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Gram-Negative Surgical Site Infections After 989 Spinal Fusion Procedures: Associated Factors and the Role of Gram-Negative Prophylactic Antibiotic Coverage

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ABSTRACT

Background: To identify, analyze, and report the patient- and procedure-related factors associated with surgical site infection (SSI) after spinal fusion (SF) surgery.

Methods: We included any SSI-SF from January 2013 to September 2015. A total of 989 spine surgeries that required instrumentation were performed.

Results: Twenty-four out of 989 (2.43%) patients presented with SSI. More than half of the SSI cases (54%) got infected with either exclusively gram-negative bacteria or a combination of gram-negative and gram-positive bacteria; 9.1% of the surgeries involved the sacral spine (90 out of 989 patients). SSI in long constructs (more than 3 levels) was performed in 66.7% compared with 33.3% with short constructs; 87.5 % of the reported SSI (21 patients) were done through a posterior approach. Of patients who had SSI, 87.5% received prophylactic antibiotics, 92% were operated on during the daytime shift, 50% required blood transfusion, and 79% required surgical debridement. Four patients out of 24 patients died (17%) due to unrelated SSI complications.

Conclusions: The overall incidence of gram-negative infections after long SFs remains low in our study population. Despite this low overall incidence, our results demonstrate a relative higher incidence of gram-negative SSIs in surgeries involving more than 3 spinal levels and for all those involving the sacral spine. We propose that there may be a potential benefit of gram-negative prophylactic antibiotic coverage in patients falling in either 1 of these categories. Further multivariate analysis and/or randomized studies may be necessary to confirm our results.

Level of Evidence: 3.

Complications

Keywords: surgical site infection, spine, fusion

INTRODUCTION

Surgical site infection (SSI) rate is an important indicator of health care quality in spine surgery.[1,2] Quality indicators such as SSI must account for patient- and procedure-specific characteristics allowing meaningful comparison between patient- and procedure-related factors.[2] SSI risk factors identification in spine surgery can help to design more effective preventative measures. Some patient-related factors such as diabetes, obesity, smoking history, alcohol abuse, anemia, coronary artery disease, and coagulopathy have been correlated to SSI.[1,3,4,5] In addition, some procedure-related factors such as prolonged operative time, posterior surgical approach, osteotomy, and blood transfusions have been associated to SSI.[1,5] Furthermore, sometimes risk factors vary from institution, country, or treated population.[5]

Spine surgery infections are most commonly monomicrobial in origin, and the most common pathogen isolated is *Staphylococcus aureus*.[3,6,7] On the other hand, gram-negative organisms represent a considerable percentage (30.5%) of all SSI.[7] Certain procedural risk factors in spine surgery have shown association with specific pathogens. Abdul-Jabbar et al[7] showed that spine surgery that involves the sacrum seems to be associated with increased gram-negative organisms, and polymicrobial infections of all gram-negative organisms in same study (61.6%) were cefazolin-resistant.[7] The use of prophylactic antibiotics has shown a significant decrease in SSI in numerous studies. A meta-analysis by Barker[8] found that postoperative spine infection rates could be reduced from 5.9% to 2.2%

with the adequate use of prophylactic antibiotics. Despite following the current clinical guidelines on antibiotic prophylaxis in spine surgery, the rate of SSI remains to be 0.7% to 10%.[9]

Cephalosporin antibiotics such as cefazolin used within 2 hours of incision has shown to improve infection rates in orthopedic surgery.[10] For uncomplicated spinal procedures, prophylaxis against gram-positive organisms has been reported to decrease SSI risk.[8,11] Cefazolin is the first-line agent used for prophylactic gram-positive coverage during spine surgery at our institution.

Current clinical guidelines suggest that patients undergoing complicated spine surgery and those with comorbidities may benefit from additional measures such as gram-negative coverage and/or intrawound vancomycin or gentamycin application.[9] Aminoglycosides including tobramycin are often used as alternative prophylactic antibiotic coverage against gram-negative organisms. Many studies have evaluated the different prophylactic regimens in the context of spine surgery, yet the superiority of 1 specific type and/or route of administration has not been clearly defined.[9]

Service reports from the orthopedic department at our institution during 2013 revealed a significant increase on the SSI rate for spinal fusion (SF) surgeries compared with previous years.[12] In 2013, SF operations accounted for 50% of the total number of SSI in the orthopedic surgery department (numbers).[1] Our infection rate on the SF group exceeded the National Healthcare Safety Network benchmark.[1] In 2014, the SF SSI rate decreased by 2.5% compared with the National Healthcare Safety Network reference rate.[13] These service report findings[1,13] led the infection prevention and control service to consider prophylaxis coverage against gram-negative bacteria in order to reduce SSI-SF rate. The purpose of this study was to dissect and identify all of those patient- and procedure-related factors that may be associated to SSI-SF in our institution.

