Postoperative Prophylactic Antibiotics in Spine Surgery

A Propensity-Matched Analysis

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Background: Surgical site infections are common and costly complications after spine surgery. Prophylactic antibiotics are the standard of care; however, the appropriate duration of antibiotics has yet to be adequately addressed. We sought to determine whether the duration of antibiotic administration (preoperatively only versus preoperatively and for 24 hours postoperatively) impacts postoperative infection rates.

Methods: All patients undergoing inpatient spinal procedures at a single institution from 2011 to 2018 were evaluated for inclusion. A minimum of 1 year of follow-up was used to adequately capture postoperative infections. The 1:1 nearest-neighbor propensity score matching technique was used between patients who did and did not receive postoperative antibiotics, and multivariable logistic regression analysis was conducted to control for confounding.

Results: A total of 4,454 patients were evaluated and, of those, 2,672 (60%) received 24 hours of postoperative antibiotics and 1,782 (40%) received no postoperative antibiotics. After propensity-matched analysis, there was no difference between patients who received postoperative antibiotics and those who did not in terms of the infection rate (1.8% compared with 1.5%). No significant decrease in the odds of postoperative infection was noted in association with the use of postoperative antibiotics (odds ratio = 1.17; 95% confidence interval, 0.620 to 2.23; p = 0.628). Additionally, there was no observed increase in the risk of *Clostridium difficile* infection or in the short-term rate of infection with multidrug-resistant organisms.

Conclusions: There was no difference in the rate of surgical site infections between patients who received 24 hours of postoperative antibiotics and those who did not. Additionally, we found no observable risks, such as more antibiotic-resistant infections and *C. difficile* infections, with prolonged antibiotic use.

Level of Evidence: Therapeutic Level III. See Instructions for Authors for a complete description of levels of evidence.

Surgical site infections (SSIs) following spine surgery are common, preventable, and costly complications. Reported rates of deep infection following spine surgery have been reported to range from approximately 1% to 2%, with variability observed between studies involving different patient populations, surgical procedures, and sample sizes¹⁻⁶. The Spine Patient Outcomes Research Trial (SPORT) demonstrated postoperative infection rates of 2% to 4% for lumbar disc herniation, spinal stenosis, and degenerative spondylolisthesis²⁻⁴. Similar rates of infection (1.1% to 1.9%) have been observed in Medicare data for cervical and lumbar spine procedures^{5.7}. Even with variable rates of infection after surgery, SSIs remain the most common complication after spine surgery. To minimize the rate of postoperative infections, a compendium of research and guidelines has been dedicated to their prevention.

In 2003, the American College of Surgeons, in conjunction with the Centers for Disease Control and Prevention (CDC), Centers for Medicare & Medicaid Services (CMS), and other professional organizations, developed the Surgical Care Improvement Project (SCIP), which established the metrics by which SSI prevention is tracked⁸⁻¹⁰. These metrics include (1) the proportion of patients who receive antimicrobial prophylaxis within 1 hour prior to incision, (2) the proportion of patients who receive a prophylactic agent within currently

Disclosure: The authors indicated that no external funding was received for any aspect of this work. On the **Disclosure of Potential Conflicts of Interest** forms, which are provided with the online version of the article, one or more of the authors checked "yes" to indicate that the author had a relevant financial relationship in the biomedical arena outside the submitted work (http://links.lww.com/JBJS/G231).

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published guidelines, and (3) the proportion of patients whose antimicrobial prophylaxis is discontinued within 24 hours after the end of surgery⁸⁻¹⁰. Growing evidence, however, indicates that 24 hours of postoperative antibiotics may pose additional risks, such as antibiotic resistance, without added prevention benefit in patients undergoing orthopaedic procedures¹¹⁻¹⁵.

Several studies in the spine literature have evaluated the duration and effectiveness of prophylactic antibiotics; however, several questions have yet to be adequately addressed. First, does the duration of antibiotic administration (preoperatively only versus preoperatively and for 24 hours postoperatively) impact postoperative infection rates? Second, is prolonged antibiotic use associated with any observable risks, such as more antibiotic-resistant infections and *Clostridium difficile* infections? To answer these questions, we conducted a retrospective, propensity-matched analysis of all inpatient spine procedures at a single tertiary academic institution.

Materials and Methods

Patient Selection and Data Collection

A retrospective review of all primary spinal procedures that were performed at a single institution from 2011 to 2018 for the treatment of degenerative conditions and scoliosis in patients ≥18 years of age, with minimum 1-year follow-up, was performed. We excluded all outpatient procedures, oncological procedures, procedures for the treatment of spine infections, and revision procedures. The patients were stratified into 2 groups: (1) those who had received preoperative antibiotics and 24 hours of postoperative antibiotics and (2) those who had received preoperative antibiotics. Postoperative redosing and no postoperative antibiotics. Postoperative antibiotics were assigned on the basis of surgeon preference.

