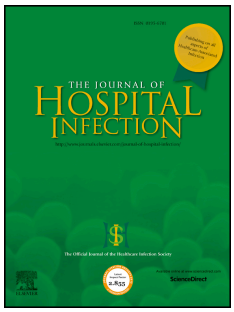
Accepted Manuscript



Predictive factors for early-onset and late-onset surgical site infections in patients undergoing elective colorectal surgery. A multicentre, prospective, cohort study

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PII: S0195-6701(17)30695-3

DOI: 10.1016/j.jhin.2017.12.017

Reference: YJHIN 5309

To appear in: *Journal of Hospital Infection*

Received Date: 13 November 2017

Accepted Date: 20 December 2017

Please cite this article as: Gomila A, Carratalà J, Biondo S, M Badia J, Fraccalvieri D, Shaw E, Diaz-Brito V, Pagespetit L, Freixas N, Brugués M, Mora L, Perez R, Sanz C, Arroyo N, Iftimie S, Limón E, Gudiol F, Pujol M, on behalf of VINCat colon surgery group, Predictive factors for early-onset and late-onset surgical site infections in patients undergoing elective colorectal surgery. A multicentre, prospective, cohort study, *Journal of Hospital Infection* (2018), doi: 10.1016/j.jhin.2017.12.017.

TITLE PAGE

Full title: Predictive factors for early-onset and late-onset surgical site infections in patients undergoing elective colorectal surgery. A multicentre, prospective, cohort study

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Running title: EO/LO SSI in colorectal surgery

[1]**Abbreviations**

[1] ASA: American Society of Anaesthesiologists; CDC: Centres for Disease Control; CLSI; Clinical Laboratory Standard Institute; EO-SSI: early-onset surgical site infection; ESBL: Extended-spectrum β-lactamase; GNB: Gram-negative bacilli; HAI: healthcare-associated infections; IBD: inflammatory bowel disease; IAP: intravenous antibiotic prophylaxis; LOS: length of stay; LO-SSI: late-onset surgical site infection; MBP: mechanical bowel preparation; MDR: multidrug-resistant; NHSN: National Healthcare Safety Network; NNIS: National Nosocomial Infections Surveillance; OAP: oral antibiotic prophylaxis; OS: organ-space; SSI: surgical site infection.

Abstract

Background: Surgical site infections (SSI) are the leading cause of healthcare-associated infections in acute care hospitals in Europe. However, the risk factors for the development of early- (EO) and late-onset (LO) SSI have not been elucidated.

Aim: This study investigated the predictive factors for EO-SSI and LO-SSI in a large cohort of patients undergoing colorectal surgery.

Methods: We prospectively followed-up adult patients undergoing elective colorectal surgery in 10 hospitals (2011-2014). Patients were divided into three groups, EO-SSI, LO-SSI or no infection (no-SSI). The cut-off defining EO-SSI and LO-SSI was 7 days (median time to SSI development). Different predictive factors were used to compare EO-SSI and LO-SSI with the no-SSI patients.

Findings: Of 3701 patients, 320 (8.6%) and 349 (9.4%) developed EO-SSI and LO-SSI, respectively. The rest had no-SSI. Patients with EO-SSI were mostly males, had colon surgery and developed organ-space SSI while LO-SSI patients frequently received chemotherapy or radiotherapy and had incisional SSI. Male sex (OR 1.92, $p<0.001$), American Society of Anaesthesiologists' physical status >2 (OR 1.51, $p=0.01$), administration of mechanical bowel preparation (OR 0.7, $p=0.03$) and stoma creation (OR 1.95, $p<0.001$) predicted EO-SSI while rectal surgery (OR 1.43, $p=0.03$), prolonged surgery (OR 1.4, $p=0.03$) and previous chemotherapy (OR 1.8, $p=0.03$) predicted LO-SSI.

Conclusions: We found distinctive predictive factors for the development of SSI before and 7 days following elective colorectal surgery. These factors could help establish specific preventive measures in each group.

Keywords

Healthcare-associated infection; surgical site infection; colorectal surgery; colorectal cancer.

Introduction

Surgical site infections (SSI) are the most frequent healthcare-associated infections (HAI) in acute care hospitals in Europe [1, 2]. The development of an SSI significantly increases length of stay (LOS), readmissions and hospital costs worldwide [3].

