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Timing of Antibiotic Prophylaxis for Preventing Surgical Site Infections in Foot and Ankle Surgery

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Abstract

Background: Surgical site infections (SSIs) are one of the most troublesome complications after foot and ankle surgery. Previous literature has emphasized the significance of appropriate timing of antibiotic prophylaxis. However, the optimal timing of antibiotic prophylaxis for SSI prevention is still inconclusive. Our study aimed to investigate the optimal timing of antibiotic administration and to elucidate the risk factors for SSIs in foot and ankle surgery.

Methods: A retrospective review of 1933 foot and ankle procedures in 1632 patients from January 1, 2011, through August 31, 2015, was performed. Demographic data; type, amount, and timing of antibiotic administration; incision; and closure time were recorded. Subsequent wound infection and incision and drainage procedure (I&D) within 30 days and 90 days were documented. Outcomes and demographic variables were compared between procedures in which antibiotics were administered less than 15 minutes and between 15 to 60 minutes prior to incision. A total of 1569 procedures met inclusion criteria.

Results: There were 17 cases (1.1%) of subsequent wound infection, of which 6 required a subsequent I&D within 30 days. There were 63 additional cases (4%) of wound complications, which did not meet SSI criteria. When comparing SSI and non-SSI groups, the only significant independent predictors were longer surgeries and nonambulatory surgeries (both $P < .05$). Stepwise multivariate logistic regression analysis demonstrated that 91.8% of the risk of an SSI could be predicted by ASA score and length of surgery alone.

Conclusion: In foot and ankle surgeries, the timing of intravenous antibiotic prophylaxis did not appear to play a significant role in the risk of SSI. Host factors and duration of surgery appear to have played a much larger role in SSI than the timing of antibiotic prophylaxis.

Level of Evidence: Level III, retrospective comparative study.

Keywords: infection, timing, antibiotic, prophylaxis, foot, ankle

Introduction

SSIs have been labeled as an important metric in value-based purchasing by the Centers for Medicare and Medicaid Services. Moreover, SSI has been hailed by nonphysicians as something that should be a "never-event." The incidence of infection in foot and ankle surgery has been noted to be higher than some other elective orthopedic procedures for a host of reasons.[8,13,21,22,30,31] Many strategies have been developed to minimize SSIs, improve patient outcomes, and subsequently reduce cost, including preoperative skin prep, antibiotic prophylaxis, operating room environmental controls, and postoperative protocols.[3,4,8,12,19,22,24]

Preoperative antibiotics represent the foundation of SSI prophylaxis by establishing a bactericidal concentration of the drug within the serum and soft tissues prior to skin incision. Administration of antibiotics too early may result in metabolism and excretion of the active antibiotic before initiation of the operative procedure. Conversely, late administration may lead to inadequate antibiotic concentration at the surgical site.

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Table 1. Comparison of Demographic Variables and Outcomes Between Procedures Administrating Intravenous Antibiotics Less Than 15 Minutes and Between 15 and 60 Minutes.

	Less Than 15 Minutes (n = 1184)	15-60 Minutes (n = 385)	*P* Value
Age, mean (SD), y	48.8 (16.7)	44.6 (16.2)	<.05[a]
BMI, mean (SD)	27.7 (5.9)	29.2 (6.4)	<.05[a]
Admission status, % (n)			<.05[b]
Ambulatory	73.2 (867)	64.9 (250)	
Non ambulatory	26.8 (317)	35.1 (135)	
Smoking status, %(n)			.07[b]
Nonsmoker	67.3 (797)	61 (235)	
Former smoker	20.4 (241)	24.9 (96)	
Current smoker	12.3 (146)	14 (54)	
Diabetes, % (n)	10.5 (124)	9.6 (37)	.63[b]
ASA classification, % (n)			.98[b]
1	28.4 (336)	28.6 (110)	
2	58.4 (692)	57.9 (223)	
3	13.2 (156)	13.5 (52)	
Length of surgery, mean (SD), min	70 (45)	104 (66)	<.05[a]
Subsequent of wound infection, % (n)	0.8 (9)	2.1 (8)	.03[b]

[a]Analysis performed using Student *t* test.
[b]Analysis performed using chi-square test.