Standardized Prophylactic Antibiotic Regimens

Patients received prophylactic cefazolin, or, if a severe allergy was documented in the chart and confirmed by patient report, vancomycin or clindamycin. Prophylactic gentamycin was additionally administered to patients undergoing lumbar surgery. Follow-up data in the chart were reviewed until a minimum of 1 year of follow-up. Culture-related data, including organism types and sensitivities from available wound cultures, were also collected.

Outcome Variables

The primary end point of the present study was deep SSI, defined as any infection after the index procedure requiring irrigation and debridement and possible removal of implants. Secondary end points included the prevalence of antibiotic-resistant organisms, gauged from wound cultures and sensitivity data, and comparison of *C. difficile* infection rates between the 2 groups. Other variables such as age, American Society of Anesthesiologists (ASA) class, body mass index (BMI), comorbidity burden, and smoking were also collected. The Charlson Comorbidity Index (CCI) was calculated from the comorbidity data. Procedural data, including estimated blood loss, operative time, instrumentation, levels of fusion, type of approach (ante-

rior, posterior, or combined), complex plastic surgery closure, drain placement, type of procedure (minimally invasive or open), and level of the procedure (cervical, thoracic, or lumbar) were collected.

Statistical Analysis

Univariate analyses were performed with the Fisher exact test for categorical variables and with the t test for continuous variables to assess differences in demographic characteristics between patients who received 24 hours of postoperative antibiotics and those who did not. Multivariate regression was performed to assess whether the administration of postoperative antibiotics was an independent risk factor for infection when controlling for age, sex, BMI, smoking, CCI, estimated blood loss, operative time, levels of fusion, complex plastic surgery closure, approach (anterior, posterior or combined), type of procedure (minimally invasive versus open), and level of involvement (cervical, thoracic or lumbar).

To adequately control for confounding variables that impact infection rates, we performed propensity score matching using 1:1 matching to nearest neighbors between patients who did and did not receive postoperative antibiotics¹⁶. Propensitymatched variables were selected on an a priori basis and included age, sex, BMI, ASA score, smoking, CCI, levels fused, operative time, estimated blood loss, complex plastic surgery closure, approach (anterior, posterior or combined), type of procedure (minimally invasive versus open), and level of involvement (cervical, thoracic or lumbar). Because we included scoliosis cases, adding the number of levels fused was important to adequately match these cases and their postoperative antibiotic regimen. Balance after matching was assessed with use of standardized mean differences with a threshold of <0.1. After balancing, 1,162 patients remained in each group, for a total of 2,324 patients. Further assessment of balance was conducted with use of univariate analyses on baseline demographic data. Both the Fisher exact test and the McNemar test were used to compare the infection rates after propensity score matching, and bivariate regression was then performed to assess the odds ratio (OR) for postoperative infection associated with the use of postoperative antibiotics.

With use of an SSI difference of 1.4% based on previous studies of SSI rates, an alpha level of 0.05, and power of 0.80, the total projected sample size needed was approximately 2,054 $(1,027 \text{ per arm})^{17}$. All statistical analysis was performed with use of R (version 3.6.2; R Foundation for Statistical Computing). The level of significance was set at p < 0.05. Institutional review board approval was obtained prior to initiation of the study.

Results

A total of 6,655 patients were evaluated for inclusion, and a total of 4,454 patients were included for analysis after inclusion and exclusion criteria were applied. In the unmatched cohort, 1,782 patients (40%) received no postoperative antibiotics and 2,672 patients (60%) received postoperative antibiotics. Demographic characteristics are shown in Table I. Patients

