

EFFICACY OF VARIOUS MODES OF BOWEL PREPARATION TO
PREVENT SURGICAL SITE INFECTION FOLLOWING
ELECTIVE COLORECTAL RESECTION

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ABSTRACT

Purpose: Administration of a mechanical bowel preparation (MBP) has long been standard before colorectal surgery with the aim of preventing complications such as surgical site infection (SSI). Newer evidence suggests that MBP does not reduce the risk of infection and that oral antibiotic (OA) use may be important in reducing post-operative infectious complications, however, there is little evidence comparing MBP, OA, and combination preparations. Our goal was to determine the relationship between type of bowel preparation and SSI in patients undergoing elective colorectal resections

Methods: All patients within the American College of Surgeons-National Surgical Quality Improvement Program (ACS-NSQIP) database undergoing elective colorectal resections from 2012 to 2013 were identified. The primary outcomes of interest were: any post-operative SSI, wound SSI, and organ/space SSI. Secondary outcomes were anastomotic leak, post-operative ileus, cardiac complications, renal complications, death, unplanned readmission, and length of stay (LOS). Univariate models were used to compare frequencies of patient and surgical characteristics across types of bowel preparation, and propensity adjustment was used to study the relationship between type of bowel preparation and all outcomes of interest.

Results: Among the study sample, 25.5% received no bowel preparation, 40.8% received MBP, 3.3% received OA, and 30.4% received OA+MBP. A total of 1,844 patients (9.5%) developed any type of post-operative SSI. 1,231 (6.4%) developed a wound SSI and 672 (3.5%) developed an organ/space SSI. MBP was not associated with a reduced risk of any type of SSI compared to no bowel preparation. Both OA and OA+MBP were significantly associated with a decreased risk of any SSI and wound SSI compared to both no preparation and compared to MBP. No differences were observed for any SSI or

wound SSI between OA and OA+MBP. Compared to no preparation, OA+MBP was associated with a decreased risk of anastomotic leak and post-operative ileus. No differences were observed between MBP and OA, or between these preparation methods and no preparation, for these secondary outcomes. There were no significant associations between type of bowel preparation and cardiac or renal complications, mortality, or readmissions. Both OA and OA+MBP were associated with a reduction in LOS.

Conclusion: These results suggest that a combination oral and mechanical bowel preparation may be most effective at preventing SSI after elective colorectal resection and that OA alone may also be effective. Future prospective studies comparing combination and OA preparations may be warranted to explore this relationship further.

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CHAPTER 1

INTRODUCTION

Up to 30% of patients undergoing colorectal resections may develop a surgical site infection (SSI),¹ with SSI representing a significant source of post-operative morbidity. SSIs are associated with increased length of stay,^{2,3} increased ICU admissions,³ and increased mortality.³ A recent study by Merkow, et al demonstrated that SSI was the leading cause of hospital readmission following surgery in the U.S.⁴ Thus, SSIs place a strain on the healthcare system, with increased hospitalization costs due to SSI averaging about \$5,000 for the total hospital stay.³ Therefore, identifying methods to reduce SSIs is of critical importance.

Since the beginning of modern surgery, surgeons have used mechanical bowel preparation (MBP) prior to elective colorectal surgery in an attempt to decrease the rate of SSI. MBP was believed to lower risk of SSI by decreasing the fecal mass, and therefore the bacterial load, of the colon.^{5,6} MBP was accepted as surgical dogma until the past several decades. With the advent of the discovery of antibiotics in the 1930s, surgeons began combining MBP with oral antibiotics (OA) in an attempt to further decrease the rate of SSI, and the combination of the two became widely utilized.⁷ In the 1970s, several studies by Nichols and Condon demonstrated a reduced rate of SSI for patients who received a combination of OA and MBP compared to those who received MBP alone.⁸⁻¹⁰ As a result of those studies, a combined preparation became generally accepted as the superior type of bowel preparation to decrease the risk of SSI.

In the 1980s and 1990s, there was increased interest in comparing the efficacy of MBP alone to no preparation. Numerous studies have demonstrated no difference in the

rate of SSI, anastomotic leak, and other non-surgical complications among patients who received MBP compared to those who received no bowel preparation.^{6, 11, 12} Further, an increased rate of infectious complications^{13, 14} as well as slower return of bowel function¹³ and increased rate of cardiac complications,¹⁵ electrolyte disturbances,^{16, 17} and post-operative diarrhea⁶ among patients receiving MBP has been observed in some studies.

Recent literature has focused to a large extent on MBP and less on the combination of OA and MBP specifically. There is persistent controversy regarding which type of bowel preparation most effectively reduces SSI, and there exists substantial variation in preparation utilization among surgeons. Because of the lack of consensus regarding best practice, further evidence to clarify the benefits, as well as adverse effects, of the different types of bowel preparation is necessary.

Given this need, the purpose of the current study is to use the NSQIP database, a large, retrospective surgical database containing patient information collected from hundreds of hospitals in the U.S., to determine the association between four different types of bowel preparation- none, MBP, OA, and OA plus MBP- and SSI for patients undergoing elective colorectal resections, as well as to look for possible associations between bowel preparation and other adverse postoperative outcomes. The routine use of bowel preparation is not standardized within the surgical community, and further evidence using large surgical databases is needed in order to more clearly delineate these relationships in order to enable surgeons to make the most well-informed decisions.

