Modifiable and non-modifiable risk factors for surgical site infection after colorectal surgery: a single-center experience

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Abstract
Purpose Surgical site infection (SSI) is the most common complication of colorectal surgery, resulting in significant burden in terms of morbidity and length of hospital stay. The aims of this study were to establish the incidence of SSI in patients undergoing colorectal surgeries and to identify potentially modifiable risk factors to reduce overall SSI rates.
Methods This retrospective study analyzed patients who underwent colorectal resection at our Department. Patients were identified using a prospective SSI database. Univariate and multivariate analyses were used to identify risk factors.
Results A total of 687 patients were enrolled in the study and the overall SSI rate was 19.9% (137 patients). Superficial incisional surgical site infections (SSSIs) developed in 52 (7.6%) patients, deep incisional surgical site infections (DSSIs) developed in 15 (2.2%), and organ/space infections (OSIs) developed in 70 (10.1%). Univariate and multivariate analyses confirmed that age, diabetes, emergency surgery, and a high infection risk index are risk factors for SSI.
Conclusions There are some modifiable and non-modifiable risk factors for SSI. IRI and age are non-modifiable, whereas the timing of surgery and diabetes can be modulated by trying to defer some emergency procedures to elective ones and normalizing the glycemia of diabetic patients.

Keywords Abdominal infections · Surgical site infection · Colorectal surgery

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Introduction

Surgical site infections (SSIs) are one of the most common issues on surgical wards and the second most frequent nosocomial infection after urinary tract infections [1]. They encompass a wide spectrum of possible clinical features and, according to the Centers for Disease Control and Prevention (CDC) [2], SSIs can be classified into three distinct types: superficial incisional SSIs (SSSIs), involving only the skin and subcutaneous tissue of the incision; deep incisional SSIs (DSSIs), involving deep soft tissues such as the fascia and muscle layers, and organ space infections (OSIs), involving any part of the anatomy that was opened or manipulated during an operation, other than the incision [3, 4].

Despite these clinical differences, SSIs represent a high burden in terms of morbidity, mortality, prolonged length of hospital stay and additional healthcare costs [5, 6]. The associated mortality rate is 3%, and up to 75% of SSI-associated deaths are directly related to the SSI [5, 7]. Most SSIs become apparent within 30 days of surgery and the incidence varies widely depending on the surgical procedure, the surveillance criteria, and the quality of data collected [8, 9]. The problem is of particular relevance in colorectal surgery, for which SSI rates swing from 15% to 30% [10–17]; thus, reducing the occurrence of SSIs has become a major target of quality improvement initiatives [18–21].

The causes of SSI can be related to the patient, the contaminating organism, and the surgical procedure [4]. Among these, the most frequent factors called into question are age, malnutrition, poor tissue perfusion, obesity, diabetes, steroids and other immunosuppressant drugs, timing of surgery, poor skin preparation, long operation time (> 180 min), inappropriate antibiotic prophylaxis use, and hypothermia. Since numerous patient-related and procedure-related factors influence the risk of SSI, any preventive measure requires a "bundle" approach with systematic attention to these multiple risk factors [22–26].

The aims of the present study were to establish the SSI incidence in patients undergoing colorectal surgery and to identify potentially modifiable risk factors to reduce overall SSI rates.

Methods

The Department of General Surgery, University Hospital of Trieste in Italy has participated in the Hospital Infection Committee surveillance program since January, 2011 (Ministry of Health Circulars no. 52/1985 and no. 8/1988–Italy). All patients undergoing laparoscopic and laparotomic colorectal operations at our Department, between June, 2010 and July, 2014 were identified using a prospective SSI database, followed by a retrospective analysis of data. Patients were subdivided into four different time-frames according to the period of study: (1) June, 2010–May, 2011; (2) June, 2011–May, 2012; (3) June, 2012–May, 2013; (4) June, 2013–July, 2014. SSIs were assessed according to the National Nosocomial Infections Surveillance (NNIS) System [2] and classified into SSSIs, DSSIs, and OSIs. The association between an OSI and concurrent anastomotic leakage (defined by the presence of clinical and/or radiological findings of peritonitis, fistula, or intra-abdominal abscess) was also recorded. Patients with a superficial or deep SSI had a bacterial wound culture done and patients with an OSI had cultures done of liquid drained surgically or at the bedside.