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| TABLE I Characteristics of Patients Managed with and without Postoperative Antibiotics* | | | | | | | |
|---|---------------------------------------|-------------------------------------|---------------------------------|---------|--|--|--|
| | No Postop. Antibiotics (N = 1,782) | Postop. Antibiotics (N = 2,672) | Standardized Mean Difference | P Value | | | |
| Age† (yr) | 59.7 ± 14.3 | 58.1 ± 14.4 | 0.11 | <0.001‡ | | | |
| Male sex (no. of patients) | 909 (51.0%) | 1,372 (51.3%) | 0.01 | 0.849 | | | |
| Smoking (no. of patients) | 256 (14.4%) | 451 (16.9%) | 0.07 | 0.027‡ | | | |
| BMI† (kg/m ²) | 29.1 ± 6.1 | 29.8 ± 6.2 | 0.12 | <0.001‡ | | | |
| BMI category (no. of patients) | | | | <0.001‡ | | | |
| Underweight | 28 (1.6%) | 38 (1.4%) | | | | | |
| Normal | 427 (24.0%) | 494 (18.5%) | | | | | |
| Overweight | 612 (34.3%) | 963 (36.0%) | | | | | |
| Class-1 obesity | 440 (24.7%) | 673 (25.2%) | | | | | |
| Class-2 obesity | 184 (10.3%) | 337 (12.6%) | | | | | |
| Class-3 obesity | 91 (5.1%) | 167 (6.3%) | | | | | |
| ASA score (no. of patients) | | | | 0.028‡ | | | |
| 1 | 553 (31.0%) | 839 (31.4%) | | | | | |
| 2 | 632 (35.5%) | 1,030 (38.5%) | | | | | |
| 3 | 567 (31.8%) | 747 (28.0%) | | | | | |
| 4 | 30 (1.7%) | 56 (2.1%) | | | | | |
| CCI† | $\textbf{2.3} \pm \textbf{1.8}$ | 2.0 ± 1.8 | 0.15 | <0.001‡ | | | |
| Diabetes mellitus (no. of patients) | 233 (13.1%) | 336 (12.6%) | 0.02 | 0.657 | | | |
| COPD (no. of patients) | 99 (5.6%) | 138 (5.2%) | 0.02 | 0.616 | | | |
| CHF (no. of patients) | 15 (0.8%) | 19 (0.7%) | 0.02 | 0.753 | | | |
| CKD (no. of patients) | 50 (2.8%) | 41 (1.5%) | 0.09 | 0.005‡ | | | |
| IA (no. of patients) | 78 (4.4%) | 75 (2.8%) | 0.08 | 0.006‡ | | | |
| MIS (no. of patients) | 178 (10.0%) | 347 (13.0%) | 0.09 | 0.003‡ | | | |
| Instrumentation (no. of patients) | 1,419 (79.6%) | 2,261 (84.6%) | 0.13 | <0.001‡ | | | |
| No. of levels fused† | 2.7 ± 3.5 | $\textbf{2.8} \pm \textbf{3.8}$ | 0.03 | 0.330 | | | |
| Approach (no. of patients) | | | | <0.001‡ | | | |
| Anterior | 369 (21.5%) of 1,720 | 459 (17.8%) of 2,579 | | | | | |
| Posterior | 1,181 (68.7%) of 1,720 | 1,741 (67.5%) of 2,579 | | | | | |
| Combined | 170 (9.9%) of 1,720 | 379 (14.7%) of 2,579 | | | | | |
| EBL† (<i>mL</i>) | 446.8 ± 782.24 | 590.6 ± 993.8 | 0.16 | <0.001‡ | | | |
| Operative time† (min) | 237.4 ± 134.38 | $\textbf{245.3} \pm \textbf{132.1}$ | 0.06 | 0.055 | | | |
| Level of procedure (no. of patients) | | | | | | | |
| Cervical | 515 (28.9%) | 579 (21.7%) | 0.17 | <0.001‡ | | | |
| Thoracic | 216 (12.1%) | 273 (10.2%) | 0.06 | 0.050 | | | |
| Lumbar | 1,188 (66.7%) | 1,933 (72.3%) | 0.12 | <0.001‡ | | | |
| Drain (no. of patients) | 1,020 (57.2%) | 1,628 (60.9%) | 0.08 | 0.015† | | | |
| Complex plastic surgery closure (no. of patients) | 92 (5.2%) | 77 (2.9%) | 0.12 | <0.001‡ | | | |

*CCI = Charlson Comorbidity Index, COPD = chronic obstructive pulmonary disease, CHF = congestive heart failure, CKD = chronic kidney disease, IA = inflammatory arthritis, MIS = minimally invasive surgery, and EBL = estimated blood loss. †The values are given as the mean and the standard deviation. ‡Significant.

in the postoperative antibiotics group were more likely to be male, to have a history of smoking, and to have a higher BMI. The postoperative antibiotics group also had a higher proportion of ASA class-3 and 4 patients and a greater mean CCI. In terms of specific comorbidities, the group that did not receive postoperative antibiotics had higher rates of diabetes, chronic

obstructive pulmonary disease, and congenital heart failure, but the differences were not significant. Additionally, the postoperative antibiotics cohort had a greater percentage of procedures involving instrumentation, more levels fused, greater estimated blood loss, and longer operative time. The rate of infection in the group that received postoperative antibiotics was not significantly different from that in the group that did not (1.6% compared with 1.6%; p = 0.99) (Fig. 1). The rate of infection with *C. difficile* was also not significantly different between the groups that did and did not receive postoperative antibiotics (0.04% compared with 0%; p = 0.99).

