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*WILEY*
Surgical Site Infection Affects Length of Stay After Complex Head and Neck Procedures

Nicole L. Lebo, MD; Alexandra E. Quimby, MD; Lisa Caulley, MD; Kednapa Thavorn, PhD; Natasha Kekre, MD; Sarah Brode, MD; Stephanie Johnson-Obaseki, MD

**Objectives/Hypothesis:** Quality improvement (QI) initiatives emphasize a need for reduction in hospital length of stay (LOS). We sought to determine the impact of surgical site infections (SSIs) on LOS after complex head and neck surgery (HNS).

**Study Design:** Retrospective cohort analysis.

**Methods:** An analysis of the American College of Surgeons National Surgical Quality Improvement Program was undertaken. All adult patients undergoing complex HNS from 2005 to 2016 were included in the analysis. Our main outcomes were SSI incidence and increase in hospital LOS attributable to SSI.

**Results:** Of 4,014 patients identified, 16.5% developed SSI. History of smoking, diabetes, preoperative wound infection, contaminated or dirty wound classes, and prolonged operative time were found to significantly predict postoperative SSI. Adjusting for potential preoperative and postoperative factors, SSI was associated with significantly increased LOS (hazard ratio = 0.486, 95% confidence interval: 0.419-0.522).

**Conclusions:** SSI following complex HNS is associated with significantly increased hospital LOS. This result supports the need for institutional QI strategies that target SSIs after head and neck procedures in an effort to provide the highest quality care at the lowest possible cost. Our analysis identifies risk factors that can allow identification of patients at high risk of SSI and prolonged hospitalization.

**Key Words:** Surgical site infection, surgical site infection, length of stay, head and neck surgery, quality improvement.

**Level of Evidence:** 2b

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INTRODUCTION

Surgical site infection (SSI), defined by the Centers for Disease Control and Prevention (CDC) as an infection related to an operative procedure that occurs at or near the surgical incision within 30 days of the procedure, is the most common nosocomial infection among surgical patients.1,2 Despite antibiotic prophylaxis, complex head and neck surgery (HNS) is associated with high rates of SSI, with an estimated incidence of 3% to 41% in the literature.3–6 Rates vary widely due to heterogeneous definitions of SSI and depending on the particular subset of patients studied.3,5 Studied risk factors for SSI in HNS include length of surgery, contamination of the neck via communication with the oral cavity, and more complex surgery, among others.7–12 The recent increased complexity of HNS cases is largely due to the implementation of free tissue transfer for reconstruction of surgical defects. This has led to an increase not only in operative times, but also in the number of exposed body sites during surgery.13

SSIs increase morbidity, but also contribute to increased hospital resource utilization, both costs per admission, readmission rates, and length of stay (LOS).14–21 To improve quality in medical care, it is important to identify sources of significant perioperative morbidity and their consequential burden on healthcare systems; this information is critical for establishing and monitoring quality improvement strategies. However, despite the emphasis that quality improvement strategies place on reducing LOS, objective data evaluating predictors of prolonged admission in HNS are largely limited to single-center studies or specific head and neck subpopulations.20,21

This study sought to analyze the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) accrued international data to evaluate factors predisposing to SSI following complex HNS, and the impact of SSI on LOS following surgery in these patients.

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Additional supporting information may be found in the online version of this article.

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MATERIALS AND METHODS

Study Population
The ACS-NSQIP is a risk-adjusted, validated, observational cohort study of patients undergoing noncardiac procedures under general, spinal, or epidural anesthesia in over 500 medical centers in the United States, and has expanded internationally to include hospitals in Canada, Lebanon, the United Kingdom, Saudi Arabia, and United Arab Emirates. Demographic, surgical, preoperative, intraoperative, and 30-day postoperative data are collected by trained clinical reviewers in accordance with a standard protocol. Routine audits of the NSQIP database are performed to ensure the accuracy of its reported data. The information contained within the ACS-NSQIP database is described in detail in the Participant Use Data File user guide. For the purpose of this study, access was granted to the ACS-NSQIP database through a contractual Data Use Agreement. All ACS-NSQIP data were stripped of personal identifiers. This information was exempted as nonhuman subject research, and thus, ethics review was not necessary for this study.