Prior studies report that optimal timing for antibiotic administration ranges from 15 minutes prior to incision in certain procedures to as high as 60 minutes prior to incision in general orthopedic procedures.[1,4,7,20,26,27] However, the correlation between SSI occurrence and the timing of antibiotic administration in foot and ankle surgery and other orthopedic subspecialties remains unclear.[*]

Therefore, the purpose of this study was to investigate the optimal timing for preoperative prophylactic antibiotic administration as well as to elucidate the risk factors for SSIs in foot and ankle surgery.

Methods

A priori power analysis was performed in order to detect a 4% absolute increase in infection rate with inadequate timing of antibiotic prophylaxis, based on a presumed baseline SSI rate of 4% in foot and ankle surgeries from previous literature ranging from 2% to 4.5% (n = 1204 to achieve a power of 0.80).[8,22,29-31] After approval by our institutional review board, a retrospective review was performed using the electronic medical record of 1933 foot and ankle procedures in 1632 patients from January 2011 through August 2015. All patients were treated by 2 senior surgeons, who also determined the postoperative SSIs. The study group included patients who underwent foot and ankle procedures. Cases with preexisting infections, open wounds, intentionally withheld antibiotic prophylaxis, or procedures performed specifically to address potential infections (eg, incision and drainage) were excluded from analysis. Recorded information included demographic data, type and amount of antibiotics, the timing of antibiotic administration, incision time, and closure time.

A total of 1569 procedures in 701 males (44.7%) and 868 females (55.3%) met inclusion criteria. The following cases were excluded: (1) soft tissue infection (n = 25), (2) osteomyelitis (n = 38), (3) potential infection (n = 23), (4) open wound (n = 89), (5) intentionally withheld prophylactic antibiotic (n = 26), and (6) incomplete data (n = 163). In the majority of cases, antibiotics were administered less than 15 minutes prior to incision (1184 of 1569, 75.5%). Most of the key demographic variables were similar between the <15 minutes and 15-60 minutes groups, including tobacco use, ASA score, and diabetes (Table 1). The patients who received antibiotics less than 15 minutes prior to incision tended to have more ambulatory surgery and tended to have a shorter average length of surgery than the 15-60 minutes group.

Postoperative wound infections and incision and drainage procedures (I&D) within 30 days and 90 days of the original procedure were documented. SSIs were identified according to the Centers for Disease Control and Prevention (CDC) definitions.[15] According to the CDC definition, superficial incisional SSI is defined as occurring within 30 days after an operation involving only skin and subcutaneous tissue with either purulent drainage or an organism isolated from an aseptically obtained culture of the superficial incision and at

[*]References [2, 5, 6, 10, 11, 17, 25, 27, 32]

least one of the following signs and symptoms: pain or tenderness, localized swelling, redness, or deliberately opened superficial incision by surgeon. Deep incisional SSI is defined as an infection occurring within 30 days after an operation that involves deep soft tissue and either purulent drainage or spontaneous dehiscence when the patient has at least one of the following signs and symptoms: fever (>38°C), localized pain, tenderness, or other evidence of infection involving the deep incision. Superficial and deep incisional infections were combined in this study.

Patient and surgical covariates known to predict the occurrence of SSI were obtained from the database including age, gender, tobacco use, body mass index (BMI), American Society of Anesthesiology (ASA) score, diabetes, admission status, type and amount of antibiotic, type of diagnosis (injury occurred within 30 days or elective procedure), duration of surgery, and type of procedures (digit, forefoot, midfoot, hindfoot, ankle, arthroscopy, soft tissue, and combined procedures). Patients' admission status was classified as inpatient if there was an admission to the hospital greater than 24 hours either preoperatively or postoperatively; otherwise, the case was classified as ambulatory surgery.

