Surgical Site Infection in Elective Operations for Colorectal Cancer After the Application of Preventive Measures

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Objectives: To assess the prevalence of surgical site infection (SSI) after elective operations for colon and rectal cancer after the application of evidence-based preventive measures and to identify risk factors for SSI.

Design: Prospective, observational, multicenter.

Setting: Tertiary and community public hospitals in Catalonia, Spain.

Patients: Consecutive patients undergoing elective surgical resections for colon and rectal cancer during a 9-month period.

Main Outcome Measures: The prevalence of SSI within 30 days after the operations and risk factors for SSI.

Results: Data from 611 patients were documented: 383 patients underwent operations for colon cancer and 228 underwent operations for rectal cancer. Surgical site infection was observed in 89 (23.2%) colon cancer patients (superficial, 12.8%; deep, 2.1%; and organ/space, 8.4%) and in 63 (27.6%) rectal cancer patients (superficial, 13.6%; deep, 5.7%; and organ/space, 8.3%). For colon procedures, the following independent predictive factors were identified: for incisional SSI, open procedure vs laparoscopy; for organ/space SSI, hyperglycemia at 48 hours postoperatively (serum glucose level, >200 mg/dL), ostomy, and National Nosocomial Infection System index of 1 or more. In rectal procedures, no risk factors were identified for incisional SSI; hyperglycemia at 48 hours postoperatively (serum glucose level, >200 mg/dL) and temperature lower than 36°C at the time of surgical incision were associated with organ/space SSI.

Conclusion: The prevalence of SSI in elective colon and rectal operations remains high despite the application of evidence-based preventive measures.

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SURGICAL SITE INFECTION (SSI) is the most frequent cause of nosocomial infection in surgical patients, accounting for 38% of the total.1 Surgical site infection doubles the risk of postoperative mortality, increases intensive care unit stay by 60%, and is associated with a 5-times increased likelihood of readmission.2 It also prolongs hospital stay between 5 and 20 days, with a substantial increase in hospital costs.3-6 The high prevalence and the financial burden associated with SSI have led investigators in many countries to develop infection control systems. A good example is the National Nosocomial Infection System (NNIS) of the US Centers for Disease Control and Prevention, which modified the definition of surgical wound infection by introducing the concept of surgical site infection, divided into wound infection and organ/space infection.7-8 In an attempt to compare the prevalence of SSI between hospitals, the NNIS developed an SSI risk index based on the American Society of Anesthesiologists score, the degree of contamination of the wound, and duration of the operation. A modified version of the index is used in laparoscopic procedures.9,10 Many studies on the frequency of SSI in colorectal operations fail to separate the results of procedures for benign vs malignant neoplasms.11-13 Frequency of SSI differs in the colon and the rectum.14,15 Rectal cancer operations are often associated with the creation of ostomies, preoperative radiotherapy, and total excision of the mesorectum with anastomoses close to the anal margin. These procedures lengthen surgical time and increase the likelihood of bacterial contamination15,17; for this reason, rectal operations are associated with a greater risk of SSI.

The application of protocols for the prevention of SSI has proved to be effective in reducing postoperative infections.15,18 It
is important, however, to assess these protocols at least 30 days after surgery. Currently, with enhanced recovery programs, patients are discharged within 7 days,\textsuperscript{13,19} and the figures for in-hospital SSI may differ substantially from those recorded at 30 days.\textsuperscript{20}

Most studies published to date have been conducted at a single institution or report the results obtained by a single surgeon\textsuperscript{11-13,21} and have not separately assessed SSI for colon and rectal cancer resections. The purpose of the present study was to evaluate, in a prospective multicenter design, the prevalence of SSI in colon and rectal cancer resections and to identify predictive factors for SSI after the application of a protocol of preventive measures with a follow-up of 30 days.

**METHODS**

**STUDY DESIGN**

We conducted a prospective, observational, multicenter study of the application of evidence-based preventive measures to control SSI. The target population comprised patients receiving elective operations for colon or rectal cancer in a group of public hospitals in Catalonia, Spain.

**INCLUSION AND EXCLUSION CRITERIA**

Colon operation was defined as any resection above the peritoneal reflection. The inclusion criteria were the application of all the preventive measures and colon cancer surgery with oncologic resection. Rectal operation was defined pragmatically as any resection below the peritoneal reflection. The inclusion criteria were the application of all preventive measures and rectal cancer operations with oncologic resection. Exclusion criteria for both types of procedures were failure to apply any of the preventive measures, procedures associated with the excision of other organs, and total coloproctectomy.

