β-Lactam vs Non-β-Lactam Antibiotics and Surgical Site Infection in Colectomy Patients

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BACKGROUND: Surgical site infections (SSIs) represent a significant preventable source of morbidity, mortality, and cost. Prophylactic antibiotics have been shown to decrease SSI rates, and β-lactam antibiotics are recommended by national guidelines. It is currently unclear whether recommended β-lactam and recommended non-β-lactam antibiotic regimens are equivalent with respect to SSI risk reduction in colectomy patients.

STUDY DESIGN: We conducted a retrospective cohort study of SSI rates between prophylactic intravenously administered recommended β-lactam and non-β-lactam in colectomy patients (25 CPT codes) collected by the Michigan Surgical Quality Collaborative from January 2013 to February 2018. Surgical site infection rates were compared as a dichotomous variable (no SSI vs SSI). Mixed-effects regression was used to compare the association between receiving a β-lactam or non-β-lactam antibiotic and likelihood of having an SSI.

RESULTS: Of 9,949 patients, 9,411 (94.6%) received β-lactam antibiotics and 538 (5.4%) received non-β-lactam antibiotics. Overall, there were 622 (6.3%) patients with SSIs. Of the patients receiving β-lactam antibiotics, SSIs developed in 571 (6.1%) compared with 51 (9.5%) patients in the non-β-lactam group. After applying mixed-effects logistic regression, prophylactic treatment with a non-β-lactam regimen was associated with significantly higher odds of surgical site infection (odds ratio 1.65; 95% CI 1.20 to 2.26; $p < 0.01$).

CONCLUSIONS: Colectomy patients receiving β-lactam antibiotics had a lower likelihood of SSI compared with those receiving non-β-lactam antibiotics, even when antibiotics were compliant with national recommendations. Our findings suggest that surgeons should prescribe β-lactam antibiotics for prophylaxis whenever possible, reserving alternatives for those rare patients with true allergies or clinical indications for non-β-lactam antibiotic prophylaxis. (J Am Coll Surg 2019;229:487–496. © 2019 by the American College of Surgeons. Published by Elsevier Inc. All rights reserved.)

Surgical site infection (SSI) represents a significant preventable source of morbidity, mortality, and cost.[1-3] With estimates of 1 million additional hospital days and $1.5 billion in added costs,[3] reducing SSIs is an imperative patient safety and quality improvement opportunity. For patients undergoing operations, the rate of SSI is approximately

CME questions for this article available at http://jacscme.facs.org

Disclosure Information: Authors have nothing to disclose. Timothy J Eberlein, Editor-in-Chief, has nothing to disclose.

Disclosures outside the scope of this work: Drs Campbell, Englesbe, and Krapohl's institution receives a partial salary paid for by the Blue Cross Blue Shield of Michigan value partnerships for the Michigan Surgical Quality Collaborative.

Support: Dr Vu's institution is supported by the Ruth L Kirstein National Service Research Service Award/National Institute of Diabetes, Digestive, and Kidney Diseases grant #1F32DK115340-01A1. Mr Kuriakose institution was supported by the University of Michigan Institute for Healthcare Policy & Innovation Summer Fellowship Program.

Received June 2, 2019; Revised July 17, 2019; Accepted July 23, 2019.

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https://doi.org/10.1016/j.jamcollsurg.2019.07.011
ISSN 1072-7515/19

2%,[4-6] but in colectomy procedures, where there is removal of a section or all of the colon, the rate is reported to be more than 5 times as high (11% to 25%).[7-10] With more than 300,000 colectomies performed each year,[11] and SSI infections costing approximately $20,000 per occurrence,[3,12] SSIs for colectomy procedures alone can account for hundreds of millions of dollars each year. Because of the increased morbidity, SSI in colectomy is in the national spotlight as one of the 2 surgical quality improvement initiatives incorporated into the Hospital Acquired Condition Reduction Program, whereby a payment penalty is levied for hospitals in the bottom quartile.[13]

Most hospitals systems have adopted prophylactic antibiotic guidelines to reduce SSIs based on the recommendations from the Surgical Care Improvement Project[14] and/or the Clinical Practice Guidelines for Antimicrobial Prophylaxis in Surgery, developed as a joint effort by the American Society of Health-System Pharmacists, The Infectious Disease Society of America, The Surgical Infection Society, and the Society for Healthcare Epidemiology of America.[15] Prophylactic β-lactam antibiotics are the mainstay of these protocols, as they are known to be associated with decreased SSI rates,[16] with alternative antibiotics recommended for patients with a reported β-lactam allergy.

