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Operative duration and risk of surgical site infection in neurosurgery

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ABSTRACT

Background. The association of surgical duration with the risk of surgical site infection (SSI) has not been quantified in neurosurgery. We investigated the association of operative duration in neurosurgical procedures with the incidence of SSI.

Methods. We performed a retrospective cohort study involving patients who underwent neurosurgical procedures from 2005-2012 and were registered in the ACS National Quality Improvement Project (NSQIP) registry. In order to control for confounding, we used multivariable regression models, and propensity score conditioning.

Results. During the study period there were 94,744 patients who underwent a neurosurgical procedure and met the inclusion criteria. Of these, 4.1% developed a postoperative SSI within 30 days. Multivariable logistic regression demonstrated an association between longer operative duration with higher incidence of SSI (OR, 1.18; 95% CI, 1.16-1.20). Compared with procedures of moderate duration (third quintile, 40-60th percentile), patients undergoing the longest procedures (>80th percentile) had higher odds (OR, 2.07; 95% CI, 1.86-2.31) of developing SSI. The shortest procedures (<20th percentile) were associated with decreased incidence of SSI (OR, 0.72; 95% CI, 0.61-0.83) in comparison to those of moderate duration. The same associations were present in propensity score adjusted models, and models stratified by subgroups of cranial, spinal, peripheral nerve, and carotid procedures.

Conclusions. In a cohort of patients from a national prospective surgical registry, longer operative duration was associated with increased incidence of SSI for neurosurgical
procedures. These results can be used by neurosurgeons to inform operative management, and to stratify patients with regard to SSI risk.

**Key words:** surgical site infection; operative duration; neurosurgery; NSQIP
INTRODUCTION

Surgical site infections (SSI) are common and potentially lethal complications of all surgical procedures. In neurosurgery, their rates vary and have ranged from 1% to 8% for cranial procedures, and 0.5% to 18.8% for spine interventions. SSI can result in higher morbidity and mortality, prolonged length of stay, increased readmission rate, and higher healthcare expenditures. Accordingly, minimizing SSI has been a central goal of payers, policy-makers, providers, and patients. Several investigators have identified contributing risk factors and have devised predictive models of this complication. Most drivers of SSI are not easily modifiable. Prolonged operative duration has been identified as a potentially modifiable driver of SSI in general surgery patients. However, the relationship between operative duration and SSI has not been quantified previously in neurosurgery. Quantifying this association could guide the decision to proceed with longer or combined procedures, or conversely, inform the utility of technique advancements that shorten the duration of operations.

Several prior investigations have recognized that prolonged operations are associated with a higher incidence of SSI in multiple surgical subspecialties. Studies of SSI risk factors in neurosurgical patients were not specifically designed to study or quantify the relationship of infection and operative duration. In addition, some of them have been retrospective analyses of single institution experiences, demonstrating results with limited generalization given their inherent selection bias. There has been no prior national study quantifying the magnitude of the effect of prolonged operative duration on SSI for a wide range of neurosurgical procedures.
The American College of Surgeons’ National Quality Improvement Program (NSQIP) database contains prospectively collected data from more than 180 private and academic hospitals across the country. It allows for the unrestricted study of the patient population in question, through high quality and reliable data sets. Using this registry, we employed multivariable regression models, and propensity score conditioning to quantify the association of operative duration with SSI. We additionally utilized a battery of approaches to test the sensitivity of our conclusions.
METHODS

National Surgical Quality Improvement Program (NSQIP) Database

All patients undergoing neurosurgical procedures in the American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP) Database between 2005 and 2012 were included in the analysis. The ACS-NSQIP prospectively collects data on over 200 variables pertaining to patient characteristics, co-morbid conditions, operative details, and 30-day postoperative outcomes for a variety of surgical procedures. The latest inter-rater reliability audit for participating sites has revealed an overall disagreement rate of 1.99%. More information about ACS NSQIP, including diagnostic criteria for the risk factors included in this analysis, is available at http://www.acsnsqip.org.

Cohort Definition

In order to establish a cohort of patients undergoing neurosurgical procedures, we used CPT (Current Procedural Terminology) codes (Table S1) to identify such patients in the registry between 2005 and 2012.

Outcome variables
The primary outcome was any SSI in the first 30-days postoperatively. This was defined as an episode of superficial, or deep SSI in this time period. Deep SSI was defined as an infection that involves deep soft tissues (e.g., fascial and muscle layers) or the operated organ, appears to be related to the operation, and occurs within 30 days postoperatively. It has at least one of the following: purulent drainage, dehiscence, or abscess.