MATERIALS AND METHODS

We retrospectively collected data on SSI-SF cases occurring in a Level 1 trauma center from January 2013 to September 2015. The cases that have been treated for SSI either exclusively with antibiotics or with antibiotics combined with surgery were collected by the infection prevention and control surveillance service. Ethical approval from the Institutional Research Ethics Board was received for this study.

Table 1. Demographic data for 24 cases with surgical site infection.

Parameter	Value
Patient demographics (N = 24)	
Age, mean (range), y	64.8 (34–82)
Sex, n (%)	
Female	11 (46)
Male	13 (54)
Comorbidity, n (%)	
Active malignancy	6 (25)
Immunocompromised	5 (21)
Smoking	5 (21)
Diabetes mellitus	4 (17)
COPD	3 (12)
CAD	3 (12)
Obesity	2 (8)
Renal insufficiency	2 (8)

Abbreviations: CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease.

Inclusion Criteria

Adult patients with a SSI within 12 months of receiving instrumented SF surgery at Montreal General Hospital (MGH) were included as cases. All types of preoperative diagnoses were eligible. SSI was detected during regular in hospital surveillance using Information Systems screening.[1,13] Both these systems identified the following clinical clues as indicative of an infection: clinical culture specimens from surgical sites, antibiotic prescription, reoperation, and re-admission.[1,13]

Collected Variables

The data collected were validated by the infection prevention and control service. Collected patient and procedure factors included the following: patient demographics, comorbidities, preoperative diagnosis, procedure, procedural characteristics, and SSI complications. Also, information about preoperative antibiotic prophylaxis used and pathogen characteristics such as isolated organism, gram stain, pathogen profile, and antibiotic resistance were identified via orthopedic surgery, anesthesia, and nursing electronic charts.

RESULTS

A total of 989 spine fusion surgical procedures were performed at our institution during 2013–2015. Twenty-four cases (2.43%) were diagnosed with SSI; the demographic details of these 24 cases were included in Table 1. Malignancy, immunocomprom-

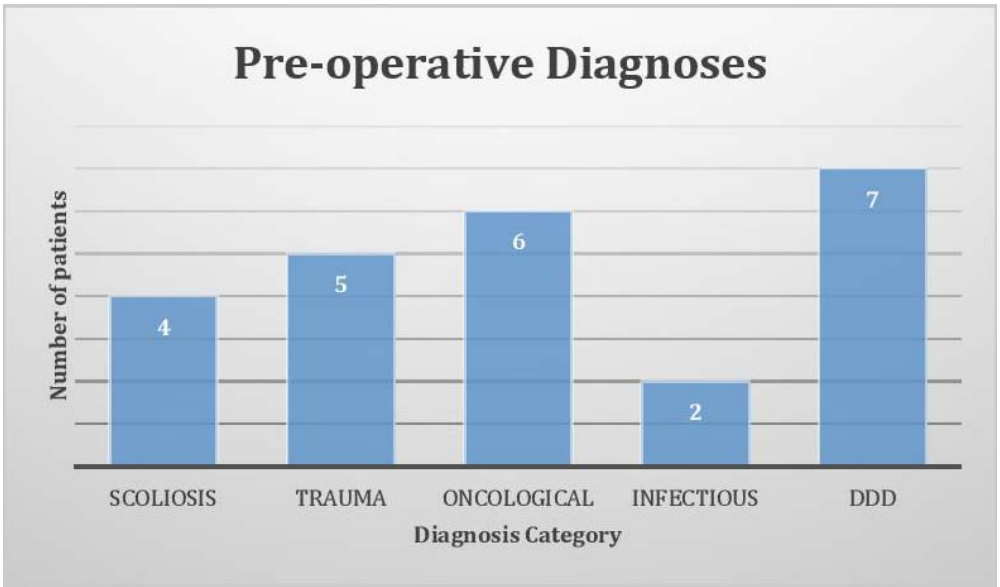

Figure 1. Preoperative diagnoses.

isation, and smoking were the most frequent associated risk factors among our population.