Operative cases were classified into 2 groups according to the timing of antibiotic administration: less than 15 minutes prior to incision or 15-60 minutes prior to incision. This cutoff was used because previous literature has suggested that the administration of preoperative antibiotics in orthopedic procedures should occur between 15 and 60 minutes prior to incision.[9,28] No patients had antibiotics administered more than 60 minutes prior to incision. A comparison of outcomes and demographic variables between these groups of patients was performed, and the association between SSI and independent variables was analyzed using a regression model.

Statistical Analysis

Descriptive statistics were performed by using frequencies (percentage) for categorical variables and mean ± standard deviation (SD) for continuous variables. Pearson chi-square tests and univariate logistic regression analysis were used to evaluate categorical variables for their associates with the primary outcome (infections) as well as to determine the associations between patients receiving antibiotics 15-60 minutes and less than 15 minutes prior to incision. Two-tailed heteroscedastic *t* test was used to compare the means of continuous variables (ie, length of surgery etc) between 2 cohorts as well as to determine the association with the primary outcome. Significance was set at an α level of 0.05 ($P \leq .05$) and 95% confidence interval. Stepwise multivariate logistic regression analysis was applied to estimate the strength of association between SSI and all independent variables. The magnitude of associations between the predictor variables and outcome was analyzed by using the odds ratio and the 95% confidence interval. All analyses were performed using IBM SPSS Statistics, version 21.0, statistical software (IBM Corp, Armonk, NY).

Result

There were a total 17 cases (1.1%) of subsequent wound infection, of which 6 required a subsequent I&D within 30 days and 11 required a subsequent I&D within 30 to 90 days. There were 63 additional cases (4%) of wound complications, which did not meet SSI criteria including mild wound erythema, wound swelling, and mild wound dehiscence that received a short course of oral antibiotics (5-7 days) and subsequently healed without signs of infection or any further procedures.

When comparing the patients who had subsequent SSIs to those who did not, the only significant independent predictors were longer surgery (117 minutes in SSIs vs 78 minutes), and nonambulatory surgery (52.9% vs 28.5%) (both $P < .05$) (Table 2). Furthermore, when a stepwise multivariate logistic regression was performed to see which variables would predict an SSI, it was found that 91.8% of the risk of an SSI could be predicted by ASA score and length of surgery alone. A more involved model also including BMI, tobacco use, type of antibiotic, gender, and whether or not a surgery was ambulatory could predict 92.3% of the risk of SSI.

Discussion

The incidence of surgical site infection (SSI) in foot and ankle surgery is higher than other orthopedic subspecialties.[8,13,21,22,30,31] Previous literature reported the mean incidence of SSI ranges from 2% to 4.5% in the general healthy population and could be more than 10% in high-risk patients especially those with complicated diabetes mellitus.[8,22,30,31] Studies of the incidence of SSI in general orthopedic surgery have reported SSI rates that range between 0.7% and 2.1%.[13,14,16,18,23] Our study reports an incidence of SSI in a set of patients undergoing foot and ankle surgery at 1.1%. However, there were 63 patients (4%) who had wound complications including mild erythema, swelling, and superficial wound dehiscence that did not meet the criteria of a clear infection. Many of these patients were treated with a short course of oral antibiotics. However, it is ultimately not clear whether these patients actually had an infection or not. If we used the most liberal definition of SSI and counted all of those cases as infections (although many of them were not), the incidence of SSI in this study is 5%, which is comparable to the mean incidence of previous studies.

Table 2. Comparison of Demographic Variables Between Non-SSI and SSI Groups.