The concept of early- (EO) and late-onset (LO) infections has been widely applied to different types of HAI. This distinction is based on differing infection risk factors, pathogenesis, microbiology and outcomes depending on when they develop. Moreover, this classification has led to the adoption of specific prevention measures and different empirical treatments in each infection type [4–7].

However, despite SSI currently being the leading cause of HAI, the risk factors for EO-SSI vs LO-SSI development have not yet been elucidated. Studies focusing on this topic are scarce [8], and none of them address the large population undergoing colorectal surgery. In this setting, an EO-SSI may be associated with more severe sepsis, requiring expeditious source control and adequate antibiotic therapy [9]. Taking into account that colorectal surgery has the highest SSI rates among elective procedures [10, 11], the identification of specific risk factors of severe SSI is of paramount importance for the adoption of targeted preventive strategies. Therefore, the aim of this study was to identify the distinctive predictive factors for EO-SSI and LO-SSI in a large cohort of patients who underwent elective colorectal surgery.

Methods

Study location and patients

We performed a multicentre, prospective, cohort study from January 2011 to December 2014 in 10 Spanish hospitals. Three of the hospitals were tertiary care university hospitals with >500 beds, five had 200-500 beds and two had <200 beds. All of them participated in the VINCat program [12]. All consecutive patients hospitalized for elective colorectal surgery with bowel resection were enrolled and followed up by trained infection control staff members until 30 days after surgery. Active post-discharge surveillance was mandatory and consisted of electronic clinical records review in primary and secondary care, checking readmissions and emergency visits, and reviewing microbiological and radiological data [13]. Patients with a pre-existing infection at the surgical site at the time of surgery were excluded.

Surveillance program

The VINCat program [12] is a nosocomial infection surveillance program in Catalonia, Spain, based on the National Healthcare Safety Network (NHSN) model [14]. It prospectively collects preoperative demographics, comorbidities, operative characteristics, microbiological and treatment data, and 30-day postoperative outcomes for eligible cases [15].

Study design

All the patients in the cohort were classified into three groups according to SSI development: (i) EO-SSI patients; (ii) LO-SSI patients; (iii) patients with no SSI within 30 days after surgery (no-SSI). The cut-off distinguishing EO-SSI and LO-SSI was 7 days (the median time for SSI development) after surgery.

Firstly, univariate analysis comparing clinical, epidemiological and microbiological characteristics of EO-SSI and LO-SSI was performed. Secondly, following the methodology described by *Harris* et al. [16], two separate analyses were performed to establish the distinctive predictive factors for: (1) EO-SSI , and (2) LO-SSI, each in comparison to no-SSI occurrence. Variables with statistical significance in the first analysis but not in the second, and those significant in the second analysis but not in the first were considered distinctive factors for EO-SSI and LO-SSI, respectively. Significant factors present in both analyses were considered common predictive factors of SSI. This analysis would avoid the bias of considering these common predictive factors of SSI as specific of a determined time point (EO-SSI or LO-SSI).

Definitions

SSI was defined according to the Centres for Disease Control and Prevention (CDC) [17] as superficial incisional, deep incisional or organ-space (OS), and was stratified into categories according to surgical infection risk as defined by the NHSN [14]. EO-SSI was defined as occurrence within the first week after surgery, and LO-SSI as occurrence between the 8^{th} and 30^{th} day after surgery.

Standardised data collection included age, sex, American Society of Anaesthesiologists' (ASA) physical status, administration of mechanical bowel preparation (MBP) and oral antibiotic prophylaxis (OAP) in combination with adequate intravenous antibiotic prophylaxis (IAP), surgical risk index category according to the National Nosocomial Infections Surveillance (NNIS) system criteria [18], operation date, prolonged operation time ($\geq 75^{th}$ percentile for the procedure), laparoscopic surgery, wound classification, date of SSI, infection site (superficial incisional, deep

incisional or OS), microbiology and underlying disease (neoplasia, inflammatory bowel disease [IBD] or others).

Adequate IAP occurred when the following three conditions were met: antibiotics administered according to the evidence-based local protocol at each hospital, completion of the infusion within 60 minutes before the surgical incision and perioperative antibiotic redosing if indicated.

The use of OAP the day before surgery was not mandatory but based on the local protocol at each hospital. It was administered jointly with MBP and the IAP mentioned above, as internationally recommended [19].

