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ORIGINAL ARTICLE

Oral antibiotic prophylaxis induces changes in the microbiology of surgical site infection after colorectal surgery. A matched comparative study

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Abstract

Aim: Oral antibiotic prophylaxis (OAP) lowers rates of surgical site infection (SSI) and may aid anastomotic healing in colorectal surgery. The aim of this study was to analyse the understudied impact of OAP on SSI microbiology after colorectal surgery.

Method: A post hoc analysis was performed on a previous prospective, multicentre study of elective colorectal surgery. For 1000 patients with SSI, this study compared the microbiology of SSIs in procedures without OAP (SSI/OAP–) and with OAP (SSI/OAP+).

Results: There were 340 patients in the SSI/OAP– group and 660 in the SSI/OAP+ group. The use of OAP increased the presence of Gram-positive cocci (GPC) (OR 1.542, 95% CI 1.153–2.062) and fungi (OR 2.037, 95% CI 1.206–3.440), but reduced rates of Gram-negative bacteria (GNB) (OR 1.461, 95% CI 1.022–2.088) and anaerobe isolation (OR 0.331, 95% CI 0.158–0.696). Specifically, it led to increases in the isolation of *Enterococcus faecium* (OR 1.450, 95% CI 0.812–2.591), methicillin-resistant *Staphylococcus aureus* (OR 2.000, 95% CI 1.043–3.834) and *Candida* spp. (OR 2.037, 95% CI 1.206–3.440). In colon surgery with OAP, GPC infections were more likely (OR 1.461, 95% CI 1.022–2.088). In rectal surgery, organ/space SSIs had a higher risk of harbouring GPC (OR 1.860, 95% CI 1.153–2.999) and a lower risk of GNB (OR 0.321, 95% CI 0.200–0.515).

Conclusion: OAP reduced the presence of anaerobes and GNB in SSIs, but increased the isolation of GPCs and fungi, with *E. faecium* and *Candida* being of particular concern. This information should guide empirical antibiotic therapy for postoperative colorectal SSIs in patients who have received preoperative OAP.

KEYWORDS
adverse effects, cohort studies, colorectal surgery, microbiology, surgical site infection, surgical wound infection/prevention and control

INTRODUCTION

Colorectal surgery has the highest incidence of surgical site infections (SSIs) after elective abdominal procedures, ranging from 9% to 20% [1–3]. SSIs are linked to prolonged length of stay (LOS) and higher morbidity and mortality rates, and impose a significant financial burden on healthcare systems [4, 5]. In colorectal surgery, organ/space SSI (O/S-SSI) results in a threefold increase in LOS and is associated with a 23% readmission rate, a 60% reoperation rate and a 29% likelihood of needing intensive care [6].

Among the multiple approaches to reduce SSIs, perioperative intravenous antibiotic prophylaxis is a cornerstone, alone or in combination with oral antibiotic prophylaxis (OAP) [2]. This latter strategy involves the administration of antibiotics orally prior to surgery to target the local microbiota in the gastrointestinal tract, and has proven effective for prevention of SSI [1, 7, 8]. Although most of the evidence is based on the combined use of OAP and mechanical bowel preparation (MBP) methods, oral antibiotics alone appear to be the second-best option [8], although the data available on this approach are still limited [9, 10]. In the study from which this subanalysis is derived, the implementation of a SSI-preventive bundle including OAP and MBP reduced the

What does this paper add to the literature?

This study provides evidence on the impact of oral antibiotic prophylaxis (OAP) on the microbiology of surgical site infection in colorectal surgery. It underscores significant microbial shifts, including increased Gram-positive cocci and fungal isolation associated with OAP use, providing critical guidance for optimizing empirical treatment of postoperative infections.

probability of overall SSI (OR 0.44, 95% CI 0.40–0.48) and O/S-SSI rates (OR 0.53, 95% CI 0.47–0.59). Multivariate analysis confirmed that, among other measures, OAP decreased both overall colorectal SSI (OR 0.68, 95% CI 0.59–0.79) and O/S-SSI (OR 0.82, 95% CI 0.68–0.98), while MBP was not an individual protective factor for SSI [11].

While the systemic effects of intravenous antibiotic prophylaxis are well documented, limited attention has been given to the local impact of OAP on SSI microbiology in this specific surgical context.

New advances in the understanding of the gut microbiota and its possible influence on the occurrence of anastomotic leaks and O/S-SSI make manipulation of the intestinal microbiota by OAP an exciting area of future research [12, 13]. Before being able to do this, it is important to investigate the effects that the antibiotics currently used in OAP may have on the infection-causing microbiota in this type of surgery.

This study uses prospectively collected data from a population-based cohort of patients undergoing elective colorectal surgery in the framework a nationwide SSI surveillance system using US Centers for Disease Control and Prevention (CDC) criteria, which recommend a preventive bundle including OAP.

The main objective was to analyse the effect of OAP on the post-operative infecting microbiota, comparing two cohorts of patients who had/had not received oral antibiotics.

METHOD

Study design

The results of a pragmatic cohort study investigating the efficacy of two SSI preventive bundles in elective colorectal surgery (ClinicalTrials.gov identifier NCT06244836) within a nationwide quality improvement programme have been reported elsewhere [11]. The present research is a post hoc analysis of data from the period in which the preventive bundles were implemented with a specific focus on the effect of OAP (2016–2022).

This multicentre cohort study compared patients with infection either with OAP administration (SSI/OAP+ group) or without (SSI/OAP− group), with the aim of uncovering potential OAP-induced alterations in SSI microbiology that could guide and optimize empirical antibiotic therapy for these infections.

Setting, patients and data source

Only elective cases of wound class 2 (clean-contaminated) and class 3 (contaminated) according to the National Healthcare Safety Network classification [14] were followed. Patients with previous ostomies or active infection at the time of intervention (wound class 4) and emergency procedures were excluded. The patients had not received prior antibiotic therapy, and 98% of the procedures involved oncological surgery.

Basic demographic data were recorded, including age, gender, American Society of Anesthesiologists (ASA) score, information on surgical details (including surgical approach), wound contamination class and duration of surgery. The National Nosocomial Infection Surveillance (NNIS) score was also calculated for each patient.

In 2016–2017 a bundle comprising six measures was proposed to the participating hospitals for implementation on a voluntary basis. These measures were: adequate antibiotic intravenous prophylaxis (antibiotic type, dose, timing within 60 min, intraoperative redosing and duration <24 h), OAP, MBP, laparoscopic surgery, maintenance of normothermia (goal >36°C) and the use of a double-ring plastic wound retractor in minimally invasive surgery (MIS) and open surgery.

The recommended guidelines for systemic prophylaxis were metronidazole 15 mg/kg plus gentamycin 5 mg/kg, cefuroxime 1.5 g plus metronidazole 15 mg/kg or amoxicillin-clavulanate 2 g, and were ultimately decided on the basis of the protocol in place at each hospital. Oral antibiotics and recommended doses were neomycin 1 g combined with metronidazole 500 mg (in three doses ingested 3 h after the end of the MBP and 19, 18 and 9 h prior to surgery). From 2018 to 2022, a second bundle added four new measures (adequate hair removal, skin antisepsis with 2% chlorhexidine gluconate alcohol solution, perioperative glucose monitoring and change of instruments before wound closure). All measures included in both bundles were adopted with an average adherence rate of over 70%, which increased over time. In the second bundle period, adherence rates were 98.0% for OAP and 81.9% for MBP.