It is currently unclear whether recommended β-lactam and recommended non-β-lactam antibiotic regimens are equivalent with respect to SSI risk reduction in colectomy patients. Studies evaluating various types of surgical procedures show that recommended β-lactam antibiotic regimens (cefazolin with metronidazole, cefoxitin, cefotetan, ampicillin with sulbactam, ceftriaxone with metronidazole, and ertapenem) are associated with significantly lower SSI rates, both superficial and deep/organ space compared with those of recommended alternative non-β-lactam antibiotics (clindamycin with aztreonam, ciprofloxacin, levofloxacin, or gentamicin, and metronidazole with ciprofloxacin, levofloxacin, or gentamicin).[17,18] Although these studies suggest that β-lactam antibiotics might be superior to non-β-lactam antibiotics for SSIs,[18-20] studies specifically focused on colectomy have found some β-lactam choices to be inferior to non-β-lactam regimens.[16,19] If β-lactam prophylactic antibiotics were convincingly shown to be superior in SSI prevention in colectomy, then the use of alternate antibiotics would represent a potential preventable SSI risk.

In this context, the purpose of this study was to compare recommended β-lactam and non-β-lactam antibiotic regimens with respect to the rate of SSI after colectomy. We hypothesized that patients receiving non-β-lactam antibiotic regimens would have a higher rate of SSIs than those receiving β-lactam antibiotic regimens.

METHODS

This is a retrospective cohort study of patients in the Michigan Surgical Quality Collaborative (MSQC) undergoing colectomy between January 2013 and February 2018. Funded by the Blue Cross and Blue Shield of Michigan/Blue Care Network, the MSQC is a collaborative of 70 academic and community hospitals across the state of Michigan that voluntarily share data to improve surgical quality, safety, and value. As determined by the University of Michigan IRB, the MSQC data collection does not meet the definition of human subjects research and is considered "not regulated" (HUM00147337).

Data source

Trained nurse abstractors review medical records to abstract patient information, such as characteristics, intraoperative care processes, and 30-day postoperative outcomes for general, vascular, and gynecologic surgery, collecting approximately 50,000 cases per year. Phone calls, letters, and chart review are used to contact patients and to identify and collect data from readmissions to other institutions. Cases are sampled using a stratified random algorithm to reduce selection bias, proportionally selecting cases from procedure groups based on population size and variability.

Study cohort

Patients older than 18 years of age who underwent elective colectomy were identified using 25 CPT codes (eTable 1). Only patients who received Surgical Care Improvement Project/American Society of Health-System Pharmacists-recommended antibiotics were included. Patients without any recorded antibiotic information or without a 30-day follow-up were excluded. Those who received recommended antibiotics along with additional antibiotics were labeled as "over-treated" and were excluded from analysis due to the possibility of antibiotic resistance as a reason for over-treatment.

Variables

The explanatory variable of interest was prophylactic IV antibiotic choice, which was separated into 2 categories: recommended β-lactam and recommended non-β-lactam. The primary end point was SSI as a dichotomous variable (no SSI vs SSI as reported by MSQC and defined by the CDC).[21] American Society of Anesthesiologist (ASA) class, age, race, sex, insurance type, obesity (BMI), COPD status, steroid use, tobacco use, functional status, peripheral vascular disease, bleeding disorder, hypertension, dialysis, open wound, alcohol consumption, preoperation sepsis, mechanical bowel preparation with oral antibiotics, wound class, diabetes, surgical approach, and a body weight loss of >10% were used as covariates in this study (eTable 2). A

de-identified code was used to indicate the hospital site for each patient. This variable was used as a random intercept to account for clustering in the data. No information about whether patients have a penicillin allergy was collected.

Statistical analyses

First, simple logistic regression was used to analyze the effect of each sociodemographic variable and clinical risk factor on the odds of experiencing any postoperative SSI. Then, Pearson's chi-square tests were used to compare sociodemographic characteristics and clinical risk factors between those who received a β-lactam antibiotic regimen and non-β-lactam antibiotic regimen. The difference in duration of the surgery between the β-lactam and non-β-lactam group was compared using a Mann-Whitney U test.

A forward stepwise logistic regression was used to select sociodemographic characteristics and clinical risk factors to be included in the final risk models and results compared with known medical literature on SSIs. The area under the receiver operating characteristics curve was used to measure the discriminating power of the variables in the final logistic regression model. Finally, a mixed-effects logistic regression was used to compare the odds of experiencing any SSI, controlling for the variables identified during the model selection procedure, and the random effects due to the hospital using complete case analysis (using a random intercept). The intraclass correlation coefficient was used to assess the amount of variation in the model that was accounted for by the clustering and the need for a mixed model. All statistical analyses were performed in STATA software, version 15 (Stata Corp). The a priori α level was set at 5% for all statistical significance testing.

RESULTS

The MSQC database contained 20,942 colectomy patients. After excluding 8,460 non-elective colectomy patients, 561 patients without follow-up, 3 patients with missing antibiotic data, 1,241 patients who received a non-recommended regimen, and 728 patients who were "overtreated," 9,949 patients were included in the analysis (Fig. 1). Of the analyzed cases, 9,411 (94.6%) patients received β-lactam antibiotics, and 538 (5.4%) received non-β-lactam antibiotics (Fig. 1).

