Invited Commentary

Oral Antibiotics for Colon Surgery
The Questions Remain the Same, as Do the Answers

Marc D. Basson, MD, PhD, MBA

Nichols et al[1] first demonstrated the effectiveness of adding oral antibiotics to mechanical bowel preparation in 1973, yet in this issue of *JAMA Surgery*, Vo and colleagues[2] are publishing a retrospective analysis demonstrating the efficacy of oral antibiotics in reducing superficial and deep space infections in left colon resections in 2017. Oral antibiotics are inexpensive and generally well tolerated. So why are we still addressing the issue? First, virtually all patients, at least in the United States, now receive appropriate prophylactic parenteral antibiotics in a timely fashion, something not necessarily true in 1973. Second, mechanical bowel preparation has evolved, including the use of isotonic polyethylene glycol preparations, and is even skipped completely by some surgeons. Third, minimally invasive procedures have reduced the number of wound infections. Fourth, an increasing understanding of the beneficial as well as deleterious effects of the colonic microbiome suggests that disrupting the colonic microbial ecology may have adverse effects ranging from the obvious, such as *Clostridium difficile* infection, to the less obvious, such as adverse effects with regard to anastomotic healing,[3] and crosstalk between the microbial community within the intestine and the host's immune system that in turn mediates host immune responses.[4]

Related article

The article by Vo and colleagues[2] is retrospective and limited by a small sample size and potential historical confounders. Nevertheless, even with the small sample size, substantial and statistically significant decreases in the numbers of superficial and deep space infections were observed with combined oral antibiotics and mechanical bowel preparation, with a trend toward lower rates of anastomotic leaks. Parallel cases of right colon resection demonstrated a similar trend, although even smaller numbers of patients precluded statistical significance. Critics may point to the use of a hypertonic bowel preparation for the patients studied here and the potentially confounding effect of the introduction of a perioperative decontamination protocol that does not seem to have been effective. However, these results build on a multitude of other studies, including a recent review based on the American College of Surgeons National Surgical Quality Improvement Program demonstrating that, in the real world, the combination of mechanical bowel preparation and oral antibiotics decreased the rates of surgical site infections separately in both left and right colon procedures, and decreased the rate of anastomotic leakage on the left side.[5]

Future research may more conclusively address the perhaps still-controversial effects of oral antibiotics in right colonic surgery and evaluate whether oral antibiotics can be effective without mechanical bowel preparation. However, the study by Vo and colleagues[2] does seem to confirm what we have known since 1973; preoperative oral antibiotics reduce the number of wound infections in elective surgery on the mechanically prepared colon. Surgical site infections produce substantial morbidity among our patients. Given all the efforts that we have made to reduce infection rates by ineffective methods such as mandating compliance with the Surgical Care Improvement Project and experimenting with varieties of decontamination and skin preparation techniques, perhaps it is time to stop studying this issue and simply (re)adopt the practice of oral antibiotic use more universally, at least for elective surgery on the mechanically prepared left colon.

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Association of the Addition of Oral Antibiotics to Mechanical Bowel Preparation for Left Colon and Rectal Cancer Resections With Reduction of Surgical Site Infections

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IMPORTANCE Surgical site infections (SSIs) after colorectal surgery remain a significant complication, particularly for patients with cancer, because they can delay the administration of adjuvant therapy. A combination of oral antibiotics and mechanical bowel preparation (MBP) is a potential, yet controversial, SSI prevention strategy.

OBJECTIVE To determine the association of the addition of oral antibiotics to MBP with preventing SSIs in left colon and rectal cancer resections and its association with the timely administration of adjuvant therapy.

DESIGN, SETTING, AND PARTICIPANTS A retrospective review was performed of 89 patients undergoing left colon and rectal cancer resections from October 1, 2013, to December 31, 2016, at a single institution. A bowel regimen of oral antibiotics and MBP (neomycin sulfate, metronidazole hydrochloride, and magnesium citrate) was implemented August 1, 2015. Patients receiving MBP and oral antibiotics and those undergoing MBP without oral antibiotics were compared using univariate analysis. Multivariable logistic regression controlling for factors that may affect SSIs was used to evaluate the association between use of oral antibiotics and MBP and the occurrence of SSIs.