The preoperative diagnoses of the 24 SSI cases were mainly degenerative disc disease (DDD; 29% [7 patients]), followed by tumors 25% (6 patients) (Figure 1). Interestingly, there were 2 infection-related diagnoses: spondylodiscitis and osteomyelitis.

All of the SSI were cultured and analyzed, and the classes of organism cultured for each specimen were monomicrobial in 62.5% (predominantly gram-positive organisms, 73%), and polymicrobial being 37.5% (Figure 2). Bacteremia was found to be present in 3 of the 24 SSI patients (12.5%).

Larger surgeries involving multiple spinal regions were most likely to become infected with thoraco-lumbo-pelvic having the highest incidence of infection of 9.1% (Table 2; Figure 3). Of the 24 SSI cases, 21 (87.5%) were done via a posterior approach, 3 were dual approach procedures, none were performed exclusively via an anterior approach, and all of the 24 cases had instrumentation.

In terms of the time of the day during which the surgeries resulting in SSI were performed, 22 (92%)

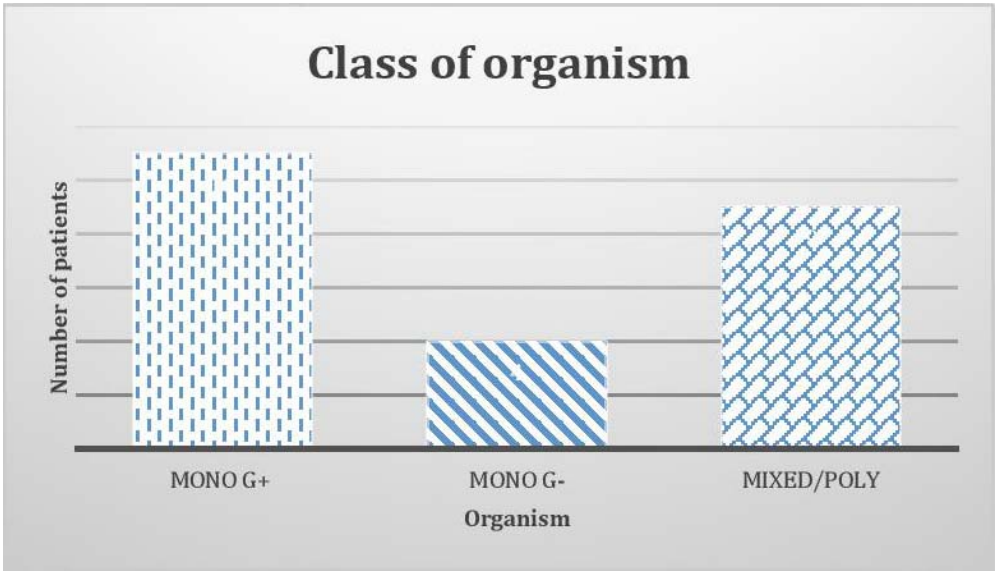

Figure 2. Class of organisms reported in surgical site infection cases.

Table 2. SSI incidence according to spinal region.

Spinal Region	Total Number of Surgeries	Number of SSIs	SSI incidence (%)
C	185	2	1.1
T	104	2	1.9
L	276	5	1.8
S	6	0	0.0
CT	30	2	6.7
TL	116	3	2.6
LS	228	6	2.6
TLS	44	4	9.1
Total	989	24	

Abbreviations: C, cervical; CT, cervicothoracic; L, lumbar; LS, lumbosacral; S, sacrum; SSI, surgical site infection; T, thoracic, TL, thoracolumbar; TLS, thoracolumbosacral.

were performed between 6 AM and 6 PM, and 2 were performed after hours between 6 PM and 6 AM (both patients were polytrauma, required intensive care unit admission, and had unstable spine fractures).

A total of 21 of 24 SSI patients received some kind of antibiotic prophylaxis (Figure 4), 17 (71%) received cephazolin (Ancef), and the rest had combination of Ancef with either vancomycin or gentamycin. Of the 21 patients who received antibiotic prophylaxis, 19 (90%) received the initial dose prior to the first incision (up to 100 minutes before), and 2 received it postincision at the 2- and 3.5-hour marks. One of the 2 patients who received cephazolin after surgical incision, the antibiotic was delayed until specimen collection for the reason of spondylodiscitis. Of the SSI patients, 10 received blood transfusions, which represented 40% (Figure 5).