In multivariate logistic regression, male sex, increased BMI, and greater estimated blood loss were significant independent risk factors for postoperative infection. However, administration of postoperative antibiotics was not protective against infection (Table II).

After propensity-matched analysis, there were no significant differences in demographic characteristics between the 2 groups (Table III). The infection rate was 1.8% in the group that received postoperative antibiotics and 1.5% in the group that did not (Fisher exact test, p = 0.859; McNemar test, p = 0.748). No significant decrease in the odds of postoperative infection was noted in association with the use of postoperative antibiotics (OR = 1.17; 95% confidence interval [CI], 0.620 to 2.23; p = 0.628).

For culture data, there were no significant differences between the group that received postoperative antibiotics and the group that did not in terms of the prevalence of different types of organisms (Fig. 2). The most common organism isolated was *Staphylococcus aureus*, which comprised 47% of the cultures that yielded an organism. All 3 patients who were infected with methicillin-resistant *S. aureus* (MRSA) had received postoperative antibiotics.

Discussion



Our propensity-matched analysis demonstrated no difference in SSI between patients who received postoperative

Infection rates for the group that received no postoperative antibiotics and the group that received postoperative antibiotics, prior to matching and after propensity score matching. POSTOPERATIVE PROPHYLACTIC ANTIBIOTICS IN SPINE SURGERY

TABLE II Regression Analysis Assessing Independent Variables Associated with Infection*

| | OR (95% CI) | P Value |
|---------------------------|-----------------------|---------|
| Postoperative antibiotics | 0.896 (0.542, 1.506) | 0.672 |
| Age | 0.983 (0.960, 1.008) | 0.167 |
| Male sex | 1.913 (1.147, 3.279) | 0.015† |
| BMI | 1.074 (1.040, 1.107) | <0.001† |
| Smoking | 1.745 (0.916, 3.157) | 0.076 |
| CCI | 1.128 (0.919, 1.349) | 0.219 |
| Diabetes mellitus | 1.784 (0.885, 3.486) | 0.096 |
| EBLŧ | 1.027 (1.003, 1.049) | 0.018† |
| Operative time | 0.999 (0.997, 1.002) | 0.655 |
| MIS | 0.381 (0.086, 1.180) | 0.135 |
| No. of levels fused | 1.008 (0.926, 1.073) | 0.833 |
| Anterior approach | 0.136 (0.005, 3.728) | 0.176 |
| Posterior approach | 2.312 (0.492, 41.300) | 0.411 |
| Combined approach | 1.217 (0.184, 23.934) | 0.861 |
| Cervical | 0.794 (0.259, 2.094) | 0.661 |
| Thoracic | 0.876 (0.331, 2.065) | 0.775 |
| Lumbar | 0.686 (0.384, 1.239) | 0.206 |
| Drain | 1.425 (0.781, 2.755) | 0.268 |
| Complex plastics closure | 0.970 (0.299, 2.624) | 0.956 |

OR = odds ratio, CI = confidence interval, BMI = body mass index, CCI = Charlson Comorbidity Index, EBL = estimated blood loss, and MIS = minimally invasive surgery. †Significant. †EBL was scaled by 100.

antibiotics and those who did not (1.8% compared with 1.5%). Among those who received postoperative antibiotics, we detected no increase in resistant organisms from wound cultures and no increased rates of *C. difficile* infection. In the published literature, there is limited evidence to support postoperative antibiotic prophylaxis for patients undergoing spine surgery. Our study, with adequate sample size, statistical methodology, and follow-up, adds to this evidence and improves on the previous literature.

In the spine literature to date, studies evaluating preoperativeonly versus preoperative and postoperative antibiotics have shown no added benefit but have had limited generalizability due to underpowered sample sizes and heterogenous control and comparison groups^{12,15,18,19}. Hellbusch et al. performed a randomized controlled trial of 269 patients undergoing instrumented lumbar fusion who received either a preoperative-only dose or an extended 10-day antibiotic protocol¹⁸. Patients who were randomized into the extended postoperative protocol received the standard preoperative and intraoperative prophylactic dosing as well as cefazolin for 3 days followed by oral cephalexin for 7 days. The infection rate was 4.3% in the preoperative-only cohort and 1.7% in the extended protocol cohort (p > 0.25). The trial was underpowered by approximately 1,100 patients to detect significant differences in infection rates. Additionally, the authors did not report adverse events associated