MAIN OUTCOMES AND MEASURES Surgical site infections within 30 days of the index procedure and time to adjuvant therapy.

RESULTS Of the 89 patients (5 women and 84 men; mean [SD] age, 65.3 [9.2] years) in the study, 49 underwent surgery with MBP but without oral antibiotics and 40 underwent surgery with MBP and oral antibiotics. The patients who received oral antibiotics and MBP were younger than those who received only MBP (mean [SD] age, 62.6 [9.1] vs 67.5 [8.8] years; $P = .01$), but these 2 cohorts of patients were otherwise similar in baseline demographic, clinical, and cancer characteristics. Surgical approach (minimally invasive vs open) and case type were similarly distributed; however, the median operative time of patients who received oral antibiotics and MBP was longer than that of patients who received MBP only (391 minutes [interquartile range, 302-550 minutes] vs 348 minutes [interquartile range, 248-425 minutes]; $P = .03$). The overall SSI rate was lower for patients who received oral antibiotics and MBP than for patients who received MBP only (3 [8%] vs 13 [27%]; $P = .03$), with no deep or organ space SSIs or anastomotic leaks in patients who received oral antibiotics and MBP compared with 9 organ space SSIs (18%; $P = .004$) and 5 anastomotic leaks (10%; $P = .06$) in patients who received MBP only. Despite this finding, there was no difference in median days to adjuvant therapy between the 2 cohorts (60 days [interquartile range, 46-73 days] for patients who received MBP only vs 72 days [interquartile range, 59-85 days] for patients who received oral antibiotics and MBP; $P = .13$). Oral antibiotics and MBP (odds ratio, 0.11; 95% CI, 0.02-0.86; $P = .04$) and minimally invasive surgery (odds ratio, 0.22; 95% CI, 0.05-0.89; $P = .03$) were independently associated with reduced odds of SSIs.

CONCLUSIONS AND RELEVANCE The combination of oral antibiotics and MBP is associated with a significant decrease in the rate of SSIs and should be considered for patients undergoing elective left colon and rectal cancer resections.

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Invited Commentary

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Surgical site infection (SSI) after colorectal surgery is a common postoperative complication, with rates of 15% to 20%, and significantly affects patient morbidity and mortality.[1-3] For cancer patients specifically, postoperative infections are a common cause of delay to adjuvant therapy and can result in decreased overall and cancer-free survival.[4,5] Several efforts, such as the Surgical Care Improvement Project and preoperative care bundles, have been implemented to reduce rates of SSIs, but few have proved to be effective.[6]

Bowel preparation prior to colorectal cancer resections is a potential, yet controversial, strategy to prevent SSIs.[1,2] Nichols et al[7] first demonstrated a reduction in the rate of SSIs using a bowel regimen of oral antibiotics and mechanical bowel preparation (MBP) in 1973. However, with the introduction of perioperative intravenous antibiotics and the discontinuation of preadmitting patients to perform inpatient bowel cleansing, the benefit of bowel preparation was questioned because it was burdensome, potentially harmful, and ineffective.[1,2] Recently, the combination of oral antibiotics and MBP with perioperative intravenous antibiotics has been evaluated in several studies and has demonstrated a significant decrease in the rate of SSIs.[8-11]

Despite evolving data that appear to support the use of the combination of oral antibiotics and MBP, there remains notable variation in practice, with less than 40% of patients receiving this combination for bowel preparation.[12,13] In addition, studies do not differentiate between right and left colon resection, and reports on the utility of the combination of oral antibiotics and MBP in right colons are inconclusive. Therefore, we sought to examine the association of the combination of oral antibiotics and MBP with SSIs in left colon and rectal cancer resections. We hypothesized that the combination of oral antibiotics and MBP with perioperative intravenous antibiotics would be associated with a decrease in the rate of SSIs in left colon and rectal cancer resections and would potentially increase the number of patients receiving timely administration of adjuvant therapy.

Key Points

Question Do oral antibiotics with mechanical bowel preparation reduce the risk of surgical site infections after left-sided colorectal cancer surgery?

Findings In this cohort study, the rate of surgical site infections was 27% with mechanical bowel preparation only and 8% with oral antibiotics combined with mechanical bowel preparation.