We retrospectively identified adult patients (aged >18 years) in the ACS-NSQIP database who underwent complex HNS between the years of 2005 and 2016. The authors defined complex HNS as any procedure involving free tissue transfer following mucosal or composite tissue excision in the head and neck or laryngectomy, a procedure that the authors considered complex but which commonly does not require free tissue transfer. Patients were selected for inclusion on the basis of current procedural terminology (CPT) codes. For patients undergoing laryngectomy, inclusion was based on the selection of the following CPT codes: 31360, 31365, 31368, 31390, 31395. For patients undergoing free tissue transfer, patients were included on the basis of having two linked CPT codes, one indicating head and neck mucosal or composite resection (CPT: 21034, 21044, 21045, 21047, 31230, 31255, 40814, 40816, 41116, 41120, 41130, 41135, 41140, 41145, 42120, 41150, 41153, 41155, 42845, 42894) and one indicating use of either a soft tissue, osseous, or osseocutaneous free flap (CPT: 15756, 15757, 15758, 20955, 20956, 20962, 20969, 20970).

Covariates
Data related to pertinent patient demographic variables as well as covariates determined a priori were identified and extracted from the database. Age was evaluated as a continuous variable. Operative variables included the American Society of Anesthesiologists (ASA) physical status classification, and operative time. ASA class was assessed categorically as class 1 or 2 versus class 3 or 4. No patients in the study population were classified as class 5 or 6. Operative time was stratified into a dichotomous variable, evaluated as operative time ≥490 and <490 minutes, based on the median operative time in our cohort. Clinically relevant patient comorbidities included smoking (within 1 year prior to surgery), diabetes, history of chronic obstructive pulmonary disease, congestive heart failure, hypertension requiring medication, chronic steroid use, and more than 10% loss in body weight in the last 6 months. Because postoperative complications other than SSI can have a significant impact on duration of hospitalization, data on other postoperative complications were also extracted and controlled for including pneumonia, stroke, pulmonary embolism (PE), deep vein thrombosis (DVT), and renal failure. All postoperative complications, including SSI, were treated as time-varying covariates when examining their impact on LOS.

End Points and Statistical Analyses
All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC). Statistical tests were two-tailed, with the level of significance set at .05.

Part I: Predictors of SSI. The end point of interest was the occurrence of postoperative SSI within 30 days of

| Table I. Demographic and Basic Clinical Characteristics of Case and Control Groups for Patients Developing SSI Versus Those With No SSI. |
|---|---|---|---|
| Variable | No. of Patients Without SSI (%) | No. of Patients With SSI (%) | P Value |
| No. of patients | 3,352 | 662 |  |
| Age, yr, mean ± SD | 61.6 ± 12.2 | 61.6 ± 11.1 | .9819 |
| Sex, n (%) |  |  |  |
| Female | 936 (27.9%) | 197 (29.8%) | .3401 |
| Male | 2,415 (72.1%) | 465 (70.2%) |  |
| Body mass index, kg/m², n (%) |  |  |  |
| <18.5 | 340 (10.2%) | 72 (10.9%) | .5679 |
| ≥18.5 | 2,993 (89.8%) | 586 (89.1%) |  |
| Comorbidities, n (%) |  |  |  |
| Current smoker within 1 year | 1,340 (40.0%) | 309 (46.7%) | .0014 |
| Weight loss >10% body weight in last 6 months | 381 (11.4%) | 96 (14.5%) | .0227 |
| Diabetes | 421 (12.6%) | 101 (15.3%) | .0594 |
| History severe COPD | 435 (13.0%) | 72 (10.9%) | .137 |
| Congestive heart failure in 30 days before surgery | 32 (1.0%) | 6 (0.9%) | .9066 |
| Hypertension requiring medication | 1,579 (47.1%) | 317 (47.9%) | .7137 |
| Steroid use for chronic condition | 139 (4.2%) | 32 (4.8%) | .4238 |
| Dialysis | 13 (0.4%) | 3 (0.5%) | .8074 |
| Bleeding disorder | 75 (2.2%) | 20 (3.0%) | .2255 |
| Functional status, n (%) |  |  |  |
| Dependent | 122 (3.7%) | 27 (4.1%) | .5899 |
| Independent | 3,215 (96.3%) | 633 (95.9%) |  |
| ASA class, n (%) |  |  |  |
| 1–2 | 556 (16.6%) | 85 (12.9%) | .0159 |
| 3–5 | 2,789 (83.4%) | 576 (87.1%) |  |
| Wound class, n (%) |  |  |  |
| Clean or clean–contaminated | 3,254 (97.1%) | 620 (93.7%) | <.0001 |
| Contaminated or dirty | 98 (2.9%) | 42 (6.3%) |  |
| Operative time, min, n (%) |  |  |  |
| <490 | 1,743 (52.0%) | 262 (39.6%) | <.0001 |
| ≥490 | 1,608 (48.0%) | 399 (60.4%) |  |
| Length of stay in hospital, d |  |  |  |
| Mean ± SD | 10.5 ± 7.2 | 23.8 ± 14.5 | <.0001 |
| Median | 9 | 20 |  |