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| TABLE III Characteristics of Patients After Propensity Score Matching* | | | | | | |
|--|---------------------------------------|------------------------------------|---------------------------------|---------|--|--|
| | No Postop. Antibiotics (N = 1,162) | Postop. Antibiotics (N = 1,162) | Standardized Mean Difference | P Value | | |
| Age† (yr) | 58.9 ± 14.1 | 59.0 ± 14.0 | 0.00 | 0.976 | | |
| Male sex (no. of patients) | 577 (49.7%) | 578 (49.7%) | 0.00 | 1.000 | | |
| Smoking (no. of patients) | 193 (16.6%) | 181 (15.6%) | 0.03 | 0.535 | | |
| BMI† (kg/m ²) | 29.6 ± 6.1 | 29.6 ± 5.7 | 0.01 | 0.848 | | |
| ASA score† | 2.0 ± 0.8 | 2.0 ± 0.8 | 0.00 | 0.960 | | |
| CCI† | 2.1 ± 1.7 | 2.1 ± 1.8 | 0.01 | 0.819 | | |
| Diabetes mellitus (no. of patients) | 145 (12.5%) | 154 (13.3%) | 0.02 | 0.620 | | |
| COPD (no. of patients) | 55 (4.7%) | 60 (5.2%) | 0.02 | 0.702 | | |
| CHF (no. of patients) | 5 (0.4%) | 6 (0.5%) | 0.01 | 1.000 | | |
| CKD (no. of patients) | 26 (2.2%) | 15 (1.3%) | 0.07 | 0.114 | | |
| IA (no. of patients) | 42 (3.6%) | 39 (3.4%) | 0.01 | 0.821 | | |
| MIS (no. of patients) | 145 (12.5%) | 134 (11.5%) | 0.03 | 0.523 | | |
| No. of levels fused† | $\textbf{2.3}\pm\textbf{3.1}$ | 2.4 ± 3.1 | 0.02 | 0.713 | | |
| EBL† (mL) | 410.5 ± 702.9 | 428.3 ± 651.3 | 0.03 | 0.527 | | |
| Operative time† (min) | 229.7 ± 130.1 | 232.1 ± 126.7 | 0.02 | 0.650 | | |
| Approach (no. of patients) | | | | | | |
| Anterior | 225 (19.4%) | 219 (18.8%) | 0.01 | 0.792 | | |
| Posterior | 785 (67.6%) | 788 (67.8%) | 0.01 | 0.929 | | |
| Combined | 114 (9.8%) | 121 (10.4%) | 0.02 | 0.680 | | |
| Level of procedure (no. of patients) | | | | | | |
| Cervical | 286 (24.6%) | 289 (24.9%) | 0.01 | 0.923 | | |
| Thoracic | 97 (8.3%) | 111 (9.6%) | 0.04 | 0.345 | | |
| Lumbar | 838 (72.1%) | 822 (70.7%) | 0.03 | 0.494 | | |
| Drain (no. of patients) | 697 (60.0%) | 719 (61.9%) | 0.04 | 0.372 | | |
| Complex plastic surgery closure (no. of patients) | 29 (2.5%) | 31 (2.7%) | 0.01 | 0.896 | | |

*BMI = body mass index, ASA = American Society of Anesthesiologists, CCI = Charlson Comorbidity Index, COPD = chronic obstructive pulmonary disease, CHF = congestive heart failure, CKD = chronic kidney disease, IA = inflammatory arthritis, MIS = minimally invasive surgery, and EBL = estimated blood loss. †The values are given as the mean and the standard deviation.

with the antibiotics. The sample size and lack of adverse event reporting unfortunately limited that study's ability to assess the risks and benefits associated with postoperative antibiotics.

Dobzyniak et al., in a study of 635 patients undergoing lumbar laminotomy for disc herniation, compared a single preoperative dose of antibiotics (192 patients) with multiple doses of preoperative and postoperative antibiotics (418 patients) and found no difference between the groups in terms of the postoperative infection rate (1.56% compared with 1.20%, respectively; p = 0.71)¹². The postoperative antibiotic dosing was undefined, and, with an average length of stay of 2 days, it is unclear whether antibiotics were standardized to a 24-hour postoperative period or until discharge. One of the strengths of that study was the sample size; the study was adequately powered at 0.885 to detect differences between the 2 groups. However, the duration of follow-up may have artificially deflated postoperative infection rates as patients' charts were reviewed with a minimum of 6 weeks follow-up, which would have inadvertently missed deep infections presenting 1.5 months after the index procedure.