Meaning Oral antibiotics combined with mechanical bowel preparation should be considered for all patients undergoing left-sided colorectal cancer resections.

Methods

A retrospective review was performed to identify patients undergoing elective surgery for colorectal cancer between October 1, 2013, and December 31, 2016. Emergency cases, nonprimary tumor resections, and patients without 30 days of postoperative follow-up were excluded. Electronic medical records were reviewed for all patients to determine whether the combination of oral antibiotics and MBP was prescribed for bowel preparation. Institutional review board approval was obtained from the Baylor College of Medicine and the Michael E. DeBakey Veterans Affairs Medical Center. As this was a retrospective review, patient consent was waived.

Implementation of Standardized Bowel Regimen

Starting August 1, 2015, as part of a quality improvement initiative, a standardized regimen of oral antibiotics and MBP was implemented for patients undergoing colorectal surgery. This regimen began the day prior to surgery and included 1 g of neomycin sulfate and 1 g of metronidazole hydrochloride 3 times per day plus 296 mL of magnesium citrate 2 times per day. This regimen was prescribed routinely for left colon and rectal resections. Throughout the study period, there were no changes in rates of compliance (>95%) with Surgical Care Improvement Project guidelines[14] (appropriate and timely administration of prophylactic intravenous antibiotics and discontinuation within 24 hours) as reported by the US Department of Veterans Affairs external peer review program. In addition, all patients underwent skin preparation with chlorhexidine gluconate and isopropyl alcohol immediately prior to surgical incision. During the study period, a preoperative decontamination protocol was implemented as part of a separate SSI prevention initiative that began in October 2014 and was offered to all patients undergoing elective surgery. The preoperative decontamination protocol, as described previously by Bebko et al,[15] included a 3-site approach using chlorhexidine gluconate wipes, 2%, chlorhexidine gluconate oral rinse, 0.12%, and intranasal povidone iodine, 5%, the night before and the morning of surgery.

Left Colon and Rectal Cancer Resections Data Collection

Patients who underwent left colon and rectal cancer resections in the prestandardization period (before August 2015) typically received MBP alone with perioperative intravenous antibiotics and were part of a cohort. Patients prescribed oral antibiotics in the prestandardization period were excluded from the study because they potentially received a nonstandard regimen. Patients who underwent surgery in the poststandardization period (after August 1, 2015) and who were prescribed the combination of oral antibiotics and MBP were part of another cohort.

Data on baseline characteristics, such as demographics, body mass index (calculated as weight in kilograms divided by height in meters squared), American Society of Anesthesiologists score, and serum albumin levels, were collected. The body mass index and American Society of Anesthesiologists score served as surrogates for severity of comorbid disease, and the serum albumin level served as a biomarker for nutritional status. These variables were chosen based on previous studies that have associated a body mass index greater than 30, an American Society of Anesthesiologists score higher than 3, and malnutrition with increased risk of postoperative infectious complications.[16] Age was further categorized into 65 years of age or older for the logistic regression model.

Specific cancer variables were examined including tumor site (colon vs rectum), receipt of neoadjuvant therapy, and cancer stage. Operative characteristics included perioperative intravenous antibiotic used, surgical approach (minimally invasive surgery [MIS] vs open), type of operation (left or sigmoid colectomy, low anterior resection, abdominoperineal resection, or subtotal or other colectomy), operative duration, and transfusion of intraoperative blood product(s). At our institution, most surgeons used ertapenem sodium for intravenous antibiotic prophylaxis. Thus, we summarized intravenous antibiotics into ertapenem with or without additional antibiotic(s) or non-ertapenem antibiotics. Minimally invasive surgery included laparoscopic, hand-assisted laparoscopic, and robotic surgery. Cases converted to laparotomies were categorized as open. Operative time was calculated from the time of surgical incision to skin closure.

