrition is present and preoperative hyperalimentation is planned in an attempt to avert postoperative morbidity and mortality, the preoperative serum prealbumin level may be useful as a monitor of the response to nutritional supplementation.

There are several important study limitations. First, all diagnoses of incisional SSI were recorded retrospectively. We are also well aware of small study group. But we could not include patients operated in 2009, because we started with routinely testing of serum protein, albumin and prealbumin in 2010. On the other hand, single-centre nature of our study minimizes variations in observer differences and environmental factors (e.g. operating room discipline, skin preparation, operation technique).

In conclusion, according to our study, the most important predictor of surgical site infections is serum total protein level and albumin level, more powerful than gender, obesity, diabetes, ASA score and tumor stage. Positively, the latter are relatively resistant to overcome in the pre-operative period, whereas nutritional status may be improved.

Despite compelling evidence that malnutrition increases postoperative morbidity and mortality following major elective surgery, preoperative nutrition is sometimes ignored. Our findings suggest that at least preoperative serum albumin testing should be performed. The cost of the test is low in relation to its prognostic value.

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