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Major article

Antimicrobial prophylaxis may not be the answer: Surgical site infections among patients receiving care per recommended guidelines

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Background: It is believed that compliance with all 3 components of perioperative antimicrobial prophylaxis, ie, timing, choice, and duration, yields greater reduction in surgical site infections (SSI).

Methods: An observational study was performed among patients in the surgical care improvement project at a tertiary public academic hospital in the United States. The rates of SSI among patients who received appropriate antimicrobial agent(s) per current guidelines were compared with patients who did not. Medical record review was performed to compare the clinical characteristics of patients with SSI (cases) and an equal number of patients without SSI (matched controls).

Results: From January 2008 to June 2009, 762 patients underwent 763 eligible surgical procedures. Forty-seven (6.2%) developed SSI. The rate of SSI in patients who received appropriate antimicrobial prophylaxis per guidelines was not different from those who did not (42/611, 6.9% vs 5/152, 3.3%, respectively; P value = .13). Patients with SSI were more likely to have an elevated body mass index (median and interquartile range in cases: 28.7 [27.0-34.9] vs 25.0 [22.4-30.4] in controls; P value = .02) and more likely to have diabetes (36% vs 9%, respectively; odds ratio, 5.71; 95% confidence interval: 1.43-22.8; P value = .02).

Conclusion: Compliance with timing, choice, and duration of antimicrobial prophylaxis as a whole did not lead to lower SSI. Elevated body mass index and diabetes were associated with a higher rate of SSI.

Surgical site infections (SSI) comprise a major proportion of health care-associated infections,[1] leading to increased morbidity and mortality as well as increased cost and length of stay.[2,3] Efforts to reduce SSI gained momentum with the national implementation of the Surgical Infection Prevention project in 2002.[4] This effort focused on perioperative antibiotic selection and administration, including (1) timing of parenteral antimicrobial administration, (2) selection of a procedure-appropriate antibiotic, and (3) discontinuation of antibiotics within 24 hours of the end time of surgery. The Surgical Infection Prevention guidelines were then incorporated into the Surgical Care Improvement Project (SCIP)[4] that added additional recommendations for SSI prevention including proper hair removal for all patients, maintenance of normothermia for patients undergoing colorectal surgery, and glucose control for those undergoing cardiac surgery. SCIP has subsequently expanded to include additional recommendations to prevent SSI, cardiovascular, and thromboembolic complications.[4] The study institution participated in the SCIP since 2006 and has a robust surveillance program for SSIs. During the study period of January 2008 to June 2009, the average compliance with SCIP measures was 99% for appropriate hair removal, 94% for appropriate timing of antibiotic (SCIP-1), 97% for appropriate choice of antibiotic (SCIP-2), 87% for appropriate duration of antibiotic (SCIP-3), and 87% for post-operative normothermia for all patients. Perioperative glucose control was not measured because cardiac surgery was not performed at the institution. We undertook this study to evaluate whether complete compliance with all 3 SCIP antimicrobial prophylaxis criteria (SCIP-1, SCIP-2, and SCIP-3) was associated

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Table 1
Receipt of perioperative antimicrobial prophylaxis and rate of surgical site infection

	Antimicrobial agent received within 1 hour prior to incision: n (%)	Appropriate antimicrobial agent selected: n (%)	Antimicrobial agent discontinued appropriately: n (%)	Care compliant with all 3 measures: n (%)	SSI in those meeting all 3 criteria: n (%)	SSI in those who did not meet at least 1 criterion: n (%)	Odds ratio (95% Confidence interval)	*P* value
All procedures (N = 763)	725 (95)	748 (98)	664 (87)	610 (80)	42 (6.9)	5 (3.3)	2.19 (0.85-5.63)	.10
Hip arthroplasty (n = 133)	129 (97)	132 (99)	105 (79)	101 (76)	3 (3)	0	2.03 (0.10-40.52)	.64
Knee arthroplasty (n = 223)	221 (99)	223 (100)	178 (80)	176 (79)	1 (0.6)	0	0.79 (0.03-19.72)	.89
Colon surgery (n = 115)	105 (91)	105 (91)	95 (83)	79 (69)	27 (34.2)	5 (13.9)	3.22 (1.12-9.23)	.03*
Hysterectomy (n = 261)	243 (93)	258 (99)	253 (97)	232 (89)	8 (3.4)	0	2.23 (0.13-39.71)	.58
Vascular surgery (n = 31)	27 (87)	30 (97)	29 (94)	24 (77)	3 (12.5)	0	1.29 (0.06-29.38)	.87

*$P \leq .05$.

with a lower rate of SSI compared with compliance with ≤2 SCIP antimicrobial prophylaxis criteria. We also evaluated clinical variables associated with development of SSI.