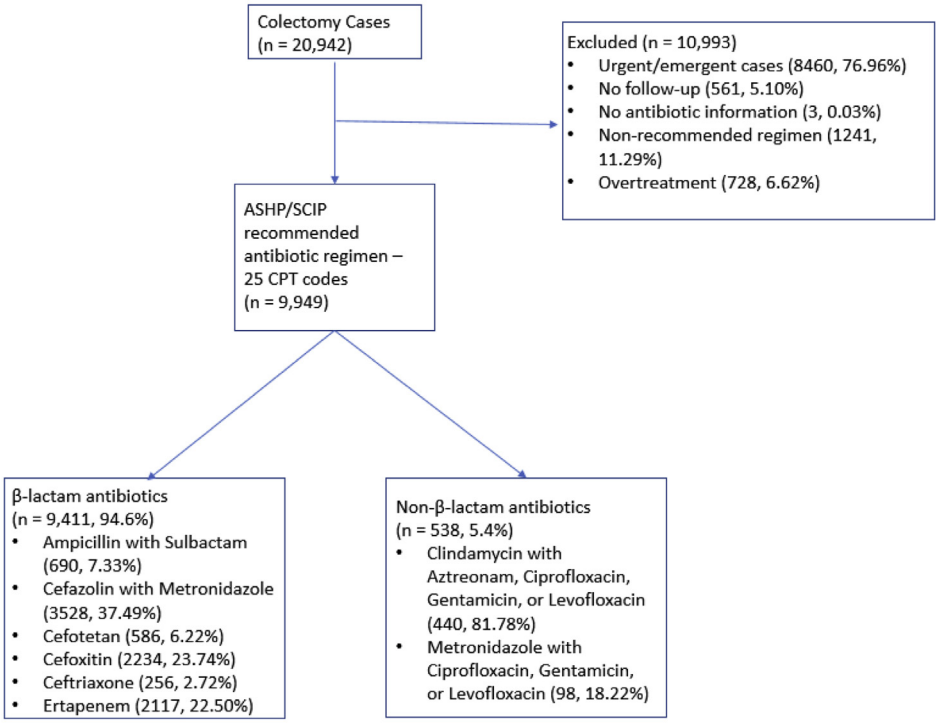

Figure 1. Breakdown of antibiotic categories. Categories based on national guidelines. Patients receiving a recommended regimen, β-lactam or non-β-lactam, alongside other antibiotics are considered "overtreated." Patients receiving antibiotics aside from the recommended regimen were excluded as "non-recommended." ASHP, American Society of Health-System Pharmacists; SCIP, Surgical Care Improvement Project.

Table 1. Baseline Comparison of Sociodemographic and Clinical Characteristics of Cohort by Antibiotic Regimen

Characteristic	Recommended β-lactam antibiotic (n = 9,411)	Recommended non-β-lactam antibiotic (n = 538)	p Value
Age, n (%)			
Younger than 45 y	904 (9.6)	34 (6.3)	
45 to 64 y	4,165 (44.3)	220 (40.9)	0.003*
65+ y	4,342 (46.1)	284 (52.8)	
Race, n (%)			
White	7,989 (87.7)	460 (88.6)	0.527
Non-white	1,121 (12.3)	59 (11.4)	
Functional status, independent, n (%)			
No	9,198 (97.9)	523 (97.2)	0.306
Yes	200 (2.1)	15 (2.8)	
Bleeding disorder, n (%)			
No	9,193 (97.7)	515 (95.7)	0.004*
Yes	218 (2.3)	23 (4.3)	
Body weight loss, n (%)			
No	9,060 (96.3)	520 (96.7)	0.647
Yes	351 (3.7)	18 (3.3)	
Sex, n (%)			
Male	4,538 (48.2)	164 (30.5)	<0.001†
Female	4,873 (51.8)	374 (69.5)	
Steroid, n (%)			
No	8,895 (94.5)	499 (92.8)	0.083
Yes	516 (5.5)	39 (7.2)	
Alcohol consumption, n (%)			
No	9,109 (96.8)	524 (97.4)	0.435
Yes	302 (3.2)	14 (2.6)	
Dialysis, n (%)			
No	9,371 (99.6)	536 (99.6)	0.853
Yes	40 (0.4)	2 (0.4)	
COPD, n (%)			
No	8,608 (91.5)	478 (88.8)	0.036‡
Yes	803 (8.5)	60 (11.2)	
Tobacco use, n (%)			
No	7,389 (78.5)	435 (80.9)	0.198
Yes	2,022 (21.5)	103 (19.1)	
Diabetes, n (%)			
No	7,566 (80.4)	408 (75.8)	0.01*
Yes	1,845 (19.6)	130 (24.2)	
Hypertension, n (%)			
No	4,336 (46.1)	206 (38.3)	<0.001†
Yes	5,075 (53.9)	332 (61.7)	
Peripheral vascular disease, n (%)			
No	9,193 (97.7)	525 (97.6)	0.881
Yes	218 (2.3)	13 (2.4)	
Open wound, n (%)			
No	9,308 (98.9)	531 (98.7)	0.656
Yes	103 (1.1)	7 (1.3)	