**Exposure variables**

Total operative duration was the primary exposure variable. This was measured in minutes. For ease of interpretation the unit of measurement for this variable was transformed to hours in some of the analyses.

**Covariates**

Age and BMI were defined as continuous variables. Five race categories (Asian/Pacific Islander, Black/African American, Native American/Alaska Native, White/Caucasian, and Other/Unknown) and 2 ethnicity categories (Hispanic, not Hispanic) were defined. We additionally created 9 categories for types of anesthesia (General, MAC, Regional, Spinal, Epidural, Local, None, Other, and Unknown), and 4 categories for the functional status of the patients (Independent, Partially dependent, Totally dependent, and Unknown), at baseline and peri-operatively. The patients’ American Society of Anesthesiology (ASA) was treated as a binary variable with values
greater than or equal to 3 considered a high ASA score. The logarithm of the total relative value units (RVUs) in every operation was used as a surrogate for the complexity of the procedure.

Comorbidities, for which outcomes were adjusted (Table S2), included: current smoking, chronic obstructive pulmonary disease (COPD), peripheral vascular disease (PVD), history of MI, angina, TIA, stroke with and without residual symptoms, congestive heart failure, alcohol consumption, prior coronary angioplasty, major cardiac surgery, diabetes mellitus, immunocompromise, coagulopathy, pre-operative ventilator dependence, and dialysis.

Statistical analysis

To investigate the association of 30-day risk of SSI and operative duration we used several methods to address confounding. Initially we used a multivariable logistic regression controlling for all the covariates mentioned above. Subsequently, we repeated this analysis substituting operative duration with 5 indicator variables (representing the quintiles of operative duration) of increasingly longer operative duration (the 3rd quintile was used as the reference variable).

In an alternate way to control for confounding we employed a propensity score adjusted logistic regression model. Operative duration was transformed to a binary variable, which received a value of 1 when patients had longer operative durations than the average value. To derive the propensity of having a “longer than average” operative duration we developed a prediction model using logistic regression based on all the
covariates described above. We subsequently employed a logistic regression with
adjustment (stratification) by quantiles (we chose the number of quantiles to be 20) of the
propensity score.

As part of the sensitivity analysis, we examined these associations using a Poisson
regression to calculate risk ratios. We additionally repeated the above analyses
considering deep and superficial SSI as independent outcomes. We also investigated the
association of operative duration and 30-day SSI in pre-specified subgroups of cranial,
spinal, carotid, and peripheral nerve procedures. Missing values were imputed, using
multiple imputation methods (5 imputed datasets), and the analyses were repeated. Our
results were remarkably robust in the latter sensitivity analysis, and therefore only the
complete case analysis is presented further. Additionally, we controlled for prior
chemotherapy, repeat surgery, steroid use 30-days prior to the procedure, posterior
approach to the spine, and spinal fusion. The observed associations were identical to the
initial analyses, and therefore these results are not reported further. Lastly, we performed
specific analyses of the most common procedures in every subgroup (carotid
endarterectomy, craniotomy for metastasis resection, lumbar laminectomy, and carpal
tunnel release). The relationship between operative time and risk of infection was
identical to the broader groups, and these results are not reported further.

Regression diagnostics were performed for all analyses. Given that the
distribution of the operative duration had a mean of 206.9 minutes and a standard
deviation of 113.2 minutes, we had an 80% power to detect a difference in SSI as small
as 0.9%, at an \( \alpha \)-level of 0.05. All probability values were the result of two sided tests.
Stata version 13 (StataCorp, College Station, TX) was used for statistical analysis.
RESULTS

Patient characteristics

From 2005-2012, there were 94,744 patients who underwent neurosurgical procedures (mean age 62.9 years, 45.5% female), and met the inclusion criteria for the study. The respective distribution of exposure variables across quintiles of operative duration can be found in Table S3.

30-day SSI and operative duration

Overall, 3,884.5 (4.1%) patients developed SSI within 30 days postoperatively. As demonstrated in Table 1, increasing operative duration was associated with higher incidence of SSI (OR, 1.22; 95% CI, 1.21-1.23) 30 days postoperatively in the unadjusted analysis. Similarly, adjusting for confounders with a multivariable logistic regression model (Table 1) demonstrated that every additional hour of anesthesia was associated with a 1.18 times higher odds of SSI (95% CI, 1.16-1.20) in the first 30 days postoperatively. This association persisted after propensity score adjustment, with patients undergoing operations longer than average having 1.56 higher odds of SSI (95% CI, 1.45-1.68) 30 days postoperatively. Our regressions demonstrated a linear relationship and therefore there is no specific cutoff time below which infection risk is minimal.