METHODS

We performed a retrospective observational cohort with nested case control study at Parkland Health and Hospital System, a public tertiary academic center affiliated with University of Texas Southwestern Medical Center, Dallas, TX. The system comprises a hospital with 672 operating beds and a large network of outpatient clinics. Over 13,000 surgical procedures are performed every year at Parkland. Services include level I trauma, burn, transplantation, and high-risk obstetrics.

The study period was January 2008 to June 2009. Patients who were reviewed for meeting SCIP criteria for the purpose of national hospital inpatient quality measures were included in the study. At the study institution, these patients underwent the following types of surgical procedures: hip or knee replacement, vaginal or abdominal hysterectomy, colorectal surgery, or vascular surgery. Data collection was performed by a certified quality improvement professional using methodology specified in the Specifications Manual for National Hospital Inpatient Quality Measures.[5] Patients who were excluded for any of the 3 SCIP antimicrobial prophylaxis criteria (timing of antibiotic administration [SCIP-1], choice of appropriate antibiotic [SCIP-2], and duration of antibiotic(s) [SCIP-3]) per the prespecified methodology[5] were excluded from the study. Examples of these exclusion criteria are age <18 years, length of stay >120 days, diagnosis of preoperative infection, laparoscopy, enrollment in clinical trials, or receipt of antibiotics for >24 hours prior to surgery.

All patients were reviewed for the occurrence of SSI within 30 days from the date of surgery in patients without an implant and within 1 year if implant was involved. SSI was defined per the surveillance criteria published by the National Health Safety Network (NHSN).[6] Trained infection prevention staff and a trained infectious diseases fellow performed review for occurrence of SSI. We also determined the NHSN risk index category[6] for all patients included in the study.

To assess potential risk factors for SSI beyond adherence to SCIP criteria, a nested case control study was conducted. Cases were patients who developed SSI among the patients included in the study. An equal number of matched controls were selected among the patients included in the study. The controls met the following criteria: (1) underwent the same procedure (identical procedure code) as the case patient, (2) underwent surgery within a 3-month window before or after the date of the surgery as the case patient, and (3) did not develop an SSI within 30 days from the date of surgery. If more than 1 potential control patient was identified, then the patient whose surgery was closest to the case patient was chosen. Review of medical records was performed on cases and controls to collect data on demographic, laboratory, and clinical variables. The variables included age, gender, body mass index (BMI), obesity (BMI ≥ 30), age-adjusted Charlson comorbidity risk index,[7,8] number of units of red blood cells transfused perioperatively, duration of endotracheal intubation, duration of central venous catheters, and duration of indwelling urinary catheters.

Table 2
Comparison of rates of SSI between patients receiving care compliant with all 3 SCIP antibiotic measures compared with those receiving care compliant with <3 measures, stratified by NHSN risk index

NHSN risk index (n = 763)	Percent cases compliant with all 3 measures that developed infection: n (%)	Percent cases compliant with <3 measures that developed infection: n (%)	RR	95% CI	*P* value
3 (n = 2)	1 (50)	0	NA	NA	NA
2 (n = 108)	16 (20)	3 (10)	2.2	0.59-8.2	.27
1 (n = 321)	19 (7)	1 (2)	3.6	0.47-27.6	.33
0 (n = 332)	6 (2)	1 (1)	1.7	0.21-14.7	1

RR, relative risk.

The association between any clinical variable and development of SSI was determined using Fisher exact test, χ^2 test, or Mann-Whitney *U* test as indicated. Stratified analysis by NHSN risk index was performed to evaluate the association between receipt of perioperative antimicrobial prophylaxis per recommended guidelines and development of SSI. All tests were 2-tailed, and the critical level of α was .05. Statistical analyses were performed using SPSS for Windows v17.0 (SPSS Inc, Chicago, IL). The Institutional Review Board at the study institution approved this study.