(Continued)

Table 1. Continued

Characteristic	Recommended β-lactam antibiotic (n = 9,411)	Recommended non-β-lactam antibiotic (n = 538)	p Value
Preoperative sepsis, n (%)			
No	9,393 (99.8)	538 (100.0)	0.31
Yes	18 (0.2)	0 (0.0)	
Mechanical bowel preparation with oral antibiotic, n (%)			
No	4,026 (42.8)	229 (42.6)	0.922
Yes	5,385 (57.2)	309 (57.4)	
American Society of Anesthesiologists class, n (%)			
<3	4,381 (46.6)	216 (40.1)	0.004*
≥3	5,023 (53.4)	322 (59.9)	
Obesity status, n (%)			
No	5,776 (61.4)	324 (60.2)	0.594
Yes	3,635 (38.6)	214 (39.8)	
Wound class, n (%)			
Clean or clean/contaminated	7,963 (84.3)	465 (86.4)	0.058
Contaminated	1,005 (10.7)	41 (7.6)	
Dirty/infected	470 (5)	32 (6.0)	
Surgical approach, n (%)			
Open	3,031 (32.2)	162 (30.1)	0.311
Minimally invasive	6,380 (67.8)	376 (69.9)	
Insurance, n (%)			
Commercial (non-HMO)	3,028 (32.4)	148 (27.7)	0.003*
HMO	1,712 (18.3)	110 (20.6)	
Government/Medicaid	4,341 (46.4)	271 (50.7)	
Other/uninsured/self-pay	277 (3.0)	5 (1.0)	
Operation time, min	162.82	167.19	0.049‡

*p < 0.01.
†p < 0.001.
‡p < 0.05.

Table 1 provides a comparison of patient characteristics between the β-lactam and non-β-lactam antibiotic groups. Patients who received non-β-lactam antibiotic had a higher proportion of patients who were older, had a bleeding disorder, were female, have COPD, have diabetes, have hypertension, have a higher ASA class, and have government insurance (Table 1). The unadjusted SSI rates were 6.1% for those receiving β-lactam antibiotics (n = 571) and 9.5% for the non-β-lactam antibiotic group (n = 51).

The rate of any SSI across the 9,949 elective colectomy cases was 6.3% (n = 622). Patient and care factors associated with SSI are provided in Table 2. Patients with SSIs were younger, more likely to have a bleeding disorder, report steroid use, receive dialysis, be functionally dependent, have an open wound, report tobacco use, be obese, and have diabetes. In terms of surgical factors, patients with SSIs were also less likely to receive mechanical bowel preparation with oral antibiotic, less likely to have a clean or clean/contaminated wound class, more likely to undergo open colectomy, more likely to have an open wound, more likely to have a higher ASA class, and less likely to receive a β-lactam antibiotic (Table 2).

Analysis of the intercept-only model with a random effect for hospital showed that the intraclass correlation coefficient for SSI was 0.01 (SE 0.003). The intraclass correlation coefficient is a proportion of the variance in the outcomes variable that is explained by the grouping structure of the hierarchical model. We used a mixed-effects logistic regression to estimate the effect of the type of antibiotic on SSI rate controlling for patient-level fixed effects (identified from the stepwise logistic regression) and the hospital random effects. After controlling for the surgical approach, wound class, bowel preparation, total operative time, ASA grade, obesity, steroid, and age, receipt of a non-β-lactam regimen was associated with a significantly higher odds of SSI (odds ratio 1.65; 95% CI 1.20 to 2.27; p < 0.01) (Fig. 2). The effect of mechanical bowel

Table 2. Sociodemographic and Clinical Characteristics of Cohort by Surgical Site Infection with Unadjusted Predictors