**EVIDENCE-BASED PREVENTIVE MEASURES**

Preoperative preventive measures included shower,\textsuperscript{22} serum glucose determination (in patients with diabetes mellitus, a glycosylated hemoglobin level was required\textsuperscript{23,24}), and hair removal with a disposable electronic clipper.\textsuperscript{7}

Perioperative measures included prophylactic antibiotics, administered 30 minutes prior to the surgical incision.\textsuperscript{19,25} A single antibiotic was preferred to a combination, provided that its spectrum included fecal bacterial flora.\textsuperscript{26} Amoxicillin–clavulanate potassium, 2 g/200 mg, was administered intravenously and repeated 4 hours after the first dose if surgery was prolonged. In the case of allergy to penicillin, metronidazole hydrochloride, 1500 mg, and gentamicin sulfate, 240 mg, were administered in a single intravenous dose. On closing the laparotomy, gowns and gloves were changed, a new table was used with specific surgical material (needle holders, forceps, and separators), and a clean, dry field was obtained with use of new sterile drapes.\textsuperscript{27,28} The surgical wound was washed with 500 mL of normal saline before skin closure.\textsuperscript{29} Measures were applied to achieve normothermia (\textasciitilde36.6°C) during the procedure and for 3 to 6 hours after the operation;\textsuperscript{30} body temperature was maintained with an esophageal probe. Serum glucose level was maintained below 200 mg/dL (to convert glucose levels to millimoles per liter, multiply by 0.0555) for 24 to 48 hours after the operation in all patients.\textsuperscript{31}

Patients who met the inclusion criteria were enrolled consecutively at each of the hospitals. The coordinating surgeon at each hospital supervised the application of the preventive measures.

**END POINT AND PATIENT VARIABLES**

The aim of the study was to establish the prevalence of SSI (superficial or deep incisional or organ/space) in elective operations for cancer of the colon and rectum, based on the Centers for Disease Control and Prevention definitions.\textsuperscript{32} The diagnosis of SSI was made after discussion among surgeons and nurses who inspected the surgical wound once daily. For cases in which there was initial disagreement, consensus was obtained by a member of the infection control staff. Infections involving both organ/space and the incision (superficial or deep) were categorized as organ/space. Organ/space infections were diagnosed most commonly by radiologic or reoperative findings consistent with an intra-abdominal infection. The final assessment was made by the surgeon after 30 days, during an outpatient visit.

Patient-dependent variables included age, sex, body mass index (calculated as weight in kilograms divided by height in meters squared: \(<30 \text{ kg/m}^2 \text{ vs } \geq 30 \text{ kg/m}^2\)), high blood pressure, ischemic heart disease, arrhythmia due to atrial fibrillation, diabetes, smoking, previous surgical incision, history of weight loss of more than 10% of body weight, preoperative use of corticosteroids, Charlson comorbidity index (\(<2 \text{ vs } \geq 2\)), hemoglobin A\textsubscript{1c} (\(<8\% \text{ vs } \geq 8\%\) [to convert to a proportion of 1.0, multiply by 0.01]), preoperative hemoglobin level (\(<10\text{ or } \geq 18\text{ g/dL}\), [to convert to grams per liter, multiply by 10]), American Society of Anesthesiologists score (1-2 vs 3-4), preoperative radiotherapy, preoperative serum glucose level (\(<200\text{ mg/dL vs } \geq 200\text{ mg/dL}\)), diagnosis of colon or rectal cancer, and mechanical colon preparation.