CHAPTER 2

METHODS

This study was a cross-sectional analysis of data collected in 2012 and 2013 by the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP). The ACS NSQIP database was created in 2004 with the goal of reducing surgical complications. A hospital's participation in ACS NSQIP is optional. In 2014, more than 500 hospitals around the country were enrolled in NSQIP, representing about 10% of all hospitals in the U.S. For participating hospitals, preoperative through 30-day postoperative data is collected from medical charts by a trained Surgical Clinical Reviewer at each site. Data is collected for 21 morbidities, as well as mortality. Sites are compared to one another for outcomes and are encouraged to correct deficiencies in care.¹⁸

For this study, all patients undergoing elective, non-emergent colorectal resections were included in the analysis (N=26,688). Patients were excluded if they were missing data regarding bowel preparation (N=6,882), if they were ventilator-dependent (N=3), if they had diagnosed infections (N=187), or if they had documented evidence of an open wound at the time of surgery (N=244). As all cases included were colorectal resections and by definition cannot be considered "clean," cases with a recorded wound classification of "clean" were reclassified as "clean/contaminated" (N=193).

Measures

Bowel Preparation Method

Bowel preparation was separated into four categories based on the way it is recorded in the NSQIP database: none, mechanical bowel preparation (MBP), oral antibiotics (OA) and both OA and MBP (OA+MBP).

Primary Surgical Site Infection Outcomes

The primary outcomes of interest were: (1) any post-operative SSI, defined as the presence of a superficial, deep incisional, or organ/space SSI, (2) wound SSI, defined as the presence of a superficial and/or deep incisional SSI, and (3) organ/space SSI. These measures were recorded as binary variables.

Secondary Outcomes

In addition to SSI outcomes, a range of outcomes associated with morbidity, mortality, and healthcare system burden were examined. These secondary outcomes were: (1) anastomotic leak, (2) post-operative ileus, (3) cardiac complications, defined as either myocardial infarction or cardiac arrest, (4) renal complications, defined as either acute renal insufficiency not requiring dialysis or acute renal failure requiring dialysis, (5) death within 30 days, and (6) unplanned readmission to the hospital within 30 days of discharge. These variables were all recorded dichotomously. Total hospital length of stay (LOS) in days was also examined.

Covariates

Covariates included in the analysis consisted of demographic data, preoperative co-morbidities and lab values, and operative characteristics that were selected based on knowledge gained from the literature regarding possible cofounders of the bowel

preparation-SSI relationship. The different colorectal procedures were classified into the following 4 types of resections based on the principal current procedural terminology (CPT) code: ileocolic resection (CPT codes 44160 and 44205), partial colectomy (CPT codes 44140, 44141, 44143, 44144, 44147, 44204, and 44206), total colectomy (CPT codes 44150, 44151, and 44210) and rectal resection (CPT codes 44145, 44146, 44207, and 44208).

Statistical Analysis

Bivariate analyses were conducted using tests to examine frequencies in the distribution of patient characteristics, as well as outcomes, across patients receiving the four different types of bowel preparation. Chi-square tests were used to compare frequencies, and ANOVAs were used to compare mean values of continuous variables. To account for the non-random receipt of type of bowel preparation by patients, propensity-adjustment was performed using inverse probability of treatment (IPT) weights developed using all theoretically and empirically-identified covariates.^{19, 20} Pairwise comparisons between IPT-weighted odds ratios (ORs) were conducted in order to identify differences in the occurrence of all primary and secondary outcomes between each type of bowel preparation compared to no preparation. Similar pairwise comparisons between MBP, OA, and OA+MBP were conducted for all study outcomes. $P < 0.05$ was used to indicate significant differences between ORs. All analyses were completed using STATA 13.1.

CHAPTER 3

RESULTS

A total of 19,372 patients who underwent elective colorectal resections between 2012 and 2013 were included in the analysis. Patient demographics and co-morbidities stratified by type of bowel preparation are shown in Table 1, with IPT weight-adjusted covariates shown in Table 2. Among the study sample, 25.5% received no bowel preparation, 40.8% received MBP, 3.3% received OA, and 30.4% received OA+MBP.

Table 1. Cohort Demographics and Co-Morbidities

	Overall N (%)	None N (%)	MBP Only N (%)	OA Only N (%)	OA+MBP N (%)	<i>P</i>
Overall	19,372	4,941 (25.5)	7,905 (40.8)	634 (3.3)	5,892 (30.4)	
Age (mean (SD))	45.21 (14.66)	45.21 (15.61)	45.69 (14.20)	41.79 (17.17)	44.92 (14.09)	<0.001
Gender						
Female	10,035 (51.8)	2,596 (52.5)	4,090 (51.7)	329 (51.9)	3,020 (51.3)	0.616
Race/Ethnicity						
White	14,992 (77.4)	3,597 (72.8)	6,099 (77.2)	483 (76.2)	4,813 (81.7)	<.001
Black	1,456 (7.5)	377 (7.6)	604 (7.6)	56 (8.8)	419 (7.1)	
Hispanic	821 (4.2)	167 (3.4)	363 (4.6)	28 (4.4)	263 (4.5)	
Asian	629 (3.3)	122 (2.5)	306 (3.9)	25 (3.9)	176 (3.0)	
Other	1,474 (7.6)	678 (13.7)	533 (6.7)	42 (6.6)	221 (3.8)	
BMI						
<18.5	532 (2.8)	180 (3.6)	192 (2.4)	24 (3.8)	136 (2.3)	<.001
≥18.5 and <25	5,713 (29.5)	1,545 (31.3)	2,278 (28.8)	221 (34.9)	1,669 (28.3)	
≥25 and <30	6,521 (33.7)	1,656 (33.5)	2,667 (33.7)	177 (27.9)	2,021 (34.3)	
≥30	6,606 (34.1)	1,560 (31.6)	2,768 (35.0)	212 (33.4)	2,066 (35.1)	
Hypertension	9,140 (47.2)	2,306 (46.7)	3,859 (48.8)	266 (42.0)	2,709 (46.0)	<.001
CHF	96 (0.5)	34 (0.7)	37 (0.47)	1 (0.2)	24 (0.4)	0.101
Dyspnea	1,284 (6.6)	363 (7.3)	518 (6.6)	32 (5.0)	371 (6.3)	0.05
COPD	827 (4.3)	211 (4.3)	339 (4.3)	20 (3.2)	257 (4.4)	0.56
Diabetes	2,704 (14.0)	649 (13.1)	1,153 (14.6)	77 (12.2)	825 (14.0)	0.068
Weight loss	680 (3.5)	192 (3.9)	255 (3.2)	31 (4.9)	202 (3.4)	0.054
Steroid use	1,660 (8.6)	533 (10.8)	507 (6.4)	115 (18.1)	505 (8.6)	<.001
Smoking	3,186 (16.5)	793 (16.0)	1,279 (16.2)	109 (17.2)	1,005 (17.1)	0.418
Sodium <135	845 (4.7)	265 (5.9)	298 (4.1)	31 (5.5)	251 (4.6)	<.001