Data on the treatment methods for the SSI patients were gathered as well. It was determined that 19 patients (79%) required surgical debridement (incision and drainage), and the remaining 5 patients (21%) simply received a course of intravenous antibiotics (Figure 6). All patients were noted to have improved post SSI treatment. It is important to note that 4 of the 24 patients died during the time span of the study. However, their causes of death were not related directly to the SSI in itself.

DISCUSSION

The incidence of SSI at our center between January 2013 and September 2015 was 2.43%. This result is congruent and with the reported 0.7% to 12.0% incidence of SSI after adult spinal surgery reported in the literature.[14]

The preoperative diagnosis that was shown to have the highest number of SSI was DDD with 7 cases, and interestingly the diagnosis with the lowest number of SSI was "spinal infection" (osteomyelitis and spondylodiscitis) with 2 cases. With our total amount of patients with SSI being 24, the difference between these 2 groups (DDD and spinal infection) is insignificant (29% vs 8% respectively). In a previous study with a sample of patients greater than 6000, the diagnosis of neoplasm was identified as being a risk factor for SSI.[15] This was associated to the overall immune and nutritional state of oncological patients.[20] In our series, we observed the same trend. Although, the fact that our sample was

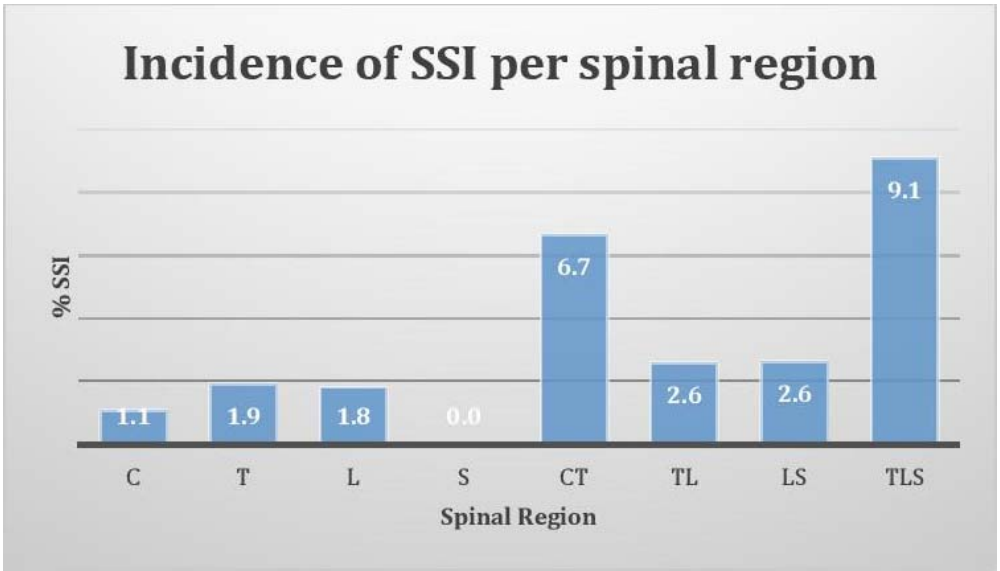

Figure 3. Surgical site infection incidence according to spinal region.