Dependent perioperative variables included type of surgical procedure (open, laparoscopic, or conversion); surgeon (senior or resident); prophylactic antibiotic regimen (amoxicillin–clavulanate or metronidazole/gentamicin); time of antibiotic administration in relation to the time of the incision (\(\leq 1\text{ vs } >1\) hour); \(\leq 30\text{ minutes and } >3\text{ hours vs } >30\text{ minutes and } \leq 3\text{ hours}\); central body temperature at baseline, time of resection, and end of the intervention (\(<36\text{°C vs } \geq 36\text{°C}\)); duration of the operation (\(<120\text{ vs } >120\) minutes); glycemic control at 24 hours and 48 hours (serum glucose level, \(<200\text{ mg/dL vs } >200\text{ mg/dL}\) ); perioperative blood transfusion; surgical technique used; use of anastomoses (absence or presence and type); type of laparotomy closure; creation of an ostomy; classification of surgical wound (clean-contaminated vs contaminated-dirty); NNIS score for SSI risk (\(<1/0 \text{ vs } 1/2/3\)\textsuperscript{33,34} and scores of POSSUM (Physiological and Operative Severity Score for the Enumeration of Mortality and Morbidity),\textsuperscript{35} P-POSSUM (Portsmouth POSSUM),\textsuperscript{36} and CR-POSSUM (Colorectal POSSUM) scales.\textsuperscript{37}

Postoperative variables (in-hospital) included presence of superficial, deep, or organ/space SSI; date of detection of the SSI; type of treatment; microorganisms identified; date of hospital discharge; presence of other medical and surgical complications; and death, with cause of death. Postoperative variables (after discharge) included readmission because of an SSI, date of outpatient visit (at least 30 days after the operation), presence or absence of SSI, tumor stage, and death during 30 days after the operation, with cause of death. Variables were recorded in an online electronic database on the Web site of the Avedis Donabedian University Institute, Barcelona, Spain. Using a password, each center accessed its own form and all data were stored in the centralized database. Each center could access the data of its own patients, but not those from other hospitals. Data were analyzed monthly.
At the end of the study, an external audit was performed by independent staff who visited the hospitals and inspected the data processing. The study was approved by the Ethics Committee of the Corporacio´n Sanitària Parc Taulı´, the coordinating hospital.

Risk factors were studied for incisional SSI (superficial and deep infections) and for organ/space SSI. Superficial and deep SSIs were grouped because their negative influence on the healing of the abdominal incision is very similar.12

STATISTICAL ANALYSIS

Descriptive and statistical analysis was performed (SPSS, version 14; SPSS, Inc, Chicago, Illinois). For the quantitative variables, mean (SD) was used when the distribution was considered normal; otherwise, the median, interquartile interval, and range were used. Categorical variables were reported in absolute numbers and percentages. The parametric t test was used for statistical analysis of the quantitative variables with independent groups if the conditions for its application were met. For categorical variables, Pearson 𝜒² test was used. The results of the statistical tests are given, whenever possible, with a confidence interval (CI) of 95%, and P < .05 was considered statistically significant. Variables that were statistically significant or presented a trend (P < .20)13 were introduced in the multivariate logistic regression analysis for the study of the risk factors in incisional and organ/space SSI in cancer of the colon and rectum in 4 independent models.

RESULTS

The recruitment period lasted from June 1, 2007, to March 31, 2008, in 19 hospitals in Catalonia. Four had fewer than 250 beds; 6 were medium sized, with 250 to 500 beds; and 9 had more than 500 beds.

Data on 611 patients were included, with operations on 383 patients for colon cancer and 228 for rectal cancer. The mean (SD) number of patients included per hospital was 32 (29). Table 1 demonstrates the results for SSI in colorectal cancer as well as data for superficial, deep, and organ/space SSI for each group. The prevalence of infection differed between colon and rectal cancer (89/383 [23.2%] vs 63/228 [27.6%]).

The Figure shows the results for SSI according to the type of operation and site and time of infection. In-hospital superficial wound infection occurred in 64 of 611 procedures (10.5%) overall, with similar values for the colon and the rectal operations. The Figure also stresses the importance of measuring SSI at 30 days. More than one-fifth of the infections were detected after discharge: 20 of 89 (22.5%) in colon operations and 15 of 63 (23.8%) in rectal operations.

Table 2 reports the variability among centers. There was a trend toward higher SSIs in small hospitals (<250 beds) and, in incisional SSIs, in colon cancer the difference was statistically significant. With application of the POSSUM-Morbidity risk model, no statistically significant differences were found between patients with and those without SSI. In the risk models that measure mortality, significant differences were found with the P-POSSUM, but with the model for colorectal operations (CR-POSSUM), no statistically significant differences were observed.

