Original Article

Length of preoperative hospital stay is the dominating risk factor for surgical site infection in neurosurgery: A cohort data-driven analysis

Emilio Garzón Cediel1,3, Varina Louise Boerwinkle2, Juan Fernando Ramon1, Diana Arias4, Jose Antonio De la Hoz-Valle5, Jose Dario Mercado4, Darwin Cohen4, Maria Claudia Niño4

1Department of Neurosurgery, Clínica de Marly Jorge Cavelier Gaviria, Chía, Cundinamarca, Colombia, 2Department of Pediatric Neurology, Barrow Neurological Institute at Phoenix Children’s Hospital, Phoenix, Arizona, United States, Departments of 3Neurosurgery, 4Anesthesiology, 5Clinical Research, Hospital Universitario Fundación Santa Fe de Bogotá, Bogotá, Cundinamarca, Colombia.

E-mail: *Emilio Garzón Cediel - 2emiliodn@gmail.com; Varina Louise Boerwinkle - vboerwinkle@phoenixchildrens.com; Juan Fernando Ramon - juanfernandoramont@yahoo.com; Diana Arias - d.arias@uniandes.edu.co; Jose Antonio De la Hoz-Valle - jossedela@hotmail.com; Jose Dario Mercado - md.jose.dmg@hotmail.com; Darwin Cohen - cohendarwin@yahoo.com; Maria Claudia Niño - gigi87@yahoo.com

*Corresponding author: Emilio Garzón Cediel, Department of Neurosurgery, Clínica de Marly Jorge Cavelier Gaviria, Chía, Cundinamarca, Colombia.

ABSTRACT

Background: The number of days of preoperative hospital stay (PHS) is a modifiable variable that has shown contradictory surgical site infection (SSI) risk factor results in neurosurgery. We sought to pinpoint the day of PHS length related with a marked increase of risk of SSI.

Methods: From a tertiary teaching hospital, January 2015–December 2017, prospectively collected nonpercutaneous neurosurgery procedures with standard antibiotic prophylaxis and 1-year follow-up were evaluated. SSI risk factors were assessed through multiple logistic regression models with different thresholds of PHS.

Results: A total of 1012 procedures were included in the study. Incidence of SSI was 4.4%. The median PHS was higher in those with SSI than in those without (1 day, interquartile range [IQR]: 7 vs. 0 days, IQR: 1, respectively, P = 0.002). By the amount of six days of PHS, this exposure risk past the threshold of significance for impact on wound infection (OR 2.8; CI 1.23–6.39, P = 0.014). Operative time past 4 h (OR 2.11; CI 1.12–3.98; P = 0.021), and in some models, previous surgery at same admission were also identified by multivariate analysis as increasing postoperative SSI risk.

Conclusion: The gradual increase of the SSI OR associated with longer PHS days was the highest risk factor of SSI in our cohort of patients. Studies directed to reduce this complication should consider the PHS.

Keywords: Antibiotic prophylaxis, Hospitalization, Neurosurgery, Preoperative period, Risk factor, Surgical site infection

INTRODUCTION

The U.S. News and World Report rankings of Best Hospitals list minimization of hospital-acquired infection 7 times in its criteria. Neurosurgical studies report surgical site infection (SSI) incidence of 3.5–6.2%, related to morbidity and mortality, making prevention of SSI a high priority. Surgical antibiotic prophylaxis is well known in preventing SSI, thus is common
However, some found no benefit, and others even a negative role, possibly related to the antibiotic resistance patterns.\textsuperscript{[10,24]}

Although the length of preoperative hospital stay (PHS) is factored in some neurosurgery SSI studies and has been related to this complication,\textsuperscript{[1,7,31]} the specific number of days of PHS is less well understood, with mixed findings.\textsuperscript{[3,8,11,13,18,23,25,27,29,33,36-38,40,41]} Moreover, to the knowledge of the authors, there are no prior characterizations of PHS as a quantitative variable for the determination of the point at which it becomes a relevant risk factor for SSI.