Table 1 continued.

		Overall	None	MBP Only	OA Only	OA+MBP	P
		N (%)	N (%)	N (%)	N (%)	N (%)	
Creatinine >1.2		1,823 (10.2)	472 (10.3)	778 (10.6)	46 (8.1)	527 (9.6)	0.089
Albumin ≤3.5		9,535 (49.2)	2,497 (50.5)	3,930 (49.7)	323 (51.0)	2,785 (47.3)	0.003
Bilirubin >1		1,259 (6.5)	331 (6.7)	528 (6.7)	46 (7.3)	354 (6.0)	0.298
SGOT >40		820 (6.9)	214 (7.0)	341 (7.1)	27 (6.5)	238 (6.6)	0.828
Hematocrit >45		1,922 (10.4)	368 (7.8)	786 (10.5)	53 (8.8)	715 (12.6)	<.001
Platelets >400		1,289 (7.0)	395 (8.5)	470 (6.3)	54 (9.0)	370 (6.6)	<.001
Chemotherapy		1,112 (5.8)	269 (5.5)	443 (5.6)	34 (5.4)	366 (6.2)	0.296
Disseminated cancer		1,055 (5.5)	384 (7.8)	406 (5.1)	24 (3.8)	241 (4.1)	<.001
ASA class	1-2	10,465 (54.0)	2,561 (51.9)	4,236 (53.7)	361 (56.9)	3,307 (56.2)	<.001
	3	8,281 (42.8)	2,200 (44.6)	3,425 (43.4)	248 (39.1)	2,408 (40.9)	
	4	601 (3.1)	174 (3.53)	232 (2.9)	25 (3.94)	170 (2.9)	

Table 2. Propensity Adjusted Cohort Demographics and Co-Morbidities

		Overall, %	None, %	MBP Only, %	OA Only, %	OA+MBP, %
Age (mean (SD))			14.9	14.8	14.9	14.8
Gender						
	Female	51.7	51.5	51.6	52.3	51.6
Race						
	White	77.4	77.5	77.5	77.1	77.4
	Black	8.1	8.2	8.0	8.2	8.1
	Hispanic	4.3	4.3	4.2	4.5	4.3
	Asian	3.4	3.3	3.4	3.3	3.4
	Other	6.8	6.7	6.8	6.8	6.8
BMI						
	<18.5	2.9	2.9	3.0	2.8	2.9
	≥18.5 and <25	30.3	30.1	30.3	30.6	30.3
	≥25 and <30	33.1	33.0	33.2	33.4	32.8
	≥30	33.7	34.0	33.6	33.1	34.0
Diabetes		14.1	14.0	14.3	13.6	14.4
COPD		4.6	4.6	4.6	4.5	4.6
Dyspnea		7.1	7.1	7.1	7.4	7.0
Hypertension		48.4	47.5	48.0	50.3	47.9
CHF		0.4	0.5	0.5	0.1	0.5
Smoking		16.1	16.3	16.2	15.5	16.4
Steroid use		9.4	9.5	9.4	9.3	9.6
Weight loss		4.1	4.2	4.3	3.8	4.2

Table 2 continued.

		Overall, %	None, %	MBP Only, %	OA Only, %	OA+MBP, %
Bilirubin		10.1	10.2	10.2	9.8	10.2
Albumin		24.2	23.9	24.2	24.8	23.9
Creatinine		10.1	9.9	10.1	10.3	10.2
SGOT		6.8	6.9	6.9	6.6	6.9
Platelets		7.6	7.9	7.8	7.1	7.8
Sodium		4.9	4.8	5.0	4.8	4.9
Hematocrit		9.5	9.7	9.5	9.0	9.6
Chemotherapy		6.9	7.0	6.9	6.7	7.1
Disseminated cancer		6.6	6.7	6.9	6.1	6.8
ASA class	1-2	50.6	50.1	50.2	52.0	50.0
	3	45.8	46.3	46.3	44.1	46.4
	4	3.7	3.6	3.6	3.9	3.5

The most common indication for surgery was neoplasm (42.5%), followed by other (26.8%), diverticulitis (22.9%), and inflammatory bowel disease (7.7%). The most frequently performed type of procedure was partial colectomy (45.1%), followed by rectal resection (28.6%), ileocolic resection (21.8%), and total colectomy (4.5%). 37.4% underwent a minimally invasive approach, 27.6% had an open procedure, 27.4% had a minimally invasive approach with hand assist, and 7.6% underwent a minimally invasive approach that was converted to open. Operative characteristics are shown in Table 3, and IPT weight-adjusted operative characteristics are shown in Table 4. Tables 2 and 4 demonstrate that use of the IPT-weights sufficiently balanced all demographic and operative characteristics, as well as co-morbidities, across bowel preparation type.