Study outcomes, variables and definitions

The main outcome of the study was the comparison of the type of microorganism causing SSI according to the administration/non-administration of oral antibiotics. The results were analysed in the overall group of interventions and separately for colon and rectal surgery. Other outcomes were the rate and type of infection, which were also analysed overall or by type of intervention.

The definitions of the CDC National Healthcare Safety Network were used [15, 16]. SSIs were defined as superficial incisional (S-SSI), deep incisional (D-SSI) or O/S-SSI. The term 'overall SSI' refers to the sum of the SSIs at all three anatomical levels, while 'incisional SSI' (I-SSI) combines S-SSI and D-SSI. The incidence of SSIs was measured as events per 100 procedures included.

The CDC and Surveillance of Healthcare Related Infections in Catalonia Program criteria state that all infections should be sampled for microbiological study by needle aspiration, wound swab or from a tissue sample obtained from a surgical procedure. In instances of I-SSI, the acquisition of biological specimens was consistently feasible prior to the initiation of treatment. However, as some O/S-SSI were diagnosed early by ultrasound or abdominal CT and treated exclusively with antibiotics, biological samples were initially unavailable from these nonoperated or nonpercutaneously drained infections. In patients in whom conservative antibiotic treatment proved

ineffective, microbiological samples were obtained at the time of percutaneous or surgical drainage procedures. The microbiology laboratory of each participating hospital identified the organisms from samples obtained aseptically from any level of the surgical site. Standardized microbiological analysis methods (Clinical Laboratory Standard Institute and European Committee on Antimicrobial Susceptibility Testing), typically employing the matrix-assisted laser desorption ionization-time of flight mass spectrometry technique, were used for clinical diagnosis or treatment purposes to study aerobic, anaerobic and fungal organisms.

Prospective surveillance was conducted by the infection control team (ICT) at each participating hospital to ensure standardized data collection. This surveillance followed a structured protocol from the day of surgery until hospital discharge, incorporating comprehensive reviews of the patient's electronic health records, temperature charts and antibiotic treatments. Additionally, the ICT examined microbiology cultures and relevant radiological findings, supplemented by direct information exchange among healthcare providers. This systematic approach ensured consistent and thorough monitoring of SSI indicators across all study sites.

Mandatory active surveillance after discharge was conducted until postoperative day 30 using a multimodal approach, including electronic review of medical records (with access to out-of-hospital care notes), checking of readmissions and of emergency department visits, and review of microbiological and radiological data.

Ethical issues

Data extraction was approved by the institutional research committee (code no. 20166009), and the study was approved by the research ethics committee of the Hospital General de Granollers (code no. 2021006). Anonymity and data confidentiality (access to records, data coding and archiving of information) were maintained throughout the research process. Confidential patient information was protected in accordance with European regulations. The study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement [17] (Table A1).

Statistical analysis

Data are summarized as frequencies and proportions for categorical variables and as medians and interquartile ranges (IQRs) or means and standard deviations for continuous variables. Infection rates are expressed as cumulative incidence, that is, the crude percentage of operations resulting in SSIs/number of surgical procedures. The quantitative variables did not follow a normal distribution, therefore the nonparametric Wilcoxon test was used to compare means. To compare two qualitative variables, the chi-square test or the likelihood ratio test was performed. This analysis was performed for the overall sample, distinguishing between colon and rectal surgery.

A contingency table was made between the different microorganisms according to the variable OAP and the variable type of SSI. Secondly, a contingency table was made between each microorganism (both by taxonomic group and individually) according to the variables OAP and type of SSI. To analyse whether these variables affect the isolation of a microorganism, a logistic regression model was performed with these two variables and the interaction between them. If the interaction was statistically significant it was left in the model, otherwise it was removed and only the two main variables were left. The interaction was added to the model to determine the combined effect of the two explanatory variables, i.e. whether the OAP effect is different according to the SSI level. The significance level was set at 0.05 for all tests. Analyses were performed with SAS v.9.4 software (SAS Institute Inc., Cary, NC, USA).

RESULTS

In 25 951 procedures, 2499 SSIs were detected (Figure 1). Of these, microbiological SSI results were available for 1533 patients. One thousand patients for whom information on preoperative OAP administration was available were selected and constituted the study cohort, which was split into two groups: the SSI/OAP– group (340 patients) and the SSI/OAP+ group (660 patients). Sixty-two per cent of procedures were for the colon while 38% were for the rectum.

The demographic characteristics and risk factors for SSI of the procedures included are displayed in Table 1. In the SSI/OAP+ group there was more colon surgery than rectal surgery (46.0% vs. 53.9%). However, 80% of the rectal surgery cases were in the SSI/OAP+ group, in contrast to 20% who belonged to the SSI/OAP– group ($p < 0.001$). No other significant differences were detected between the two study groups, except for the duration of the surgical

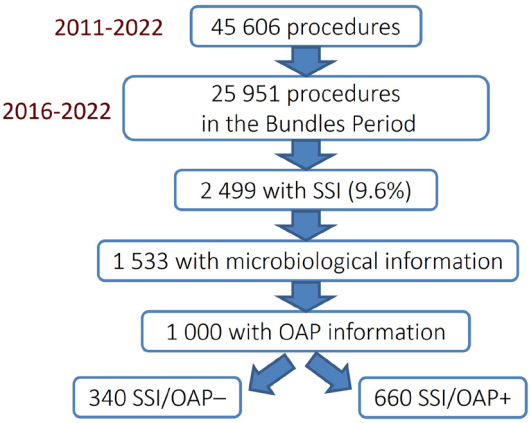

FIGURE 1 Flow chart of the origin of the study patient cohort. The present investigation was a post hoc analysis of data from a cohort study investigating the efficacy of two preventive surgical site infection (SSI) bundles in elective colorectal surgery (2016–2022). Data were obtained for the period of the bundles, from which patients with SSI were identified. From these, cases for which microbiological and oral antibiotic prophylaxis (OAP) administration data were available were selected.

TABLE 1 Characteristics of patients and comparison between the two groups of study.