Hospital stay has been associated with changes in the bacteria flora,\textsuperscript{[4,18]} increasing the amount of isolated pathogens resistant to antibiotics used in surgery that targets common community-acquired bacteria. This colonization may cause increased risk of SSI for patients with longer PHS, as it is widely documented in the literature of different surgical specialties.\textsuperscript{[7,34,35,39]} In the present study, the number of days of the PHS is evaluated for its possible role as a SSI risk factor in those undergoing open neurosurgical procedures with standard antibiotic prophylaxis against community usual bacteria.\textsuperscript{[28]}

\section*{MATERIALS AND METHODS}

The Institutional Research Ethics Committee approved the study. According to the STROBE guideline, retrospective analysis of the institutional neuroanesthesia database consecutive cohort was conducted. All the nonpercutaneous procedures performed by the neurosurgery or orthopedic spine surgery divisions between January 2015 and December 2017, classified by the surgeon as clean wound, and received antibiotic prophylaxis with cefazolin or clindamycin were selected, including those of the same patient. Surgeries to anatomical areas with on-going local infections or with positive microbiological isolates from samples taken during the procedure were excluded, as well as those cases with SSI wherein the clinical infection signs appeared after the exposure of inert prosthetic or fixation material through the skin during the ambulatory follow-up. Data were also extracted from the prospectively recorded neuroanesthesia database and the patient’s electronic medical records. Several variables were collected, including age, sex, diagnosis, surgery, antibiotic prophylaxis, emergency procedure, previous surgery during the same hospital admission, previous surgery on the same anatomical area, operative time, maximum number of people in the operating room, American Society of Anesthesiologists classification (ASA), aseptic product for skin preparation, training level of the physician closing the wound, intraoperative transfusion, ICU stay during the admission, ICU stay before the surgery during the same hospital admission, history of diabetes mellitus, and days of PHS.

SSI cases were identified from the database with up to 1 year postoperative follow-up and from the institutional epidemiology group register. Afterward, the data were verified by manual review of the clinical records according to the Centers of Disease Control and prevention criteria\textsuperscript{[30]} and the study exclusion criteria. Included patients received 2 g of intravenous cefazolin or 600 mg of clindamycin if they had history of allergy, administered within 1 h before incision. In those with operative time longer than 4 h or need of transfusion, a half the dose was repeated. Outcomes of positive cultures at the time of SSI diagnosis were gathered for further analysis. The bacteria were classified as cutaneous origin (\textit{Staphylococcus aureus}, coagulase-negative staphylococci, and \textit{Propionibacterium acnes}) and noncutaneous origin (\textit{Escherichia coli}, \textit{Pseudomonas aeruginosa}, Acinetobacter spp., streptococci, enterococci, and Gram-positive bacillus) similarly to Korinek \textit{et al.}\textsuperscript{[24]}

\subsection*{Statistical analysis}

Data were analyzed using STATA\textsuperscript{®} software version 16. A univariate analysis was carried out to describe the characteristics of the patients included. Categorical data are presented as percentages and were analyzed using the Chi-square test. For continuous data, the median (interquartile range [IQR]) and mean (standard deviation [SD]) are presented. Comparisons of continuous data were performed using the Mann–Whitney U-test for nonnormally distributed variables.

As the main goal of the study was to characterize the odds of SSI in function of the PHS, 15 logistic regression models were made, each one of them using its own dichotomized variable PHS with a different cut point of time in days, from 0 to 15+ days. The characteristics identified as potential risk factors based on univariate analysis underwent the multivariate logistic regression analysis, and $P \leq 0.05$ represented statistical significance.

\section*{RESULTS}

\begin{table}[h]
\centering
\begin{tabular}{|c|c|}
\hline
\textbf{Variable} & \textbf{SSI}}
The overall SSI rate was 4.4% (n: 45) and positive cultures at the time of SSI identification were obtained in the 84.4% (n: 38) of the cases. The most frequent isolated microorganism was *Staphylococcus epidermidis* in 34.2% (n: 13) followed by *S. aureus* 26.3% (n: 10). In 11 cases, out of those 38 (26.3%) positive culture cases, more than 1 microorganism species was isolated and 55.3% of the times, at least one microorganism was among the defined as noncutaneous origin bacteria. Cefazolin was used as antibacterial prophylaxis in 94.3% of the cases, while clindamycin just in the 5.7%, without having a statistical difference on their relation to SSI (P = 0.704).

The overall median preoperative hospitalization time was 0 (IQR 1) days, 0 (IQR 1) for non-SSI, and 1 day (IQR 7) for SSI cases (P = 0.002). ICU stay during the hospitalization was observed in a 54.2%. However, only in 10.6% was the ICU stay preoperative, which was associated with SSI in the bivariate analysis (OR 2.2; CI 1.04–4.74; P = 0.035). Intraoperative transfusion (OR 2.1; CI 1.07–4.22; P = 0.027), surgical time ≥4 h (OR 2.3; CI 1.27–4.24; P = 0.005), and any previous surgery during the same hospital admission (OR 4.76; CI 1.99–11.3; P < 0.001) were also associated with SSI. Bivariate analysis of the other variables, type of surgery (P = 0.124), emergency surgery (P = 0.538), asepsis product (P = 0.871), level of training of the professional closing the wound (P = 0.546), maximum number of persons in the operating room (P = 0.316), ASA score (P = 0.09), and diabetes mellitus (P = 0.925) showed no difference in the SSI rate [Tables 1 and 2].