Primary outcomes of interest were the occurrence of any SSI and the type of SSI (superficial, deep incisional, and organ space) within 30 days of the index procedure based on the Centers for Disease Control and Prevention and National Nosocomial Infection Society criteria.[17] Secondary outcomes included anastomotic leak, length of stay, 30-day readmission, receipt of adjuvant therapy, and timely administration of adjuvant therapy. Anastomotic leak was included under organ space SSI and defined as postoperative fluid collection adjacent to the anastomotic site seen on imaging scans and may have required a percutaneous drainage procedure and/or an operative intervention. Recommendations for adjuvant therapy were based on National Cancer Comprehensive Network guidelines (high-risk stage 2 or 3 colon cancer and stage 2 or 3 rectal cancer).[18,19] Patients with stage 4 cancer were excluded from this part of the analysis. Time to initiation of adjuvant therapy was determined through medical oncology and pharmacy records. Timely administration was defined as 60 days or less from the index procedure based on literature suggesting that adjuvant therapy for colorectal cancer begin 6 to 8 weeks after the operation for optimal oncologic outcomes.[5,20]

Comparison With Right Colon Cancer Resections

We performed additional analyses of right colon cancer resections to examine any change in rates of SSIs between prestandardization and poststandardization periods to potentially address historical biases such as the preoperative decontamination protocol. Patients undergoing right colon cancer resections were stratified into similar cohorts: those who received MBP only (prestandardization) and those who received oral antibiotics and MBP (poststandardization). At our institution, most patients undergoing a right colon resection were not prescribed MBP and received only perioperative intravenous antibiotics. Preoperative decontamination use and the MIS approach were also examined. Rates of SSIs were compared between left colon or rectal resection and right colon resection cases.

Statistical Analysis

Univariate analysis was performed using the χ^2 test or the Fisher exact test for categorical variables and the *t* test or the Wilcoxon rank sum test for continuous variables. The Shapiro-Wilk test was used to test for normal distribution. Variables significant on univariate analysis were placed in a logistic regression model to identify independent factors that were significantly associated with the occurrence of SSIs. The Hosmer-Lemeshow test was used to test the goodness of fit of the model. $P < .05$ (2-sided) was considered statistically significant, and all analyses were performed using STATA, version 14.1 (StataCorp).

Results

Of the 191 patients who underwent elective colorectal cancer resection during the study period, 105 were left colon or rectal cases and 86 were right colon cases. A total of 16 patients who underwent left colon or rectal resection in the prestandardization period were excluded because they potentially received a nonstandard combination of oral antibiotics and MBP. The rate of SSIs for these 16 patients was 19% (2 [13%] superficial and 1 [6%] organ space). All patients undergoing left colon or rectal resections in the poststandardization period were given the standard combination of oral antibiotics and MBP. Of the patients who underwent right colon resections, 18 were excluded because they were not prescribed the combination of oral antibiotics and MBP in the poststandardization period, and 3 were emergency cases. No patients received oral antibiotics alone, and no patients were lost to follow-up at 30 days.

Univariate Analyses

Outcomes of Patients Who Underwent Left Colon and Rectal Cancer Resections With Oral Antibiotics and MBP

Overall, 89 patients were included in the analysis of left colon and rectal resections (49 received MBP only and 40 received oral antibiotics and MBP). The mean (SD) age was 65.3 (9.2) years, with a majority of patients being male (84 [94%]) and white (59 [66%]) (**Table 1**). Most patients were overweight (median body mass index, 27.8 [interquartile range, 25.2-32.0]) and had many comorbidities, with 80 (90%) having American Society of Anesthesiologists scores of 3 or higher. Table 1 summarizes the baseline characteristics of the study cohort. Compared with the patients who received MBP only, the patients who received oral antibiotics and MBP were younger (mean [SD] age, 62.6 [9.1] years vs 67.5 [8.8] years; $P = .01$), had a higher percentage of rectal malignant tumors (23 [58%] vs 25 [51%]; $P = .54$), and received neoadjuvant therapy more frequently (20 [50%] vs 15 [31%]; $P = .06$). In addition, more patients who received oral antibiotics and MBP performed preoperative decontamination than did patients who received MBP only (27 [68%] vs 3 [6%]; $P = .001$). Most patients received intravenous ertapenem with or without additional antibiotics (82 [92%]) and underwent MIS (68 [76%]), with similar distribution between cohorts (**Table 2**). Median operative times were longer for patients who received oral antibiotics and MBP than for patients who received MBP only (391 minutes [interquartile range, 302-550 minutes] vs 348 minutes [interquartile range, 248-425 minutes]; $P = .03$). Other operative variables are shown in Table 2.