	SSI/OAP−	SSI/OAP+	*p*-value
Colorectal surgery			
Type of surgery			
Colon surgery	264 (42.6%)	356 (57.4%)	<0.001
Rectal surgery	76 (20.0%)	304 (80.0%)	
Age (years), median (IQR)	71.96 (64.31–79.50)	70.41 (60.81–78.70)	0.030
Male:female	237:103	456:204	0.842
Appropriate intravenous antibiotic prophylaxis	264 (78.3%)	535 (81.3%)	0.265
Duration of intervention (min), median (IQR)	180 (136.5–230.5)	210 (156.0–275.0)	<0.001
ASA			
I	15 (4.5%)	18 (2.8%)	0.070
II	129 (39.0%)	307 (46.9%)	
III	178 (53.8%)	310 (47.4%)	
IV	9 (2.7%)	19 (2.9%)	
MIS			
No	131 (38.9%)	224 (34.2%)	0.146
Yes	206 (61.1%)	431 (65.8%)	
NNIS			
-1	57 (16.8%)	114 (17.3%)	0.750
0	136 (40.0%)	256 (38.8%)	
1	110 (32.4%)	226 (34.2%)	
2	35 (10.3%)	63 (9.6%)	
3	2 (0.6%)	1 (0.2%)	
Colon surgery			
Age (years), median (IQR)	72.77 (64.38–79.91)	71.46 (61.02–78.70)	0.166
Male:female	179:85	240:116	0.919
Appropriate intravenous antibiotic prophylaxis	201 (76.4%)	294 (82.6%)	0.058
Duration of intervention (min), median (IQR)	165.0 (130.0–213.0)	185.0 (135.5–234.5)	0.009
ASA			
I	10 (3.9%)	10 (2.8%)	0.5076
II	104 (40.3%)	162 (45.8%)	
III	135 (52.3%)	168 (47.5%)	
IV	9 (3.5%)	14 (4.0%)	
MIS			
No	111 (42.2%)	133 (37.7%)	0.256
Yes	152 (57.8%)	220 (62.3%)	
NNIS			
-1	44 (16.7%)	51 (14.3%)	0.665
0	101 (38.3%)	143 (40.2%)	
1	86 (32.6%)	123 (34.6%)	
2	32 (12.1%)	39 (11.0%)	
3	1 (0.4%)	0 (0%)	
Rectal surgery			
Age (years), median (IQR)	68.56 (64.15–77.01)	68.71 (59.92–78.67)	0.287
Male:female	58:18	216:88	0.360
Appropriate intravenous antibiotic prophylaxis	63 (85.1%)	241 (79.8%)	0.296

(Continues)

TABLE 1 (Continued)

	SSI/OAP−	SSI/OAP+	*p*-value
Duration of intervention (min), median (IQR)	226.5 (171.0–293.0)	245.0 (185.5–310.0)	0.249
ASA			
I	5 (6.9%)	8 (2.7%)	0.040
II	25 (34.3%)	145 (48.3%)	
III	43 (58.9%)	142 (47.3%)	
IV	0 (0%)	5 (1.7%)	
MIS			
No	20 (27.0%)	91 (30.1%)	0.510
Yes	54 (72.1%)	211 (69.9%)	
NNIS			
-1	13 (17.1%)	63 (20.7%)	0.382
0	35 (46.1%)	113 (37.2%)	
1	24 (31.6%)	103 (33.9%)	
2	3 (1.3%)	24 (7.9%)	
3	1 (1.3%)	1 (0.3%)	

Note: Values are *n* (%) unless otherwise indicated.

Abbreviations: ASA, American Society of Anesthesiologists physical status classification score; IQR, Interquartile range; MIS, minimally invasive surgery; NNIS, National Nosocomial Infection Surveillance System risk index; OAP, oral antibiotic prophylaxis (− no OAO; + with OAP); SSI, surgical site infection.

procedure, which was longer in the SSI/OAP+ group (210 min vs. 180 min, $p < 0.001$). When colon and rectal procedures were analysed separately, in both cases the duration of surgery was longer in the SSI/OAP+ group, although the difference was only significant for colon surgery [165 min vs. 185 min ($p = 0.009$) and 226.5 min vs. 245 min ($p = 0.249$), respectively]. Additionally, a significant difference in ASA scores was observed for rectal surgery, with higher scores in the SSI/OAP− group. For colon surgery, ASA scores were also higher in the SSI/OAP− group; however, this difference did not reach statistical significance.

Type of SSI

The type of SSI according to the use or nonuse of OAP is shown in Table 2. I-SSIs were more frequent in the SSI/OAP− group than in the SSI/OAP+ group (49.0% vs. 40.6%, $p = 0.010$), while O/S-SSIs were more frequent in the SSI/OAP+ group (59.6% vs. 51.0%, $p = 0.010$). These differences were maintained for colon surgery (49.8% vs. 62.4%, $p = 0.002$) but did not reach significance for rectal procedures ($p = 0.877$).

TABLE 2 Localization of the surgical site infection (SSI) according to the type of surgery and the group of study. The *p*-value is obtained from the chi-square test of independence analyses of whether there is a relationship between the distribution of infection type (organ/space or incisional SSI) and the category of the oral antibiotic prophylaxis (OAP) variable.

	SSI/OAP−	SSI/OAP+	*p*-value*
Colorectal surgery			
I-SSI, *n* (%) (95% CI)	166 (49.0), (43.65, 54.29)	267 (40.6), (36.71, 44.19)	0.010
O/S-SSI, *n* (%) (95% CI)	173 (51.0), (45.71, 56.35)	393 (59.6), (55.81, 63.29)	
Colon surgery			
I-SSI, *n* (%) (95% CI)	132 (50.2), (44.15, 56.23)	134 (37.6), (32.61, 42.67)	0.002
O/S-SSI, *n* (%) (95% CI)	131 (49.8), (43.77, 55.85)	222 (62.4), (57.33, 67.39)	
Rectal surgery			
I-SSI, *n* (%) (95% CI)	34 (44.7), (33.56, 55.92)	133 (43.8), (38.17, 49.33)	0.877
O/S-SSI, *n* (%) (95% CI)	42 (55.3), (44.08, 66.44)	171 (56.3), (50.67, 61.83)	

Abbreviations: I-SSI, incisional surgical site infection; O/S-SSI, organ/space surgical site infection. OAP−/+ indicate nonuse/use of OAP.

*Chi-square test.

Microbiology of SSI

Table 3 shows the crude results for microbiological isolates, grouped into SSI/OAP− and SSI/OAP+ samples. Analysing the colon and rectal procedures together, statistical differences were observed in the microbiological profiles of SSIs. In the procedures where OAP was used, there was an increase in isolation of Gram-positive cocci (GPC) (25.9% vs. 35.0%, $p = 0.035$) and fungi (5.6% vs. 10.8%, $p = 0.078$) and a decrease in Gram-negative bacteria (GNB) (63.2% vs. 52.4%, $p = 0.011$) and anaerobic pathogens (5.3% vs. 1.8%, $p = 0.035$).

TABLE 3 Aetiology of surgical site infection (SSI) according to the group of study.