ASA = American Society of Anesthesiologists; COPD = chronic obstructive pulmonary disease; SD = standard deviation; SSI = surgical site infection.
surgery. The ACS-NSQIP employs CDC definitions for wound infections, where postoperative SSI includes at least one of the following variables in the ACS-NSQIP registry: superficial SSI (above fascia), deep incisional SSI (at or below fascia), organ/space SSI, or wound dehiscence (complete or partial).

Univariable followed by multivariable log binomial regression analysis assessing relative risk (RR) of developing SSI associated with the covariates described above were conducted. Variables identified as significant ($P < .05$) in the univariate analysis, as well as those deemed clinically important a priori irrespective of statistical significance in the univariable model, were included in the multivariable model. Thirty-four patients were excluded from the model due to missing data.

Part II: Impact of SSI on LOS. The second outcome of interest examined was length of hospital stay, defined as time spent in hospital from date of operation to date of discharge alive, recorded in days.

To examine the relationship between SSI and LOS, univariable followed by multivariable Cox proportional hazards regression models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs). Adjusted HRs were compared between the two groups, that is, those with versus without SSI, to estimate the difference in LOS attributable to covariates. Hazards were defined as the hazard of discharge from the hospital. In this way, HRs are interpretable as values above 1 being associated with a significantly increased hazard of discharge from hospital, that is, a significantly decreased LOS. Hazard ratios of <1 are interpreted as significantly increased LOS. The multivariable model was constructed using clinically relevant variables as well as those identified as significant in the univariable analysis. Three hundred sixty-four patients were excluded due to missing data.

Approval and Consent
Given that the study served as a retrospective review with the purpose of auditing an existing data source, institutional ethics approval and consent were not required.

RESULTS
A total of 4,014 patients underwent complex HNS procedures and had data available for analysis. Of these patients, 662 (16.5%) experienced SSI. The demographics and baseline clinical characteristics of the patients that met study criteria are illustrated in Table I. The mean age of patients in the selected study population was 61.6 years, and 28.2% were female. The median operative time was 490 minutes (mean = 497.5, standard deviation [SD] = 201.43 minutes). Figure 1 shows the distribution of operative times in the total cohort, as well as in the two groups with operative times of <490 and $\geq 490$ minutes.

Twenty-nine (0.7%) patients died in the hospital prior to discharge.