Several other studies have evaluated the duration of antibiotics in patients undergoing spine surgery; however, there has been wide variation in postoperative antibiotic protocols. Kanayama et al., in a study of 1,597 patients undergoing lumbar spine surgery who received either 1 day of postoperative antibiotics (464 patients) or 5 to 7 days of postoperative antibiotics (1,133 patients), reported no difference between the groups in terms of the infection rate (0.4% versus 0.8%, respectively)¹⁵. In another study, Kakimaru et al. evaluated patients undergoing microscopic spinal decompression without instrumentation who received no postoperative antibiotic dose (143 patients) or postoperative antibiotics (141 patients)¹⁹. That study also THE JOURNAL OF BONE & JOINT SURGERY • JBJS.ORG VOLUME 103-A • NUMBER 3 • FEBRUARY 3, 2021



Fig. 2

Culture results after revision surgery for infections in unmatched cohorts. MSSA = methicillin-susceptible *Staphylococcus aureus*, MRSA = methicillinresistant *S. aureus*, Coag.-neg Staph = coagulase-negative staphylococci, *E. coli = Escherichia coli*, *P. Aeruginosa = Pseudomonas aeruginosa*, *P. Acnes = Propionibacterium acnes* (now reclassified as *Cutibacterium acnes*), and *E. faecalis = Enterococcus faecalis*. Other includes *Enterobacter cloacae*, *Streptococcus agalactiae*, and *Klebsiella aerogenes*.

demonstrated no added prophylactic benefit in association with postoperative antibiotics in terms of the infection rate (2.8% in the group that received the postoperative dose compared with 1.4% in the group that did not; p = 0.335). The postoperative antibiotic protocol was heterogenous. Some patients received antibiotics throughout postoperative day 0, and some received antibiotics until discharge (average length of stay = 2.7 days). Our study improves on the heterogeneity of those studies in terms of the postoperative antibiotic protocols and adds to the evidence that antibiotics administered after wound closure have no significant effect on preventing infection.

With respect to other orthopaedic surgical procedures, there has been no demonstrated benefit of postoperative antibiotics in addition to a single preoperative dose^{11,20-23}. In the hip and knee arthroplasty literature, several studies have shown no difference in infection rates between preoperative-only antibiotic regimens and 24-hour perioperative regimens or between 1-day regimens and 7-day regimens of postoperative antibiotics^{11,23}. Tan et al., in a retrospective study of 20,862 primary total hip and knee arthroplasties, found no difference in the postoperative infection rate between patients who received 1 dose of antibiotics and those who received multiple doses¹¹.

Prophylactic antibiotics have been shown to be most effective if an adequate concentration is maintained within 2 hours after incision²¹. In order to be effective for prophylaxis, antibiotic concentrations in serum, soft tissue, and bone must exceed the minimum inhibitory concentration (MIC) for a specific bacterium^{8,21,24}. The MIC must be maintained throughout the duration of the procedure in order to effectively control the bacterial burden²¹. Postoperative antibiotics may be superfluous if the MIC was adequately maintained throughout the procedure.

The administration of antibiotics is not without associated risks. Proper antibiotic stewardship ensures that patients only receive antibiotics when such agents are clinically indicated and have been demonstrated to provide a benefit²¹. The administration of antibiotics beyond the intraoperative period increases financial cost and the long-term risk of multidrug-resistant organisms²¹. Prolonged antibiotic use is also associated with a risk of *C. difficile* infection. Previous laboratory studies have shown that a single dose of cephalosporin antibiotics is sufficient to allow for *C. difficile* colonization, and clinical studies have demonstrated a strong association between cephalosporin antibiotics and *C. difficile* infections^{25,26}. However, in the present study, no increased risk of *C. difficile* infections, this finding was consistent with those reported by Tan et al. for patients undergoing elective total knee and hip arthroplasty¹¹.

Our study demonstrated no significant increase in multidrugresistant organisms in patients who received 24 hours of postoperative antibiotics. All patients who demonstrated growth of MRSA on culture had received postoperative antibiotics, although there was no significant difference when compared with those who had not received postoperative antibiotics (p = 0.427). The development of antibiotic-resistant bacteria could occur over a longer period of time than what is captured in our study. The microbial ecosystem of a hospital may have a higher proportion of antibiotic-resistant organisms due to prolonged antibiotic use. However, isolating the impact of extended postoperative antibiotics on an institutional-specific biome is difficult. Antibiotic resistance poses a tremendous challenge to administering effective prophylactic agents and treating surgical site infections. Our study demonstrated no discernible short-term emergence of multidrug-resistant bacteria in patients managed with postoperative antibiotics; however, it did not clarify the broader impact on the hospital biome and the long-term impact on a patient's microbiome caused by more extended antibiotic administration.