	SSI/OAP−	SSI/OAP+	OR (95% CI)	*p*-value
Colorectal surgery				
Gram-positive cocci	88 (25.9)	231 (35.0)	1.542 (1.153–2.062)	0.035
Enterococcus faecalis	30 (8.8)	76 (11.5)	1.345 (0.862–2.097)	0.192
Enterococcus faecium	23 (6.8)	75 (11.4)	1.767 (1.086–2.875)	0.022
Enterococcus spp.	4 (1.2)	3 (0.5)	0.384 (0.085–1.724)	0.211
Staphylococcus coag. negative	3 (0.9)	13 (2.0)	2.257 (0.639–7.975)	0.206
MRSA	12 (3.5)	45 (6.8)	2.000 (1.043–3.834)	0.037
Others	16 (4.7)	19 (2.9)	0.600 (0.305–1.183)	0.140
Gram-negative bacteria	215 (63.2)	346 (52.4)	0.641 (0.490–0.838)	0.001
Enterobacter spp.	24 (7.1)	33 (5.0)	0.693 (0.403–1.192)	0.185
Escherichia coli	127 (37.4)	164 (24.9)	0.555 (0.418–0.735)	<0.001
Klebsiella spp.	17 (5.0)	52 (7.9)	1.625 (0.925–2.856)	0.092
Proteus spp.	3 (0.9)	19 (2.9)	3.33 (0.978–11.332)	0.054
Pseudomonas spp.	25 (7.4)	50 (7.6)	1.033 (0.627–1.701)	0.900
Others	16 (4.7)	24 (3.6)	0.764 (0.400–1.459)	0.415
Anaerobes	18 (5.3)	12 (1.8)	0.331 (0.158–0.696)	0.004
Bacteroides spp.	17 (5.0)	9 (1.4)	0.263 (0.116–0.596)	0.001
Clostridium spp.	1 (0.3)	2 (0.3)	1.030 (0.093–11.400)	0.981
Fungi	19 (5.6)	71 (10.8)	2.037 (1.206–3.440)	0.078
Candida spp.	19 (5.6)	71 (10.8)	2.037 (1.206–3.440)	0.008
Colon surgery				
Gram-positive cocci	65 (24.6)	115 (32.3)	1.461 (1.022–2.088)	0.038
Enterococcus faecalis	22 (8.3)	36 (10.1)	1.237 (0.710–2.158)	0.453
Enterococcus faecium	19 (7.2)	36 (10.1)	1.450 (0.812–2.591)	0.209
Enterococcus spp.	3 (1.1)	1 (0.3)	0.245 (0.025–2.369)	0.224
Staphylococcus coag. negative	1 (0.4)	8 (2.3)	6.046 (0.752–48.633)	0.091
MRSA	9 (3.4)	25 (7.0)	2.140 (0.982–4.665)	0.056
Others	11 (4.2)	9 (2.5)	0.597 (0.244–1.461)	0.258
Gram-negative bacteria	170 (64.4)	199 (55.9)	0.701 (0.505–0.972)	0.033
Enterobacter spp.	19 (7.2)	17 (4.8)	0.647 (0.329–1.270)	0.205
Escherichia coli	104 (39.4)	102 (28.7)	0.618 (0.441–0.866)	0.005
Klebsiella spp.	13 (4.9)	36 (10.1)	2.172 (1.128–4.183)	0.020
Proteus spp.	2 (0.8)	9 (2.5)	3.398 (0.728–15.858)	0.120
Pseudomonas spp.	18 (6.8)	20 (5.6)	0.813 (0.421–1.570)	0.539
Others	11 (4.1)	14 (3.9)	0.942 (0.420–2.109)	0.884
Anaerobes	15 (5.7)	5 (1.4)	0.236 (0.085–0.659)	0.006
Bacteroides spp.	14 (5.3)	3 (0.8)	0.152 (0.043–0.534)	0.003
Clostridium spp.	1 (0.4)	2 (0.6)	1.485 (0.134–16.463)	0.747
Fungi	14 (5.3)	37 (10.4)	2.071 (1.096–3.916)	0.025
Candida spp.	14 (5.3)	37 (10.4)	2.071 (1.096–3.916)	0.025
Rectal surgery				
Gram-positive cocci	23 (30.2)	116 (38.2)	1.422 (0.827–2.443)	0.203
Enterococcus faecalis	8 (10.5)	40 (13.2)	1.288 (0.576–2.879)	0.538
Enterococcus faecium	4 (5.2)	39 (12.8)	2.649 (0.916–7.655)	0.072
Enterococcus spp.	1 (1.3)	2 (0.7)	0.497 (0.044–5.550)	0.570

(Continues)

TABLE 3 (Continued)

	SSI/OAP−	SSI/OAP+	OR (95% CI)	*p*-value
Staphylococcus coag. negative	2 (2.6)	5 (1.6)	0.619 (0.118–3.252)	0.571
MRSA	3 (4.0)	20 (6.6)	1.714 (0.496–5.924)	0.395
Others	5 (6.6)	10 (3.3)	0.483 (0.160–1.457)	0.197
Gram-negative bacteria	45 (59.2)	147 (48.4)	0.645 (0.387–1.074)	0.092
Enterobacter spp.	5 (6.6)	16 (5.3)	0.798 (0.278–2.294)	0.654
Escherichia coli	23 (30.2)	62 (20.4)	0.590 (0.336–1.037)	0.067
Klebsiella spp.	4 (5.2)	16 (5.3)		
Proteus spp.	1 (1.3)	10 (3.3)	2.550 (0.322–20.228)	0.376
Pseudomonas spp.	7 (9.2)	30 (9.9)	1.079 (0.455–2.561)	0.863
Others	5 (6.6)	10 (3.3)	0.483 (0.160–1.457)	0.197
Anaerobes	3 (4.0)	7 (2.3)	0.574 (0.145–2.272)	0.429
Bacteroides spp.	3 (4.0)	6 (2.0)	0.490 (0.120–2.005)	0.321
Clostridium spp.	0 (0.0)	0 (0.0)		
Fungi	5 (6.6)	11.2	1.788 (0.675–4.738)	0.242
Candida spp.	5 (6.6)	34 (11.2)	1.788 (0.675–4.738)	0.242

Note: Values are *n* (%) unless otherwise indicated.

Abbreviations: MRSA, methicillin-resistant *Staphylococcus aureus*; OR, odds ratio; SSI/OAP−, patients with surgical site infection without OAP administration; *Staphylococcus* coag, negative, *Staphylococcus* coagulase negative; SSI/OAP+, patients with surgical site infection with OAP administration.

Specifically, the higher growth of GPC and fungi was due to increases in the isolation of *Enterococcus faecium*, methicillin-resistant *Staphylococcus aureus* (MRSA) and *Candida* spp., while the decrease in GNB and anaerobes was due to the lower rate of detection of *Escherichia coli* and *Bacteroides* spp. The occurrence of *Pseudomonas* spp. was twice as high in the SSI/OAP+ cohort, although the differences were not statistically significant.

Similar results were obtained when analysing colon surgery cases separately, but with an added significant increase in *Klebsiella* spp. in the SSI/OAP+ group. In the individual analysis of rectal procedures, similar trends were found to the general group in microbiology between the two groups, although without reaching statistical significance.

Table 4 shows the probability of isolating each microorganism according to the SSI location level. A higher risk of isolation of *E. faecium* (OR 3.534, 95% CI 2.106–5.929) and *Candida* spp. (OR 2.393, 95% CI 1.464–3.912) was found on O/S-SSI in the analysis of all procedures overall and also when analysing colon surgery (*E. faecium*, OR 3.300, 95% CI 1.670–6.522; *Candida* spp., OR 2.348, 95% CI 1.224–4.502) and rectal surgery separately (*E. faecium*, OR 3.908, 95% CI 1.761–8.674; *Candida* spp., OR 2.474, 95% CI 1.169–5.236). Similarly, a lower probability of MRSA being the causative agent of O/S-SSI was recorded (overall OR 0.130, 95% CI 0.063–0.276; colon procedures OR 0.065, 95% CI 0.20–0.215; rectal procedures OR 0.256, 95% CI 0.099–0.664). Finally, in rectal surgery, lower rates of *Enterobacter* spp. (OR 0.294, 95% CI 0.111–0.775) and *Pseudomonas* spp. (OR 0.499, 95% CI 0.250–0.996) were observed.