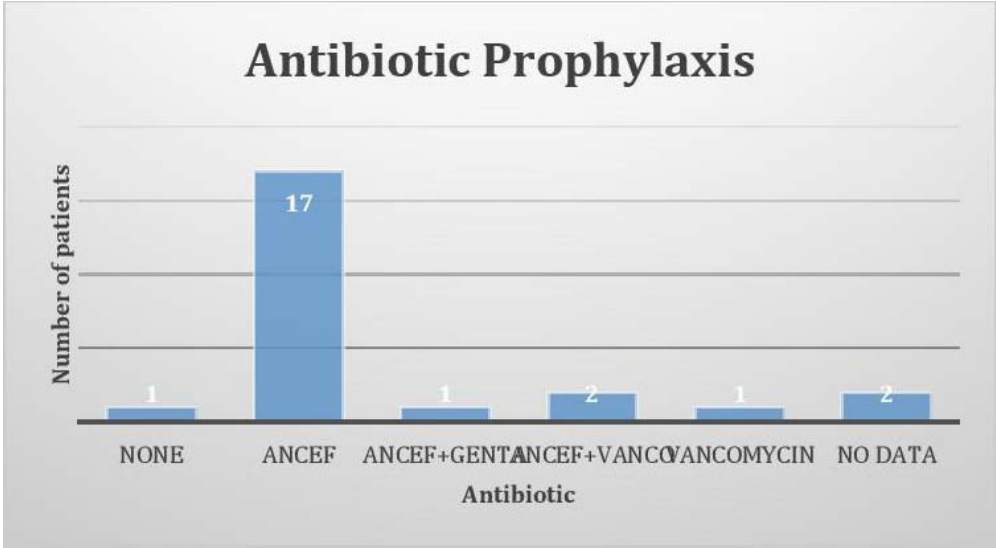

Figure 4. Antibiotic prophylaxis use.

smaller may have affected the result leaving "oncological" diagnosis as the second most common group presenting with SSI in our study.

Other main risk factors that have been associated with higher incidences of SSI are surgeries involving 8 or more levels and surgeries involving the sacrum or the pelvis.[15] This was also found in our results as the majority of SSI (9.1%) involved thoraco-lumbo-pelvic instrumentations and therefore, longer surgical time and greater surgical area exposed and estimated blood loss.

Of the 24 SSI cases, all of them required instrumentation thereby suggesting that the introduction of a foreign body such as instrumentation is a risk factor for SSI. This is consistent with previous studies that have demonstrated how the use of instrumentation is high risk factor associated with SSI.[16]

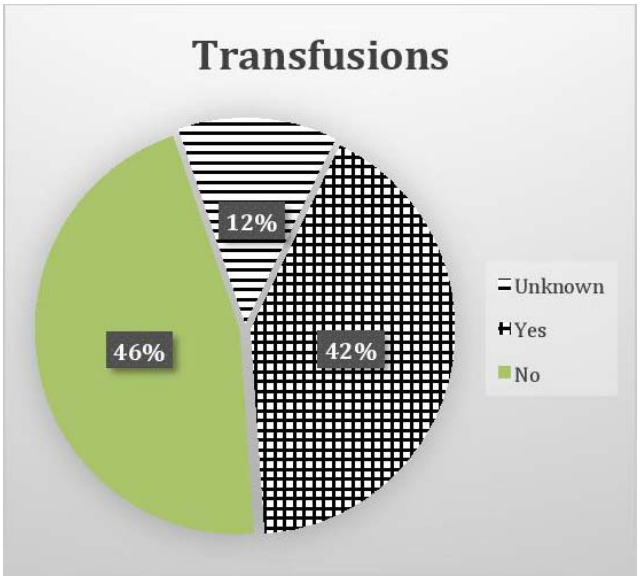

Figure 5. Transfusions.

We hypothesized that nonpatient related factors such as surgeon or operating team variation during the night shift (6 PM to 6 AM) could have led to an increased risk of SSI. However, our results did not show that the time of surgery is a remarkable risk for SSI as 22 of the 24 SSI cases were performed during day time hours. As expected, almost all the patients in the SSI group received antibiotic prophylaxis.

We know from the literature that using a cephalosporin antibiotic such as cefazolin within 2 hours of incision has shown to improve infection rates in orthopedic surgery.[11] Our data show that 19 of the 21 SSI patients who received prophylaxis (gram-positive coverage only) received it according to this recommendation. We then asked ourselves whether adequate therapeutic antibiotic levels were maintained throughout the entire duration of the procedures, especially for the longer cases. However, we assumed the subsequent doses were given. While collecting data, we realized that the only prophylaxis protocol for anesthesia is to document the time at which the initial antibiotic was given. Despite this difficulty, the results we would have gathered may not have affected our results. Previously reported evidence showed that patients with prolonged procedures that are re-dosed have a similar infection rate to those were there was not a "subsequent dose" given.[17]