RESULTS

Seven hundred sixty-two (762) patients underwent 763 procedures meeting inclusion criteria during the 18-month period from January 2008 to June 2009. These patients underwent the following procedures: hip arthroplasty (133, 17.4%), knee arthroplasty (223, 29.2%), colon surgery (115, 15.1%), hysterectomy (261, 34.2%), and vascular surgery (31, 4.1%). Administration of antimicrobial agent was correctly timed (SCIP-1) for 95% of cases; 98% received the appropriate type of antibiotic (SCIP-2); in 87% of cases, antibiotics were discontinued within 24 hours of the end of surgery (SCIP-3). The rate of adherence to all 3 parameters was 80%. Patients

Table 3
Clinical variables associated with development of surgical site infection

	Patients who developed SSI (cases: n = 33)	Patients who did not develop SSI (controls: n = 33)			
Clinical parameter	Median (IQR) or n (%)	Median (IQR) or n (%)	Unadjusted odds ratio	95% Confidence interval	*P* value
Age, yr	47 (40.5-61)	50 (36.5-63.5)			.73
Female sex	21 (64%)	18 (55%)	0.69	0.26-1.84	.62
Charlson comorbidity score adjusted for age	2 (0-5.5)	2 (0-5)			.57
BMI	28.7 (27.0-34.9)	25 (22.4-30.4)			.02*
ASA score	2 (0-5)	2 (0-5)			.37
Obesity (BMI $\geq$ 30)	15 (45%)	8 (24%)	0.43	0.15-1.24	.19
Diabetes present	12 (36%)	3 (9%)	5.71	1.43-22.8	.02*
Total duration of surgery (min)	185 (125.5-269)	156 (110-239)			.24

ASA, American Society of Anesthesiologists; *IQR*, interquartile range.
**P* $\leq$ .05.

undergoing hysterectomy were most likely to have met all 3 SCIP antimicrobial prophylaxis criteria, whereas patients with colon surgery were least likely to have met all 3 criteria. (Table 1)

Forty-seven of the 763 procedures (6.2%) developed SSI within 30 days after surgery. Of these, 32 underwent colon surgery, 8 underwent hysterectomy, 3 each underwent vascular and hip surgeries, and 1 underwent knee replacement. The median time to development of infection was 11 days (range, 3-30 days). Thirty-four (72%) infections were superficial: cultures were obtained in 22 of these, demonstrating 14 polymicrobial infections; 3 methicillin-resistant *Staphylococcus aureus* (MRSA); 2 *Escherichia coli*; and 1 each *Bacteroides fragilis, Enterococcus faecalis*, and *Proteus mirabilis.* Seven (15%) infections were classified as deep: 1 was culture negative; 3 were polymicrobial; and 1 each grew *B fragilis*, MRSA, and methicillin-sensitive *Staphylococcus aureus*. Of the 6 (13%) organ-space infections, 5 were polymicrobial, and no culture was obtained in 1.

There was no difference in the overall rates of SSI among patients with compliance to all 3 measures compared with patients having compliance with less than 3 measures (Table 1). The lack of difference remained even after performing a stratified analysis by NHSN risk index category (Table 2). The lack of difference also remained in all surgical procedure types except colon surgery (Table 1). In the colon surgery group, patients who had received care per all 3 SCIP measures were more likely to develop SSI compared with those who did not.

Of the 47 patients who developed SSI, controls meeting criteria were available for 33 cases (1:1 matching) within the retrospective cohort. Fourteen case patients (12 colon surgery patients and 2 vascular surgery patients) could not be matched because an uninfected patient with an identical procedure code was not available within the cohort. Case patients were more likely than control patients to have diabetes (36% vs 9%, respectively; unadjusted odds ratio, 5.71; 95% confidence interval: 1.43-22.8; *P* value = .02) and more likely to have elevated BMI (median BMI and interquartile range in case patients, 28.7 (27.0-34.9) vs 25.0 (22.4-30.4) in control patients; Mann-Whitney *U* test 2-tailed *P* value = .02). There was no difference between the groups with respect to gender, age, NHSN risk index, duration of central venous catheters, days of intubation, number of transfused units of red cells, duration of indwelling urinary catheters, age-adjusted Charlson comorbidity score, or diagnosis of obesity (BMI $\geq$ 30). Key results are shown in Table 3. Multivariable analysis was not performed because of small sample size.