A total of 1,844 patients (9.5%) developed any type of post-operative SSI. 1,231 (6.4%) developed a wound SSI and 672 (3.5%) developed an organ/space SSI. There was a significant difference in the prevalence of all types of SSI by type of bowel preparation in the unadjusted analysis ($P<0.001$) The highest rates of SSI were observed in the group

who received no preparation, followed by those who received MBP, OA, and OA+MBP (Table 5).

Table 3. Cohort Operative Characteristics

	Overall, N(%)	None, N(%)	MBP Only, N (%)	OA Only, N (%)	OA+MBP, N (%)	P
Indication						
Neoplasm	8,238 (42.5)	2,102 (42.5)	3,535 (44.7)	218 (34.4)	2,383 (40.4)	<.001
IBD	1,490 (7.7)	528 (10.7)	396 (5.0)	131 (20.7)	435 (7.4)	
Diverticulitis	4,445 (22.9)	757 (15.3)	1,914 (24.4)	135 (21.3)	1,639 (27.8)	
Other	5,199 (26.8)	1,554 (31.5)	2,060 (26.1)	150 (23.7)	1,435 (24.4)	
Type of procedure						
Ileocolic resection	4,215 (21.8)	1,469 (29.7)	1,456 (18.4)	180 (28.4)	1,110 (18.8)	<.001
Partial colectomy	8,737 (45.1)	2,070 (41.9)	3,561 (45)	270 (42.6)	2,836 (48.1)	
Total colectomy	874 (4.5)	282 (5.7)	295 (3.7)	39 (6.2)	258 (4.4)	
Rectal resection	5,546 (28.6)	1,120 (22.7)	2,593 (32.8)	145 (22.9)	1,688 (28.6)	
Operative approach						
MIS	7,252 (37.4)	1,724 (34.9)	3,058 (38.7)	239 (37.7)	2,231 (37.9)	<.001
MIS with hand assist	5,297 (27.4)	1,185 (24)	2,238 (28.3)	179 (28.2)	1,695 (28.8)	
MIS converted to open	1,468 (7.6)	384 (7.8)	553 (7.0)	51 (8.0)	480 (8.1)	
Open	5,350 (27.6)	1,647 (33.3)	2,054 (26.0)	165 (26.0)	1,484 (25.2)	
Wound classification						
Clean/Contaminated	16,426 (84.79)	4,188 (84.76)	6,735 (85.20)	495 (78.08)	5,008 (85)	<.001
Contaminated	2,069 (10.68)	508 (10.28)	844 (10.68)	87 (13.72)	630 (10.69)	
Dirty	877 (4.53)	245 (4.96)	326 (4.12)	52 (8.2)	254 (4.31)	
Operative time						
<180 min	11,268 (58.2)	2,984 (60.4)	4,606 (58.3)	357 (56.3)	3,321 (56.4)	<.001
≥180 min	8,104 (41.8)	1,957 (39.6)	3,299 (41.7)	277 (43.7)	2,571 (43.6)	
Stoma creation						
No	17,522 (90.5)	4,440 (89.9)	7,155 (90.5)	565 (89.1)	5,362 (91.0)	0.143
Yes	1,850 (9.5)	501 (10.1)	750 (9.5)	69 (10.9)	530 (9.0)	

Table 4. Propensity-Adjusted Cohort Operative Characteristics

	Overall, %	None, %	MBP Only, %	OA Only, %	OA+MBP, %
Indication					
Neoplasm	45.9	45.6	45.9	46.7	45.4
IBD	8.4	8.5	8.3	8.4	8.5
Diverticulitis	21.5	21.3	21.1	22.1	21.3
Other	24.2	24.6	24.7	22.7	24.8
Type of procedure					
Ileocolic resection	22.4	22.6	22.4	22.2	22.5
Partial colectomy	42.9	42.7	43.8	42.0	43.2
Total colectomy	4.5	4.7	4.6	4.0	4.7
Rectal resection	30.2	30.1	29.2	31.9	29.7
Operative approach					
MIS	33.2	32.7	33.1	33.6	33.2
MIS with hand assist	29.5	29.2	28.9	31.1	29.5
MIS converted to open	8.0	8.2	8.0	8.0	8.0
Open	29.2	29.9	30.0	27.3	29.2
Wound classification					
Clean/Contaminated	84.4	84.7	84.4	84.1	84.5
Contaminated	10.7	10.3	10.7	11.4	10.5
Dirty	4.9	5.0	4.9	4.5	5.0
Operative time					
<180 min	56.3	55.5	56.3	57.7	55.7
≥180 min	43.7	44.5	43.8	42.3	44.3
Stoma creation					
No	89.3	88.8	89.0	90.3	89.3
Yes	10.7	11.2	11.0	9.7	10.7

Table 5. Rates of Adverse Outcomes by Type of Bowel Preparation, Unadjusted

	Overall	None	MBP Only	OA Only	OA + MBP	P
	N (%)	N (%)	N (%)	N (%)	N (%)	
Any SSI	1,844 (9.5)	618 (12.5)	844 (10.7)	50 (7.9)	332 (5.6)	<.001
Wound SSI	1,231 (6.4)	416 (8.4)	574 (7.3)	31 (4.9)	210 (3.6)	<.001
Organ/Space SSI	672 (3.5)	221 (4.5)	293 (3.7)	21 (3.3)	137 (2.3)	<.001
Anastomotic leak	608 (3.1)	204 (4.2)	265 (3.4)	18 (2.8)	121 (2.1)	<.001
Prolonged ileus	2,260 (11.7)	679 (13.8)	947 (12.0)	67 (10.6)	567 (9.6)	<.001
Cardiac complications	158 (0.8)	48 (1.0)	66 (0.8)	5 (0.8)	39 (0.7)	0.355
Renal complications	167 (0.9)	41 (0.8)	60 (0.8)	8 (1.3)	58 (1.0)	0.353
Readmission	1,784 (9.2)	524 (10.6)	722 (9.1)	58 (9.2)	480 (8.2)	<.001
Mortality	164 (0.8)	64 (1.3)	67 (0.8)	4 (0.6)	29 (0.5)	<.001
LOS (Mean, SD)	6.2 (6.6)	6.9 (8.3)	6.2 (6.7)	6.1 (4.7)	5.5 (4.6)	<.001