Table 1. Baseline Characteristics

Characteristic	Patients, No. (%)		P Value
	No OA (n = 49)	OA + MBP (n = 40)	
Age, mean (SD), y	67.5 (8.8)	62.6 (9.1)	.01
Male sex	47 (96)	37 (93)	.65
Race/ethnicity			
Black	7 (14)	12 (30)	.17
Hispanic	6 (12)	2 (5)	
White	35 (71)	24 (60)	
Other	1 (2)	2 (5)	
BMI, median (IQR)	27.8 (25.8-32.7)	27.7 (24.8-30.8)	.28
Obese (BMI > 30)	19 (39)	15 (38)	.90
ASA score			
2	6 (12)	3 (8)	.48
3	36 (73)	34 (85)	
4	7 (14)	3 (8)	
Serum albumin, mean (SD), g/dL	3.7 (0.4)	3.7 (0.4)	.92
Preoperative decontamination use	3 (6)	27 (68)	.001
Tumor site			
Colon	24 (49)	17 (43)	.54
Rectum	25 (51)	23 (58)	
Cancer stage			
0	3 (6)	1 (3)	.93
1	12 (24)	10 (25)	
2	14 (29)	11 (28)	
3	17 (35)	14 (35)	
4	3 (6)	4 (10)	
Neoadjuvant therapy	15 (31)	20 (50)	.06

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); IQR, interquartile range; No OA, no oral antibiotic; OA + MBP, combined oral antibiotic and mechanical bowel preparation.

SI conversion factor: To convert albumin to grams per liter, multiply by 10.0.

Table 2. Operative Characteristics

Characteristic	Patients, No. (%)		P Value
	No OA (n = 49)	OA + MBP (n = 40)	
Perioperative intravenous antibiotics[a]			
Ertapenem	43 (88)	39 (98)	.09
Non-ertapenem	6 (12)	1 (3)	
Type of operation			
Left colectomy	8 (16)	6 (15)	.89
Sigmoid colectomy	10 (20)	6 (15)	
Low anterior resection	19 (39)	16 (40)	
Abdominoperineal resection	6 (12)	8 (20)	
Subtotal colectomy or other colectomy	6 (12)	4 (10)	
Surgical approach			
Open	13 (27)	8 (20)	.47
Minimally invasive surgery	36 (73)	32 (80)	
Operative time, median (IQR), min	348 (248-425)	391 (302-550)	.03
Transfusion of blood products	4 (8)	1 (3)	.37

Abbreviations: IQR, interquartile range; No OA, no oral antibiotic; OA + MBP, combined oral antibiotic and mechanical bowel preparation.

[a] Ertapenem includes ertapenem use with and without additional antibiotics.

Overall, 16 patients (18%) had SSIs: 13 patients (27%) who received MBP only and 3 patients (8%) who received oral antibiotics and MBP (P = .03) (**Table 3**). By SSI type, organ space SSIs decreased from 9 patients (18%) who received MBP only to 0 patients who received oral antibiotics and MBP (P = .004). The hospital lengths of stay and the 30-day unplanned readmission rates were similar between the 2 groups (Table 3). A total of 46 patients (52%) were recommended adjuvant therapy; 39 of these patients (85%) received adjuvant therapy (5 declined, 1 was noncompliant with medical oncology appointments, and 1 was deemed a poor candidate). No statistically significant differences in median time to adjuvant therapy or in the number of patients who received timely adjuvant therapy were found between the 2 groups of patients. Additional sensitivity analysis was performed to include the previously excluded left colon/rectal cases (n = 16) and reaffirmed that the combination of oral antibiotic and MBP was associated with a decrease in overall rates of SSIs (6 of 56 [11%] vs 13 of 49 [27%]; P = .01) and in rates of organ space SSIs (1 of 56 [2%] vs 9 of 49 [18%]; P = .01).