Patients who died during follow-up for reasons unrelated to the SSI, those who underwent only the creation or closure of a stoma, and those who underwent another procedure apart from the colorectal surgery within 30 days for reasons unrelated to the first operation were excluded from the analysis. Patient demographics, preoperative comorbidities, intraoperative factors, and 30-day outcomes were examined. For each patient, the following variables were recorded: age, gender, smoking status, nutritional status evaluated as body mass index (BMI), American Society of Anesthesiologists (ASA) score, preoperative levels of serum albumin (when available, cut-off level: 3 g/dL), preoperative levels of hemoglobin (cut-off level: 10 mg/dL), hyperglycemia (cut-off level: 180 mg/dL), preoperative diagnosis of diabetes, indication for surgery (benign vs. malignant disease), adjuvant radiotherapy and/or chemotherapy for rectal cancer.

Perioperative details included the procedure (identified by the DRG—Diagnosis-Related Groups; ICD9-CD), surgical site (right colon, transverse colon, left colon, rectum), timing of surgery (elective/emergency), surgical approach (laparoscopic/laparotomic), wound classification as defined by the American College of Surgeons (ACS), and the CDC (ClassI: clean, ClassII: clean/contaminated, ClassIII: contaminated, ClassIV: dirty/infected), length of operation (cut-off level: > 180 min), simultaneous creation or closure of a diverting ostomy. Each patient was stratified according to the NNIS Infection Risk Index (IRI) [2] to create an individual risk profile. For this, each stratum was based on the presence of three major risk factors: surgery lasting more than the duration cut point hours (where the duration cut point is approximately the 75th percentile of the duration of surgery in minutes for the operative procedures); contaminated (Class III) or dirty/infected (Class IV) wound class; and ASA class 3 or higher. The patient's SSI risk category was defined by the number of these factors present at the time of the operation (IRI 0, 1, 2, or 3). Special attention was paid to preoperative skin preparation and surgical scrubs, including hair removal and the use of antiseptic soap. Antibiotic prophylaxis was based on local guidelines and resistance profiles: all patient received cefazolin 2 g plus metronidazole 500 mg, about 30 min before incision. Patients with penicillin or cephem allergy, were given gentamicin 3 mg/Kg plus metronidazole 500 mg. If the surgical procedure lasted more than 180 min, a booster dose of cefazolin 1 g was administered. In the presence of both ASA 3 and an operation time > 180 min, the prophylaxis was given for 24 h.

Both general surgeons and nursing staff participated in an effective educational program. Mechanical bowel preparation was routinely done for all patients undergoing elective surgery. Hypothermia was carefully prevented during every surgical procedure, using forced-air warming devices, and adequate oxygen saturation levels were maintained during the hospital stay. Re-scrubbing was done and plastic drapes were changed before abdominal wall closure at every operation. Moreover, the abdominal wall closure was delayed in case there was a major spill of colonic contents during surgery and/or when an intra-abdominal abscess was found intraoperatively.

The SSI onset, rates, and pathogens were reported. The length of hospital stay was also recorded for every patient and compared between those with an SSI and those without an SSI.

Statistical analysis

Data were collected on an Excel 2010 spreadsheet and statistical analyses were performed using software R version 3.0.3. Quantitative data were reported as medians and the interquartile range. Qualitative variables were expressed as absolute frequencies and percentages. The student t test or Mann–Whitney test were used to compare the groups (SSI versus no SSI) for continuous variables. A proportion test was used to compare the SSI incidence rates during the four different time-frames according to the period of study. Univariate logistic regression was conducted to identify potential risk factors significantly associated with SSI; namely: age, gender, smoking BMI, ASA score, preoperative albumin, preoperative hemoglobin, glycemia, history of diabetes, diagnosis, neoadjuvant therapy, timing of surgery, surgical approach, length of procedure, IRI, site of intervention, and ostomy.