Primary SSI Outcomes

After propensity adjustment to address confounding, compared to no preparation, both OA and OA+MBP were significantly associated with decreased risk of any SSI and wound SSI compared to no preparation (Table 6). No differences were observed for any SSI or wound SSI between OA and OA+MBP (OR =0.81, 95%CI=0.52-1.28 and OR=1.03, 95%CI=0.58-1.83, respectively) (Table 7). For the outcome of organ/space SSI, compared to no preparation, the prevalence of organ/space SSI with use of OA was not different from that observed with no preparation (OR 0.94, 95%CI 0.50-1.77). MBP was not significantly different than no preparation for any of the SSI outcomes examined (any SSI OR=0.95, 95% CI=0.82-1.10; wound SSI OR=0.91, 95%CI=0.76-1.09; organ/space SSI OR=1.00, 95%CI=0.79-1.27).

Table 6. Unadjusted and Propensity Adjusted Associations Between Type of Bowel Preparation and Adverse Outcomes Compared to No Preparation

<u>Primary Outcomes</u>		Unadjusted %	Propensity Adjusted %	Propensity Adjusted OR (95% CI) Compared to None
Any SSI				
	None	12.50	11.87	--
	MBP	10.70	11.31	0.95 (0.82-1.10)
	OA	7.90	7.01	0.56 (0.36-0.87)
	OA+MBP	5.60	5.78	0.46 (0.38-0.55)
Wound SSI				
	None	8.42	8.30	--
	MBP	7.26	7.62	0.91 (0.76-1.09)
	OA	4.89	3.56	0.41 (0.23-0.72)
	OA+MBP	3.56	3.66	0.42 (0.33-0.53)
Organ/Space SSI				
	None	4.47	4.06	--
	MBP	3.71	4.07	1.00 (0.79-1.27)
	OA	3.31	3.82	0.94 (0.50-1.77)
	OA+MBP	2.33	2.43	0.59 (0.44-0.78)

Table 6 continued.

		Unadjusted %	Propensity Adjusted %	Propensity Adjusted OR (95% CI) Compared to None
<u>Secondary Outcomes</u>				
Anastomotic leak				
	None	4.15	3.63	--
	MBP	3.36	3.45	0.95 (0.73-1.23)
	OA	2.84	2.34	0.64 (0.29-1.39)
	OA+MBP	2.05	2.1	0.57 (0.42-0.78)
Post-operative ileus				
	None	13.81	13.07	--
	MBP	12.01	13.32	1.02 (0.89-1.18)
	OA	10.58	9.29	0.68 (0.47-1.00)
	OA+MBP	9.63	10.62	0.79 (0.68-0.92)
Cardiac complications				
	None	0.97	0.82	--
	MBP	0.83	0.94	1.14 (0.69-1.90)
	OA	0.79	0.96	1.18 (0.44-3.13)
	OA+MBP	0.66	0.78	0.95 (0.52-1.72)
Renal complications				
	None	0.83	1.00	--
	MBP	0.76	0.77	0.76 (0.47-1.24)
	OA	1.26	1.29	1.29 (0.54-3.08)
	OA+MBP	0.98	1.25	1.25 (0.76-2.04)
Mortality				
	None	1.30	1.02	--
	MBP	0.85	0.97	0.96 (0.61-1.51)
	OA	0.63	0.89	0.87 (0.29-2.64)
	OA+MBP	0.49	0.70	0.68 (0.38-1.22)
Readmissions				
	None	10.61	10.49	--
	MBP	9.13	9.86	0.93 (0.80-1.09)
	OA	9.15	8.17	0.76 (0.51-1.12)
	OA+MBP	8.15	9.03	0.85 (0.71-1.01)
LOS*				
	None	6.93 (8.28)	6.74 (5.93)	--
	MBP	6.21(6.69)	6.61 (5.68)	-0.14 (-0.41 to 0.13)
	OA	6.14 (4.72)	5.91 (4.39)	-0.83 (-1.30 to -0.36)
	OA+MBP	5.55 (4.64)	5.91 (5.13)	-0.83 (-1.12 to -0.55)

*numbers are changes in means

Table 7. Pairwise Comparisons of Propensity Adjusted Associations Between Type of Bowel Preparation and Adverse Outcomes

		<u>MBP</u>	<u>OA</u>
<u>Primary Outcomes</u>			
Any SSI			
	OA	0.60 (0.38-0.93)	--
	OA+MBP	0.48 (0.40-0.57)	0.81 (0.52-1.28)
Wound SSI			
	OA	0.45 (0.26-0.78)	--
	OA+MBP	0.46 (0.37-0.57)	1.03 (0.58-1.83)
Organ/Space SSI			
	OA	0.93 (0.50-1.75)	--
	OA+MBP	0.59 (0.45-0.76)	0.63 (0.33-1.19)
<u>Secondary Outcomes</u>			
Anastomotic leak			
	OA	0.67 (0.31-1.45)	--
	OA+MBP	0.60 (0.45-0.80)	0.90 (0.41-1.98)
Post-operative ileus			
	OA	0.67 (0.46-0.97)	--
	OA+MBP	0.77 (0.67-0.89)	1.16 (0.79-1.70)
Cardiac complications			
	OA	1.03 (0.40-2.63)	--
	OA+MBP	0.83 (0.49-1.41)	0.81 (0.30-2.17)
Renal complications			
	OA	1.69 (0.71-4.00)	--
	OA+MBP	1.63 (1.02-2.60)	0.97 (0.41-2.30)
Mortality			
	OA	0.92 (0.31-2.70)	--
	OA+MBP	0.71 (0.41-1.24)	0.78 (0.25-2.47)
Readmissions			
	OA	0.81 (0.56-1.19)	--
	OA+MBP	0.91 (0.78-1.06)	1.12 (0.76-1.65)
Length of stay*			
	OA	1.44 (0.88 to 4.17)	--
	OA+MBP	-0.70 (-0.95 to -0.45)	0.00 (-0.46 to 0.45)