Readmission and mortality rates, whether directly attributable to SSI or not, and length of hospitalization were also recorded.

Microbiological studies

In patients with suspected SSI, microbiological samples (blood, wounds and/or peritoneal fluid or abscesses) were usually taken for culture.

Polymicrobial infection was defined as the isolation of ≥2 microorganisms in the samples. If there were ≥3 microorganisms, the laboratory reported the sample as polymicrobial without identifying the species of microorganisms isolated.

Antibiotic susceptibility was tested and interpreted using the microdilution method based on the Clinical Laboratory Standard Institute (CLSI) guidelines [20]. Screening of multidrug-resistant (MDR) phenotypes including extended-spectrum β-lactamase (ESBL) and carbapenemase production was conducted according to the CLSI recommendations [21]. Selected isolates from each centre were characterized by PCR and DNA sequencing using established methods.

MDRGNB were defined as those resistant to at least three classes of antibiotics: carbapenems, ureidopenicillins, cephalosporins (ceftazidime and cefepime), monobactams, aminoglycosides and fluoroquinolones. The following Gram-negative bacilli (GNB) were considered as MDR: (i) ESBL-producing Enterobacteriaceae, (ii) carbapenemase-producing Enterobacteriaceae, and (iii) MDR strains of *Pseudomonas aeruginosa*.

Statistical analysis

All statistics were calculated using SPSS version 20.0 (Chicago, Ill). Continuous variables were compared using Student's *t*-test or the Mann-Whitney *U*-test as appropriate. Categorical variables were analysed using the chi-square test or Fisher's exact test, as appropriate. The multivariate logistic regression model was performed using significant variables from the univariate analysis with a *P* value ≤0.05. Adjusted Odds Ratio (OR) was calculated with 95% confidence intervals (95%CI).

Ethical considerations

This study was approved by the Ethics Committee at Hospital Universitari de Bellvitge (reference: PR305/15).

Results

Overall, 3701 patients were included. Of these, 320 (8.6%) developed EO-SSI, 349 (9.4%) developed LO-SSI and 3032 (81.9%) had no-SSI. Among the 669 (18.1%) patients with SSI, 333 (49.7%) had incisional (superficial and deep) SSI while 336 (50.2%) had OS-SSI.

Epidemiological and clinical characteristics

The comparison among the three groups (EO-SSI, LO-SSI and no-SSI) is shown in Table I. Patients in the EO-SSI group were mostly males, underwent colon surgery, developed OS-SSI and had longer hospitalization. Patients in the LO-SSI group more frequently received MBP, chemotherapy and radiotherapy, had incisional SSI and higher readmission rate.

Predictive factors

The distinctive predictive factors for EO-SSI and LO-SSI on univariate and multivariate regression analysis are shown in Tables II and III. Each cohort was compared with the no-SSI patient group. Compared with no-SSI, EO-SSI patients were mostly males (OR 1.92, 1.46-2.53; p<0.001), with an ASA score III-IV (OR 1.5, 1.10-2.07; p=0.01), had fewer laparoscopic procedures (OR 0.47, 0.35-0.63; p<0.001), less frequently received OAP (OR 0.5, 0.44-0.76; p<0.001) and MBP (OR 0.7, 0.54-0.96; p=0.03) and more frequently received a stoma (OR 1.95, 1.50-2.53; p<0.001). Patients with LO-SSI more frequently underwent rectal surgery (OR 1.43, 1.03-1.97; p=0.03), had prolonged operation time (OR 1.4, 1.02-1.93; p=0.03), had fewer laparoscopic procedures (OR 0.47, 0.30-0.60; p<0.001), less frequently received OAP (OR 0.5, 0.50-0.80; p<0.001) and more frequently had received previous chemotherapy (OR 1.8, 1.06-3.10; p=0.03).