A multivariate logistic regression model, including significant factors of SSI and controlling for confounders, was also performed. The stepwise backward method was used for variable selection (inclusion $p < 0.05$; permanence $p < 0.1$). With the stepwise forward procedure, the results were similar. The fit for logistic regression was tested with the Hosmer and Lemeshow test. P values < 0.05 were considered significant.

Results

Between June, 2010 and July, 2014, 687 patients underwent colorectal surgery at the Department of General Surgery, University Hospital of Trieste. The median age was 71 years (range 19-93 years) and 58.8% of the patients were men, with ASA scores of 2 and 3 (54.9 and 38.2%, respectively). Most of the procedures were performed for malignant disease (80.5%). Table 1 summarizes the univariate analysis of the patients' characteristics.

SSIs developed in 137 patients over the entire period, representing an overall rate of 19.9%. Overall, there were 52 cases of SSSI (37.95%), 15 cases of DSSI (10.95%), and 70 cases of OSI (51.1%). Among patients with an OSI, 56 (80%) were associated with anastomotic leakage and 14 (20%) were associated with intra-abdominal abscesses. The patients were subdivided into four subgroups according to the period in which they underwent surgery. After an initial slight increase, there was a remarkable decrease (7.3%) in overall SSI rates with the best outcomes evident in the last period. Between June, 2013 and July, 2014, among the 165 patients who underwent colorectal surgery, SSI developed in 25, as SSSIs in 11 (44%), DSSIs in 2 (8%), and OSIs in 12 (48%), with an overall rate of 15.1%. These results represent an absolute decrease of 7.3% vs. the first subgroup of patients operated on between June, 2010 and May, 2011, whose overall SSI rate was 22.4%, although the difference did not reach significance (22.4 vs. 19.9%, $p = 0.12$). Moreover, when the incidence of incisional SSIs and OSIs were compared in the two periods, the reduction did not reach significance (9.2 vs. 6.6%, $p = 0.51$ and 9.2 vs. 7.3%, $p = 0.66$, respectively).

SSIs developed during the hospital stay in 92% of the patients, whereas the remaining 8% were detected after discharge and during follow-up. The median time of onset of infection was 7 days after surgery (range 5–10 days). The most common (54%) pathogens isolated from the wound swab or drainage fluid were *Escherichia coli, Enterococcus faecium, Enterococcus faecalis,* and *Pseudomonas Aeruginosa*, although no significant difference was found among the various types of infections.

The median in-hospital stay was 11 days (range 4–111 days), being considerably longer for patients with SSIs; at 23 days (range 7–111 days) for patients with SSIs vs. 10 days, (range 4–82 days) for patients without SSIs ($p < 0.05$).

The Hospital Infection Committee report confirmed 100% compliance for antibiotic prophylaxis in colorectal surgery. Cefazolin plus metronidazole were administered to 553 (80.5%) patients and gentamicin plus metronidazole was administered to 134 (19.5%) patients with penicillin allergy. A booster dose was given to 159 (23.1%) patients, while 99 (14.4%) received 24-h prophylaxis.

Univariate analysis of the patients' characteristics revealed no difference in SSI rates for age ($p = 0.09$), gender ($p = 0.92$), or smoking status ($p = 0.64$) (Table 1). For nutritional status evaluated as BMI, statistical analysis did not show any significant association with the onset of surgical wound infection ($p = 0.50$); however, preoperative hypoalbuminemia was strongly associated with a higher risk of the development of infectious complications (OR = 3.15 [1.74–5.60], $p = 0.0002$).

A reduced risk of SSI was evident for patients with a low ASA score (ASA1: OR = 0.09 [0.01–0.41] and ASA2: OR = 0.58 [0.40–0.85]) and for those with no perioperative anemia (OR = 0.50 [0.29–0.89]). No significant difference was observed in the onset of SSI according to whether surgery was performed for benign vs. malignant disease ($p = 0.23$), or in patients receiving preoperative radiotherapy and/or chemotherapy ($p = 0.33$). Perioperative

Table 1 Preoperative characteristics of patients with vs. those without surgical site infections (SSI)