The multivariate regression analysis of the significant variables is shown with adjusted OR in [Table 3]. The identified independent risk factors were surgical time ≥4 h (OR 2.107; CI 1.12–3.98; P = 0.021), level of training of the professional closing the wound (P = 0.546), maximum number of persons in the operating room (P = 0.316), ASA score (P = 0.09), and diabetes mellitus (P = 0.925) showed no difference in the SSI rate [Tables 1 and 2].

The multivariate regression analysis of the significant variables is shown with adjusted OR in [Table 3]. The identified independent risk factors were surgical time ≥4 h (OR 2.107; CI 1.12–3.98; P = 0.021) and PHS (OR 1.13; CI 1.05–1.22; P = 0.001). The 15 time points' logistic regressions of the PHS centered analysis are summarized in [Table 4 and Graph 1]. They reveal a gradual increase of the PHS OR for SSI from 1.71 (CI 0.87–3.37; P = 0.123) to 13.26 (CI 3.94–44.63; P < 0.001), reaching and maintaining the significance at 6 days. Most of the variables have consistent values across the models with different threshold of PHS, except for previous surgery in the same hospitalization which starts with an OR of 3.1 at day 1 and ends with an OR of 1.68 in the logistic regression with PHS dichotomized at 15 days. Furthermore, the SSI association of this last variable was not significant in any of the models with PHS cut point at 6 days or more.

---

**Table 1:** Demographics and bivariate analysis according to surgical site infection event.

| Variables                                | Total, n (%) n=1012 | SSI | P-value† |
|------------------------------------------|---------------------|-----|----------|
|                                          | Yes, n (%) n=45     | No, n (%) n=967 |
| Sex                                      |                     |     |          |
| Female                                   | 524 (51.8)          | 25  (55.6) | 499 (51.6) | 0.604 |
| Male                                     | 488 (48.2)          | 20  (44.4) | 468 (48.4) |     |
| Age (years)                              |                     |     |          |
| Median (IQR)                             | 56 (32)             | 51  (39.5) | 56 (32)  | 0.248 |
| Diagnosis                                |                     |     |          |
| Tumoral                                  | 285 (28.2)          | 15  (33.3) | 270 (27.9) | 0.115 |
| Vascular                                 | 104 (0.3)           | 9    (20)   | 95 (9.8)  |     |
| Traumatic brain injury                   | 117 (1.6)           | 2    (4.4)   | 115 (1.9) |          |
| Traumatic or degenerative spine disease  | 406 (40.1)          | 15  (33.3) | 391 (40.4) |          |
| Other                                    | 100 (9.8)           | 4    (8.9)   | 96 (9.9)  |     |
| ASA                                      |                     |     |          |
| 1                                        | 85 (8.4)            | 1    (2.2)   | 84 (8.7)  | 0.090 |
| 2                                        | 343 (33.9)          | 11   (24.4) | 332 (34.3) |     |
| 3                                        | 498 (49.2)          | 26   (57.8) | 472 (48.8) |     |
| 4                                        | 79 (7.8)            | 7    (15.6) | 72 (7.5)  |     |
| 5                                        | 7 (0.7)             | 0    (0)     | 7 (0.7)   |     |
| Previous surgery at same admission       | 43 (4.2)            | 7    (15.6) | 36 (7.3)  | <0.001* |
| Previous surgery in equal location       | 197 (19.5)          | 12   (26.7) | 185 (19.1) | 0.212 |
| History of diabetes mellitus             | 71 (7)              | 3    (6.7)   | 68 (7)    | 0.925 |
| ICU stay during hospitalization          | 549 (54.2)          | 28   (62.2) | 521 (53.9) | 0.272 |
| PHS                                      |                     |     |          |
| Mean                                     | 1.5 (3.1)           | 3.8  (5.7)  | 1.4 (2.9)  |     |
| Median (IQR)                             | 0 (1)               | 1    (7)    | 0 (1)     | 0.002* |

*P ≤ 0.05 considered statistically significant difference. †P-values are calculated from Chi-square test; Fisher’s exact; and Mann–Whitney U, as appropriate.
SSI: Surgical site infection, IQR: Interquartile range, SD: Standard deviation, ASA: American Society of Anesthesiologist classification of physical state, ICU: Intensive care unit, PHS: Preoperative hospital stay
DISCUSSION

To the best of our knowledge, this study is the first study in neurosurgery to include a quantitative analysis to describe how the PHS gradually increases the SSI risk. Herein, SSI risk factors are identified for a specific but representative fraction of neurosurgical patients, with clean wounds, without late prosthetic material exposure, and with antibiotic prophylaxis directed to community acquired flora, aiming to standardize the grade of wound contamination and antibiotic selective pressure. The time of exposure to the hospital environment before surgery is shown to be the most relevant factor for this surgical complication among the factors studied in this cohort.

