Intraoperative Fraction of Inspired Oxygen Is a Modifiable Risk Factor for Surgical Site Infection after Spinal Surgery


Background: Surgical site infections (SSI) after spinal surgery increase morbidity, mortality, length of hospital stay, and costs. Most previously identified risk factors for these infections, such as severity of illness and procedure duration, are not amenable to intervention. This study sought to identify modifiable risk factors associated with SSI after spinal surgery.

Methods: This is a case-control study including case identification and review of medical records. A total of 104 patients with SSI after spinal surgery were compared to 104 randomly selected control patients without SSI after spinal surgery in a 926-bed tertiary care hospital in Baltimore, Maryland, between April 1, 2001 and December 31, 2004.

Results: Multivariate analysis identified independent risk factors for SSI after spinal surgery including prolonged procedure duration (odds ratio [OR], 4.7; 95% confidence interval [95% CI], 1.6–14; P < 0.001), American Society of Anesthesiologists score of 3 or greater (OR, 9.7; 95% CI, 3.7–25; P < 0.001), lumbar-sacral operative level (OR, 2.9; 95% CI, 1.2–7.1; P = 0.02), posterior approach (OR, 3.5; 95% CI, 1.2–9.7; P = 0.02), instrumentation (OR, 2.5; 95% CI, 1.1–6.0; P = 0.03), obesity (OR, 4.0; 95% CI, 1.6–10; P < 0.01), razor shaving before surgery (OR, 3.6; 95% CI, 1.2–11; P = 0.02), and intraoperative administration of fraction of inspired oxygen of less than 50% (OR, 12; 95% CI, 4.5–33; P < 0.001).

Conclusions: In addition to previously reported risk factors, this study identified intraoperative administration of fraction of inspired oxygen of less than 50% as an independent, modifiable risk factor for SSI after spinal surgery. Intraoperative administration of at least 50% fraction of inspired oxygen should be tested prospectively as an intervention to prevent SSI after spinal surgery.

SURGICAL site infections (SSI) are the second most common cause of healthcare-associated infection in the United States,1 and they lead to increased morbidity, mortality, length of hospital stay, and healthcare costs.2–4 Overall, patients who develop SSI are twice as likely to die and 60% more likely to spend time in the intensive care unit.2 The Centers for Disease Control and Prevention (CDC) National Healthcare Safety Network (formerly the National Nosocomial Infection Surveillance system) reports rates of between 0.72 and 4.1 SSI per 100 laminectomy or spinal fusion procedures.3 SSI after laminectomy or spinal fusion has been found to prolong total hospital stay by a median of 2 weeks per patient and increase healthcare costs more than 300%.6 These infections can lead to significant morbidity, readmission to the hospital, and additional surgeries, sometimes requiring the removal of implanted spinal hardware.7–9

The National Healthcare Safety Network risk index, a composite score calculated from the American Society of Anesthesiologists (ASA) score, duration of surgery, and wound class, is predictive of SSI for a variety of surgeries, including laminectomy and spinal fusion.10 However, compared with other surgical procedures, relatively little is known about specific risk factors for SSI after spinal surgery. Especially lacking is knowledge of risk factors that are modifiable or amenable to intervention. Previous studies have identified a range of potential risk factors, including postoperative incontinence, previous spinal surgery, tumor resection, dural tear with use of glue, surgical level, use of morphine nerve paste, posterior operative approach, instrumentation, obesity, and duration of the procedure. However, these studies include relatively small numbers of patients, there is little agreement among results, and most identified risk factors are not amenable to intervention but rather reflect the patient’s underlying severity of illness or the complexity of the required surgical intervention.3,4,8,11–18

Studies of other types of surgical procedures suggest that modifiable risk factors including the fraction of administered oxygen, glucose control, and maintenance of patients’ normothermia are associated with SSI.19–27 Two recent studies found that diabetes or elevated perioperative glucose levels were associated with SSI after spinal surgery.17,18 To our knowledge, no published studies have examined the role of maintenance of normothermia or fraction of administered oxygen as risk factors for SSI after spinal surgery.