Aetiology of SSI

Of the 669 patients who developed SSI, 496 (74.1%) had positive surgical samples; 240 (48.4%) of these were polymicrobial. Blood cultures were performed in 238 (35.5%) of 669 patients, and they were positive in 34/238 (14.3%). Concordance between blood cultures and abdominal samples was observed in 14 of 34 (41.2%) cases. The most frequent isolates were *Escherichia coli* (229/496, 46.1%), *Enterococcus* spp. (23.3%) and *P. aeruginosa* (12.5%) (Table IV). There were no significant differences regarding aetiology between EO-SSI and LO-SSI, except *E. coli*, which was more commonly observed in EO-SSI than in LO-SSI (44.1% vs 25.2% $p<0.001$) and *Staphylococcus aureus*, which was more commonly observed in LO-SSI than in EO-SSI (6.3% vs 2.2%, $p=0.009$). There were also no significant differences among groups in terms of MDR GNB, although there was a tendency of a higher proportion of MDR *P. aeruginosa* in LO-SSI than in EO-SSI.

Discussion

Our study revealed the different predictive factors of EO-SSI and LO-SSI after elective colorectal surgery. Male sex, ASA score III-IV, not receiving MBP and stoma creation predicted EO-SSI, while rectal surgery, longer duration of surgery and previous chemotherapy predicted LO-SSI. This analysis permits to establish the specific predictive factors at each time point (EO-SSI and LO-SSI), avoiding the bias of considering the common predictors of SSI.

We found several distinctive predictive factors for EO-SSI. Firstly, MBP was a protective factor in itself. We agree with the controversy about the efficacy of MBP since a large body of evidence suggests that MBP has no beneficial effect in reducing SSI rates unless it is accompanied with an OAP [22, 23]. The effect of MBP was probably influenced by the concomitant use of an OAP; however, MBP could also have had a beneficial effect in reducing patient morbidity since most EO-SSIs were OS.

Stoma creation appeared as the strongest risk factor for EO-SSI development. A previous study [24] showed that stoma creation was a risk factor for superficial and deep incisional SSI, but that analysis did not include OS-SSI. In our cohort, cases involving stoma creation were more complex and technically challenging, since surgery frequently involved the rectum and was performed due to pathologies like IBD or diverticulosis rather than for neoplasia, therefore conferring a higher risk of SSI. These SSIs were equally distributed between incisional and OS-SSI. Another study examined the effect of stoma creation in rectal cancer patients after chemotherapy and radiotherapy, and showed results similar to ours: patients in the stoma group had greater comorbidities (higher ASA score, body mass index or hypertension) than the other group [25]. This suggests that the need for stoma could be a marker of illness severity. Another study showed an increased anastomotic leakage rate in patients with a diverting

stoma, although the stoma diminished the severity of the leakage [26]. Therefore the stoma is probably a marker of surgery with high risk of SSI.

Rectal surgery was a LO-SSI distinctive predictive factor. The rectal surgical technique usually requires incision through the perineum, which is a highly-contaminated area. Manipulation of wounds in this area could increase the risk of incisional SSI (most frequent SSI type in this group), and such extensive surgery usually requires a long operation time [27], this was also an independent LO-SSI risk factor. We described higher rates of SSI associated with rectal surgery previously [28].

Chemotherapy was the strongest risk factor for developing LO-SSI. Chemotherapy with capecitabine or 5-fluorouracil is almost always administered in stage II-III rectal cancer to downstage tumour size and improve survival after surgery. Despite the beneficial effects of neoadjuvant therapy, it causes some degree of inflammation, necrosis and fibrosis of surrounding tissue. This leads to an increased risk of intraoperative bleeding, wound dehiscence and wound infection [29].

We revealed laparoscopy and OAP as protective factors in both early and late SSI, as has been previously reported [30, 31].

E. coli was significantly more common in EO-SSI than in LO-SSI since the risk of anastomotic leakage and OS-SSI is the highest within the first few days after surgery. Conversely, *S. aureus* was significantly more common in LO-SSI than in EO-SSI. Since *S. aureus* commonly colonizes human skin, wound manipulation or drains placed during hospitalization could increase the risk of wound infection [32]. Incisional SSI was the most frequent LO-SSI in our cohort. Although not significant, because of the small number of isolates, we found a tendency of a higher proportion of MDR *P. aeruginosa* in LO-SSI than in EO-SSI, probably related to antibiotic pressure.

In the outcome analyses, EO-SSI development increased LOS and mortality compared to LO-SSI or no-SSI. This was probably related to the fact that EO-SSI was predominantly OS, while LO-SSI was more frequently incisional. A previous study by our group already showed the worst outcome associated with OS-SSI [33].