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**TABLE II.**
Multivariate Analysis for Predictors of Development of Surgical Site Infection in Patients Undergoing Complex Head and Neck Procedures.*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Comparison</th>
<th>$P$ Value</th>
<th>RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking status</td>
<td>Yes vs. no (current smoker within 1 year)</td>
<td>.001</td>
<td>1.282</td>
<td>1.056-1.416</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Yes vs. no (diabetes mellitus requiring therapy with noninsulin agents or insulin)</td>
<td>.029</td>
<td>1.241</td>
<td>1.022-1.507</td>
</tr>
<tr>
<td>Preoperative wound infection</td>
<td>Yes vs. no (open or infected wound at time of surgery)</td>
<td>.043</td>
<td>1.360</td>
<td>1.010-1.831</td>
</tr>
<tr>
<td>Wound class</td>
<td>Contaminated/dirty vs. clean/clean-contaminated</td>
<td>&lt;.0001</td>
<td>1.753</td>
<td>1.337-2.300</td>
</tr>
<tr>
<td>Operative time</td>
<td>$\geq 490$ vs. $&lt;490$ minutes</td>
<td>&lt;.0001</td>
<td>1.5274</td>
<td>1.323-1.763</td>
</tr>
</tbody>
</table>

*Only variables reaching statistical significance are displayed. See Supplementary Table I for full details.

CI = confidence interval; RR = relative risk.
Part I: Predictors of SSI
Table II provides a summary of the RR for variables that were found to be significantly associated with increased postoperative risk of SSI. In multivariable analysis, the RR of SSI was found to be significantly increased by history of diabetes, smoking, preoperative wound infection, contaminated or dirty wound classes, and prolonged operative time (P < .05). The variable demonstrating the highest magnitude of influence on the RR for SSI was contaminated or dirty versus clean or clean–contaminated wound class (RR = 1.73, 95% CI: 1.34–2.237, P < .0001). (For full table detailing all variables assessed in multivariable analysis, see Supplementary Table I.)

Part II: Impact of SSI on LOS
Mean time from surgery to hospital discharge was 10.5 days (SD = 7.2 days) for patients without SSI. For patients with SSI, mean time to discharge was 23.8 days (SD = 14.5 days); this represented a significant increase in LOS (P < .0001) in the presence of SSI. Multivariable analysis of factors affecting time to discharge alive indicated SSI was associated with a significantly decreased hazard of discharge from the hospital (HR = 0.486, 95% CI: 0.431–0.547, P < .0001), indicating that SSI significantly increased LOS after controlling for covariates. Multivariable analysis results are summarized in Table III. Figure 1 demonstrates the cumulative probability of discharge, comparing SSI and no-SSI groups. The magnitude of this association between SSI and increased LOS was surpassed only by that of postoperative stroke with neurologic deficit (HR for hospital discharge = 0.416, 95% CI: 0.192–0.903, P = .0266). Multivariable analysis also identified patient characteristics including increasing age, smoking, and functional dependence as significant risk factors for prolonged LOS. The presence of a preoperative wound infection was also found to significantly increase LOS, as was increased operative time. A number of other postoperative complications also significantly increased LOS, namely, occurrence of pneumonia, PE, DVT, failure to wean from a ventilator, stroke with neurologic deficit, need for peri- or postoperative transfusion, and sepsis. (For full table detailing all variables assessed in multivariable Cox proportional hazards analysis, see Supplementary Table II.)

DISCUSSION
In this ACS-NSQIP analysis of 4,014 patients undergoing complex HNS, we demonstrated a significant impact of SSI on LOS following surgery. SSI occurred in 16.5% of this patient cohort, which falls within the range cited in current literature. To give context to the interpretation of this analysis of the impact of SSI on LOS, regression analysis of predictors of SSI in this cohort was performed. Variables identified as significant predictors of the occurrence of SSI in our population, namely, longer operative time, wound class, and smoking history, are all consistent as risk factors previously recognized in head and neck surgical literature. These variables identified as significant risk factors for SSI in multivariable analysis create potential targets for future quality improvement initiatives with the ultimate goal of reducing SSI incidence and resultant postoperative LOS. More specific predictors of increased operative time, for example, advanced tumor stage, increased reconstructive complexity, may also be targets of future analyses examining predictors of SSI in this patient population.