Delays in surgical schedule for neurosurgical patients might be common in many environments due to the requirement of multiple specialized studies and careful planning of these procedures, even though the patient is coursing with a condition that motivated an emergency consult and are not seemingly suited for discharge. Even though systematic evaluation of the length of PHS has not been previously studied, its relevance has been implicated in different surgical specialties[7,26,32,34] and identified as

Table 2: Surgical factors and bivariate analysis according to surgical site infection.

| Variables                                      | Total, n (%) | Yes, n (%) | No, n (%) | P-value† |
|------------------------------------------------|--------------|------------|-----------|----------|
| Type of surgery                                |              |            |           |          |
| Noninstrumented spinal surgery                 | 201 (19.9)   | 4 (8.9)    | 197 (20.4)| 0.124    |
| Instrumented spinal surgery                    | 254 (25.1)   | 12 (26.7)  | 242 (25.0)|          |
| Posterior fossa and cranio-cervical junction   | 54 (5.3)     | 5 (11.1)   | 49 (5.1)  |          |
| Supratentorial surgeries excluding Groups 5 and | 272 (26.9)   | 15 (33.3)  | 257 (26.6)|          |
| Drainage of extracranial collections, skull    | 132 (13.0)   | 3 (6.7)    | 129 (13.3)|          |
| Osteoarticular reduction and decompressive     |              |            |           |          |
| craniotomies                                   | 99 (9.8)     | 6 (13.3)   | 93 (9.6)  |          |
| Operative time>2 h                             | 725 (71.6)   | 36 (80)    | 689 (71.2)| 0.203    |
| Operative time>4 h                             | 304 (30.1)   | 22 (48.9)  | 282 (29.2)| 0.005*   |
| Emergency surgery                              | 253 (25)     | 13 (28.9)  | 240 (24.8)| 0.538    |
| Antibiotic prophylaxis                          |              |            |           |          |
| Cefazolin                                       | 954 (94.3)   | 43 (95.6)  | 911 (94.2)| 0.704    |
| Cillamycin                                      | 58 (5.7)     | 2 (4.4)    | 56 (5.8)  |          |
| Antiseptic product for skin preparation         |              |            |           |          |
| Iodine soap and solution                        | 561 (55.4)   | 27 (60)    | 534 (55.2)| 0.871    |
| Chlorhexidine soap and solution                | 234 (23.1)   | 8 (17.8)   | 226 (23.4)|          |
| Iodine povacrylex 0.7% and isopropyl alcohol 74% (DuraPrep, 3M) | 208 (20.6) | 10 (22.2) | 198 (20.5) |          |
| Other                                          | 9 (.9)       | 0          | 9 (.9)    |          |
| Intraoperative transfusion                     | 153 (15.1)   | 12 (26.7)  | 141 (14.6)| 0.027*   |
| Preoperative ICU stay                          | 107 (10.6)   | 9 (20)     | 98 (10.1) | 0.035*   |
| Person who closed the wound                    |              |            |           |          |
| Medicine intern                                | 10 (0.9)     | 0 (0)      | 10 (0.9)  | 0.546    |
| Younger resident                                | 389 (38.44)  | 15 (33.3)  | 374 (38.7)|          |
| Older resident                                  | 519 (51.28)  | 28 (62.2)  | 491 (50.8)|          |
| Attending neurosurgeon                         | 94 (9.29)    | 2 (4.4)    | 92 (9.5)  |          |
| Maximum number of people in the operating room |              |            |           | 0.316    |

Table 3: Multivariate analysis of patient-related factors for surgical site infection.

| Variables                                      | Odds ratio (adjusted) | 95% confidence interval | P-value† |
|------------------------------------------------|-----------------------|-------------------------|----------|
| Operative time>4 h                             | 2.107 (1.118–3.975)   | 0.021*                  |
| Intraoperative transfusion                     | 1.398 (0.651–3.000)   | 0.390                   |
| Previous surgery at same admission             | 1.743 (0.587–5.174)   | 0.317                   |
| Preoperative ICU stay                          | 1.012 (0.527–1.943)   | 0.971                   |
| PHS                                           | 1.132 (1.051–1.218)   | 0.001*                  |

†P-values are calculated from Chi-square test; Fisher’s exact; and Mann–Whitney U, as appropriate. *P≤0.05 considered statistically significant. SSI: Surgical site infection, ICU: Intensive care unit, IQR: Interquartile range.
an increased risk factor of SSI resistant to the standard antibiotic prophylaxis\(^{[15]}\) and other types of infectious complications\(^{[39]}\). The previous studies highlight the importance of PHS in neurosurgery\(^{[8,13,19,27]}\). However, the time thresholds were reportedly chosen based on clinical expertise, rather than data driven, or only included central tendency measures. Moreover, others did not find PHS to be an independent SSI risk factor\(^{[3,11,23,33,37,38,40]}\). These divergent results could be due to variability in patient selection, prophylaxis protocols, institutional care, statistical methods, or time thresholds.