Among the strengths of this study is its multicentre nature, the large number of patients included and the fact that data collection was uniformly performed by trained infection control staff members. This study has some limitations that should be acknowledged. First, the number of variables was restricted since a multicentre surveillance system must collect limited but consistent variables. Second, the cut-off used to define EO-SSI and LO-SSI was arbitrary; however, it was established after the clinical observation of SSI.

Conclusions

We identified specific predictive factors for the development of EO-SSI and LO-SSI after elective colorectal surgery. The identification of these factors could help to establish targeted preventive measures for each infection type. Although further studies are needed, according to our results, it seems appropriate to perform laparoscopic surgery whenever possible and give OAP combined with MBP. Special attention to patients with stoma creation should be paid to detect any sign of severe SSI. The duration of surgery should be shortened as much as possible.

Acknowledgements:

We would like to thank all other collaborators at *Hospital Universitari de Bellvitge*: Daniel Camprubí; *Corporació Sanitària Parc Taulí*: Marta Piriz, Xavier Serra-Aracil; *Parc Sanitari Sant Joan de Déu de Sant Boi*: Antoni Cruz, Encarna Moreno; *Consorci Sanitari de Terrassa*: Elena Espejo, Francesc Aguilar; *Hospital Universitari Mútua de Terrassa:* Carmen Nicolás, Albert Navarro; *Hospital de Viladecans*: Ana Lérida, Lydia Martin; *Fundació Privada Hospital Asil de Granollers*: Jordi Cuquet, Rosa Vázquez; *Hospital Universitari Sant Joan de Reus*: Antoni Castro, Ana Felisa Lopez. Writing assistance was provided by the Department of Languages in the Faculty of Medicine of Barcelona University.

Conflicts of interest: none.

Funding sources

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authorship and manuscript preparation: AG, JC and MP substantially contributed to the conception of the study, analysis and interpretation of data. All authors contributed to drafting the article or revising it critically for important intellectual content.

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Table I. Epidemiological and clinical characteristics of early-onset (EO-SSI), late-onset (LO-SSI) and no surgical site infection (no-SSI) patients

	EO-SSI (n=320)	LO-SSI (n=349)	No-SSI (n=3032)	p-value*
Age, mean (SD) years	68.8 (12.4)	68.5 (11.6)	68.5 (12.1)	0.7
≥ 65, n (%)	219 (68.4)	236 (67.6)	1980 (65.3)	0.8
Male sex, n (%)	243 (75.9)	232 (66.5)	1814 (59.8)	0.007
ASA III-IV, n (%)	159 (49.7)	159 (45.6)	1178 (38.9)	0.3
NNIS 1-2, n (%)	146 (45.6)	168 (48.1)	993 (32.8)	0.5
Indication for surgery, n (%):				
- Neoplasia	300 (93.8)	334 (95.7)	2868 (94.6)	0.2
- IBD	11 (3.4)	7 (2)	73 (2.4)	0.25
- Other	8 (2.5)	8 (2.3)	87 (2.9)	0.8
Type of surgery, n (%):				0.007
- Colon surgery, n (%)	215 (67.2)	199 (57)	2104 (69.4)	
- Rectal surgery, n (%)	105 (32.8)	150 (43)	928 (30.6)	
Adequate antibiotic prophylaxis, n (%)	264 (82.5)	293 (84)	2526 (83.3)	0.6
Duration of surgery ≥ 75p [a], n **(%)**	128 (40)	161 (46.1)	1163 (38.4)	0.1
Laparoscopic surgery, n (%)	156 (48.8)	166 (47.6)	1975 (65.1)	0.7
Oral antibiotic prophylaxis, n (%)	93 (29.1)	122 (35)	1352 (44.6)	0.1
Mechanical bowel preparation, n (%)	221 (70.2)	283 (81.8)	2283 (77.1)	<0.001
Stoma, n (%)	122 (38.2)	125 (35.8)	715 (23.6)	0.5
Previous chemotherapy, n (%)	52 (16.3)	88 (25.2)	471 (15.5)	0.005
Previous radiotherapy, n (%)	46 (14.4)	80 (22.9)	452 (14.9)	0.005
Diagnosis of SSI during hospitalization, n (%)	296 (92.5)	185 (53)	_	<0.001
Type of SSI, n (%):				0.001