We performed a retrospective case control study to investigate whether modifiable risk factors such as glucose control, intraoperative temperature regulation, and intraoperative oxygenation are significantly associated with SSI after spinal surgery so that interventions might be designed to reduce the risk of these infections.19–25

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Materials and Methods

Setting
The Johns Hopkins Hospital is a 926-bed tertiary care university-affiliated medical center in Baltimore, Maryland. Surgeons in the Departments of Neurosurgery and Orthopedics perform approximately 1,100 laminectomy and spinal fusion procedures each year. Since April 2001, trained infection control practitioners in the Department of Hospital Epidemiology and Infection Control have conducted active SSI surveillance by reviewing the medical records of all patients after laminectomy and spinal fusion procedures and using CDC definitions for SSI. Quarterly SSI rates are calculated by dividing the number of SSIs by the number of procedures performed and are compared to national benchmark rates from the National Healthcare Safety Network.

Case-Control Study
The population of patients who had laminectomy, spinal fusion, or both performed during the study period was identified by query of the hospital administrative database for International Classification of Diseases, Ninth Revision, Clinical Modification procedure codes for laminectomy (03.02 and 03.09), discectomy (80.50 and 80.51), or spinal arthrodesis (81.00 to 81.09). Case patients were defined as any patient aged 18 yr or older who met the CDC National Healthcare Safety Network criteria for SSI after spinal surgery performed between April 1, 2001 and December 31, 2004. Case patients were identified by infection control practitioners during routine SSI surveillance, which consists of review of the medical records of all patients at least 90 days after a laminectomy or spinal fusion procedure, as defined by the procedure codes listed above. CDC definitions of nosocomial SSI require the following criteria. For superficial incisional SSI, the infection must involve skin and/or subcutaneous tissue, occur within 30 days after the operative procedure, and have at least one of the following: purulent drainage from the incision, organisms isolated from an aseptic culture of the incisional fluid or tissue, an incision that is deliberately opened by the surgeon when the patient has signs or symptoms of infection such as pain, erythema, or edema (unless the culture is negative), or the diagnosis of a superficial incisional SSI made by the surgeon or attending physician. Deep incisional SSI must involve muscle or fascia, occur within 30 days after the operative procedure, and have at least one of the following: purulent drainage from the incision, organisms isolated from an aseptic culture of the incisional fluid or tissue, an incision that is deliberately opened by the surgeon when the patient has signs or symptoms of infection such as pain, erythema, or edema (unless the culture is negative), or the diagnosis of a superficial incisional SSI made by the surgeon or attending physician. Organ Space SSI is defined as infection involving any organ or organ space opened or manipulated during the procedure, occurring within 30 days after the operative procedure if there is no implant and within 1 yr if an implant is in place, and with at least one of the following: purulent drainage from a drain placed in the organ space, organisms isolated from an aseptic culture of the organ space fluid or tissue, an abscess in the organ space, or the diagnosis of an organ space SSI made by the surgeon or attending physician.

Patients with superficial, deep or organ space infections were included in the study. Patients with evidence of infection noted at the time of their first spinal surgery at our institution were excluded from the study. Controls were randomly selected from the list of patients without SSI who underwent spinal surgery during the study period. Proportion matching by year was employed to ensure that similar percentages of cases and controls had spinal surgery in each year of the study to control for unmeasured changes in practice, personnel, or environment during the study period. The ratio of controls to cases was 1:1. Cases and controls were not matched on any criteria.