Accordingly, this study aimed to address these methodological gaps and improve the characterization of PHS to SSI risk relationship. As such, PHS, evaluated as a quantitative variable, had significant OR in relationship to SSI. However, length of PHS as a potentially large discrete variable that could be nonlinear still needs further clarification. Thus, as the binary outcome is evaluated with respect to given time frame, but also with a risk factor of variable degree of exposure, a logistic regression model was chosen over Cox proportional hazards. Moreover, considering the low incidence of infection, the relatively short follow-up period and the assumption that its relative risk could not be constant, there are no advantages from the Cox model\(^{[8]}\). As such, multiple logistic regression models including the PHS as a dichotomous variable with progressive time points, led to the cumulative risk threshold characterization, and was more informative than Cox regression or a single logistic regression model, resulting in specific cumulative day odds ratio \(\text{Graph 1}\).

By applying these methods, it became possible to show that the day of PHS-SSI OR that reaches the threshold transition is between the 5\(^{th}\) and 6\(^{th}\) days, and the PHS-SSI OR relationship was continuous and consistent with time progression. This may be particularly helpful in light of the prior mixed findings in which some found antibiotic prophylaxis effective,\(^{[5,25]}\) no benefit,\(^{[12]}\) or yielding higher risk of meningitis by prophylaxis of resistant microorganisms.\(^{[24]}\) Because the number of days patients is admitted to the hospital before surgery in many circumstances can be modified, this study’s approach was to determine at what point PHS seems to put patients at higher risk of postoperative infection. Thus, this work may inform on the explicit risk and the drop of effectiveness of the studied prophylactic antibiotic selection for patients with PHS ≥6 days, possibly associated with higher risk of complications and worse outcomes, in the context of the difficulties in isolation of bacteria from the central nervous system.\(^{[6]}\)

### Table 4: Threshold-dependent surgical site infection risk factors.

| PHS (days) | Previous surgery at same admission | Preoperative hospital stay |
|-----------|-----------------------------------|---------------------------|
|           | OR (adjusted) | 95% CI | P-value\(^{1}\) | OR (adjusted) | 95% CI | P-value\(^{1}\) |
| 1         | 3.10         | (1.16–8.29) | 0.024* \(^{2}\) | 1.71         | (0.87–3.37) | 0.123     |
| 2         | 3.26         | (1.19–8.92) | 0.022* \(^{2}\) | 1.51         | (0.75–3.07) | 0.251     |
| 3         | 2.61         | (0.94–7.24) | 0.065          | 2.12         | (1.04–4.33) | 0.039*    |
| 4         | 2.86         | (1.02–8.05) | 0.046* \(^{2}\) | 1.83         | (0.86–3.93) | 0.120     |
| 5         | 2.82         | (0.99–8.04) | 0.053          | 1.91         | (0.85–4.30) | 0.117     |
| 6         | 2.27         | (0.79–6.52) | 0.129          | 2.80         | (1.23–6.39) | 0.014*    |
| 7         | 2.17         | (0.74–6.37) | 0.159          | 4.37         | (1.89–10.11)| 0.001*    |
| 8         | 2.09         | (0.74–5.93) | 0.167          | 3.07         | (1.18–7.74) | 0.021*    |
| 9         | 2.63         | (0.94–7.37) | 0.066          | 4.03         | (1.55–10.46)| 0.004*    |
| 10        | 2.42         | (0.86–6.86) | 0.095          | 4.51         | (1.73–11.81)| 0.002*    |
| 11        | 2.35         | (0.82–6.69) | 0.111          | 6.13         | (2.28–16.45)| <0.000*   |
| 12        | 2.19         | (0.76–6.13) | 0.147          | 8.57         | (2.99–24.6) | <0.000*   |
| 13        | 1.81         | (0.59–5.54) | 0.297          | 10.70        | (3.55–32.27)| <0.000*   |
| 14        | 1.59         | (0.50–5.08) | 0.438          | 13.26        | (3.94–44.63)| <0.000*   |
| 15        | 1.68         | (0.52–5.36) | 0.386          |             |             |           |