- Incisional SSI	138 (43.1)	195 (55.9)	_	
- Organ-space SSI	182 (56.9)	154 (44.1)	_	
Readmission, n (%)	36 (11.2)	96 (26.1)	88 (2.9)	<0.001
Readmission due to SSI, n (%)	32 (10)	85 (24.4)	_	<0.001
Total length of stay, mean (SD) days	25.3 (27.6)	22.9 (17.4)	9 (7)	<0.001
Mortality, n (%)	22 (6.9)	13 (3.7)	13 (0.4)	0.07
Mortality attributed due to SSI, n (%)	19 (5.9)	12 (3.4)	_	0.1

EO-SSI: Early-onset surgical site infection, **LO-SSI:** Late-onset surgical site infection, **SD:** standard deviation, **ASA:** American Society of Anaesthesiologists' physical status, **NNIS:** National Nosocomial Infections Surveillance Risk Index, **IBD:** inflammatory bowel disease, **SSI:** surgical site infection. [a] Greater than 75th percentile for the duration of surgery (180 min, 3 hours). * *P*-value refers to the comparison between EO-SSI and LO-SSI groups.

Table II. Univariate analysis of predictive factors associated with EO-SSI and LO-SSI (compared with 30 day no-SSI patients)

	EO-SSI (n=320)	No-SSI (n=3032)	p-value	LO-SSI (n=349)	No-SSI (n=3032)	p-value
Age, mean (SD) years	68.8 (12.4)	68.5 (12.1)	0.6	68.5 (11.5)	68.5 (12.2)	0.9
≥ 65, n (%)	219 (68.4)	1980 (65.3)	0.26	113 (32.4)	1052 (34.7)	0.4
Male sex, n (%)	243 (75.9)	1814 (59.8)	<0.001	232 (66.5)	1814 (59.8)	0.016
ASA III-IV, n (%)	159 (49.7)	1178 (38.9)	<0.001	159 (45.6)	1178 (38.9)	0.015
NNIS 1-2, n (%)	146 (45.6)	993 (32.8)	<0.001	168 (48.1)	993 (32.8)	<0.001
Indication for surgery, n (%):						
- Neoplasia	300 (93.8)	2868 (94.6)	0.5	334 (95.7)	2868 (94.6)	0.4
- IBD	11 (3.4)	73 (2.4)	0.2	7 (2)	73 (2.4)	0.64
- Other	8 (2.5)	87 (2.9)	0.7	8 (2.3)	87 (2.9)	0.53
Type of surgery, n (%):			0.4			<0.001
- Colon surgery	215 (67.2)	2104 (69.4)		199 (57)	2104 (69.4)	
- Rectal surgery	105 (32.8)	928 (30.6)		150 (43)	928 (30.6)	
Adequate antibiotic prophylaxis, n (%)	264 (82.5)	2526 (83.3)	0.7	293 (84)	2526 (83.3)	0.76
Duration of surgery ≥ 75p [a], n (%)	128 (40)	1163 (38.4)	0.56	161 (46.1)	1163 (38.4)	0.005
Laparoscopic surgery, n (%)	156 (48.8)	1975 (65.1)	<0.001	166 (47.6)	1975 (65.1)	<0.001
Oral antibiotic prophylaxis, n (%)	93 (29.1)	1352 (44.6)	<0.001	122 (35)	1352 (44.6)	0.001
Mechanical bowel preparation, n (%)	221 (70.2)	2283 (77.1)	0.006	283 (81.8)	2283 (77.1)	0.047
Stoma, n (%)	122 (38.2)	715 (23.6)	<0.001	125 (35.8)	715 (23.6)	<0.001
Previous chemotherapy, n (%)	52 (16.3)	471 (15.5)	0.7	88 (25.2)	471 (15.5)	<0.001
Previous radiotherapy, n (%)	46 (14.4)	452 (14.9)	0.8	80 (22.9)	452 (14.9)	<0.001

EO-SSI: Early-onset surgical site infection, **No-SSI:** no surgical site infection, **LO-SSI:** Late-onset surgical site infection, **SD:** standard deviation, **ASA:** American Society of Anaesthesiologists' physical status, **NNIS:** National Nosocomial Infections Surveillance Risk Index, **IBD:** inflammatory bowel disease, [a] Greater than 75th percentile for the duration of surgery (180 min, 3 hours).