	Surgical site infection (any)			
Characteristic	**No (n = 9,327)**	**Yes (n = 622)**	**Unadjusted odds ratio**	**95% CI**
Antibiotic group, n (%)				
β-lactam	8,840 (94.8)	571 (91.8)	Reference	Reference
Non-β-lactam	487 (5.2)	51 (8.2)	1.62*	1.200–2.190
Age, n (%)				
Younger than 45 y	862 (9.2)	76 (12.2)	Reference	Reference
45 to 64 y	4,102 (44.0)	283 (45.5)	0.78	0.601–1.019
65+ y	4,363 (46.8)	263 (42.3)	0.68*	0.524–0.892
Race, n (%)				
White	7,933 (87.9)	516 (86.1)	Reference	Reference
Non-white	1,097 (12.1)	83 (13.9)	1.16	0.915–1.479
Sex, n (%)				
Male	4,418 (47.4)	284 (45.7)	Reference	Reference
Female	4,909 (52.6)	338 (54.3)	1.07	0.910–1.261
Bleeding disorder, n (%)				
No	9,109 (97.7)	599 (96.3)	Reference	Reference
Yes	218 (2.3)	23 (3.7)	1.60†	1.036–2.485
Peripheral vascular disease, n (%)				
No	9,111 (97.7)	607 (97.6)	Reference	Reference
Yes	216 (2.3)	15 (2.4)	1.04	0.614–1.770
Hypertension, n (%)				
No	4,269 (45.8)	273 (43.9)	Reference	Reference
Yes	5,058 (54.2)	349 (56.1)	1.08	0.916–1.271
Steroid, n (%)				
No	8,836 (94.7)	558 (89.7)	Reference	Reference
Yes	491 (5.3)	64 (10.3)	2.06‡	1.569–2.715
Dialysis, n (%)				
No	9,291 (99.6)	616 (99.0)	Reference	Reference
Yes	36 (0.4)	6 (1.0)	2.51†	1.055–5.989
Functional status, independent, n (%)				
No	190 (2.0)	25 (4.0)	Reference	Reference
Yes	9,128 (97.9)	593 (95.3)	2.03*	1.324–3.099
Open wound, n (%)				
No	9,230 (99.0)	609 (97.9)	Reference	Reference
Yes	97 (1.0)	13 (2.1)	2.03†	1.132–3.645
COPD, n (%)				
No	8,520 (91.4)	566 (91.0)	Reference	Reference
Yes	807 (8.6)	56 (9.0)	1.05	0.786–1.387
Tobacco use, n (%)				
No	7,358 (78.9)	466 (74.9)	Reference	Reference
Yes	1,969 (21.1)	156 (25.1)	1.25†	1.037–1.510
Alcohol consumption, n (%)				
No	9,032 (96.8)	601 (96.6)	Reference	Reference
Yes	295 (3.2)	21 (3.4)	1.07	0.682–1.678
Preoperative sepsis, n (%)				
No	9,312 (99.8)	619 (99.5)	Reference	Reference
Yes	15 (0.2)	2 (0.5)	3.01	0.869–10.42

(Continued)

Table 2. Continued

Characteristic	Surgical site infection (any)		Unadjusted odds ratio	95% CI
	No (n = 9,327)	Yes (n = 622)		
Mechanical bowel preparation with oral antibiotic, n (%)				
No	3,908 (41.9)	347 (55.8)	Reference	Reference
Yes	5,419 (58.1)	275 (44.2)	0.57‡	0.485–0.673
Wound class, n (%)				
Clean or clean/contaminated	7,934 (85.1)	467 (75.1)	Reference	Reference
Contaminated	953 (10.2)	93 (15.0)	1.66‡	1.314–2.092
Dirty/infected	440 (4.7)	62 (10.0)	2.40‡	1.806–3.173
American Society of Anesthesiologists class, n (%)				
<3	4,371 (46.9)	226 (36.3)	Reference	Reference
≥3	4,949 (53.1)	396 (63.7)	1.55‡	1.308–1.831
Body weight loss, n (%)				
No	8,984 (96.3)	596 (95.8)	Reference	Reference
Yes	343 (3.7)	26 (4.2)	1.14	0.760–1.717
Obesity status, n (%)				
No	5,776 (61.9)	324 (52.1)	Reference	Reference
Yes	3,551 (38.1)	298 (47.9)	1.50‡	1.271–1.761
Diabetes, n (%)				
No	7,503 (80.4)	471 (75.7)	Reference	Reference
Yes	1,824 (19.6)	151 (24.3)	1.32*	1.090–1.595
Surgical approach, n (%)				
Open	2,902 (31.1)	291 (46.8)	Reference	Reference
Minimally invasive	6,425 (68.9)	331 (53.2)	0.51‡	0.436–0.605
Insurance, n (%)				
Commercial non-HMO	2,996 (32.3)	180 (29.4)	Reference	Reference
HMO	1,712 (18.5)	110 (18.0)	1.07	0.837–1.366
Government/Medicaid	4,310 (46.4)	302 (49.3)	1.17	0.964–1.411
Other/uninsured/self-pay	262 (2.8)	20 (3.3)	1.27	0.787–2.051
Operation time, min	161.61 (Reference)	184.75	1.00‡	1.001–1.003

*$p < 0.01$.
†$p < 0.05$.
‡$p < 0.001$.

preparation with oral antibiotics was protective against SSI (adjusted odds ratio 0.59; 95% CI 0.492 to 0.713) (Fig. 2).

DISCUSSION

This study demonstrates that colectomy patients receiving recommended β-lactam antibiotic prophylaxis had decreased postoperative SSIs compared with those receiving recommended non-β-lactam antibiotics. Our multicenter analysis contributes additional knowledge about reducing SSIs with choice of antibiotic prophylaxis that are recommended by national guidelines.[17,18,22] Given the high SSI rates among colectomy, this study suggests that colectomy patients can benefit from the increased use of β-lactam antibiotics whenever possible.