Table 5 shows the results of the logistic regression model performed with the variables OAP and type of SSI (incisional or O/S). When comparing whether isolates were from incisional or O/S-SSI, *E. faecium* (OR 3.427, 95% CI 2.040–5.759) and *Candida* spp. (OR 2.298, 95% CI 1.403–3.763) were more commonly isolated in O/S-SSI, while MRSA (OR 0.121, 95% CI 0.058–0.250) was more frequent in I-SSI. Similar results were observed in colon surgery: *E. faecium* was more commonly found in O/S-SSI (OR 3.206, 95% CI 1.617–6.357) and MRSA in I-SSI (OR 0.056, 95% CI 0.017–0.188). In rectal surgery, *E. faecium* (OR 3.931, 95% CI 1.767–8.747) and *Candida* spp. (OR 2.474, 95% CI 1.168–5.241) were also more commonly isolated in O/S-SSI. However, when OAP was administered *Enterobacter* spp. (OR 0.294, 95% CI 0.111–0.775) and *Pseudomonas* spp. (OR 0.499, 95% CI 0.250–0.995) predominated in the I-SSI group.

Finally, when the interaction of the anatomical level of the infection and OAP use was introduced into the model, only three interactions were statistically significant. In colon surgery, patients with I-SSI who were given OAP had a higher risk of GPC infection than those who did not receive OAP (OR 2.927, 95% CI 1.69–5.07, $p=0.0013$). In contrast, in rectal surgery, when there was an O/S-SSI the probability of having a GPC infection was higher in patients who received OAP (OR 1.860, 95% CI 1.153–2.999, $p=0.006$). Also, in rectal surgery, patients with O/S-SSI who had received OAP were less likely to harbour GNBs than those who had not (OR 0.321, 95% CI 0.200–0.515, $p=0.001$).

DISCUSSION

There is significant evidence to suggest that OAP, either alone or combined with MBP, decreases SSI in colorectal surgery [1, 7, 18,

TABLE 4 Aetiology of surgical site infection (SSI) according to its location.

	I-SSI	O/S-SSI	OR (95% CI)	*p*
Colorectal surgery				
Gram-positive cocci	136 (31.4)	182 (32.2)	1.035 (0.791–1.354)	0.802
Enterococcus faecalis	41 (9.5)	65 (11.5)	1.240 (0.821–1.874)	0.306
Enterococcus faecium	19 (4.4)	79 (14.0)	3.534 (2.106–5.929)	<0.001
Enterococcus spp.	1 (0.2)	6 (1.1)	4.629 (0.555–38.589)	0.157
Staphylococcus coag. negative	10 (2.3)	6 (1.1)	0.453 (0.163–1.257)	0.128
MRSA	48 (11.1)	9 (1.6)	0.130 (0.063–0.276)	<0.001
Others	17 (3.9)	17 (3.0)	0.758 (0.382–1.502)	0.427
Gram-negative bacteria	263 (60.7)	298 (52.7)	0.719 (0.558–0.926)	0.011
Enterobacter spp.	27 (6.2)	30 (5.3)	0.842 (0.493–1.438)	0.528
Escherichia coli	136 (31.4)	155 (27.4)	0.824 (0.626–1.084)	0.166
Klebsiella spp.	24 (5.5)	45 (8.0)	1.472 (0.882–2.456)	0.139
Proteus spp.	13 (3.0)	9 (1.6)	0.522 (0.221–1.233)	0.138
Pseudomonas spp.	38 (8.8)	37 (6.5)	0.727 (0.454–1.164)	0.185
Others	21 (4.9)	19 (3.4)	0.681 (0.362–1.284)	0.235
Anaerobic	11 (2.5)	19 (2.5)	1.332 (0.627–2.830)	0.455
Bacterioides spp.	10 (2.3)	16 (2.8)	1.231 (0.553–2.739)	0.611
Clostridium spp.	1 (0.2)	2 (0.4)	1.532 (0.138–16.950)	0.728
Fungus	23 (5.3)	7 (11.84)	2.393 (1.464–3.912)	<0.001
Candida spp.	23 (5.3)	7 (11.84)	2.393 (1.464–3.912)	<0.001
Colon surgery				
Gram-positive cocci	82 (30.8)	97 (27.5)	0.850 (0.599–1.206)	0.363
Enterococcus faecalis	24 (9.0)	34 (9.6)	1.075 (0.621–1.860)	0.797
Enterococcus faecium	11 (4.1)	44 (12.5)	3.300 (1.670–6.522)	<0.001
Enterococcus spp.	0 (0.0)	4 (1.1)		
Staphylococcus coag. negative	6 (2.3)	3 (0.9)	0.371 (0.092–1.499)	0.164
MRSA	31 (11.7)	3 (0.9)	0.065 (0.020–0.215)	<0.001
Others	10 (3.8)	9 (2.6)	0.670 (0.268–1.672)	0.390
Gram-negative bacteria	161 (60.5)	208 (58.9)	0.936 (0.676–1.294)	0.688
Enterobacter spp.	12 (4.5)	24 (6.8)	1.544 (0.758–3.147)	0.232
Escherichia coli	97 (36.5)	109 (30.9)	0.778 (0.556–1.090)	0.145
Klebsiella spp.	14 (5.3)	35 (9.9)	1.981 (1.043–3.763)	0.037
Proteus spp.	7 (2.6)	4 (1.1)	0.424 (0123–1.464)	0.175
Pseudomonas spp.	16 (6.0)	22 (6.2)	1.038 (0.534–2.018)	0.912
Others	13 (4.9)	12 (3.4)	0.685 (0.307–1.526)	0.354
Anaerobic	10 (3.8)	10 (2.8)	0.746 (0.306–1.820)	0.520
Bacterioides spp.	9 (3.4)	8 (2.3)	0.662 (0.252–1.739)	0.403
Clostridium spp.	1 (0.4)	2 (0.6)	1.510 (0.136–16.741)	0.737
Fungus	13 (4.9)	38 (10.8)	2.348 (1.224–4.502)	0.010
Candida spp.	13 (4.9)	38 (10.8)	2.348 (1.224–4.502)	0.010
Rectal surgery				
Gram-positive cocci	54 (32.3)	85 (39.9)	1.390 (0.909–2.125)	0.129
Enterococcus faecalis	17 (10.2)	31 (14.6)	1.503 (0.801–2.821)	0.205
Enterococcus faecium	8 (4.8)	35 (16.4)	3.908 (1.761–8.674)	0.001
Enterococcus spp.	1 (0.6)	2 (0.9)	1.573 (0.141–17.50)	0.712

(Continues)

TABLE 4 (Continued)

	I-SSI	O/S-SSI	OR (95% CI)	*p*
Staphylococcus coag. negative	4 (2.4)	3 (1.4)	0.582 (0.128–2.637)	0.483
MRSA	17 (10.2)	6 (2.8)	0.256 (0.099–0.664)	0.005
Others	7 (4.2)	8 (3.8)	0.892 (0.317–2.512)	0.829
Gram-negative bacteria	102 (61.1)	90 (42.3)	0.466 (0.308–0.705)	0.001
Enterobacter spp.	12 (9.0)	6 (2.8)	0.294 (0.111–0.775)	0.013
Escherichia coli	39 (23.4)	46 (21.6)	0.904 (0.557–1.468)	0.683
Klebsiella spp.	10 (6.0)	10 (4.7)	0.773 (0.314–1.904)	0.576
Proteus spp.	6 (3.6)	5 (2.4)	0.645 (0.193–2.151)	0.476
Pseudomonas spp.	22 (13.2)	15 (7.0)	0.499 (0.250–0.996)	0.049
Others	8 (4.8)	7 (3.3)	0.675 (0.240–1.901)	0.457
Anaerobic	1 (0.6)	9 (4.2)	7.322 (0.918–58.376)	0.060
Bacterioides spp.	1 (0.6)	8 (3.8)	6.478 (0.802–52.310)	0.080
Clostridium spp.	0 (0.0)	0 (0.0)		
Fungus	10 (6.0)	29 (13.6)	2.474 (1.169–5.236)	0.018
Candida spp.	10 (6.0)	29 (13.6)	2.474 (1.169–5.236)	0.018

Note: Values are *n* (%) unless otherwise indicated.