*numbers are changes in means

Secondary Outcomes

Compared to no preparation, only OA+MBP was associated with a decreased risk of anastomotic leak (OR 0.57, 95%CI 0.42-0.78) and post-operative ileus (OR 0.79, 95%CI 0.68-0.92) (Table 6). There were no significant associations between any type of bowel preparation and cardiac or renal complications, mortality, or readmissions. Both OA and OA+MBP were associated with a significant 0.83-day reduction in LOS (OA 95% CI -1.30 to -0.36, OA+MBP 95% CI -1.12 to -0.55).

CHAPTER 4

DISCUSSION

Given that the practice of bowel preparation has varied substantially over the years and that there are currently no official recommendations regarding this practice, the goal of this study was to contribute evidence to the existing literature about the association between various types of bowel preparation and the post-operative development of SSI, a major source of both healthcare costs and patient morbidity after elective colorectal resections. Additionally, this study aimed to determine whether these types of preparations are associated, either negatively or positively, with other adverse outcomes in order to gain a better understanding of their true risks and benefits.

It was observed that OA+MBP was associated with the greatest risk reduction for any SSI and wound SSI when compared to no preparation. These results are in line with the findings of two recent studies. One study by Cannon et al from the private sector used the Veterans Affairs Surgical Quality Improvement Program (VA-SQIP) database to compare the same four types of bowel preparations as were compared in this analysis.²¹ The study included just under 10,000 patients, and the authors compared the same four types of bowel preparation and found that OA+MBP was associated with a reduced risk of SSI compared to no bowel preparation (OR 0.43, 95%CI 0.34-0.55). A second study by Morris et al also used the NSQIP database and showed that OA+MBP was associated with the greatest reduction in SSI risk compared to no bowel preparation (OR 0.46, 95%CI 0.36-0.58).²² A 2014 retrospective study by Kim, et al compared OA+MBP to no bowel preparation and found that it was associated with a reduced risk of overall SSI (5.0% vs 9.7%, P = 0.0001).²³ That OA+MBP was also associated with a reduced risk of

all types of SSI when compared with MBP demonstrates its benefit, not only compared no bowel preparation, but to this alternative type of preparation. The finding that there was a significant risk reduction in anastomotic leak and post-operative ileus, as well as a reduction in LOS, for OA+MBP when compared to both no bowel preparation and MBP may indicate other benefits of this type of preparation.

The results of this study also showed that MBP alone was not associated with a decreased risk of SSI compared to no bowel preparation, nor was it associated with a decreased risk of anastomotic leak, post-operative ileus, cardiac or renal complications, mortality, readmissions, or a reduced LOS compared to no preparation. Despite multiple studies^{5, 6, 11, 14, 15, 24} demonstrating that the use of MBP alone does not reduce the risk of SSI compared to no bowel preparation, surgeons continue to use it. A 2010 survey of members of the American Society of Colon and Rectal Surgeons demonstrated that 76% of surgeons routinely used MBP and 36% used OA,²⁵ meaning that, at the very least, 40% of colorectal surgeons were using MBP in the absence of OA. This usage pattern is similar to the findings of this study, in which approximately 40% of patients in the NSQIP database who underwent surgery in 2012 or 2013 received MBP alone. This data shows no benefit to using MBP over any other type of bowel preparation and provides further support for abandoning the use of MBP alone prior to elective colorectal resections.

Another finding of this study was that OA alone was associated with a reduced risk of any SSI and wound SSI compared to both no bowel preparation and MBP. Further, no differences were observed in the prevalence of all types of SSI when OA was compared to OA+MBP, suggesting that the addition of MBP to OA preparation may not

result in better surgical outcomes. It is unknown whether these patients truly received this type of preparation, as it is unusual for a surgeon to use OA in the absence of MBP. In this study, patients who received OA alone were more likely to undergo surgery for the indication of inflammatory bowel disease (IBD) and were also more likely to be taking steroids, which were likely being prescribed for their IBD. These patients may have been more likely to have diarrhea prior to surgery, obviating the need for a cathartic such as MBP. Another possibility is that patients recorded as having received OA alone were simply coded incorrectly within the NSQIP database. They may have truly received a combined OA+MBP preparation, but documentation of MBP may have been missing from these patients' charts.

Relatively few studies have explored the effect of OA alone on the development of SSI. In the most recent Cochrane Review of antimicrobial prophylaxis in colorectal surgery, which found significantly lower rates of SSI in patients who received OA compared to those who received no OA (RR 0.56, 95% CI 0.43 to 0.74), the authors point out that the majority of studies that found a benefit to OA were conducted at a time when MBP was routinely prescribed. As such, the benefit of oral antibiotics alone remained uncertain at the time of the study.²⁶

There has been recent interest in exploring the association between OA alone and SSI, and the findings of this study support the current, albeit sparse, evidence that OA, when used in the absence of MBP, is associated with a reduced risk of SSI. This evidence includes that noted by Dellinger in a recent article in the *Annals of Surgery*²⁷ that three studies included in the most recent Cochrane Review of mechanical bowel preparation administered OA to both the MBP and no MBP groups.^{6, 28, 29} When these studies are

evaluated separately from those in which the intervention group received MBP alone, the reduction in SSI rates is similar for the OA+MBP group and the OA group, suggesting that OA may be effective in reducing SSI rates even in the absence of MBP.