DISCUSSION

No difference in the rates of SSIs was found between patients who received care per all 3 SCIP perioperative antimicrobial prophylaxis criteria and those who did not. The SCIP antimicrobial prophylaxis measures did not improve SSI outcome either individually or as a collective measure. Interestingly, among patients who underwent colon surgery, those who received care compliant with all 3 SCIP antimicrobial criteria had a higher incidence of SSI than those with partial compliance.

Whereas the ability to successfully implement SCIP guidelines has been demonstrated in prior studies,[9,10] results have been mixed in studies seeking to demonstrate improved patient outcomes. Nguyen et al[11] evaluated the SCIP antimicrobial guidelines and found that SCIP-1, timeliness of antibiotic administration, was the most important measure that influenced development of SSI. A cross-sectional study of 200 hospitals did not find a significant difference is SSI rates based on compliance with SCIP, although compliance specifically with SCIP-2 (appropriate antibiotic selection) did correlate with lower infections.[12] A large retrospective cohort study by Stulberg et al[13] found that composite adherence to all SCIP measures was associated with lower rate of postoperative infection. In their study, composite adherence to the antimicrobial prophylaxis measures per SCIP was associated with a trend toward lower postoperative infection rate. Although composite compliance with SCIP 1-3 did not influence SSI rates in our institution, the results are attributable to influences of other known and unknown factors associated with development of SSI. Our study highlights the fact that, whereas perioperative antimicrobial prophylaxis is a foundational strategy to prevent infections, other preventive strategies must be evaluated and employed concurrently as needed.

Interestingly, in the colorectal group, there were more infections among cases receiving appropriate care than in those who did not. It is likely that the risk of SSI in these patients outweighed the benefit afforded by the perioperative antimicrobial agent(s). Blumetti et al[14] reported different risk factors for colorectal SSI depending on the depth of infection: elevated BMI and ostomy involvement for superficial infection and perioperative transfusion and previous abdominal surgery for deep/organ space infection. The higher rate of SSI among patients compliant with SCIP antimicrobial measures may be attributable to known and unknown confounding factors.

We found that patients with diabetes and those with a higher BMI are more likely to develop SSIs. Diabetes is a well-known risk factor for development of SSI.[15,16] The impact of BMI on rates of SSI may be related to impaired wound healing and decreased tissue penetration of prophylactic antibiotics.[17] In the American College of Surgeons National Surgical Quality Improvement Project, being overweight (BMI = 25-29) was shown to be associated with increased rates of superficial infections, and being morbidly obese (BMI $\geq$ 35) was associated with superficial and deep infections and wound dehiscence.[18] Because the majority of infections in our study were superficial, this may explain why an increased BMI, but not actual obesity, was associated with SSI.

Currently, the rates of infection at our institution are significantly lower than at the time of this study. One major change is the use of chlorhexidine for skin preparation. Previously, povidone-iodine was the agent in use. Additionally, there has been increase in surgeon feedback of infection rates and overall increase in awareness related to infection prevention practices. During the last 3 months of the year 2011, the standardized incidence ratio of SSIs compared with Centers for Disease Control and Prevention-NHSN pooled mean was zero, 0.3, and 2.33 in patients undergoing vascular surgery, abdominal hysterectomy, and colon surgery, respectively. Our study has several limitations, notably those inherent in retrospective database review. This is a single institutional study with a limited sample size. Appropriate perioperative antimicrobial prophylaxis practices by themselves may not be adequate to prevent SSIs. Presence of diabetes and increased BMI appear to predispose surgical patients to development of SSI. Because of the small sample size in our case control study, it is possible that other patient or practice-related factors may account for the infections observed. Institutions seeking to reduce SSI may need to evaluate additional strategies beyond antimicrobial prophylaxis guidelines. Further studies are needed to identify preoperative, intraoperative, and postoperative factors that potentially modify the beneficial effects of perioperative antimicrobial prophylaxis.

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