\(^{1}\)P-value is calculated from logistic regression analysis. \(^{2}\)P ≤0.05 considered statistically significant difference. OR: Odds ratio, CI: Confidence interval, PHS: Preoperative hospital stay

**Graph 1:** OR of surgical site infection (SSI) according to preoperative hospital stay threshold. Solid bars represent \(P < 0.05\).
Operative time ≥4 h was a SSI risk factor in this study’s multivariate analysis, consistent with prior work.\textsuperscript{[12,23]} Further, this time doubled the risk of infection, despite institutional protocols reinforcement prophylactic antibiotic dosages at the ≥4 h time point, and other standard transoperative measures including preheating intraoperative infusions, and forced patient heating to maintain transoperative normothermia. Our institutional antibiotic redosing protocol recommends half the dose initially administrated, because at 4 h provides adequate antibiotic levels based on pharmacokinetic estimates.\textsuperscript{[20]}

The previous surgery during the same hospital admission also was found to be related to SSI and was significant in some of the logistic regression models. Counterintuitively, unlike the PHS-SSI relationship that increased markedly after day 5, the antecedent of surgery during the same hospital admission SSI across different time thresholds demonstrated decreasing strength with time [Graph 2]. Indeed, in all the logistic regression models, where one of these two variables showed statistical significance in relation to SSI, the other one failed to do so. This suggests that both variables are time related and participate as moderating variables of each other. However, it is still yet to be determined how they are related to explain this relationship. Even though the previous surgery during the same hospital admission was associated with higher median PHS ($P < 0.001$), it cannot be rule out that an impact from secondary surgical inflammatory responses or the administration of antibiotics for the prior intervention is causative.

As this was a retrospective cohort study of consecutively and prospectively collected clinical cases without control, the results are Level 3 evidence that PHS ≥6 days is a risk factor for PHS in those undergoing neurosurgery with clean wounds, without late prosthetic material exposure, and antibiotic prophylaxis directed to community-acquired flora, according to Oxford Centre for Evidence-Based Medicine.\textsuperscript{[22]} For nonpercutaneous clean neurosurgical interventions, alternative SSI prevention strategies than antibiotic prophylaxis with cefazolin or clindamycin are a consideration for those patients in whom reaching six or more hospital days could not be avoided (recommendation Grade B).\textsuperscript{[16]}

**Limitations**

The primary limitation of this study was the inability to guaranty the follow-up of some wound infection-related factors including radiation therapy or cerebrospinal fluid leak that has shown a higher risk of infection for neurosurgical patients.\textsuperscript{[21,24]} Furthermore, the influence of bacterial colonization risk from the nosocomial environment could not be confirmed by this study.

**Future work**

Further studies are needed to determine if similar PHS-SSI risk applies to patients receiving perioperative antibiotics other than cefazolin or clindamycin, which may cover a wider spectrum of microorganisms and were out of the scope of this work, as well as those with prolonged wound healing during the stay outside the nosocomial environment. Studies evaluating nosocomial bacterial colonization relation to PHS-SSI risk and selection of antimicrobial prophylaxis are indicated. Prospective and multicenter PHS-SSI studies would increase formal prophylaxis recommendations strengths in neurosurgery.

**CONCLUSION**

For nonpercutaneous clean neurosurgical procedures with antibacterial prophylaxis directed against community cutaneous flora, the odds of SSI gradually increase in relation with the amount of days of PHS, as pass threshold for significance at 6 or more days. Surgical time longer than 4 h and previous surgical interventions during the same hospital admission were also found as independent risk factors in our cohort of patients. Future studies are indicated for specific antibiotic prophylaxis recommendations in neurosurgery for patients with prolonged PHS.

**Declaration of patient consent**

Patient’s consent not required as patients identity is not disclosed or compromised.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.
REFERENCES

1. Abu Hamdeh S, Lytsy B, Ronne-Engström E. Surgical site infections in standard neurosurgery procedures—a study of incidence, impact and potential risk factors. Br J Neurosurg 2014;28:270-5.

2. Alotaibi AF, Hulou MM, Vestal M, Alkholfi F, Asgarzadeh M, Cote DJ, et al. The efficacy of antibacterial prophylaxis against the development of meningitis after craniotomy: A meta-analysis. World Neurosurg 2016;90:597-603.e1.

3. Apsisrathnanarak A, Jones M, Waterman BM, Carroll CM, Bernardi R, Fraser VJ. Risk factors for spinal surgical-site infections in a community hospital: A case-control study. Infect Control Hosp Epidemiol 2003;24:31-6.