Outcomes of Patients Who Underwent MIS and Preoperative Decontamination

Among the patients who underwent left colon or rectal resection performed only as MIS (36 patients who received MBP only and 32 patients who received oral antibiotics and MBP), a decrease in the overall rate of SSIs was found for 1 of 32 patients (3%) who received oral antibiotics and MBP compared with 8 of 36 patients (22%) who receive MBP only (P = .03). In addition, we performed a subset analysis to compare rates of SSIs among patients who underwent left colon or rectal resection who used the preoperative decontamination protocol. Only 3 patients who received MBP only performed preoperative decontamination, with no difference in the overall rate of SSIs (1 of 3 [33%] with preoperative decontamination vs 12 of 46 [26%] without; P = .99). More patients who received oral antibiotics and MBP performed preoperative decontamination (n = 27), but there was no difference in rates of SSIs with or without use of preoperative decontamination (1 of 27 [4%] vs 1 of 13 [8%]; P = .99).

Comparison With Right Colon Cancer Resections

Sixty-five patients were included in the analysis of right colon cancer resection (53 who received MBP only and 12 who received oral antibiotics and MBP). Overall, 8 patients had SSIs (12%), with a decrease from patients who received MBP only to patients who received oral antibiotics and MBP (ie, from 7 of 53 [13%] to 1 of 12 [8%]; P = .99) (**Figure**). Patients who received oral antibiotics and MBP and were undergoing right colon resection had more use of preoperative decontamination than those who received MBP only (9 of 12 [75%] vs 7 of 53 [13%]; P = .001), and more patients who received oral antibiotics and MBP underwent MIS than did patients who received MBP only (12 of 12 [100%] vs 39 of 53 [74%]; P = .06).

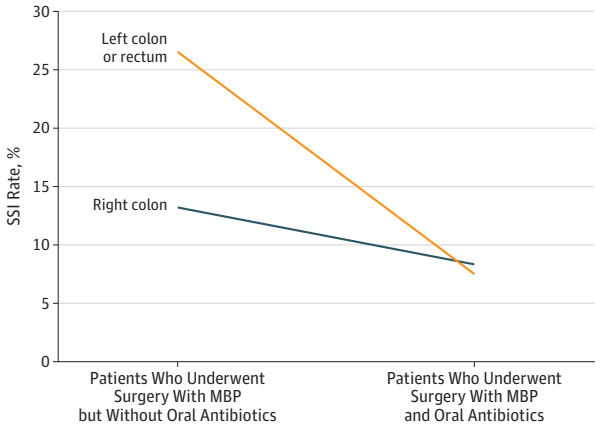
Table 3. Outcomes

Characteristic	Patients, No. (%)		P Value
	No OA (n = 49)	OA + MBP (n = 40)	
Surgical site infection[a]	13 (27)	3 (8)	.03
Superficial	4 (8)	3 (8)	.99
Deep	1 (2)	0	.99
Organ space	9 (18)	0	.004
Anastomotic leak	5 (10)	0	.06
Length of stay, median (IQR), d	5 (5-10)	6 (4-11)	.71
30-d Unplanned readmissions	10 (20)	7 (18)	.73
AT recommended	26 (53)	20 (50)	.77
Received AT	21 (43)	18 (45)	.84
Median (IQR) No. of days until AT	60 (46-73)	72 (59-85)	.13
Timely AT (<60 d)	11/21 (52)	7/18 (39)	.40

Abbreviations: AT, adjuvant therapy; IQR, interquartile range; No OA, no oral antibiotic; OA + MBP, combined oral antibiotic and mechanical bowel preparation.

[a] One patient in the no OA group had both superficial and organ space infections.

Figure. Rates of Surgical Site Infections (SSIs) With or Without Combined Oral Antibiotics and Mechanical Bowel Preparation (MBP)



A significant decrease was seen in the rate of SSIs for patients who underwent a left colon or rectal cancer resection with oral antibiotics and MBP compared with patients who underwent a left colon or rectal cancer resection with MBP but without oral antibiotics (*P* = .03). No significant difference was seen in the rates of SSIs between the 2 cohorts of patients who underwent right colon cancer resections (*P* = .99).

We performed a similar sensitivity analysis with the patients undergoing right colon resection who were excluded from the primary analysis (n = 18); no difference was found in the rate of SSIs (7 of 71 patients who received MBP only [10%] vs 1 patient who received oral antibiotics and MBP [8%]; *P* = .99).