	Non-SSIs (n = 1552)	SSIs (n = 17)	*P* Value
Age, mean (SD), years	47.78 (16.63)	48.20 (19.71)	.92[a]
BMI, mean (SD)	28.07 (6.07)	28.71 (5.88)	.67[a]
Admission status, % (n)			.03[b]
Ambulatory	71.5 (1109)	47.1 (8)	
Non ambulatory	28.5 (443)	52.9 (9)	
Smoking status, % (n)			.80[b]
Nonsmoker	65.8 (1021)	64.7 (11)	
Former smoker	21.5 (334)	17.6 (3)	
Current smoker	12.7 (197)	17.6 (3)	
Diabetes, % (n)	10.2 (159)	11.8 (2)	.84[b]
ASA classification, % (n)			.26[b]
1	28.6 (444)	11.8 (2)	
2	58.1 (902)	76.5 (13)	
3	13.3 (206)	11.8 (2)	
Type of antibiotics, % (n)			.85[b]
Cefazolin	90.1 (1399)	94.1 (16)	
Clindamycin	9.4 (146)	5.9 (1)	
Vancomycin	0.5 (7)	0 (0)	
Preoperative antibiotic administration, mean (SD), min	11 (8)	16 (9)	< .01[a]
Length of surgery, mean (SD), min	78 (53)	117 (68)	< .05[a]

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; SD, standard deviation; SSI, surgical site infection.
[a]Analysis performed using Student *t* test.
[b]Analysis performed using chi-square test.

The weaknesses of this study were not insignificant. First, and most importantly, there were many cases in which it was very difficult to tell whether an SSI actually existed or not. However, the authors felt that there was a clear difference between those patients whose symptoms and erythema improved with oral antibiotics and those that did not. The overwhelming majority of this cohort of patients simply had wound erythema that resolved with oral antibiotic administration. The authors felt that those patients that required irrigation and debridement clearly had an infection, whereas in those that did not the patient may or may not have had an infection. Ultimately, virtually every patient that required irrigation and debridement procedures had oral antibiotics beforehand and did not improve. Another weakness, and one that is perhaps equally important, relates to the fact that the rate of SSI in general is thankfully low. However, to try to prove a clear difference in infection rates with differing timing of antibiotics would require a much larger study to try to find a difference insofar as optimizing the timing of antibiotic administration.

Quality in medicine has always been a goal. More recently, especially in the United States, there has been movement toward institutionalizing mechanisms to reward quality. As a result, physicians have been feverishly working to establish ways in which quality can be recognized. Quality can, in fact, be defined in many ways and is affected by many things. The most easily defined metrics that can be used to recognize quality are process measures, that is, those things in medicine that are largely binary. It is easy to identify whether a patient did or did not receive a certain medication. Therefore, the administration of preoperative antibiotics has been assigned as one of these metrics. Some have suggested that antibiotic administration should be done between 15 (or 30) and 60 minutes prior to skin incision.[9,28] It should be noted that the first of these studies deals with the administration of vancomycin, which is simply different from other, more commonly used prophylactic antibiotics in terms of its pharmacokinetics. Also, the second study clearly relates only to cefuroxime, which is a second-generation cephalosporin that is rarely used for surgical prophylaxis in orthopedic surgery. Thus, these data are not relevant to the vast majority of orthopedic procedures in which cefazolin is used for infection prophylaxis.

The authors initiated this study somewhat in response to the idea that optimal timing of antibiotic administration is between 15 and 60 minutes prior to incision. In foot and ankle surgery, there is generally less set-up time than there is in other orthopedic surgeries, most notably in hip/knee and spine procedures. Much of the work in quality has focused on these surgical groups.[16,18,21,23,27] However, the authors' experience was that most foot and ankle patients had historically received antibiotics less than 15 minutes prior to incision without any untoward sequelae or high infection rate. This work does corroborate that theory.