The existing literature has been mixed with regard to antibiotic choice and SSI risk. Studies by Deierhoi and colleagues[19] and Hendren and colleagues[16] did not find a consistent pattern of association between β-lactam and lower risk of SSI. However, like our study, Blumenthal and colleagues[17] found that non-β-lactam antibiotics were associated with higher risk of SSI. They evaluated 9,004 patients undergoing hysterectomy, knee or hip arthroplasty, cardiac bypass, and colorectal resection from a single center during a 5-year period, finding that non-β-lactam antibiotics were associated with a 51% increased risk for SSIs (odds ratio 1.51; 95% CI 1.02 to 2.22).[17] Patients undergoing colorectal procedures comprised only 13.9% of patients, but contributed 52% of the infections, which supports the importance of evaluating β-lactams on infection rates and improving prophylaxis in this high-risk population. These

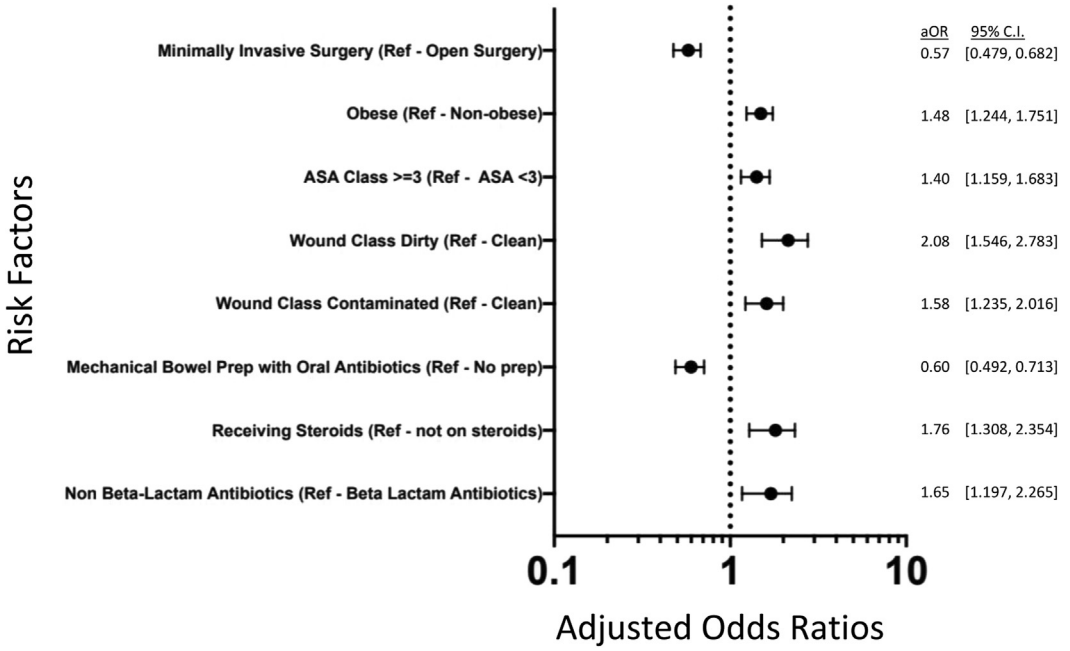

Figure 2. Mixed-effects logistic regression model. Independent effect of antibiotic regimen on surgical site infection rate. aOR, adjusted odds ratio; ASA, American Society of Anesthesiologists.

findings in colectomy are similar to those of a large multicenter study of hysterectomy patients, finding a significantly higher risk for SSIs in patients who received non-β-lactams (and non-standard regimens) than standard β-lactam regimens. One possible explanation for the increased efficacy of β-lactam antibiotics is that they are more effective against *Streptococcus* species, *Staphylococcus aureus*, and coagulase-negative *Staphylococci*, normal skin flora organisms that cause the majority of SSIs.[18,23]

The administration of β-lactam antibiotics is also considered more practical in terms of administration and cost. Non-β-lactam antibiotics require longer infusion times of 30 to 90 minutes, thereby extending the time a patient requires in the preoperative holding area before incision. Because standard β-lactam antibiotics require less than half that time (2 to 20 minutes), decreasing the number of patients receiving β-lactam antibiotics has demonstrated improved throughput by an average of 22 minutes per patient.[22] Additionally, non-β-lactam drugs are generally more expensive and in 2 small studies (1 in Canada), cost estimates were about $300 per patient during inpatient hospitalization.[24,25] In summary, reducing costs and improving operating room efficiency can provide additional potential justification for optimizing the use of recommended β-lactam antibiotics.