Table 3 presents the bivariate analysis of the variables with statistical significance for incisional and organ/space SSI in colon cancer procedures. For incisional SSI, only laparoscopy/open procedures were an indepen-

### Table 1. Overall Incidence of SSI

<table>
<thead>
<tr>
<th>Type of SSI</th>
<th>Overall Colorectal Operations (N=611)</th>
<th>Colon Operations (n=383)</th>
<th>Rectal Operations (n=228)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%) 95% CI</td>
<td>No. (%) 95% CI</td>
<td>No. (%) 95% CI</td>
</tr>
<tr>
<td>Total</td>
<td>152 (24.9) 21.4-28.4</td>
<td>89 (23.2) 18.9-27.6</td>
<td>63 (27.6) 21.6-33.7</td>
</tr>
<tr>
<td>Superficial</td>
<td>80 (13.1) 10.4-15.9</td>
<td>49 (12.8) 9.3-16.3</td>
<td>31 (13.8) 8.9-18.3</td>
</tr>
<tr>
<td>Deep</td>
<td>21 (3.4) 1.9-4.9</td>
<td>8 (2.1) 0.5-3.70</td>
<td>13 (5.7) 2.5-9</td>
</tr>
<tr>
<td>Incisional, superficial, and deep</td>
<td>101 (16.6) 13.5-19.60</td>
<td>57 (14.9) 11-18.3</td>
<td>44 (19.3) 14-24.6</td>
</tr>
<tr>
<td>Organ/space</td>
<td>51 (8.3) 6.1-10.60</td>
<td>32 (8.4) 5.4-11.3</td>
<td>19 (8.3) 4.5-12.1</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; SSI, surgical site infection.
dent predictive factor in the multivariate logistic regression analysis (odds ratio [OR], 2.76; 95% CI, 1.29-5.90; P = .009). In the case of organ/space SSI in colon cancer, the independent predictive factors in the multivariate logistic regression analysis were hyperglycemia at 48 hours (serum glucose level, >200 mg/dL) (OR, 4.48; 95% CI, 1.06-18.91; P = .04), creation of an ostomy (OR, 10.01; 95% CI, 1.31-76.29; P = .03), and NNIS risk of infection higher than 1 (OR, 7.65; 95% CI, 2.04-28.66; P = .003).

Table 4 documents the results of the bivariate analysis with statistical significance for incisional and organ/space SSI in rectal cancer operations. Although multiple risk factors were analyzed with incisional SSI, only the American Society of Anesthesiologists score showed statistically significant differences, and no independent predictive factors were identified in multivariate analysis. For organ/space SSI, the independent predictive factors in the multivariate analysis were hyperglycemia at 48 hours (serum glucose level, >200 mg/dL) (OR, 9.43; 95% CI, 1.04-85.95; P = .047) and temperature lower than 36°C at the start of the intervention (OR, 18.88; 95% CI, 2.47-144.33; P = .005).

Hospital stay was influenced by SSI. Significant differences in length of stay for patients with incisional SSI, organ/space SSI, or both were found in both colon and rectal cancer procedures. Hospital stay was much longer in cases of organ/space SSI (Tables 3 and 4).

Five hundred sixty patients received an anastomosis, 383 in colon operations and 177 in rectal operations. Overall rates of anastomotic dehiscence were 34 of 560 (6.1%), with 26 of 383 in the colon (6.8%) and 9 of 177 in the rectum (5.1%). Surgical treatment was required in 16 of 25 patients (64.0%) after colon operations and in 7 of 9 patients (77.8%) after rectal operations. The remaining anastomotic dehiscences resolved with conservative treatment.

Postoperative mortality occurred in 13 of 611 patients (2.1%): 10 of 383 after colon operations (2.6%) and 3 of 228 after rectal operations (1.3%). Two of the deaths in patients who underwent colon operations were associated with organ/space SSI; none of the deaths in patients who underwent rectal operations were related to SSI.

The external audit was performed between June 1, 2007, through March 31, 2008. Data on 50 patients from 10 of the 19 participating hospitals were reviewed in a randomized manner by an independent observer. No discrepancies were found between the information recorded in the database and that in the patients’ clinical records.