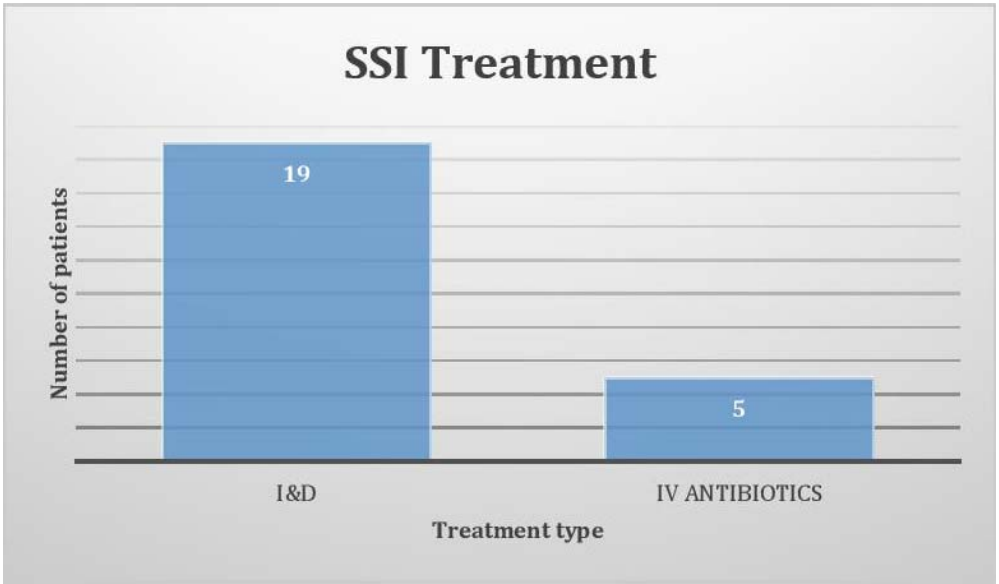

Figure 6. Surgical site infection treatment methods.

In addition, as seen in Figure 4, more than half of the SSI cases (13 out of 24) were found to be infected with either exclusively gram-negative bacteria or a combination of gram-negative and gram-positive. It is worth noting that out of the 10 SSI patients who had spine surgery involving the sacrum, 7 of them had a polymicrobial infection, 1 had a gram-negative infection and the remaining 2 had a gram-positive infection. This is consistent with the study by Abdul-Jabbar et al,[7] which showed that spine surgery involving the sacrum seems to be associated with increased gram-negative organisms and polymicrobial infections.[8] This supports our idea that there may be a benefit of using gram-negative coverage in spinal procedures, especially those involving the sacrum.

In our study, we did not find any association to blood transfusions during the procedure and SSI. However, it has been previously reported by Koutsoumbelis et al[18] that the use of packed red-blood cells for volume replacement could increase the risk for SSI following spinal procedures, but more specifically for posterior lumbar instrumented arthrodesis.

In terms of the specific SSI treatment, 19 out of 24 patients (80%) required surgical debridement (incision and drainage), and the remaining 5 (20%) patients were treated only with intravenous antibiotics. The fact that 20% of the patients responded to medical management alone is interesting. However, there are no studies that randomized the modalities of treatment. This may be a factor that is still dependent on the staff surgeon in charge of the patient most probably implemented on a case by case scenario.

It is important to note that the 4 patients who died during the time span of the study did not die due to the SSI in itself. It is well documented that the SSI-related mortality rate among spine surgical patients ranged from 1.1% to 2.3%.[19] Given these low percentages and our small sample of 24 SSI cases, it is not surprising that the number of SSI-related mortalities is 0.

LIMITATIONS

The results presented here were obtained from a retrospective analysis of prospectively collected data. Data extraction from charts should be interpreted carefully because human systematic errors can occur; for example, failure to state if a second antibiotic dose was given or just omitted. Also, retrospective cohort studies require large sample sizes especially if outcomes are rare. Our study sample of 24 cases was too low to run statistical analysis and conclude significant findings. This is a descriptive analysis and larger randomized studies are necessary to confirm our results.

CONCLUSION

The incidence of SSI at our center after reviewing 989 patients between January 2013 and September 2015 was 2.43%. SSI were associated to SFs that required multilevel constructs of instrumentation

via a posterior approach. Polymicrobial infections were identified to be present when sacral levels were involved. Blood transfusions and operating at night (from 6 PM–6 AM) were not shown to be associated with increased SSI. The role of gram-negative prophylaxis in multilevel surgeries involving the sacrum is recommended but its effectivity remains to be elucidated.