4. Baraboutis IG, Tsagalou EP, Papakonstantinou I, Marangos MN, Gogos C, Skoutelas AT, et al. Length of exposure to the hospital environment is more important than antibiotic exposure in healthcare associated infections by methicillin-resistant Staphylococcus aureus: A comparative study. Braz J Infect Dis 2011;15:426-35.

5. Barker FG. Efficacy of prophylactic antibiotic therapy in spinal surgery. Br J Neurosurg 1988;69:687-91.

6. Brouwer MC, Waites GE, Tunkel AR, van de Beek D. Risk factors for adult nosocomial meningitis after craniotomy: Role of antibiotic prophylaxis. J Neurosurg 2006;59:126-33.

7. Brouwer MC, Thwaites GE, Tunkel AR, van de Beek D. Dilemmas in the diagnosis of acute community-acquired bacterial meningitis. Lancet 2012;380:1684-92.

8. Bueno A, Rodriguez R, Delgado M, Moreno O, Lopez R, Guillen J, et al. Preoperative stay as a risk factor for nosocomial infection. Eur J Epidemiol 1991;7:670-6.

9. Buffet-Bataillon S, Saunders L, Campillo-Gimenez B, Haegelen C. Risk factors for neurosurgical site infection after neurosurgery in Rennes, France: Comparison of logistic and Cox models. Am J Infect Control 2013;41:1290-2.

10. Bullock R, van Dellen JR, Kettleby W, Reinach SG. A double-blind placebo-controlled trial of perioperative prophylactic antibiotics for elective neurosurgery. J Neurosurg 1988;69:687-91.

11. Cao Y, Pu K, Li G, Yan X, Ma Y, Xue K, et al. The role of antibiotic prophylaxis in clean neurosurgery. World Neurosurg 2017;100:305-10.

12. Cassir N, De La Rosa S, Melot A, Touta A, Troude L, Louندou A, et al. Risk factors for surgical site infections after neurosurgery: A focus on the postoperative period. Am J Infect Control 2015;43:1288-91.

13. Chen CZ, Yu S, Sun F, Ruan Q. The incidence and risk factors of meningitis after major craniotomy in china: A retrospective cohort study. PLoS One 2014;9:e101961.

14. Chiang HY, Kamath AS, Pottinger JM, Greenlee JD, Howard MA, Cavanaugh JE, et al. Risk factors and outcomes associated with surgical site infections after craniotomy or craniectomy. J Neurosurg 2014;120:509-21.

15. Davies BM, Jones A, Patel HC. Surgical-site infection surveillance in cranial neurosurgery. Br J Neurosurg 2016;30:35-7.

16. Dong ZM, Chidi AP, Goswami J, Han K, Simmons RL, Rosengart MR, et al. Prior inpatient admission increases the risk of post-operative infection in hepato-biliary and pancreatic surgery. HPB (Oxford) 2015;17:1105-12.

17. Ebell MH, Siwek J, Weiss BD, Woolf SH, Susman J, Ewigman B, et al. Strength of recommendation taxonomy (SORT): A patient-centered approach to grading evidence in the medical literature. Am Fam Physician 2004;69:548-56.

18. Esposito S, Capuano A, Noviello S, Mazzeo F, Ianniello F, Filippelli A, et al. Modification of patients’ endogenous bacterial flora during hospitalization in a large teaching hospital in Naples. J Chemother 2003;15:568-73.

19. Haleem A, Chiang HY, Vodela R, Behan A, Pottinger JM, Smucker J, et al. Risk factors for surgical site infections following adult spine operations. Infect Control Hosp Epidemiol 2016;37:1458-67.

20. Holdorf NH. Pharmacokinetics and pharmacodynamics: Rational dosing and the course of drug action. In: Basic and Clinical Pharmacology. 12th ed. New York, United States: McGraw Hill; 2012. p. 37-52.

21. How and Why We Rank and Rate Hospitals. U.S. News and World Report; 2021. Available from: https://www.health.usnews.com/health-care/best-hospitals/articles/how-and-why-we-rank-and-rate-hospitals [Last accessed on 2021 Jun 22].

22. Howick J, Chalmers I, Glasziou P, Greenhalgh T, Heneghan C, Liberati A et al. OCEBM Levels of Evidence Working Group. “The Oxford Levels of Evidence 2”. Oxford Centre for Evidence-Based Medicine; 2021. Available from: https://www.cebm.ox.ac.uk/resources/levels-of-evidence/ocemb-levels-of-evidence [Last accessed on 2021 Jun 22].

23. Kimchi G, Stylianou P, Wohl A, Hadani M, Cohen ZR, Zauberman J, et al. Predicting and reducing cranioplasty infections by clinical, radiographic and operative parameters—a historical cohort study. J Clin Neurosci 2016;34:182-6.