Abbreviations: I/SSI, incisional SSI; MRSA, methicillin-resistant *Staphylococcus aureus*; OAP, oral antibiotic prophylaxis; OR, odds ratio; *Staphylococcus* coag, negative, *Staphylococcus* coagulase negative; O/S-SSI, organ/space SSI.

19]; this practice is endorsed by recent guidelines from relevant scientific societies [20, 21]. However, little is known about the changes it may induce in the microbiota infecting the surgical site. This information may be valuable when planning empirical treatment for postoperative infection, where prior administration of OAP may prompt a change in the antimicrobial of choice.

In a previous cohort study, the application of a SSI-preventive bundle containing OAP and MBP halved the likelihood of overall SSI and O/S-SSI in elective colorectal surgery [11]. The current study is a post hoc analysis of 1000 patients from that cohort who developed SSI and for whom accurate information on OAP use or nonuse was available.

In this selected group of patients, some significant differences were observed in the location of SSI between groups in overall and colon procedures, with lower rates of I-SSI and higher rates of O/S-SSI in patients who had undergone OAP, while no differences were found in rectal surgery. In the study from which the present analysis derives, the implementation of two consecutive preventive bundles (including OAP) reduced the likelihood of overall SSI and of O/S-SSI. Furthermore, when analysing the individual effect of bundle measures on O/S-SSI rates, OAP independently reduced overall colorectal O/S-SSI. This result was similar when only colon surgery was analysed, but not in rectal procedures, where OAP did not show a significant effect on O/S-SSI (OR 0.95, 95% CI 0.67–1.35).

Historically, O/S-SSI has been associated with anastomotic leaks, which are thought to be profoundly influenced by technical factors such as maintaining good blood flow and avoiding tension on the anastomosis [22, 23]. In rectal surgery, the situation is complicated by factors such as the high rate of previous radiotherapy, the vicinity of the sphincters, the high-risk nature of distal anastomoses, the long duration of the procedure and the frequent need for a protective stoma, which may offset the advantages of measures to combat O/S-SSI [24–28]. In addition, recent research has highlighted other aspects, such as the diversity and composition of the colonic microbiota or intraoperative resuscitation, as contributing factors [29–31].

This study found substantial differences in the infecting microbiota between patients who did or did not undergo preoperative OAP. In general, the preoperative administration of OAP increased the isolation of GPC and fungi and decreased the isolation of anaerobes and GNB. Of particular concern is the increasing isolation of *E. faecium* and *Candida* spp. in O/S-SSI, both overall and in colon surgery. The study showed similar changes in rectal procedures but without reaching statistical significance, probably due to the smaller sample size [32].

It should be noted that in cases of O/S-SSI with minor suture leaks or small intra-abdominal collections and haemodynamic stability, the infection can be successfully treated with antibiotics alone, for which no microbiological data are available. Alternatively, when conservative antibiotic treatment is insufficient, these cases are treated with percutaneous or surgical drainage. This delay from diagnosis to microbiological sampling in some O/S-SSI cases, during which antibiotics are often administered, introduces a potential bias that may partly explain the observed differences in microbiota between I-SSI and O/S-SSI. However, this bias affects both study groups, those who have received OAPs and those who have not, so we believe that it may hold that the differences found are potentially due to administration of OAP.

This change in the infecting microbiota may be attributable to OAP administration. In murine studies, OAP with neomycin changed the composition of the gut microbiota and increased the

TABLE 5 Results of the logistic regression model of the microbiology of surgical site infections (SSIs) performed with the variables oral antibiotic prophylaxis (OAP) and type of SSI.

	SSI/OAP−		SSI/OAP+		O/S-SSI vs. I-SSI		OAP− vs. OAP+	
	I-SSI	O/S-SSI	I-SSI	O/S-SSI	OR (95% CI)	*p*	OR (95% CI)	*p*
Colorectal surgery								
Gram-positive cocci	40 (24.1)	47 (27.2)	96 (36.0)	135 (34.4)	1.001 (0.763–1.312)	0.994	1.559 (1.164–2.089)	0.003
Enterococcus faecalis	10 (6.0)	20 (11.6)	31 (11.6)	45 (11.5)	1.215 (0.803–1.839)	0.356	1.319 (0.844–2.060)	0.224
Enterococcus faecium	6 (3.6)	17 (9.8)	13 (4.9)	62 (15.8)	3.427 (2.040–5.759)	<0.001	1.626 (0.993–2.661)	0.053
Enterococcus spp.	1 (0.6)	3 (1.7)	0 (0.0)	3 (0.8)	5.077 (0.606–42.545)	0.134	0.342 (0.076–1.547)	0.164
Staphylococcus coag. Negative	3 (1.8)	0 (0.0)	7 (2.6)	6 (1.5)	0.427 (0.154–1.188)	0.103	2.421 (0.683–8.589)	0.171
MRSA	11 (6.6)	1 (0.6)	37 (13.9)	8 (2.0)	0.121 (0.058–0.250)	<0.001	2.392 (1.233–4.639)	0.010
Others	9 (5.4)	6 (3.5)	8 (3.0)	11 (2.8)	0.784 (0.394–1.559)	0.488	0.654 (0.327–1.307)	0.229
Gram-negative bacteria	107 (64.5)	108 (62.4)	156 (58.4)	190 (48.4)	0.741 (0.574–0.956)	0.021	0.650 (0.497–0.852)	0.002
Enterobacter spp.	12 (7.2)	12 (6.9)	15 (5.6)	18 (4.6)	0.866 (0.506–1.483)	0.601	0.699 (0.405–1.206)	0.198
Escherichia coli	64 (38.6)	63 (36.4)	72 (27.0)	92 (23.4)	0.861 (0.652–1.136)	0.289	0.559 (0.421–0.741)	<0.001
Klebsiella spp.	7 (4.2)	10 (5.8)	17 (6.4)	35 (8.9)	1.426 (0.853–2.383)	0.176	1.574 (0.894–2.772)	0.116
Proteus spp.	3 (1.8)	0 (0)	10 (3.8)	9 (2.3)	0.483 (0.204–1.144)	0.098	3.541 (1.037–12.091)	0.044
Pseudomonas spp.	11 (6.6)	14 (8.1)	27 (10.1)	23 (5.9)	0.724 (0.451–1.161)	0.180	1.059 (0.641–1.747)	0.824
Others	9 (5.4)	7 (4.1)	12 (4.5)	12 (3.1)	0.695 (0.368–1.312)	0.261	0.786 (0.411–1.504)	0.467
Anaerobes	11 (6.6)	7 (4.1)	0 (0.0)	12 (3.1)	1.471 (0.688–3.145)	0.319	0.319 (0.152–0.673)	0.003
Bacteroides spp.	10 (6.0)	7 (4.1)	0 (0.0)	9 (2.3)	1.384 (0.617–3.103)	0.431	0.255 (0.112–0.579)	0.001
Clostridium spp.	1 (0.6)	0	0 (0.0)	2 (0.5)	1.533 (0.138–17.085)	0.728	0.992 (0.089–11.061)	0.995
Fungi	8 (4.8)	11 (6.4)	15 (5.6)	56 (14.3)	2.298 (1.403–3.763)	0.001	1.915 (1.130–3.244)	0.016
Candida spp.	8 (4.8)	11 (6.4)	15 (5.6)	56 (14.3)	2.298 (1.403–3.763)	0.001	1.915 (1.130–3.244)	0.016
Colon surgery								
Gram-positive cocci	26 (19.7)	38 (29.0)	56 (41.8)	59 (26.6)	*	0.639	*	0.011
Enterococcus faecalis	7 (5.3)	15 (11.5)	17 (12.7)	19 (8.6)	1.048 (0.603–1.822)	0.868	1.225 (0.700–2.146)	0.478
Enterococcus faecium	4 (3.0)	15 (11.5)	7 (5.2)	29 (13.1)	3.206 (1.617–6.357)	0.009	1.278 (0.709–2.302)	0.415
Enterococcus spp.	0 (0.0)	3 (2.3)	0 (0.0)	1 (0.5)				
Staphylococcus coag. negative	1 (0.8)	0 (0.0)	5 (3.7)	3 (1.4)	0.310 (0.076–1.262)	0.102	6.983 (0.861–56.633)	0.069
MRSA	8 (6.1)	1 (0.8)	23 (17.2)	2 (0.9)	0.056 (0.017–0.188)	<0.001	2.935 (1.1318–6.533)	0.008
Others	6 (4.6)	4 (3.1)	4 (3.0)	5 (2.3)	0.702 (0.279–1.767)	0.453	0.686 (0.273–1.726)	0.424
Gram-negative bacteria	90 (68.2)	80 (61.1)	71 (53.0)	128 (57.7)	0.979 (0.705–1.359)	0.897	0.695 (0.500–0.968)	0.031
Enterobacter spp.	8 (6.1)	11 (8.4)	4 (3.0)	13 (5.9)	1.648 (0.803–3.382)	0.173	0.606 (0.306–1.197)	0.149
Escherichia coli	59 (44.7)	45 (34.3)	38 (28.4)	64 (28.8)	0.823 (0.585–1.158)	0.263	0.629 (0.447–0.883)	0.008
Klebsiella spp.	5 (3.8)	8 (6.1)	9 (6.7)	27 (12.2)	1.833 (0.960–3.499)	0.066	2.021 (1.044–3.910)	0.037