Table III. Multivariate analysis of predictive factors for EO-SSI and LO-SSI (significant variables of univariate analysis): logistic regression model

	EO-SSI (n= 320)			LO-SSI (n= 349)		
	p-value	**OR**	**95%CI**	**p-value**	**OR**	**95%CI**
Male sex	**<0.001**	**1.92**	**1.46-2.53**	0.15	1.2	0.93-1.51
ASA III-IV	**0.01**	**1.51**	**1.10-2.07**	0.1	1.3	0.93-1.9
NNIS 1-2	0.25	1.24	0.85-1.83	0.7	1.1	0.70-1.74
Type of surgery:						
- Colon surgery						
- Rectal surgery				**0.03**	**1.43**	**1.03-1.97**
Duration of surgery ≥75th percentile [a]				**0.03**	**1.4**	**1.02-1.93**
Laparoscopic surgery	**<0.001**	**0.47**	**0.35-0.63**	**<0.001**	**0.44**	**0.30-0.60**
Oral antibiotic prophylaxis	**<0.001**	**0.5**	**0.44-0.76**	**<0.001**	**0.63**	**0.50-0.80**
Mechanical bowel preparation	**0.03**	**0.7**	**0.54-0.96**	0.09	0.76	0.50-1.00
Stoma	**<0.001**	**1.95**	**1.50-2.53**	0.3	1.2	0.86-1.64
Previous chemotherapy				**0.03**	**1.8**	**1.06-3.10**
Previous radiotherapy				0.15	1.5	0.85-2.76

EO-SSI: Early-onset surgical site infection, **LO-SSI:** Late-onset surgical site infection, **OR:** Odds ratio, **95%CI:** 95% confidence interval, **ASA:** American Society of Anaesthesiologists' physical status, **NNIS:** National Nosocomial Infections Surveillance Risk Index, [a] Greater than 75th percentile for the duration of surgery (180 min, 3 hours).

Table IV. Aetiology of EO-SSI and LO-SSI

Number of patients	**Overall (n=496) (%)**	**EO-SSI (n=253) (%)**	**LO-SSI (n=243) (%)**	**p-value**
Gram-negative bacteria, n (%)	324 (65.3)	178 (70.4)	146 (60.1)	0.001
• *Escerichia coli*	229 (46.2)	141 (55.7)	88 (36.2)	<0.001
– MDR *E. coli*	28 (5.6)	16 (6.3)	12 (4.9)	0.5
• *Pseudomonas aeruginosa*	62 (12.5)	26 (10.3)	36 (14.8)	0.1
– MDR *P. aeruginosa*	3 (0.6)	0 (0)	3 (1.2)	0.07
• *Klebsiella pneumoniae*	30 (6)	14 (5.5)	16 (6.6)	0.6
– MDR *K. pneumoniae*	9 (1.8)	4 (1.6)	5 (2.1)	0.6
Gram-positive bacteria, n (%)	187 (28)	87 (27.2)	100 (28.7)	0.6
• *Enterococcus faecalis*	58 (11.7)	33 (13)	25 (10.3)	0.3
• *E. faecium*	58 (11.7)	30 (11.9)	28 (11.5)	0.9
• *Staphylcoccus aureus*	28 (5.6)	7 (2.8)	21 (8.6)	0.009
Anaerobes, n (%)	32 (6.5)	13 (5.1)	19 (7.8)	0.2
• *Bacteroides fragilis*	14 (2.8)	6 (2.4)	8 (3.3)	0.5
Yeast, n (%)	19 (3.8)	11 (4.3)	8 (3.3)	0.5
• *Candida albicans*	15 (3)	10 (4)	5 (2.1)	0.2
Polymicrobial**,** n (%)	240 (48.4)	123 (48.6)	117 (48.1)	0.9

EO-SSI: Early-onset surgical site infection, **LO-SSI:** Late-onset surgical site infection**,** ***E. coli:*** *Escherichia coli,* **MDR**: multidrug-resistant, ***P. aeruginosa****: Pseudomonas aeruginosa,* ***K. pneumoniae:*** *Klebsiella pneumoniae,* ***E. faecalis:*** *Enteroccocus faecalis,* ***E. faecium:*** *Enterococcus faecium,* ***S. aureus:*** *Staphylococcus aureus,* ***B. fragilis:*** *Bacteroides fragilis,* ***C. albicans:*** *Candida albicans.*