Variables	SSI, *n* (%) (137 patients)	NO SSI, *n* (%) (550 patients)	OR [95% CI]	*p* value
Age (years)				
Median [25°p–75°p]	73 [67–79]	71 [63–78]	–	0.09
Age group				
< 65	28 (20)	165 (30)	Reference	
65–74	53 (39)	188 (34)	1.66 [1.01–2.78]	0.04*
75–84	44 (32)	146 (27)	1.78 [1.06–3.02]	0.03*
> 85	12 (9)	51 (9)	1.39 [0.64-2.87]	0.39
Gender				
Female	57 (42)	226 (41)	Reference	0.92
Male	80 (58)	324 (59)	0.98 [0.66–1.46]	
Smoking habit[a]				
No	53 (40)	244 (46)	Reference	0.64
Yes	26 (20)	98 (18)	1.19 [0.70–1.99]	0.50
Ex-smoker	52 (40)	191 (36)	1.19 [0.79–1.83]	0.41
BMI (Kg/m^2)				
Median [25°p–75°p]	25.4 [23.1–27.0]	25.1 [22.4–26.7]	–	0.50
BMI group				
<25	63 (46)	268 (49)	Reference	
25–30	53 (39)	215 (39)	1.05 [0.70–1.57]	0.82
>30	21 (15)	67 (12)	1.33 [0.75–2.31]	0.32
ASA score				0.0003*
1	1 (1)	33 (6)	0.09 [0.01–0.41]	0.02*
2	64 (47)	313 (57)	0.58 [0.40–0.85]	0.005*
> 2	52 (52)	204 (37)	Reference	
Preoperative albumin (g/dL)[a]				
Median [25°p–75°p]	3.70 [3.17–4.10]	3.98 [3.60–4.22]	–	0.0001**
< 3	22 (21)	36 (8)	3.15 [1.74 5.60]	0.0001**
> = 3	83 (79)	428 (92)	Reference	
Preoperative glycaemia (mg/dL)[a]				
Median [25°p–75°p]	106 [98–127]	101 [92–113]		0.03*
<= 180	129 (95)	536 (98)	Reference	0.03*
> 180	7 (5)	10 (2)	2.91 [1.04–7.72]	
Preoperative hemoglobin (%)[a]				
Median [25°p–75°p]	12.8 [11.1–13.9]	13.2 [11.5–14.4]	–	0.02*
<10	21 (15)	46 (8)	Reference	0.02*
> = 10	115 (85)	499 (92)	0.50 [0.29–0.89]	
Diabetes				
No	110 (80)	476 (87)	Reference	0.07
Yes	27 (20)	74 (13)	1.58 [0.96–2.54]	
Diagnosis				
Malignant	105 (77)	448 (81)	Reference	0.23
Not malignant	32 (23)	102 (19)	1.34 [0.82–2.14]	
Neoadiuvant therapy (radio–chemotherapy)[b]				
Yes	9 (33)	33 (24)	Reference	0.33
No	18 (67)	107 (76)	0.62 [0.24–1.72]	

Univariate analysis of differences in the rates of SSI

[a]Numbers do not add up to the total because of missing values

[b]In patients undergoing rectal cancer resection

*$p < 0.05$

hyperglycemia did not carry a higher risk of the development of SSI and results were comparable for both diabetic and non diabetic patients.

The univariate analysis of procedure-related variables (see Table 2) showed that an SSI developed more often after emergency surgery (OR = 2.22 [1.46–3.35]; $p < 0.001$), a dirty/infected wound class (OR = 1.92 [1.00–3.58]; $p = 0.04$), and procedures lasting more than 180 min (OR = 1.69 [1.16–2.48], $p = 0.007$) (Table 2). Laparotomy resulted in risk factors (OR = 2.54 [1.68–3.93]; $p < 0.001$) increasing the rates of SSSI, DSSI, and OSI compared with laparoscopy. A high IRI score was also associated with a risk of infectious complications (IRI4: OR = 5.91 [2.77–13.79]; $p < 0.0001$). In fact, SSI developed in 7.2% of patients with an IRI score of 0, and the incidence increased with the score (15.1% of IRI1 patients, 25.6% of IRI2 patients, and 31.4% of IRI3 patients). There was no difference in SSI rates according to different procedure sites ($p = 0.20$) or the simultaneous creation or closure of an ostomy ($p = 0.10$).