24. Korinek AM, Baugnon T, Golmard JL, van EFFenterre R, Coriat P, Puybasset L. Risk factors for adult nosocomial meningitis after craniotomy: Role of antibiotic prophylaxis. Neurosurgery 2006;59:126-33.

25. Korinek AM, Golmard JL, Elcheick A, Bismuth R, van EFFenterre R, Coriat P, et al. Risk factors for neurosurgical site infections after craniotomy: A critical reappraisal of antibiotic prophylaxis on 4,578 patients. Br J Neurosurg 2005;19:155-62.

26. Legesse LT, Hiko GD, Hussen AS. Incidence and predictors of surgical site infection in Ethiopia: Prospective cohort. BMC Infect Dis 2017;17:119.

27. Lietard C, Thébaud V, Besson G, Lejeune B. Risk factors for surgical site infections in Ethiopia: A retrospective cohort study. BMC Infect Dis 2017;17:119.

28. Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for prevention of surgical site infection, 1999. Centers for disease control and prevention (CDC) hospital infection control practices advisory committee. Am J Infect Control 1999;27:97-132; quiz 133-4; discussion 96.

29. McCutcheon BA, Ubl DS, Babu M, Maloney P, Murphy M, Kerezoudis P, et al. Predictors of surgical site infection following craniotomy for intracranial neoplasms: An analysis of prospectively collected data in the American college of surgeons national surgical quality improvement program
30. National Healthcare Safety Network. Centers for Disease Control and Prevention. Surgical Site Infection (SSI) Event; 2017. Available from: http://www.cdc.gov/nhsn/pdfs/pscmanual/9pscscisicurrent.pdf [Last accessed on 2021 Feb 24].

31. Omeis IA, Dhir M, Sciubba DM, Gottfried ON, McGirt MJ, Attenello FJ, et al. Postoperative surgical site infections in patients undergoing spinal tumor surgery: Incidence and risk factors. Spine (Phila Pa 1976) 2011;36:1410-9.

32. Ortona L, Federico G, Fantoni M, Pallavicini F, Ricci F, Antinori A. A study on the incidence of postoperative infections and surgical sepsis in a University Hospital. Infect Control Hosp Epidemiol 1987;8:320-4.

33. Patir R, Mahapatra AK, Banerji AK. Risk factors in postoperative neurosurgical infection. A prospective study. Acta Neurochir (Wien) 1992;119:80-4.

34. Pereira HO, Rezende EM, Couto BR. Length of preoperative hospital stay: A risk factor for reducing surgical infection in femoral fracture cases. Rev Bras Ortop 2015;50:638.

35. Sanford DE, Strasberg SM, Hawkins WG, Fields RC. The impact of recent hospitalization on surgical site infection after a pancreatectomy. HPB (Oxford) 2015;17:819-23.

36. Schipmann S, Akalin E, Dooods J, Ewelt C, Stummer W, Molina ES. When the infection hits the wound: Matched case-control study in a neurosurgical patient collective including systematic literature review and risk factors analysis. World Neurosurg 2016;95:178-89.

37. Sherrod BA, Arynchyna AA, Johnston JM, Rozzelle CJ, Blount JP, Oakes WJ, et al. Risk factors for surgical site infection following non-shunt pediatric neurosurgery: A review of 9296 procedures from a national database and comparison with a single-center experience. J Neurosurg Pediatr 2017;19:407-20.

38. Shi ZH, Xu M, Wang YZ, Luo XY, Chen GQ, Wang X, et al. Post-craniotomy intracranial infection in patients with brain tumors: A retrospective analysis of 5723 consecutive patients. Br J Neurosurg 2017;31:5-9.

39. Vogel TR. In-hospital delay of elective surgery for high volume procedures: The impact on infectious complications. J Am Coll Surg 2010;211:784-90.

40. Walsh TL, Querry AM, McCool S, Galdys AL, Shutt KA, Saul MI, et al. Risk factors for surgical site infections following neurosurgical spinal fusion operations: A case control study. Infect Control Hosp Epidemiol 2017;38:340-7.

41. Wimmer C, Gluch H, Franzreb M, Ogon M. Predisposing factors for infection in spine surgery: A survey of 850 spinal procedures. J Spinal Disord 1998;11:124-8.

How to cite this article: Cediel EG, Boerwinkle VL, Ramon JF, Arias D, De la Hoz-Valle JA, Mercado JD, et al. Length of preoperative hospital stay is the dominating risk factor for surgical site infection in neurosurgery: A cohort data-driven analysis. Surg Neurol Int 2022;13:80.