Data were collected from the medical record and recorded on a standardized data collection form. Demographic data included age, gender, and race. Data regarding the patients’ medical history and severity of illness included tobacco use, preoperative albumin, Karnofsky performance scale, McCabe disease severity score, history of diabetes, hypertension, human immunodeficiency virus, malignancy, pulmonary disease (including both obstructive and restrictive lung disease), renal disease (including both end-stage renal disease requiring hemodialysis and chronic renal insufficiency), or cardiac disease (defined as clinical history of cardiac arrhythmia, myocardial infarction, heart failure, valvular abnormalities, or significant cardiac atherosclerotic disease), previous spinal surgery, recent trauma, chemotherapy, or radiation, obesity (defined as obesity noted in the medical record), preoperative paralysis, spinal cord compression, preoperative urinary tract infection, and ASA score. Operative risk factor data included perioperative steroids, perioperative blood transfusion, perioperative incontinence, perioperative glucose, urgency of surgery, surgical service, skin antisepsis, hair removal, operative approach, prophylactic antimicrobial administration, spinal level of surgery, instrumentation, duration of procedure, estimated blood loss, dural tear, dural patch with glue, lowest intraoperative temperature, lowest intraoperative oxygen saturation, intraoperative fraction of inspired oxygen (Fio2) administered for the longest time during surgery, intraoperative fraction of inspired nitrous oxide administered for the longest time during surgery, intraoperative average fluid infusion rate (defined as the sum of all intraoperative infused fluids and blood products minus estimated blood loss and urine.
output divided by the procedure duration), postoperative cerebrospinal fluid leak, and postoperative drains.

The Institutional Review Board at The Johns Hopkins University approved the study and granted a Health Insurance Portability and Accountability Act waiver of informed consent.

### Statistical Analysis

Fisher exact test and the chi-square test were employed to calculate odds ratios, 95% confidence intervals, and P values. We used the Wilcoxon rank sum test to compare group medians. With α = 0.05, the study had 90% or higher power to detect an absolute difference of 20% or higher between controls and cases, assuming a control proportion of 0.10. Missing values were handled by the listwise deletion method by disregarding observations with one or more missing values for the relevant variables in each analysis. All variables with P < 0.10 on univariate analysis were eligible for inclusion in the multivariable model. Variables with cells of fewer than 10 patients were not included or reported since the effect of these variables could not be accurately estimated. When multiple variables were available to assess the same construct (e.g., we measured severity of illness with several variables, including ASA score, number of comorbidities, McCabe score, and Karnofsky score), only one of these was included in the multivariable model. Once a final list of variables was constructed, stepwise, forward logistic regression was performed with thresholds of P < 0.10 and P < 0.05 to examine the relationship betweenSSI and potential risk factors. Interaction terms were used to assess for effect modification. Variance inflation factors were used to assess for evidence of collinearity. The final multivariate model was tested for goodness of fit with the Hosmer and Lemeshow test. All tests were two-tailed. All statistical analyses were performed with Stata software (version 8; StataCorp, College Station, TX).

### Results

During the study period, 3,894 laminectomy and spinal fusion procedures were performed at our institution. One hundred four patients developed SSI, for an overall infection rate of 2.67 per 100 procedures. Fifty-three (51%) of the infections were classified as deep incisional, 10 (10%) as organ space, and 41 (39%) as superficial. Missing data for study patients included race (n = 8); StataCorp, College Station, TX).

Multivariate analysis identified independent risk factors for SSI, including duration of procedure greater than the 75th percentile, instrument, lumbar-sacral level of surgery, posterior approach, dural tear, postoperative cerebrospinal fluid leak, and perioperative blood transfusion (table 1). Intraoperative administration of a FIO2 less than 50% for the majority of time during the procedure and exposure to razor shaving before surgery were also significantly associated with developing SSI. The distribution of intraoperative administered FIO2 among case and control patients is depicted in figure 1. Medical records did not contain any notation to explain why patients received higher or lower amounts of FIO2 during surgery. There was no association between SSI and the fraction of inspired nitrous oxide or the rate of volume infusion administered during surgery.
adjusted odds ratio of 12 after controlling for the other variables in the model. The final model passed the Hosmer-Lemeshow goodness-of-fit test, chi-square (9 degrees of freedom) $P = 0.79$.