(Continues)

TABLE 5 (Continued)

	SSI/OAP−		SSI/OAP+		O/S-SSI vs. I-SSI		OAP− vs. OAP+	
	I-SSI	O/S-SSI	I-SSI	O/S-SSI	OR (95% CI)	*p*	OR (95% CI)	*p*
Proteus spp.	2 (1.5)	0 (0.0)	5 (3.7)	4 (1.8)	0.368 (0.106–1.280)	0.116	3.847 (0.817–18.122)	0.088
Pseudomonas spp.	8 (6.1)	10 (7.6)	8 (6.0)	12 (5.4)	1.068 (0.546–2.087)	0.848	0.804 (0.414–1.559)	0.518
Others	7 (5.3)	4 (3.1)	6 (4.5)	8 (3.6)	0.686 (0.306–1.539)	0.361	0.984 (0.436–2.218)	0.968
Anaerobes	10 (7.6)	5 (3.8)	0 (0.0)	5 (2.3)	0.882 (0.358–2.176)	0.786	0.239 (0.085–0.671)	0.007
Bacteroides spp.	9 (6.8)	5 (3.8)	0 (0.0)	3 (1.4)	0.810 (0.304–2.157)	0.674	0.155 (0.044–0.549)	0.004
Clostridium spp.	1 (0.8)	0 (0.0)	0 (0.0)	2 (0.9)	1.448 (0.128–16.318)	0.765	1.415 (0.126–15.952)	0.779
Fungi	6 (4.6)	8 (6.1)	7 (5.2)	30 (13.5)	2.188 (1.136–4.215)	0.019	1.894 (0.997–3.601)	0.051
Candida spp.	6 (4.6)	8 (6.1)	7 (5.2)	30 (13.5)	2.188 (1.136–4.215)	0.019	1.894 (0.997–3.601)	0.051
Rectal surgery								
Gram-positive cocci	14 (41.2)	9 (21.4)	40 (30.1)	76 (44.4)	*	0.571	*	0.299
Enterococcus faecalis	3 (8.8)	5 (11.9)	14 (10.5)	26 (15.2)	1.501 (0.799–2.819)	0.206	1.284 (0.574–2.875)	0.543
Enterococcus faecium	2 (5.9)	2 (4.8)	6 (4.5)	33 (19.3)	3.931 (1.767–8.747)	0.001	2.686 (0.920–7.843)	0.071
Enterococcus spp.	1 (2.9)	0 (0.0)	0 (0.0)	2 (1.2)				
Staphylococcus coag. Negative	2 (5.9)	0 (0.0)	2 (1.5)	3 (1.8)	0.584 (0.129–2.647)	0.485	0.622 (0.118–3.272)	0.575
MRSA	3 (8.8)	0 (0.0)	14 (10.5)	6 (3.5)	0.254 (0.098–0.661)	0.005	1.755 (0.502–6.134)	0.378
Others	3 (8.8)	2 (4.8)	4 (3.0)	6 (3.5)	0.897 (0.318–2.530)	0.837	0.483 (0.160–1.459)	0.197
Gram-negative bacteria	17 (50.0)	28 (66.7)	85 (63.9)	62 (36.3)	*	0.405	*	0.197
Enterobacter spp.	4 (11.8)	1 (2.4)	11 (8.3)	5 (2.9)	0.294 (0.111–0.775)	0.0134	0.795 (0.279–2.266)	0.667
Escherichia coli	5 (14.7)	18 (42.9)	34 (25.6)	28 (16.4)	*	0.158	*	0.310
Klebsiella spp.	2 (5.9)	2 (4.8)	8 (6.0)	8 (4.7)	0.773 (0.314–1.904)	0.576	1.003 (0.325–3.092)	0.996
Proteus spp.	1 (2.9)	0 (0.0)	5 (3.8)	5 (2.9)	0.641 (0.192–2.142)	0.471	2.564 (0.323–20.348)	0.373
Pseudomonas spp.	3 (8.8)	4 (9.5)	19 (14.3)	11 (6.43)	0.499 (0.250–0.995)	0.049	1.088 (0.456–2.592)	0.850
Others	2 (5.9)	3 (7.1)	6 (4.5)	4 (2.34)	0.678 (0.240–1.913)	0.463	0.484 (0.160–1.463)	0.199
Anaerobes	1 (2.9)	2 (4.8)	0 (0.0)	7 (4.09)	7.373 (0.924–58.826)	0.059	0.561 (0.140–2.248)	0.414
Bacteroides spp.	1 (2.9)	2 (4.8)	0 (0.0)	6 (3.51)	6.540 (0.809–52.888)	0.078	0.479 (0.116–1.981)	0.309
Clostridium spp.	0 (0)	0 (0.0)	0 (0.0)	0 (0.0)				
Fungi	2 (5.9)	3 (7.1)	8 (6.0)	26 (15.20)	2.474 (1.168–5.241)	0.018	1.787 (0.671–4.762)	0.246
Candida spp.	2 (5.9)	3 (7.1)	8 (6.0)	26 (15.20)	2.474 (1.168–5.241)	0.018	1.787 (0.671–4.762)	0.246

Note: Values are *n* (%) unless otherwise indicated.