Additionally, in a multivariable setting (Table 2), relative to the third quintile of operative duration the shortest procedures were associated with decreased incidence of
30-day SSI (OR, 0.72; 95% CI, 0.61-0.83). The same was true for the second shortest quintile of operative duration (OR, 0.82; 95% CI, 0.73-0.93), albeit with a larger point estimate. The fourth (OR, 1.16; 95% CI, 1.04-1.30) and the longest quintile (OR, 2.07; 95% CI, 1.86-2.31) of operative duration were associated with an increasing incidence of 30-day SSI in comparison to the third quintile.

**Sensitivity analyses**

Similar associations (Table 1) of operative duration and incidence of superficial (OR, 1.21; 95% CI, 1.18-1.26) and deep (OR, 1.22; 95% CI, 1.19-1.25) SSI were observed individually. Our results were robust when repeating the analysis in the predefined categories of cranial (OR, 1.08; 95% CI, 1.04-1.11), spinal (OR, 1.16; 95% CI, 1.13-1.18), peripheral nerve (OR, 1.24; 95% CI, 1.03-1.51), and carotid (OR, 1.20; 95% CI, 1.15-1.26) procedures.
DISCUSSION

In a cohort of patients from a national prospective surgery registry, increased operative duration was associated with a higher incidence of 30-day postoperative SSI for neurosurgical interventions. This was consistently observed among all pre-specified subgroups of cranial, spinal, peripheral nerve, and carotid procedures. The results were remarkably robust across techniques to control for confounding. The association of operative duration with increased risk of SSI can be explained by multiple factors. Longer surgery might lead to more bacteria accessing the wound through multiple routes, including airborne spread, surgical tools, and the patient’s skin. In addition, prolonged retraction might lead to decreased local perfusion and altered immunologic responses. SSI is the most common nosocomial infection among surgical patients, constituting 38% of all such infections in the US. Given the economic and health costs associated with SSI, quantifying the relationship between SSI and operative parameters is of prime importance to policy makers, perioperative care physicians, surgeons, and anesthesiologists.

Prior investigations across multiple specialties have demonstrated that increasing operative duration is associated with a higher rate of SSI. However, the majority of such studies did not quantify this relationship or were not designed to specifically test this hypothesis. Procter et al addressed these limitations and quantified the relationship between operative duration and SSI for general surgery patients. Prior investigations in neurosurgery have failed to directly address this question. Bekelis et al used national level data to develop predictive models of the 30-day risk of SSI for
several neurosurgical interventions. However, the creation of these tools was based on preoperative patient characteristics, and did not take into account operative duration as a covariate. Other single center retrospective studies examined factors contributing to SSI, but did not quantify the relationship of SSI with operative duration. Golebiowski et al, in a retrospective analysis of a cohort from a Norwegian hospital, demonstrated that increased operative duration was associated with a higher rate of postoperative complications for patients undergoing craniotomy for tumor. The results of this study do not necessarily reflect the realities of North America and are of limited generalization, given their focus on a single center. The study was limited to cranial neurosurgical procedures, while our data captures the full spectrum of neurosurgical interventions including spine, peripheral nerve, and carotid procedures in addition to cranial procedures. Lastly, the authors failed to utilize advanced techniques to control for confounding.

Our study purposefully addresses many of these methodologic shortcomings. First, we utilized data from a multi-institution national surgical registry, in an effort to minimize selection bias associated with single center investigations. Second, by quantifying the relationship of SSI and operative duration in a neurosurgery specific cohort, our analysis allows the more accurate postoperative assessment of SSI risk in this population. Third, our analysis takes into account the functional status of the patients and it additionally quantifies the impact of surgical duration on SSI for specific procedure subgroups, giving a clinically meaningful picture of this relationship. Fourth, we used advanced observational techniques to control for confounding. Results were consistent across models, supporting the validity of the observed associations. Fifth, the
development of surgical duration quintiles presents an intuitive approach through which surgeons can adjust their SSI risk assessment.

The present study has several limitations. First, as an observational retrospective study there is still a possibility of residual confounding. We used multiple techniques to account for confounders yielding consistent results. In addition, the use of a registry allowed us to accurately control for comorbidities, and the functional status of our patients. These were recorded prospectively by trained personnel, and were not inferred from retrospective claims records designed for billing purposes. The latter is a major limitation of administrative databases and is adequately addressed by this registry analysis. Moreover, NSQIP exhibits a particularly low rate of inter-observer disagreement. Second, NSQIP provides the incidence of SSI only within 30 days postoperatively, and doesn't give information on complication rates over longer periods of time.