This work does not, however, indicate an optimal timing of antibiotic administration, and we cannot conclude that administration of antibiotics less than 15 minutes prior to incision is better than 15 to 60 minutes prior to incision. Although there is a statistical significance that arises when these 2 groups are compared en bloc, when the timing of antibiotic administration was treated as a numerical variable as part of a more sophisticated analysis taking into account other patient and surgical factors, it was not found to be an independent predictor. Although attempting to have the timing of antibiotics comply with the prescribed guidelines would likely result in at least noninferior outcomes, we have found that there are factors that are much more relevant, including optimizing patients' health and minimizing operative time. This study, thus, illustrates that there are other variables that are much more relevant and affect the risk of infection to a much greater degree. However, many of those variables are not modifiable. It is certainly a worthwhile goal to attempt to identify the most appropriate timing of antibiotic administration for different surgical patients. However, performing this type of study would require a large database of patients and almost certainly a multicenter or even national effort.

In what is perhaps the largest study on this subject, Hawn et al assessed the relationship of timing as a continuous variable with postoperative SSI in a large national surgical cohort including patients at VA hospitals undergoing hip or knee arthroplasty, colorectal procedures, vascular procedures, and hysterectomy. In more than 32 000 surgeries, 1497 SSIs were found, for an infection rate of 4.6%. A higher rate of SSI was found in those patients who had antibiotic administration greater than 60 minutes prior to incision than in those who had it less than 60 minutes prior to incision. However, in a generalized additive model that adjusted for patient, procedure, and antibiotic variables, no significant association was found between SSI and the timing of antibiotic prophylaxis.[10]

In our study, the variables that most influenced the risk of SSI were nonambulatory surgery and length of surgery. Similarly, in our regression model, the variables that predicted SSI were again length of surgery and ASA score. Nonambulatory surgery and ASA score are both simply markers of the relative health of the patient undergoing surgery, as those patients that are sicker tend to have a higher ASA and are more likely to be admitted after surgery. These factors are largely not modifiable. Length of surgery is likely related somewhat to nonambulatory surgery, as patients with more extensive, longer surgeries may be more likely to be admitted to the hospital. The length of surgery is somewhat, although not entirely, under the surgeon's control. Some surgeries will be longer by necessity. However, the necessity of adequate preoperative planning and preparation is thus reinforced, as well as the need for time-efficient action in the operating room. Interestingly, the addition of many factors that could reasonably be posited to affect infection risk (BMI, tobacco use, antibiotic choice, etc) did not seem to significantly affect risk of infection rates, highlighting how much infection rates depended on length of surgery and ASA score in our study population.

Diabetes was surprisingly not a significant independent predictor of infection in our study population. There were many reasons why this may be the case. The diagnosis of diabetes was treated as a binary variable, whereas in reality there is a spectrum of severity of disease. Because the study was examining cases in which prophylactic antibiotics may make a difference in outcome (ie, patients who were undergoing procedures for preexisting infection or open wounds were excluded), the prevalence of poorly controlled diabetes in our study was likely relatively low and thus did not have a significant effect on perioperative infection risk.

Although these data do not indicate an optimal timing for antibiotic administration in this set of patients, the authors still feel that standardization is a laudable and frankly necessary goal. Indeed, decreasing variability and developing standards are perhaps one of the most direct ways to lead change towards better safety and ultimately better quality. As before, much of the work that has been done in this arena has focused on hip/knee replacement and spine procedures, which may or may not be as relevant to foot and ankle procedures, and this distinction likely merits further exploration. Furthermore, this work serves to highlight the absolute necessity of risk stratification, as the sicker patients with more complex procedures seem to be at greater risk for SSI.

Conclusion

In foot and ankle surgery, the timing of antibiotic prophylaxis did not appear to play a significant role in the risk of SSI. Based on current evidence, antibiotic administration within 60 minutes prior to incision was most appropriate. Host factors and duration of surgery appeared to play a much larger role in SSI than the timing of antibiotic prophylaxis.

Declaration of Conflicting Interests

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