Multivariate analysis (adjusted odds ratio, controlled for confounding variables) demonstrated that age between 65–74 years, emergency surgery, diabetes, and high IRI were associated with a significantly increased SSI risk, but wound classification was not (Table 3).

The Hosmer and Lemeshow test confirmed the efficiency of the logistic regression: p value = 0.2339, indicating no evidence of poor fit. This model is correctly specified.

Discussion

SSI is one of the most common postoperative complications and a costly cause of potentially preventable morbidity and mortality. Reducing the occurrence of SSIs is the focus of numerous quality improvement initiatives and a sensitive quality indicator of good healthcare [15, 18, 19]. As a surgical specialty, colorectal surgery has one of the highest rates of SSI, ranging from 15 to 30% [8, 15–17]. Many studies have investigated the causes and risk factors for SSI and a variety of clinical interventions with different levels of supporting evidence have been implemented to reduce wound infection rates in patients undergoing colorectal surgery

Table 2 Surgical site infections (SSI) in relation to the preoperative characteristics

Variables	SSI, n (%) (137 patients)	NO SSI, n (%) (550 patients)	OR [95% CI]	p value
Timing of surgery				
Elective	91 (66)	44 (81)	Reference	
Emergency	46 (34)	102 (19)	2.22 [1.46–3.35]	0.0002**
Surgical approach				
Laparoscopy	34 (25)	251 (46)	Reference	
Laparotomy	103 (75)	299 (54)	2.54 [1.68–3.93]	0.00001**
Length of procedure (min)				
Median [25°p–75°p]	200 [155–260]	175 [135–225]		0.0002**
<= 180	55 (40)	292 (53)	Reference	
>180	82 (60)	258 (47)	1.69 [1.16–2.48]	0.007**
IRI				0.000002**
0	9 (7)	116 (21)	Reference	
1	32 (23)	179 (33)	2.30 [1.10–5.29]	0.03*
2	63 (46)	183 (33)	4.44 [2.23–9.87]	0.00007**
3	33 (24)	72 (13)	5.91 [2.77–13.79]	0.00001**
Site of intervention				0.19
Right hemicolectomy	41 (30)	161 (29)	Reference	
Left hemicolectomy	39 (28)	151 (27)	1.01 [0.60–1.71]	0.26
Transverse colectomy	7 (5)	45 (8)	0.61 [0.22–1.50]	0.32
Anterior resection of rectum	40 (29)	177 (32)	0.89 [0.53–1.49]	0.71
Total abdominal colectomy	6 (4)	10 (2)	2.34 [0.66–7.62]	0.12
Abdominoperineal resection	4 (3)	6 (1)	2.60 [0.52–11.57]	0.23
Ostomy				
Yes	19 (25)	53 (17)	Reference	0.11
No	58 (75)	264 (83)	0.61 [0.33–1.18]	

Univariate analysis of differences in the rates of SSI

*$p < 0.05$

Table 3 Multivariate regression analysis of potential risk factors for surgical site infection (SSI) development: significant variables

Variables	OR* [95% CI]	*p* value
Age group		
< 65	Reference	
65–74	1.89 [1.04–3.52]	0.04*
75–84	1.38 [0.71–2.70]	0.34
> 85	0.57 [0.19–1.48]	0.27
Diabetes		
No	Reference	
Yes	1.85 [1.04–3.24]	0.03*
Timing of surgery		
Elective	Reference	0.009**
Emergency	2.50 [1.24–4.93]	
IRI		
0	Reference	
1	1.70 [0.77–4.07]	0.21
2	3.25 1.54–7.53]	0.003**
3	4.65 [1.99–11.67]	0.0006**
Wound classifications		
Contaminated	Reference	
Dirty/infected	1.77 [0.59–5.31]	0.30

*Odds ratios were adjusted for confounding variables

[18–24, 27]. These considerations prompt us to investigate potentially modifiable risk factors for SSI, to enhance the quality of preventive "care bundles" adopted at our Institution.