Third, the hospitals participating were not a random sample from the United States but were rather motivated to improve the quality of surgical care, although individual surgeons are unaware of the inclusion of their patients in the NSQIP database preoperatively. Hospitals participating in NSQIP are expected to be larger and more likely to have an academic affiliation than the average US hospital. However, the hospitals included were still diverse with respect to size, region, and academic status, supporting the generalizability of our findings. In addition, the current analysis contains the largest cohort of NSQIP neurosurgery patients investigated to date. Fourth, although NSQIP has the highest granularity among the nationally available surgical datasets, it does not include data on specific pathogens related to infections, and therefore we could
not analyze the association of operative time and specific pathogens. Lastly, causal inference is hard to establish based on observational data, even when using advanced methods to control for confounding.

Conclusions

The association of operative duration with the risk of SSI has not been quantified before in neurosurgery. In a cohort of patients from a national quality improvement registry, increased operative duration was associated with higher incidence of SSI. Our results were remarkably robust with the use of several techniques to control for confounding. These results can be used by neurosurgeons to plan operative management, and to stratify their patients on SSI risk.
REFERENCES

25. Surgical Care Improvement Project: in, Vol 2008
Table 1. Correlation of operative time\* with the incidence of SSI in the first 30 days postoperatively

<table>
<thead>
<tr>
<th>Models</th>
<th>All</th>
<th>30-day SSI</th>
<th>OR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crude</td>
<td>1.22 (1.21-1.23)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multivariable regression</td>
<td>1.18 (1.16-1.20)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Propensity score adjustment*</td>
<td>1.56 (1.45-1.68)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>RR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poisson regression</td>
<td>1.17 (1.14-1.19)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Subgroups</th>
<th>Cranial procedures</th>
<th>Multivariable regression</th>
<th>1.08 (1.04-1.11)</th>
<th>&lt;0.001</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spinal procedures</td>
<td>Multivariable regression</td>
<td>1.16 (1.13-1.18)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Peripheral nerve procedures</td>
<td>Multivariable regression</td>
<td>1.24 (1.03-1.51)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Carotid procedures</td>
<td>Multivariable regression</td>
<td>1.20 (1.15-1.26)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Superficial SSI</td>
<td>Multivariable regression</td>
<td>1.21 (1.18-1.26)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Deep SSI</td>
<td>Multivariable regression</td>
<td>1.22 (1.19-1.25)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

OR: Odds Ratio; 95% CI: 95% Confidence Interval; SSI: Surgical Site Infection
\*Quintiles of operative time
*Dependent variable was binary and took the value of 1 when it was longer than the average operative time. Propensity score calculation was based on age, gender, race, functional status preoperatively and postoperatively, American Society of Anesthesiology (ASA) score higher than 3, logarithm of the total relative value units (RVUs), and all available comorbidities
\$Analyses based on logistic regression §Analyzed based on a Poisson regression
Table 2. Correlation of operative time with the incidence of SSI in the first 30 days postoperatively

<table>
<thead>
<tr>
<th>Quintiles of operative time</th>
<th>30-day SSI*</th>
<th>OR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 130 minutes</td>
<td>0.72</td>
<td>(0.61-0.83)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>130 to 163 minutes</td>
<td>0.82</td>
<td>(0.73-0.93)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>164 to 201 minutes</td>
<td>1.00</td>
<td>(Reference)</td>
<td></td>
</tr>
<tr>
<td>202 to 265 minutes</td>
<td>1.16</td>
<td>(1.04-1.30)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Over 265 minutes</td>
<td>2.07</td>
<td>(1.86-2.31)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

OR: Odds Ratio; 95% CI: 95% Confidence Interval; SSI: Surgical Site Infection
¶Calculated in hours
*Analyses based on logistic regression. Adjusted for age, gender, race, functional status at baseline and peri-operatively, American Society of Anesthesiology (ASA) score greater than or equal to 3, logarithm of the total relative value units (RVUs), and all available comorbidities
Highlights

1. The association of operative duration with the risk of SSI has not been quantified before in neurosurgery.

2. In a cohort of patients from a national quality improvement registry, increased operative duration was associated with higher incidence of SSI.

3. Our results were remarkably robust with the use of several techniques to control for confounding.

4. These results can be used by neurosurgeons to plan operative management, and to stratify their patients on SSI risk.
Abbreviations

SSI: Surgical Site Infection
NSQIP: National Quality Improvement Project
ACS: American College of Surgeons
ASA: American Society of Anesthesiology
RVU: Relative Value Units
COPD: Chronic Obstructive Pulmonary Disease
PVD: Peripheral Vascular Disease
Disclosures: The authors have no conflicts of interest to disclose