Multivariable Logistic Regression Analysis

Factors that were significant on univariate analysis and those known to be associated with SSIs in the patients undergoing left colon or rectal resection were entered into a logistic regression model (**Table 4**). Use of oral antibiotics and MBP (odds ratio, 0.11; 95% CI, 0.02-0.86; *P* = .04) and the MIS approach (odds ratio, 0.22; 95% CI, 0.05-0.89; *P* = .03) were the 2 significant factors independently associated with a reduced odds of SSI occurrence. Although the preoperative decontamination protocol was implemented as an SSI prevention measure, it was not a significant factor in our logistic regression model. The model was considered a good fit (*P* = .62, determined by use of the Hosmer-Lemeshow goodness-of-fit test; C statistic, 0.76).

Table 4. Logistic Regression Model to Identify Factors Independently Associated With Surgical Site Infections

Independent Variable	OR (95% CI)	P Value
Age >65 y	1.29 (0.35-4.85)	.70
BMI > 30	0.84 (0.23-3.04)	.79
Use of preoperative decontamination	1.80 (0.26-12.64)	.55
Use of OA + MBP	0.11 (0.02-0.86)	.04
ASA score >2	1.68 (0.15-19.07)	.68
Neoadjuvant therapy	1.06 (0.20-5.66)	.95
Rectal tumor site	0.38 (0.06-2.25)	.29
Minimally invasive surgery approach	0.22 (0.05-0.89)	.03
Operative time	1.00 (1.00-1.01)	.07
Ertapenem use	0.79 (0.11-5.50)	.81

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); OA + MBP, combined oral antibiotic and mechanical bowel preparation; OR, odds ratio.

Discussion

Surgical site infections are a common postoperative complication after surgery for colorectal disease and significantly affect patient morbidity and mortality. Given the high rate of SSIs after colorectal surgery as well as the lack of effectiveness of other preventive programs, the use of oral antibiotics and MBP, which was initially evaluated in the 1970s and subsequently fell out of favor, has resurfaced as a potential intervention. Our study demonstrated that use of oral antibiotics and MBP was associated with a decrease in overall rates of SSIs and organ space SSIs for patients undergoing left colon and rectal cancer resections. In our logistic regression model, use of oral antibiotics and MBP was associated with an almost 90% reduced odds of having an SSI. However, even with the significant decrease in SSIs with oral antibiotics and MBP, there was no significant difference in the number of patients receiving timely adjuvant therapy, suggesting that there may be other factors affecting this outcome.

Across many institutions, bowel regimens prior to elective colorectal surgery are not routinely used and remain largely dependent on the surgeon. Typically, the use of oral antibiotics is optional, and even the type of MBP differs. In a 2010 survey of members of the American Society of Colon and Rectal Surgeons, respondents indicated that less than 40% of patients always used oral antibiotics as part of routine bowel preparation prior to elective colorectal surgery.[12] Several reasons for this variation in practice may exist. First, data from Finland and Sweden that were published in the early 2000s

demonstrated no difference in rates of SSIs with or without the use of MBP[21,22]; therefore, many surgeons began abandoning the practice of bowel preparation altogether. In particular, studies on no bowel preparation for patients undergoing left colon and rectal resections demonstrated low rates of SSIs ranging from 8% to 13%[23-25]; however, these studies excluded cases with stoma formations and abdominoperineal resections. The overall rate of SSIs in our study was 8% for patients who received oral antibiotics and MBP and is not only comparable to the results of the studies in which no bowel preparation was used but also encompasses the high-risk cases that have been traditionally associated with increased rates of SSIs.[26,27] Second, many of the data for bowel preparation studies come from large administrative databases that do not differentiate between cases of right colon resection and cases of left colon resection, and most surgeons use different bowel regimens depending on the site of resection.[8,9,11] Several studies have demonstrated a lower risk of SSIs for right colon resections compared with left colon and rectal resections[28,29]; therefore, some surgeons advocate not using MBP for right colon resections.[30] The right colon can be expected to have less of a fecal burden than the left colon or rectum; therefore, MBP may not yield the same benefit. However, right colon resections may benefit from oral antibiotics alone to decrease the intraluminal bacterial load. We examined our own institutional data for right colon cancer resections during the study period and, although our sample size was small, found lower rates of SSIs (7 of 53 [13%]) for right colon cancer resections compared with left colon or rectal cancer resections (27%) among the patients who received MBP only. Because the number of patients who received oral antibiotics and MBP for right colon cancer resections (n = 12) was small, we were unable to draw conclusions regarding the benefit of oral antibiotics and MBP for patients undergoing right colon resection.