Given the advantages and efficacy of β-lactam antibiotics, there is potential opportunity to optimize patients before elective surgical procedures with standard β-lactam antibiotics regimens to reduce the risk of SSI, especially in higher-risk procedures, such as colectomy. Patients in the general population with a documented β-lactam intolerance due to a penicillin allergy are estimated to be about 10%.[26,27] Interestingly, of the patients that self-report a penicillin allergy, >95% are found to safely tolerate penicillin after skin testing and/or oral dose challenge (single or graded dose).[17,28-30] Many of these patients have likely been misclassified as a penicillin allergy due family history, non-allergic adverse drug events, a childhood incident, or a rash that was a consequence of the illness, not a true mediated allergic response.[28] In addition, >80% of patients with a history of penicillin allergy will be able to tolerate penicillin antibiotics just 10 years after the reaction occurred.[31] Patients designated as penicillin allergic are also associated with an increased risk of healthcare-associated infections, including MRSA, vancomycin-resistant *Enterococcus*, and *Clostridium difficile* infections.[27,30,32-34] With the cost of penicillin allergy testing, from simple oral challenge to more complex skin testing estimated to be between US$200 and US$500,[35] incorporating penicillin testing protocols for high-risk colectomy patients seems a worthy pursuit as part of a comprehensive strategy to increase adherence to the recommended β-lactam guidelines.

There are several limitations to our study, many of which are inherent to conducting a retrospective analysis and also the constraints of the MSQC data set. Most importantly, we did not have data about whether patients actually had a penicillin allergy, and there might have been other clinical reasons that patients received a recommended non-β-lactam antibiotic. However, the proportion of cases (5.4%)

is consistent with empiric literature reporting penicillin allergies in the general population.[26-28] The second limitation is the possibility of selection bias. Unknown confounders and selection bias could influence the difference in SSI rates between the 2 groups of antibiotics. In addition, a larger proportion of patients who received non-β-lactam antibiotics were older or had diabetes, hypertension, or COPD. However, the 2 groups were similar with respect to wound class, proportion of open operations, and tobacco use (all risk factors for SSI) and the increased likelihood of SSI for the non-β-lactam group remained even after adjusting for SSI risk factors.

Another limitation of this study was the exclusion of 2,533 cases from the cohort due to missing data (564 cases) or because of receiving a non-recommended antibiotic combination for prophylaxis (1,969 cases). We designed the study to only include cases that received antibiotic prophylaxis concordant with national guidelines because our research question focused on the use of non-β-lactam alternative antibiotics compared with standard β-lactam antibiotics. Nevertheless, excluding patients from a cohort study always raises concerns about bias, if the excluded patients are systematically different from included patients. Fortunately, the rich clinical data in the MSQC allow for adjustment for relevant patient risk factors, and this should decrease the risk for bias. In addition, data did not include the timing of antibiotics (infusion completion before incision), which might have also influenced the rate of SSI.

CONCLUSIONS

This multicenter study of colectomy patients showed that patients who received recommended non-β-lactam antibiotics had an increased likelihood of SSIs compared with patients receiving β-lactam antibiotics. Our findings suggest that surgeons should prescribe β-lactam antibiotics for prophylaxis whenever possible, reserving alternatives for those rare patients with true allergies or clinical indications for non-β-lactam antibiotic prophylaxis.

Author Contributions

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eTable 1. List and Description of Colorectal CPT

CPT code	CPT description
44140	Partial colectomy with anastomosis
44141	Partial colectomy with skin level cecostomy or colostomy
44143	Partial colectomy with end colostomy and closure of distal segment (Hartmann type procedure)
44144	Partial colectomy with resection and colostomy or ileostomy and creation of mucofistula
44145	Partial colectomy with coloproctostomy (low pelvic anastomosis)
44146	Partial colectomy with coloproctostomy (low pelvic anastomosis) and colostomy
44147	Partial colectomy using abdominal and transanal approach with anastomosis
44150	Total abdominal colectomy without proctectomy with ileostomy or ileoproctostomy
44151	Total abdominal colectomy without proctectomy with continent ileostomy
44155	Total abdominal colectomy with proctectomy and ileostomy
44156	Total abdominal colectomy with proctectomy and continent ileostomy
44157	Total abdominal colectomy with proctectomy, ileonal anastomosis, loop ileostomy, and rectal mucosectomy (when performed)
44158	Total abdominal colectomy with proctectomy, ileonal anastomosis, creation of ileal reservoir (S or J), loop ileostomy, and rectal mucosectomy (when performed)
44160	Partial colectomy with removal of terminal ileum with ileocolostomy
44204	Surgical laparoscopy; partial colectomy with anastomosis
44205	Surgical laparoscopy; partial colectomy with removal of terminal ileum and ileocolostomy
44206	Surgical laparoscopy; partial colectomy with end colostomy and closure of distal segment (Hartmann type procedure)
44207	Surgical laparoscopy; partial colectomy with anastomosis and coloproctostomy (low pelvic anastomosis)
44208	Surgical laparoscopy; partial colectomy with anastomosis, coloproctostomy (low pelvic anastomosis), and colostomy
44210	Surgical laparoscopy; total abdominal colectomy without proctectomy with ileostomy or ileoproctostomy
44211	Surgical laparoscopy; total abdominal colectomy with proctectomy, ileonal anastomosis, creation of ileal reservoir (S or J), loop ileostomy, and rectal mucosectomy (when performed)
44212	Surgical laparoscopy; total abdominal colectomy with proctectomy and ileostomy
44238	Unlisted laparoscopy procedure in large or small intestine (except rectum)
44799	Unlisted procedure in small intestine
45399	Unlisted procedure in colon