Additionally, the Cannon study found that OA alone was associated with a reduced risk of SSI compared to no preparation (OR = 0.33, 95%CI 0.21–0.50).²¹ For years, a commonly held belief and oft-cited adage in the literature was that oral antibiotics will not prevent SSI in a colon that has not first been cleared of its fecal burden by MBP.^{21, 27, 30} However, there has been no evidence in favor of this hypothesis, and the results of this study, in addition to those of the several studies mentioned, provide support for beginning to reconsider this assumption.

This study provides several benefits over the Cannon and Morris studies. Because the VA-SQIP database contains data from exclusively VA hospitals, and therefore almost exclusively older, male patients, there is the question as to the generalizability of the findings of the Cannon study to the public sector. Another advantage of this study is that it included two years of NSQIP data, and therefore over 10,000 more patients than the Morris study, which made possible the comparison of four different types of bowel preparation and allowed for additional confidence in the results. An additional strength of this study is that a propensity-adjusted analysis was used to account for the non-randomized prescription of bowel preparation type to patients. This type of adjustment also allowed for the determination of the effect of the four types of bowel preparation, not only on SSI, but on multiple adverse outcomes, providing additional information about any true additional risks and benefits of the types of bowel preparations. Finally, the pairwise comparison of each type of bowel preparation to the others provides insight into

advantages and disadvantages of the types of bowel preparations, not solely compared to no preparation, but also compared to the other types of preparations as well. This is the first study to conduct a propensity-adjusted analysis in order to compare all four types of bowel preparation to both no preparation and also to each other to further explore the true benefits and risks of bowel preparation. This is also the first study to conduct propensity-adjusted analyses of numerous adverse outcomes to determine whether an association exists between type of bowel preparation and these outcomes.

There are several limitations of this study. Due to its retrospective nature, the patients in this cohort were not randomized to type of bowel preparation, which could have introduced bias if the groups were similar in other ways. Conducting a propensity-adjusted analysis helps reduce the possibility of bias, but it is possible that there are additional confounders that were not considered in this analysis. Also, the way in which bowel preparation variables are collected and recorded in the NSQIP database make it impossible to determine which type of OA, MBP, or combination each patient received. Further, there is an aspect of human error inherent to the way in which bowel preparation variables were collected and recorded by NSQIP chart reviewers. There is also no data about patient compliance; the fact that a patient was prescribed a certain type of bowel preparations does not mean he or she took it as prescribed, or even at all. Additionally, there is no data within the NSQIP database regarding whether or not patients received appropriate parenteral antibiotic prophylaxis. However, national compliance rates with SCIP Infection Process measures is approximately 99%, so this is unlikely to have biased the results.³¹ Finally, while OA was associated with a reduced risk of any SSI and wound SSI, the findings of this study did not show a significant risk reduction in organ/space SSI

for OA alone. This is likely due to the relatively small number of patients who both received OA and who developed an organ/space SSI.

Although there have been numerous studies that have demonstrated the benefit of using OA in combination with MBP^{26, 30, 32, 33} since the first studies conducted by Nichols and Condon four decades earlier, use of OA has remained controversial, and its use by colorectal surgeons has declined from 86% in 1997 to 36% in 2010.^{25, 34} There does not seem to be a good reason to omit the use of OA. The results of this study do not show an association between OA+MBP and other outcomes commonly believed to be associated with bowel preparation, such as anastomotic leak, ileus, cardiac and renal complications resulting from electrolyte disturbances, readmissions, and mortality. In fact, these results suggest that OA+MBP may be associated with a decreased risk of some complications, such as leak and ileus, as well as a reduced LOS. Regarding the concern that has sometimes been expressed that the use of OA prior to colorectal resections will increase rates of *C. difficile*, studies have found no association between an OA bowel preparation and this type of infection.^{21, 35}

While any bias due to non-randomization of patients to bowel preparation groups should have been accounted for by propensity adjustment, a lack of confidence that patients recorded as receiving OA alone truly received that type of preparation warrants conducting prospective, randomized trials to compare OA and OA+MBP. Such studies would also eliminate unknowns not accounted for by this analysis, such as specific type of OA and MBP administered, patient compliance, possible errors in data collection, and other confounders that may be unknown at this point in time. In the meantime, it is the recommendation of these authors that surgeons abandon the use of MBP alone and

routinely prescribe OA as part of an effective bowel preparation prior to elective colorectal resections.

REFERENCES CITED

1. Smith RL, Bohl JK, McElearney ST, et al. Wound infection after elective colorectal resection. *Ann Surg* 2004;239:599-605; discussion 605-7.
2. Mahmoud NN, Turpin RS, Yang G, et al. Impact of surgical site infections on length of stay and costs in selected colorectal procedures. *Surg Infect (Larchmt)* 2009;10:539-544.
3. Kirkland KB, Briggs JP, Trivette SL, et al. The impact of surgical-site infections in the 1990s: attributable mortality, excess length of hospitalization, and extra costs. *Infect Control Hosp Epidemiol* 1999;20:725-730.
4. Merkow RP, Ju MH, Chung JW, et al. Underlying reasons associated with hospital readmission following surgery in the United States. *JAMA* 2015;313:483-495.
5. Cao F, Li J, Li F. Mechanical bowel preparation for elective colorectal surgery: updated systematic review and meta-analysis. *Int J Colorectal Dis* 2012;27:803-810.
6. Zmora O, Mahajna A, Bar-Zakai B, et al. Colon and rectal surgery without mechanical bowel preparation: a randomized prospective trial. *Ann Surg* 2003;237:363-367.
7. Fry DE. Colon preparation and surgical site infection. *Am J Surg* 2011;202:225-232.
8. Nichols RL, Condon RE, Gorbach SL, et al. Efficacy of preoperative antimicrobial preparation of the bowel. *Ann Surg* 1972;176:227-232.
9. Nichols RL, Broido P, Condon RE, et al. Effect of preoperative neomycin-erythromycin intestinal preparation on the incidence of infectious complications following colon surgery. *Ann Surg* 1973;178:453-462.