Abbreviations: I/SSI, incisional SSI; MRSA, methicillin-resistant *Staphylococcus aureus*; OR, odds ratio; SSI/OAP−, patients with surgical site infection without OAP administration; O/S-SSI, organ/space SSI; *Staphylococcus* coag, negative, *Staphylococcus* coagulase negative; SSI/OAP+, patients with surgical site infection with OAP administration; 95% CI, 95% confidence interval.

*Indicates models where the interaction is significant. In these cases, ORs are not calculated for each variable separately because the interaction makes it advisable to interpret these variables jointly. The results of these interactions are shown in the text.

abundance of potentially pathogenic genera such as *Enterococcus* [33]. A risk of selection of resistant Enterobacteriaceae has been reported following treatment with oral colistin and neomycin [34], as observed in the present study, with a main reduction of *E. coli* but not as marked a decrease in other more concerning GNB. Similarly, OAP with erythromycin and neomycin may be an independent risk factor for selection of resistant nosocomial strains of Enterococci [35].

It has been speculated that the gut microbiota plays an important role in the fate of intestinal anastomoses and that disruption of the normal gut microbiota may be a direct cause of the anastomotic leakage [29]. Several studies in animal models have shown that alteration of the gut microbiome involving the growth of specific microorganisms such as *Pseudomonas aeruginosa* and *Enterococcus* spp. may lead to tissue destruction and anastomotic leakage [36, 37]. Leading experts in the field advocate the development of a new generation of technology leading to the design of an OAP that selects beneficial pathogens while controlling those that cause SSI [12, 38].

Fungal isolation is a rare finding in intra-abdominal infections, predominantly reported in immunocompromised or intensive care patients [32, 39, 40]. In this study, prior OAP administration was associated with a twofold increase in the incidence of fungal infections. Knowledge of these data can guide empirical antibiotic therapy in patients who develop SSI after colorectal surgery and have received preoperative OAP. In such cases, the addition of antifungal therapy and antibiotics effective against *E. faecium* should be considered, especially for O/S-SSI.

Limitations and strengths

This work has several limitations. Firstly, changes in the infecting microbiota may also be due to the interaction of systemic prophylaxis with OAP; however, there was no difference in the use of systemic prophylaxis between the two study groups. Secondly, as in other infection surveillance databases, the number of variables collected was restricted, leaving out potentially valuable information such as the patient's nutritional status, body mass index, certain comorbidities such as diabetes and smoking, diagnosis of anastomotic leakage, the extent of implementation of enhanced recovery after surgery programmes, technical details such as the type of anastomosis and data on bacterial resistance. Finally, due to the length of the study over time, the cohort's MIS rate can be considered low and is lower than the programme's current rate of 85%. This study also has several strengths. It was carried out in a large population and a high volume of patients were followed up in accordance with a consolidated, audited reporting method. Although the programme was based on voluntary hospital participation, almost all public hospitals in the area and several private institutions were included. We believe that the inclusion of different types and sizes of hospital may make the results generalizable to other settings.

CONCLUSIONS

In this study, prescription of OAP increased the isolation of GPC and fungi and decreased the isolation of anaerobes and GNB in SSI. A notable level of isolation of *E. faecium* and *Candida* was detected in O/S-SSI in both colon and rectal surgery. Awareness of these data may guide empirical antibiotic treatment in patients who develop severe SSI after colorectal surgery and have received preoperative OAP.

AUTHOR CONTRIBUTIONS

Miriam Flores-Yelamos: Investigation; writing – original draft; writing – review and editing; methodology. **Montserrat Juvany:** Conceptualization; methodology; validation; writing – original draft; writing – review and editing; supervision. **Josep M. Badia:** Conceptualization; investigation; writing – original draft; writing – review and editing; methodology; validation; supervision; formal analysis. **Ana Vázquez:** Conceptualization; investigation; methodology; validation; formal analysis; writing – review and editing; writing – original draft; software. **Marta Pascual:** Investigation; writing – review and editing; methodology. **David Parés:** Investigation; methodology; writing – review and editing. **Alexander Almendral:** Methodology; writing – review and editing; formal analysis. **Enric Limón:** Conceptualization; investigation; writing – review and editing; methodology; validation; supervision; project administration. **Miquel Pujol:** Conceptualization; investigation; writing – review and editing; writing – original draft; methodology; validation; supervision; project administration. **Aina Gomila-Grange:** Conceptualization; investigation; writing – original draft; writing – review and editing; validation; methodology; formal analysis; supervision.

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CONFLICT OF INTEREST STATEMENT

All authors declare no conflict of interest relevant to this article. All authors submitted the ICMJE form for disclosure of potential conflicts of interest, and the conflicts that the editors consider relevant to this work are disclosed here.

DATA AVAILABILITY STATEMENT

The research data are prospectively registered and belong to the Surveillance of Healthcare Related Infections in Catalonia (VINCat) programme, a programme from the Catalan Health Service,

Department of Health, Generalitat de Catalunya. All data will be made available on request.

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APPENDIX A

TABLE A1 STROBE statement—checklist of items that should be included in reports of cohort studies.

	Item no.	Recommendation	Page no.
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1, 6
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	7
Objectives	3	State specific objectives, including any prespecified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	7
Setting	5	Describe the setting, locations and relevant dates, including periods of recruitment, exposure, follow-up and data collection	8
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	8
		(b) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders and effect modifiers. Give diagnostic criteria, if applicable	9
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8
Bias	9	Describe any efforts to address potential sources of bias	9
Study size	10	Explain how the study size was arrived at	8, 10
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	9
		(b) Describe any methods used to examine subgroups and interactions	
		(c) Explain how missing data were addressed	
		(d) If applicable, explain how loss to follow-up was addressed	
		(e) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study, e.g. numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10
		(b) Give reasons for nonparticipation at each stage	
		(c) Consider use of a flow diagram	

TABLE A1 (Continued)

		Item no.	Recommendation	Page no.
Descriptive data		14*	(a) Give characteristics of study participants (e.g. demographic, clinical, social) and information on exposures and potential confounders	10
			(b) Indicate number of participants with missing data for each variable of interest	
			(c) Summarize follow-up time (e.g. average and total amount)	
Outcome data		15*	Report numbers of outcome events or summary measures over time	10–12
		(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g. 95% confidence interval). Make clear which confounders were adjusted for and why they were included		10–12
		(b) Report category boundaries when continuous variables were categorized		
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period		
Main results	16			
Other analyses	17	Report other analyses done, e.g. analyses of subgroups and interactions and sensitivity analyses		NA
Discussion				
Key results	18	Summarize key results with reference to study objectives		12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias		13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies and other relevant evidence		12,13
Generalizability	21	Discuss the generalizability (external validity) of the study results		14
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based		14