eTable 2. Definition of Variables

Variable	Michigan Surgical Quality Collaborative definition
Bleeding disorder	Any condition that places the patient at risk for excessive bleeding due to a deficiency of blood clotting elements (ie vitamin K deficiency, hemophilias, thrombocytopenia, chronic anticoagulation therapy that has not been discontinued before operation).
PVD	PVD must be documented within the chart and also requires 1 of the following (current or past): revascularization of the upper and/or lower extremities for PVD (include angioplasty or revascularization procedures such as aorta-femoral, femoral-femoral, femoral-popliteal; exclude resection of an abdominal aortic aneurysm, carotid endarterectomy), amputation for PVD (include toe, metatarsal, below the knee, above the knee amputations; exclude amputation for trauma), rest pain (exclude intermittent claudication), gangrene (include ischemic ulceration and/or tissue loss related to PVD; exclude Fournier's gangrene).
Hypertension	The patient has a persistent elevation of systolic blood pressure >140 mmHg or a diastolic blood pressure >90 mmHg or requires an antihypertensive treatment (eg diuretics, β-blockers, angiotensin-converting enzyme inhibitors, calcium channel blockers) at the time the patient is being considered as a candidate for operation (which should be no longer than 30 d before operation).
Steroid use	The regular administration of oral or parenteral corticosteroids (eg prednisone or dexamethasone/Decadron) for a chronic medical condition (eg COPD, asthma, rheumatologic disease, rheumatoid arthritis, or inflammatory bowel disease) and/or has required the regular administration of immunosuppressive medications as chemotherapy, to prevent the rejection of a transplanted organ, to treat an autoimmune disease, and/or to treat a non-autoimmune inflammatory disease in the 30 d before operation.
Dialysis	Acute or chronic renal failure requiring treatment with peritoneal dialysis, hemodialysis, hemofiltration, hemodiafiltration, or ultrafiltration within 2 wk before operation.
Functional status- independent	The patient's abilities to perform ADLs independently (without partial dependence or total dependence) in the 30 d before operation. ADLs are defined as the activities usually performed in the course of a normal day in a person's life. ADLs include bathing, feeding, dressing, toileting, and mobility.
Open wound	Evidence of an open wound that communicates to the air by direct exposure, with or without cellulitis or purulent exudate.
COPD status	COPD (such as asthma, emphysema, and/or chronic bronchitis) requires a diagnosis and additionally 1 or more of the following: functional disability from COPD (eg dyspnea or inability to perform activities of daily living), hospitalization in the past for treatment of COPD, requires chronic bronchodilator therapy with oral or inhaled agents, a forced expiratory volume of <75% of predicted on pulmonary function testing.
Tobacco use	Usage of cigarette(s), which must contain tobacco, within 1 y. Use of electronic cigarettes/e-cigarettes/vaping without tobacco does not meet the criteria for this variable.
Alcohol consumption	The patient admits to drinking more than 2 oz of hard liquor, more than two 12-oz cans of beer, or more than two 6-oz glasses of wine per day in the 2 wk before admission.
Preoperative sepsis	Captured the presence of sepsis or severe sepsis within 72 h before the POP. All criteria must be supported by preoperative documentation; intraoperative findings/results cannot be used. If all required criteria are met, assign sepsis/severe sepsis, even if there is no diagnosis of sepsis/severe sepsis documented. Conversely, if all required criteria are not met, do not assign sepsis/severe sepsis, even if there is a sepsis/severe sepsis diagnosis documented. Report the greatest level of sepsis.
Mechanical bowel preparation with oral antibiotic	Indicated any mechanical bowel preparation and oral antibiotics ordered preoperatively.
Wound class	Indicate the wound classification assigned to the case as indicated by the description of the procedure in the operative report.
ASA class	Recorded the ASA physical status classification of the patient's present physical condition on a scale from 1 to 5 as it appears on the anesthesia record.
Body weight loss	A >10% decrease in body weight in the 6-mo interval immediately preceding operation as manifested by 1 or more of the following: serial weights in the chart, report by the patient, a change in clothing size, or severe cachexia.
Obesity status	Indicated by a BMI $\geq$30 kg/m^2.
Diabetes	Reported the treatment of the patient's chronic, long-term management (>2 wk) of diabetes.
Surgical approach	Indicated the approach taken by the surgeon to perform the POP.
Insurance type	Indicated by the patient's primary insurance payer at the time of discharge.

ADL, activity of daily living; ASA, American Society of Anesthesiologists; POP, principal operative procedure; PVD, peripheral vascular disease.