**Discussion**

This is the largest study to date designed to examine risk factors for SSI after spinal surgery. The study analyzed a wide variety of risk factors, including those that were previously identified, clinically plausible, and potentially modifiable.

We found that the intraoperative administered $\text{FiO}_2$ was a significant, independent, and modifiable risk factor for SSI after spinal surgery. Patients who received less than 50% $\text{FiO}_2$ during surgery were at significantly higher risk of developing a SSI. Administered $\text{FiO}_2$ remained a strong independent risk factor after adjusting for other
variables in the multivariate analysis. The effect was seen whether FIO2 was analyzed as a continuous or categorical variable, and administered FIO2 had the strongest association with SSI of any variable in this study. The association between supplemental oxygen and SSI risk has been studied previously for other types of surgery. In colorectal surgery, three randomized controlled trials found that the administration of supplemental oxygen at 80% FIO2 during surgery and for several hours after surgery significantly reduced the risk of SSI compared to patients who received 30% FIO2.20,26,27 Another randomized controlled trial by Pryor et al. reported the opposite result for patients undergoing a variety of abdominal surgeries.31 The association between supplemental oxygen and SSI is biologically plausible because oxygen is vital to oxidative processes used for bacterial killing in leukocytes.32 Studies show that the perioperative tissue oxygen tension is associated with risk of SSI.21,33 To our knowledge, supplemental oxygen during surgery has not been widely implemented as an intervention to lower SSI rates. Our data suggest that such an intervention, which is relatively simple to implement at little cost, has the potential to substantially reduce patients’ risk of SSI after spinal surgery.

Administration of nitrous oxide limits the inspired oxygen concentration that can be administered during surgery, and the gas has several properties to suggest that it may be associated with inhibition of wound healing and wound infections.34,35 Myles et al. found that nitrous oxide administration increased overall complications, including wound infection, after major surgery.34 However, the inspired oxygen concentrations varied significantly, and it was impossible to conclude whether the observed effect was due to nitrous oxide, oxygen, or other factors. In a recent randomized control trial, Fleischmann et al. found that nitrous oxide did not increase the incidence of surgical wound infection.35 Similarly, in our study, we found no association between nitrous oxide administration and SSI.

Perioperative glucose control and intraoperative temperature regulation were two other modifiable risk factors that were assessed in this study. We did not detect a difference in intraoperative temperature regulation between case and control patients. Others have found that diabetes and elevated perioperative glucose levels are risk factors for SSI after spinal surgery.3,17,18 In this study, an elevated glucose measurement greater than 126 mg/dl was associated with SSI on univariate analysis, but it was not an independent risk factor for SSI after adjusting for other variables. Many study patients did not have measurement of glucose in the preoperative and intraoperative periods, and it is possible that this limited our ability to adequately assess this variable.

We found that obesity was a significant, independent risk factor for SSI after spinal surgery. Obesity was defined by a clinical diagnosis indicated in the medical record, and the average weight of obese patients was 97.8 kg. We could not calculate body mass index because the majority of subjects did not have height recorded in the medical record. Other investigators have also found that obesity is associated with SSI after spinal surgery.3,17,18 Interestingly, obesity has been shown to decrease perioperative tissue oxygenation,36 and we found evidence to suggest an interaction between obesity and administered FIO2 in this study. Recently, Hilbrand et al. speculated that an inadequate volume of intraoperative fluid infusion in obese patients might contribute to reduced tissue oxygenation.37 We examined intraoperative average fluid infusion rate and found no association with SSI among obese or nonobese patients. The majority of the spinal surgeries in this study were elective, and only 5% were performed for emergent or urgent reasons. For obese patients, who were at fourfold risk for SSI in this study, delaying elective spinal surgery whenever possible to pursue weight reduction would likely reduce the risk of SSI.