10. Clarke JS, Condon RE, Bartlett JG, et al. Preoperative oral antibiotics reduce septic complications of colon operations: results of prospective, randomized, double-blind clinical study. *Ann Surg* 1977;186:251-259.
11. Ram E, Sherman Y, Weil R, et al. Is mechanical bowel preparation mandatory for elective colon surgery? A prospective randomized study. *Arch Surg* 2005;140:285-288.
12. Saha AK, Chowdhury F, Jha AK, et al. Mechanical bowel preparation versus no preparation before colorectal surgery: A randomized prospective trial in a tertiary care institute. *J Nat Sci Biol Med* 2014;5:421-424.
13. Bucher P, Gervaz P, Soravia C, et al. Randomized clinical trial of mechanical bowel preparation versus no preparation before elective left-sided colorectal surgery. *Br J Surg* 2005;92:409-414.
14. Slim K, Vicaut E, Launay-Savary MV, et al. Updated systematic review and meta-analysis of randomized clinical trials on the role of mechanical bowel preparation before colorectal surgery. *Ann Surg* 2009;249:203-209.
15. Gravante G, Caruso R, Andreani SM, et al. Mechanical bowel preparation for colorectal surgery: a meta-analysis on abdominal and systemic complications on almost 5,000 patients. *Int J Colorectal Dis* 2008;23:1145-1150.
16. Frizelle FA, Colls BM. Hyponatremia and seizures after bowel preparation: report of three cases. *Dis Colon Rectum* 2005;48:393-396.
17. Beloosesky Y, Grinblat J, Weiss A, et al. Electrolyte disorders following oral sodium phosphate administration for bowel cleansing in elderly patients. *Arch Intern Med* 2003;163:803-808.

18. Maggard-Gibbons M. The use of report cards and outcome measurements to improve the safety of surgical care: the American College of Surgeons National Surgical Quality Improvement Program. *BMJ Qual Saf* 2014;23:589-599.
19. Rosenbaum PR RD. Reducing bias in observational studies using subclassification on the propensity score. *JASA* 1984;79:516-524.
20. Lunceford JK, Davidian M. Stratification and weighting via the propensity score in estimation of causal treatment effects: a comparative study. *Stat Med* 2004;23:2937-2960.
21. Cannon JA, Altom LK, Deierhoi RJ, et al. Preoperative oral antibiotics reduce surgical site infection following elective colorectal resections. *Dis Colon Rectum* 2012;55:1160-1166.
22. Morris MS, Graham LA, Chu DI, et al. Oral Antibiotic Bowel Preparation Significantly Reduces Surgical Site Infection Rates and Readmission Rates in Elective Colorectal Surgery. *Ann Surg* 2015.
23. Kim EK, Sheetz KH, Bonn J, et al. A statewide colectomy experience: the role of full bowel preparation in preventing surgical site infection. *Ann Surg* 2014;259:310-314.
24. Guenaga KF, Matos D, Wille-Jorgensen P. Mechanical bowel preparation for elective colorectal surgery. *Cochrane Database Syst Rev* 2011;(9):CD001544. doi:CD001544.
25. Markell KW, Hunt BM, Charron PD, et al. Prophylaxis and management of wound infections after elective colorectal surgery: a survey of the American Society of Colon and Rectal Surgeons membership. *J Gastrointest Surg* 2010;14:1090-1098.

26. Nelson RL, Gladman E, Barbateskovic M. Antimicrobial prophylaxis for colorectal surgery. *Cochrane Database Syst Rev* 2014;5:CD001181.
27. Dellinger EP. Should a Scheduled Colorectal Operation Have a Mechanical Bowel Prep, Preoperative Oral Antibiotics, Both, or Neither? *Ann Surg* 2015.
28. Alcantara Moral M, Serra Aracil X, Bombardo Junca J, et al. A prospective, randomised, controlled study on the need to mechanically prepare the colon in scheduled colorectal surgery. *Cir Esp* 2009;85:20-25.
29. Jung B, Pahlman L, Nystrom PO, et al. Multicentre randomized clinical trial of mechanical bowel preparation in elective colonic resection. *Br J Surg* 2007;94:689-695.
30. Bellows CF, Mills KT, Kelly TN, et al. Combination of oral non-absorbable and intravenous antibiotics versus intravenous antibiotics alone in the prevention of surgical site infections after colorectal surgery: a meta-analysis of randomized controlled trials. *Tech Coloproctol* 2011;15:385-395.
31. Timely and Effective Care - National. Available at: <https://data.medicare.gov/Hospital-Compare/Timely-and-Effective-Care-National/isrn-hqyy>.
32. Lewis RT. Oral versus systemic antibiotic prophylaxis in elective colon surgery: a randomized study and meta-analysis send a message from the 1990s. *Can J Surg* 2002;45:173-180.
33. Playforth MJ, Smith GM, Evans M, et al. Antimicrobial bowel preparation. Oral, parenteral, or both? *Dis Colon Rectum* 1988;31:90-93.

34. Nichols RL, Smith JW, Garcia RY, et al. Current practices of preoperative bowel preparation among North American colorectal surgeons. *Clin Infect Dis* 1997;24:609-619.

35. Englesbe MJ, Brooks L, Kubus J, et al. A statewide assessment of surgical site infection following colectomy: the role of oral antibiotics. *Ann Surg* 2010;252:514-9; discussion 519-20.