The present study improves on the prior literature on the basis of the statistical analysis performed, minimum 1-year

follow-up, standardization of the postoperative antibiotics group, and large sample size with adequate power. With a minimum follow-up of 1 year after the index procedure, we believe that the majority of infections were captured in the data collection²⁷. Additionally, all patients who received postoperative antibiotics received the prophylactic agent for 24 hours. Our study is not without limitation as our evaluation was retrospective and therefore was not truly randomized. To address this limitation, we propensity-matched comorbidities to control for any confounding. In addition, there was a low rate of infection with C. difficile in our cohort and, as such, it is possible that our study was not adequately powered to detect differences between the 2 groups. The antibiotic regimen, whether a cephalosporin, vancomycin, or clindamycin, was not further pharmacodynamically evaluated to test for differences in clinical outcomes. Finally, our study included all inpatient spinal procedures and, as such, there may be some nuance in outcomes that might be appreciated with more granular data. Future studies should investigate antibiotic use in subgroups of patients undergoing spinal procedures associated with a higher risk of infection, such as revision procedures and procedures for the treatment of deformity.

Conclusions

Our propensity-matched analysis of 4,454 patients undergoing spine surgery demonstrated no additional prophylactic benefit of 24 hours of postoperative antibiotics. In patients who received the additional postoperative antibiotics, there was no increased risk of *C. difficile* infection or short-term

1. O'Toole JE, Eichholz KM, Fessler RG. Surgical site infection rates after minimally invasive spinal surgery. J Neurosurg Spine. 2009 Oct;11(4):471-6.

2. Weinstein JN, Lurie JD, Tosteson TD, Tosteson AN, Blood EA, Abdu WA, Herkowitz H, Hilibrand A, Albert T, Fischgrund J. Surgical versus nonoperative treatment for lumbar disc herniation: four-year results for the Spine Patient Outcomes Research Trial (SPORT). Spine (Phila Pa 1976). 2008 Dec 1;33(25):2789-800.

3. Weinstein JN, Lurie JD, Tosteson TD, Zhao W, Blood EA, Tosteson AN, Birkmeyer N, Herkowitz H, Longley M, Lenke L, Emery S, Hu SS. Surgical compared with non-operative treatment for lumbar degenerative spondylolisthesis. Four-year results in the Spine Patient Outcomes Research Trial (SPORT) randomized and observational cohorts. J Bone Joint Surg Am. 2009 Jun;91(6):1295-304.

4. Weinstein JN, Tosteson TD, Lurie JD, Tosteson A, Blood E, Herkowitz H, Cammisa F, Albert T, Boden SD, Hilibrand A, Goldberg H, Berven S, An H. Surgical versus nonoperative treatment for lumbar spinal stenosis four-year results of the Spine Patient Outcomes Research Trial. Spine (Phila Pa 1976). 2010 Jun 15; 35(14):1329-38.

5. Kurtz SM, Lau E, Ong KL, Carreon L, Watson H, Albert T, Glassman S. Infection risk for primary and revision instrumented lumbar spine fusion in the Medicare population. J Neurosurg Spine. 2012 Oct;17(4):342-7. Epub 2012 Aug 24.

6. Beiner JM, Grauer J, Kwon BK, Vaccaro AR. Postoperative wound infections of the spine. Neurosurg Focus. 2003 Sep 15;15(3):E14.

7. Wang MC, Shivakoti M, Sparapani RA, Guo C, Laud PW, Nattinger AB. Thirtyday readmissions after elective spine surgery for degenerative conditions among US Medicare beneficiaries. Spine J. 2012 Oct;12(10):902-11. Epub 2012 Oct 22.

8. Bratzler DW, Houck PM; Surgical Infection Prevention Guideline Writers Workgroup. Antimicrobial prophylaxis for surgery: an advisory statement from the National Surgical Infection Prevention Project. Am J Surg. 2005 Apr;189(4): 395-404.

9. Hawn MT, Richman JS, Vick CC, Deierhoi RJ, Graham LA, Henderson WG, Itani KM. Timing of surgical antibiotic prophylaxis and the risk of surgical site infection. JAMA Surg. 2013 Jul;148(7):649-57.

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emergence of multidrug-resistant organisms. Future studies should further stratify patient populations and identify whether postoperative antibiotics are useful for targeted populations.

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References

 Bratzler DW, Hunt DR. The Surgical Infection Prevention and Surgical Care Improvement Projects: national initiatives to improve outcomes for patients having surgery. Clin Infect Dis. 2006 Aug 1;43(3):322-30. Epub 2006 Jun 16.
Tan TL, Shohat N, Rondon AJ, Foltz C, Goswami K, Ryan SP, Seyler TM,

Parvizi J. Perioperative antibiotic prophylaxis in total joint arthroplasty: a single dose is as effective as multiple doses. J Bone Joint Surg Am. 2019 Mar 6;101(5): 429-37.