REFERENCES

1. Abdul-Jabbar A, Takemoto S, Weber M, et al. Surgical site infection in spinal surgery. *Spine*. 2012;37(15):1340–1345.
2. Biscione F. Rates of surgical site infection as a performance measure: are we ready? *World J Gastrointest Surg*. 2009;1(1):11–15.
3. Fang A, Hu SS, Endres N, Bradford DS. Risk factors for infection after spinal surgery. *Spine*. 1460;30(12):1460–1465.
4. Olsen MA, Nepple JJ, Riew KD, et al. Risk factors for surgical site infection following orthopaedic spinal operations. *J Bone Joint Surg Am*. 2008;90(1):62–69.
5. Nota S, Braun Y, Ring D, Schwab J. Incidence of surgical site infection after spine surgery: what is the impact of the definition of infection? *Clin Orthop Relat Res*. 2014;473(5):1612–1619.
6. Maesani M, Doit C, Lorrot M, et al. Surgical site infections in pediatric spine surgery: comparative microbiology of patients with idiopathic and nonidiopathic etiologies of spine deformity. *Pediatr Infect Dis J*. 2016;35(1):66–70.
7. Abdul-Jabbar A, Berven SH, Hu SS, et al. Surgical site infections in spine surgery: identification of microbiologic and surgical characteristics in 239 cases. *Spine*. 2013;38:E1425–E1431.
8. Barker FG 2nd. Efficacy of prophylactic antibiotic therapy in spinal surgery: a metaanalysis. *Neurosurgery*. 2002;51(2):391–400; discussion 400–401.
9. Shaffer WO, Matz P, Baisden J, Fernand R. Clinical guidelines for multidisciplinary spine care antibiotic prophylaxis in spine surgery. North American Spine Society. Published 2013. http://www.spine.org. Accessed October 4, 2015.
10. Luer MS, Hatton J. Appropriateness of antibiotic selection and use in laminectomy and microdiskectomy. *Am J Hosp Pharm*. 1993;50(4):667–670.
11. Rubinstein E, Findler G, Amit P, Shaked I. Perioperative prophylactic cephazolin in spinal surgery. A double-blind placebo-controlled trial. *J Bone Joint Surg Br*. 1994;76B(1):99–102.
12. Infection Prevention and Control Service. *Service Report for Orthopedic Surgical Site Surveillance at the MGH–2013*. McGill University Health Center; 2013:1–9.
13. Infection Prevention and Control Service. *Service Report for Orthopedic Surgical Site Surveillance at the MGH–2014*. McGill University Health Center; 2014.
14. Pull ter Gunne AF, Cohen DB. Incidence, prevalence, and analysis of risk factors for surgical site infection following adult spinal surgery. *Spine*. 2009;34(13):1422–1428.
15. Abdul-Jabbar A, Takemoto S, Weber MH, et al. Surgical site infection in spinal surgery: description of surgical and patient-based risk factors for postoperative infection using administrative claims data. *Spine*. 2012;37(15):1340–1345.
16. Chahoud J, Kanafani Z, Kanj SS. Surgical site infections following spine surgery: eliminating the controversies in the diagnosis. *Front Med*. 2014;1:7. doi:10.3389/fmed.2014.00007
17. Hellbusch LC, Helzer-Julin M, Doran SE, et al. Single-dose vs. multiple-dose antibiotic prophylaxis in instrumented lumbar fusion—a prospective study. *Surg Neurol*. 2008;70(6):622–627; discussion 627.
18. Koutsoumbelis S, Hughes AP, Girardi FP, et al. Risk factors for postoperative infection following posterior lumbar instrumented arthrodesis. *J Bone Joint Surg Am*. 2011;93(17):1627–1633.
19. Patel H, Khoury H, Girgenti D, et al. Burden of surgical site infections associated with select spine operations and involvement of Staphylococcus aureus. *Surg Infect*. 2017;18(4):461–473.
20. Gradl G, Bas de Witte P, Evans BT, Hornicek F, Raskin K, Ring D. Surgical site infection in orthopaedic oncology. *J Bone Joint Surg Am*. 2014;96(3):223–230.

Disclosures and COI: The authors of this study have no commercial or financial association with regards to this project and, therefore, have no affiliation that may pose a conflict of interest with the manuscript enclosed. The authors had full access to all the data in the study and take responsibility for the integrity and accuracy of the data, as well as the decision to submit for publication.

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