In 2016, SSI guidelines from the American College of Surgeons and Surgical Infection Society[31] and a consensus guideline statement from the American Society for Enhanced Recovery and Perioperative Quality Initiative[3] recommended oral antibiotics for bowel preparation. Holubar et al[3] also recommended MBP using isosmotic solutions (ie, polyethylene glycol) vs hyperosmotic solutions (ie, magnesium citrate) because they may cause less significant electrolyte imbalances. However, isosmotic bowel preparations require patients to drink large volumes of solution, making it less likely for patients to comply. In our practice, we used magnesium citrate in an elderly veteran population and did not observe significant adverse events. Critics of bowel preparation with oral antibiotics also cite the increased risk of *Clostridium difficile* infections.[1,32] We did not examine this outcome in our study and did not actively screen for *C difficile*, so asymptomatic patients with *C difficile* would have been undiagnosed.

In addition, implementation of a preoperative decontamination protocol may have had an unknown effect in our study. Preoperative decontamination has been effective at decreasing SSI rates in cases with a clean wound class (Bebko et al[15] demonstrated that the SSI rate decreased from 3.8% before intervention to 1.1% after intervention with preoperative decontamination in orthopedic hardware implantation cases); however, its value in colorectal surgery is still under investigation. Recently, our group presented our institutional results at the 2017 Surgical Infection Society Annual Meeting in which there was a nonstatistically significant decrease in the overall rate of SSIs among elective clean contaminated oncologic resections (19% of controls vs 11% of patients who underwent preoperative decontamination; $P = .11$) (E.V., unpublished data, 2017). In the present study, use of preoperative decontamination increased in both the right colon and the left colon or rectal resection cohorts receiving oral antibiotics and MBP. However, on multivariable analysis, use of the preoperative decontamination protocol was not independently associated with reduced odds of SSIs. In addition, on subset analysis, there was no difference in rates of SSIs between patients who performed preoperative decontamination and those who did not, further strengthening our conclusion that preoperative decontamination was likely not a confounder in this study.

Finally, we anticipated that the use of oral antibiotics and MBP would translate into more patients receiving timely adjuvant therapy; however, this hypothesis was not demonstrated in our study. When examining rates of SSIs among the subset of patients who received adjuvant therapy, we found that there was a significant decrease in the rate SSIs among the patients who received oral antibiotics and MBP (0%) compared with the patients who received MBP only (6 of 21 [29%]). Delays to adjuvant therapy for the patients who received oral antibiotics and MBP were attributed to poor healing of perineal wounds after abdominoperineal resection without evidence of infection and early ileostomy reversals. Other reasons for delays could have involved systems issues with scheduling and patient compliance with clinic visits. Further efforts to improve postoperative outcomes after colorectal cancer resections are needed to increase the number of patients receiving timely adjuvant therapy.

Limitations

Our study had several limitations. First, it was a small, single-institution retrospective study of a veteran population, which limits the external validity of our findings. Second, we did not have a reliable method for assessing patient compliance. Third, historical bias may have been present, which we attempted to minimize by underscoring that no changes occurred in compliance with the Surgical Care Improvement Project during the study period, recognizing the effect of MIS, and discussing the possible implications of preoperative decontamination. However, we acknowledge that residual bias may still exist with unmeasured and unknown changes in surgeon practices.

Conclusions

Use of oral antibiotics and MBP was associated with a significant decrease in the overall rate of SSIs. Because there have been no contemporaneous randomized clinical trials evaluating the use of oral antibiotics and MBP, to our knowledge, it may be time for a trial to demonstrate whether the findings in our work and other recent studies are truly attributable to use

of oral antibiotics and MBP. Future work is also needed to understand whether the benefits of oral antibiotics and MBP are also present for patients undergoing right colon resections. Until such data become available, clinicians should consider using oral antibiotics and MBP for all patients undergoing left-sided colorectal cancer resections.

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