Shaving with a razor before surgery is a well-documented risk factor for SSI, and guidelines from the CDC Healthcare Infection Control Practices Advisory Committee recommend avoidance of hair removal before surgery when possible and the use of clippers if hair removal is necessary.38 Despite this, we were surprised to find that 20% of study patients were shaved with a razor before spinal surgery, and this was a significant, independent risk factor for SSI. Avoiding razor shaving before surgery is a straightforward intervention to reduce the risk of SSI.

Our data confirm previous reports that an ASA score of 3 or more and a prolonged duration of surgery, both elements of the National Healthcare Safety Network risk index, are significant independent risk factors for the development of SSI after laminectomy or spinal fusion.3,13 Duration of procedure is dictated primarily by the surgical complexity of the procedure; however, there are some surgeons or methods of practice (e.g., involvement of trainees, etc.) that are faster than others and that may be modifiable under certain circumstances.

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>OR (95% CI)*</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedure duration &gt; 75th percentile*</td>
<td>4.7 (1.6–14)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>ASA score ≥ 3</td>
<td>9.7 (3.7–25)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Lumbar-sacral level of surgery</td>
<td>2.9 (1.2–7.1)</td>
<td>0.02</td>
</tr>
<tr>
<td>Posterior surgical approach</td>
<td>3.5 (1.2–9.7)</td>
<td>0.02</td>
</tr>
<tr>
<td>Instrumentation</td>
<td>2.5 (1.1–6.0)</td>
<td>0.03</td>
</tr>
<tr>
<td>Obesity</td>
<td>4.0 (1.6–10)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Razor shaving before surgery</td>
<td>3.6 (1.2–11)</td>
<td>0.02</td>
</tr>
<tr>
<td>FIO2 &lt; 50%</td>
<td>12 (4.5–33)</td>
<td>&lt; 0.001</td>
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</tbody>
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* 75th percentile duration of procedure for the study patients was 352 minutes.

ASA = American Society of Anesthesiologists; CI = confidence interval; FIO2 = fraction of inspired oxygen; OR = odds ratio.
The role of procedure duration highlights the need to complete surgical procedures as expeditiously as possible while not compromising the completeness of the procedure or the safety of the patient. Among severity of illness measures, the ASA score was the strongest predictor of SSI, although the Karnofsky performance score, the number of comorbidity illnesses, and the McCabe disease severity score were also significantly associated with SSI. Similar to other reports, we found that posterior surgical approach, instrumentation, and lumbar-sacral operative level were also significant, independent risk factors for SSI after spinal surgery.13

This study had several limitations, including a relatively small sample size. The study included both laminectomy and fusion procedures and a mixture of deep, organ space, and superficial infections, which may have distinct risk factors. The retrospective study design and missing data limited our ability to accurately measure and estimate the effect of some variables such as obesity, preoperative albumin, and perioperative glucose. Postdischarge SSI among control patients may not have been detected if patients did not return to the same surgeon for care or if the medical record lacked sufficient detail to meet criteria for SSI. This is a potential source of misclassification bias. Case control studies can demonstrate an association between factors such as administered FIO2 and the risk of SSI, but they cannot lead to conclusions regarding causality. All variables considered for inclusion in our exploratory model were biologically plausible and tested for colinearity. However, data-driven modeling strategies can lead to biased regression coefficients and falsely narrow confidence intervals. Because we did not perform resampling techniques to assess reproducibility of results, our results cannot be used to form a prediction model to assess an individual's risk of SSI.

In conclusion, this study identified several variables, including an ASA score of 3 or more, prolonged duration of surgery, posterior surgical approach, instrumentation, and lumbar-sacral operative level, as independent risk factors for SSI after spinal surgery. We also identified variables that are potentially amenable to intervention, including obesity, razor shaving before surgery, and intraoperative administered FIO2 of less than 50% as independent risk factors for SSI after spinal surgery. Addressing obesity before elective spinal surgery and avoiding razor shaving would likely reduce the risk of SSI. Intraoperative administration of at least 50% FIO2 should be tested prospectively as an intervention to prevent SSI after spinal surgery.

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References


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