**COMMENT**

To our knowledge, no studies to date have assessed the incidence of SSI only in colorectal cancer—with results specified for colon and rectal resections—or the factors that influence incisional (superficial and deep) SSI, and organ/space SSI in each of these types of operations. Over-
all, we found SSI in 152 patients (24.9%) with colorectal cancer (colon cancer, 89 [23.2%]; and rectal cancer, 63 [27.6%]). Historically, the incidence of SSI in colorectal cancer has ranged widely, mostly due to differences in the definition of the phenomenon and because not all studies have considered a 30-day follow-up period.5 Recent studies continue to show a wide range in prevalence (3%-26%),12,16,36 despite the fact that they use the currently accepted definitions7 for SSI. This variability may reflect the fact that the studies mix results from single-center and multicenter settings, benign and malignant neoplasms, and colon and rectal disease. For this reason, Konishi et al15 recommend that factors related to colon and rectal operations be studied separately. Few studies have distinguished between incisional (superficial and deep) and organ/space SSI, although the 2 forms of infection have different pathogenesis and risk factors.12

The supervised application of a set of evidence-based preventive measures is usually associated with an improvement in results.15 In our study, the prevalence of SSI was higher than expected, despite the application of preventive measures selected on the basis of scientific evidence and recommended by the National Institute for Health and Clinical Excellence clinical guidelines.37 However, in our study, the results differed for overall SSI incidence in-hospital and at 30 days. Kobayashi et al38 also found substantial discrepancies in their results depending on the time of follow-up.

The prevalence of SSI in the present study is in the high range of that reported in the literature38 and similar to that reported by Konishi et al.15 Other recent studies have also reported figures above 20%,5,12,13 indicating that colorectal SSI is probably underreported and is in fact higher than the internationally accepted prevalence.13 The SSI rate varied substantially depending on the hospital size; small hospitals (<250 beds) presented higher rates of SSI, especially for incisional SSI in colon cancer. This may reflect the fact that community hospitals have less experience with colorectal operations, as most of them do not have specialist units.

Patient-dependent variables had little effect on the prevalence of SSI. In the univariate analysis, the American Society of Anesthesiologists score was identified as a predictive factor in incisional SSI in the rectum and preoperative hemoglobin level was identified in organ/space SSI also in the rectum, but neither of these factors was confirmed in the multivariate analysis. In recent studies of these patient-dependent factors, only body mass index more than 30 kg/m2 was found to be predictive.5,12,10,21

Almost all the variables related to SSI are dependent on the surgical technique.15,36 In our study, the factors...
related to incisional SSI after colectomy were the laparoscopic approach and the temperature at the end of the operation; however, only laparoscopy was confirmed in the multivariate analysis, in agreement with other publications. In some studies, a laparoscopic procedure was not decisive owing to selection bias: the patients had lower body mass index, fewer comorbid conditions, and less-advanced tumors. We found no predictive variables for incisional SSI in the rectum, whereas Konishi et al identified preoperative radiotherapy, corticosteroid treatment, and the creation of an ostomy as predictive factors.

In organ/space SSI, predictive variables in the colon were hyperglycemia at 48 hours, the creation of an ostomy, and NNIS score greater than 1. In the rectum, these predictive variables were hyperthermia at the beginning of surgery and hyperglycemia at 48 hours. The protective role of normothermia has not been established, although the harmful effects of hypothermia are well known. In our study, normothermia protected against SSI, although the results in incisional SSI in the colon were not conclusive. Control of serum glucose levels reduces mortality in critically ill patients, but its effect has not been definitively shown in other studies.

Other predictive variables in multivariate analyses in recent studies were the time since administration of the antibiotic (>60 minutes), surgical time longer than 120 minutes, incorrect application of asepsis measures in the surgical area, and perioperative hypotension. Anastomotic dehiscence was associated with organ/space SSI. Our results are within the range published in the literature. After colectomy, the dehiscence rate was higher than expected, although surgical treatment was required in only 64.0% of instances.

A limitation of this study is that it included only patients who were administered all the preventive measures selected. For this reason, the efficacy of each measure could not be assessed. Furthermore, the fact that patients who were not administered 1 or more of the preventive measures were excluded may have biased the final results. In addition, SSI after 30 days was assessed by participating surgeons. This potential bias was mitigated by an external audit.

The true rates of SSI in colorectal operations are probably higher than those commonly reported. In further studies of SSI, the location criteria and time of follow-up should be standardized and the pathologic findings should be clearly identified. Although general postoperative morbidity is related to patient-dependent risk factors and the complexity of the operation, our results and those of other recent studies indicate that the measures applied to reduce both incisional and organ/space SSI should be aimed at controlling all perioperative variables as well as patient-dependent factors.

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