12. Dobzyniak MA, Fischgrund JS, Hankins S, Herkowitz HN. Single versus multiple dose antibiotic prophylaxis in lumbar disc surgery. Spine (Phila Pa 1976). 2003 Nov 1;28(21):E453-5.

13. Tang WM, Chiu KY, Ng TP, Yau WP, Ching PTY, Seto WH. Efficacy of a single dose of cefazolin as a prophylactic antibiotic in primary arthroplasty. J Arthroplasty. 2003 Sep;18(6):714-8.

14. Mastronardi L, Tatta C. Intraoperative antibiotic prophylaxis in clean spinal surgery: a retrospective analysis in a consecutive series of 973 cases. Surg Neurol. 2004 Feb;61(2):129-35; discussion 135.

15. Kanayama M, Hashimoto T, Shigenobu K, Oha F, Togawa D. Effective prevention of surgical site infection using a Centers for Disease Control and Prevention guideline-based antimicrobial prophylaxis in lumbar spine surgery. J Neurosurg Spine. 2007 Apr;6(4):327-9.

 Thomas L, Li F, Pencina M. Using propensity score methods to create target populations in observational clinical research. JAMA. 2020 Feb 4;323(5):466-7. Epub 2020 Jan 10.
Lewis A, Lin J, James H, Krok AC, Zeoli N, Healy J, Lewis T, Pacione D, A single-

17. Lewis A, Lin J, James H, Krok AC, Zeoli N, Healy J, Lewis T, Pacione D. A singlecenter intervention to discontinue postoperative antibiotics after spinal fusion. Br J Neurosurg. 2018 Apr;32(2):177-81. Epub 2017 Nov 2.

18. Hellbusch LC, Helzer-Julin M, Doran SE, Leibrock LG, Long DJ, Puccioni MJ, Thorell WE, Treves JS. Single-dose vs multiple-dose antibiotic prophylaxis in instrumented lumbar fusion—a prospective study. Surg Neurol. 2008 Dec;70(6): 622-7; discussion 627. Epub 2008 Jan 18.

19. Kakimaru H, Kono M, Matsusaki M, Iwata A, Uchio Y. Postoperative antimicrobial prophylaxis following spinal decompression surgery: is it necessary? J Orthop Sci. 2010 May;15(3):305-9. Epub 2010 Jun 18.

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24. Yamada K, Matsumoto K, Tokimura F, Okazaki H, Tanaka S. Are bone and serum cefazolin concentrations adequate for antimicrobial prophylaxis? Clin Orthop Relat Res. 2011 Dec;469(12):3486-94. Epub 2011 Oct 4.

21. Bryson DJ, Morris DLJ, Shivji FS, Rollins KR, Snape S, Ollivere BJ. Antibiotic prophylaxis in orthopaedic surgery: difficult decisions in an era of evolving antibiotic resistance. Bone Joint J. 2016 Aug;98-B(8):1014-9.

20. Kim B, Moon SH, Moon ES, Kim HS, Park JO, Cho IJ, Lee HM. Antibiotic microbial

prophylaxis for spinal surgery: comparison between 48 and 72-hour AMP protocols.

Asian Spine J. 2010 Dec;4(2):71-6. Epub 2010 Nov 24.

22. Takemoto RC, Lonner B, Andres T, Park J, Ricart-Hoffiz P, Bendo J, Goldstein J, Spivak J, Errico T. Appropriateness of twenty-four-hour antibiotic prophylaxis after spinal surgery in which a drain is utilized: a prospective randomized study. J Bone Joint Surg Am. 2015 Jun 17;97(12):979-86.

23. Nelson CL, Green TG, Porter RA, Warren RD. One day versus seven days of preventive antibiotic therapy in orthopedic surgery. Clin Orthop Relat Res. 1983 Jun;176:258-63.

25. Ambrose NS, Johnson M, Burdon DW, Keighley MRB. The influence of single dose intravenous antibiotics on faecal flora and emergence of Clostridium difficile. J Antimicrob Chemother. 1985 Mar;15(3):319-26.

26. Privitera G, Scarpellini P, Ortisi G, Nicastro G, Nicolin R, de Lalla F. Prospective study of Clostridium difficile intestinal colonization and disease following single-dose antibiotic prophylaxis in surgery. Antimicrob Agents Chemother. 1991 Jan; 35(1):208-10.

27. Weinstein MA, McCabe JP, Cammisa FP Jr. Postoperative spinal wound infection: a review of 2,391 consecutive index procedures. J Spinal Disord. 2000 Oct;13(5):422-6.