The main focus of this study was to examine the impact of SSI on duration of hospital admission. Multivariable analysis found SSI to be significantly associated with increased LOS, with a mean increase in...
postoperative LOS of 13.3 days. Though estimation of hospital costs was beyond the scope of our data source for the present study, a crude estimate of hospital costs attributed to SSI may be obtained by multiplying the number of SSI patients identified in our cohort by the incremental hospital cost attributed to SSI (US$22,001) obtained from a recent study that used data derived from the National Readmissions Database to estimate outcomes and hospital costs attributed to SSI in head and neck surgery. After adjusting for inflation to reflect the 2019 US dollar, as per the inflation calculator of the Bureau of Labor Statistics, and using a bootstrapping method to derive 95% CIs to reflect the uncertainty of the impact of SSI on cost, the estimated total hospital cost of SSI in our cohort would be US$14,564,662 (95% CI: $14,434,927-$14,693,934). This amount is consistent with a 2008 prospective study from a French center, which studied 261 patients undergoing head and neck oncologic surgery. In their cohort, SSI was associated with an average increase in LOS of 16 days, which carried an increased cost of €17,434 in 2005 (findings comparable to those of the current study after taking into account the average euro inflation rate from 2005–2019, and the average euro-to-US dollar exchange rate in 2019). Some variations in LOS between institutions may be due to institutional policy and culture, as well as surgeon preference. As the present study includes data collected from many institutions, it likely provides a more generalizable average value of the increased LOS in patients with SSI. Regardless, it stands to reason that the increase in LOS as a result in SSI is associated with increased hospital costs. This should provide yet another motivation for efforts to curtail SSI rates.

The limitations of this study include those of information bias, and unmeasured and residual confounding. Information bias is mitigated in part by the level of training and clinical experience required of ASC-NSQIP data collectors. Confounding is an issue in the present study by virtue of the complex association between intrinsic patient characteristics—some unmeasured and others incompletely controlled for—and postoperative complications. Multivariable analyses were used to reduce confounding by measured variables. However, several potential confounders of our analysis could not be controlled for due to lack of availability or robust reporting with the NSQIP database; particularly, data on perioperative antibiotic prophylaxis, previous radiation therapy, postoperative wound therapy, and patient alcohol use were not available. These variables are recognized in the literature as influencing SSI occurrence. This limitation is inherent in the use of the ACS-NSQIP database to answer this clinical question. A broad definition of SSI was used in an effort to capture all possible SSIs, which included cases recorded as wound breakdown in the ACS-NSQIP database. This description is expected to capture cases of postoperative fistula formation, which some argue does not constitute a true SSI, although such tracts are typically infected. It is important to note that risk factors associated with the development of postoperative fistula likely differ from those predisposing to development of typical SSI; however, some overlap may exist.

Operative closure type, for example, (e.g., free tissue transfer vs. primary closure for laryngectomy defects) is likely to impact the risk of fistula formation. However, this and other risk factors for fistula formation could not be evaluated in the present study due to the limitation of our data source and its definition of SSI. This choice of definition will limit comparability to other studies, which exclude fistula formation from SSI analysis. In addition, we sought to examine SSI within the population of complex HNS, defined as procedures involving either free tissue transfer or laryngectomy. Use of this definition may limit comparability of these results to certain other studies in the literature that examine SSI in either more narrow or more broad HNS populations, for example, those that include patients undergoing local or regional tissue transfer.

The main strength of this study lies in our data source. Data collection from a multi-institutional international database with strict inclusion criteria lends strength to our results and increases external validity. There is near-complete follow-up in ASC-NSQIP data with little to no loss to follow-up for 30-day complications. Furthermore, the high level of training and strict criteria for data collectors results in minimal misclassification of data.

CONCLUSION

In this risk-adjusted multivariable analysis, SSI was found to be associated with significantly increased duration of hospital stay following complex head and neck surgery. These results support the need for quality improvement strategies that target SSIs after head and neck procedures in an effort to provide the highest quality care at the lowest possible cost. This analysis identifies risk factors that can allow identification of patients at high risk of SSI and prolonged hospitalization, allowing surgeons to flag these individuals for closer monitoring while in the hospital, focus quality improvement programs, and make efforts to involve patients, families, and allied health professionals to target timely discharge.

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