We reported the findings of a prospective trial of colorectal surgery cases retrospectively assessed for SSIs during ongoing intervention to lower SSI. During the study period, the overall SSI rate among colorectal patients was 19.9%. Overall, SSSIs developed in 7.6% of patients, DSSIs developed in 2.2%, and OSIs developed in 10.1%. Our current findings, apart from those in relation to OSIs, are consistent with literature data [18, 22–24, 28]. This discrepancy may be due to different definitions of this category of infections, since anastomotic leakage is sometimes excluded from analyses; thus determining a lower rate of OSIs and making it difficult to assess the problem accurately. The downward trend in SSI rates during the study period was noteworthy. This tendency was especially evident for superficial and deep incisional infections (although not significantly) and associated with the implementation of preventive "care bundles", such as delayed primary closure for contaminated procedures and the routine change of sterile drapes and gloves before abdominal wall closure. In this regard, the absolute reduction of 7.3% in overall SSI rates, from 22.4% in the first time-frame to 15.1% in the last timeframe, mirrors the effectiveness of our surveillance program and confirms the importance of preventive care measures [18, 27]. In reference to predictable risk factors, patient variables such as age, gender, and smoking status, seemed not to be correlated with the development of wound infection. In contrast to the literature data [12, 28–31], our study failed to corroborate an association between indications for surgery and SSI rates, as well as between neoadjuvant radio-chemotherapy for rectal cancer and the risk of SSI. However, we confirmed that diabetic patients and those with a high ASA score (≥ 3) are at higher risk of the development of SSI. We also demonstrated that hypoalbuminemia (< 3 g/dL) is strongly associated with infectious complications, highlighting a potentially modifiable risk factor of which practitioners should be aware of [32–35].

All our patients received mechanical bowel preparation according to local protocols, as well as adequate preservation of normothermia and oxygen saturation; therefore, we cannot discuss a possible correlation between these factors and the risk of wound infection. In contrast to the literature data [14, 23, 30], the concurrent creation or closure of an ostomy did not seem to influence SSI rates in our study. However, it is known that patients undergoing emergency surgery and those undergoing contaminated (Class III) or dirty/infected (Class IV) procedures are more at risk of SSI [36–38]. Furthermore, our research confirmed that surgeons may mitigate SSI risk by using laparoscopic techniques and reducing, whenever possible, the operation time (< 180 min) [18, 22, 39–41].

Finally, the IRI score appeared to be significantly correlated with the onset of SSI, thus providing an easy and accurate tool to predict the individual risk of wound infection. Watanabe et al. [42] reported the usefulness of the risk index category for SSI after colorectal surgery but pointed out the necessity to review the method of setting the 75th percentile of the operation time for colorectal surgery, separating that for open vs. laparoscopic surgery.

Our study has some limitations. First, it focused on colorectal surgery at a single institution; therefore, the same results may not be obtained in other patient populations, specialties, or institutions. Second, data regarding subcutaneous fat, evidence of septic shock and duration of postoperative antibiotic use were not recorded in our prospective database, so discerning these outcomes in all patients retrospectively was not possible. Despite these limitations, this single-center experience study reveals an acceptable rate of SSI in a modern colorectal population. Univariate and multivariate analysis confirmed that both modifiable and non-modifiable factors are associated with SSI. IRI and age result as non-modifiable risk factors, while the timing of surgery, diabetes, and nutritional status can be modulated by trying to defer some emergency surgery to an elective procedure, normalize glycemia of diabetic patients, and give nutritional support to hypoalbuminemic patients. These findings may guide our future steps to accurately assess the risk of SSI for each patient through the routine use of an IRI score and by the implementation of standardized glucose control protocols in the preoperative period. From a strictly technical point of view, a laparoscopic approach has advantages and significantly reduces the risk of SSSI and DSSI. There is still a lack of consensus on the optimal system of care. Surgical risk mitigation is multifactorial and multidisciplinary commitment is required. Drawing from the existing evidence base, together with expert opinion and group consensus, it is appropriate to implement national and international registers on SSI to establish new guidelines to reduce their risk.

Compliance with ethical standards

Conflict of interest We declare no conflicts of interest in relation to this study.

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