

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

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**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; 94% CI, 1.6–10;  $P < 0.01$ ), razor shaving before surgery (OR, 3.6; 95% CI, 1.2–11;  $P = 0.02$ ), and intraoperative administered fraction of inspired oxygen of less than 50% (OR, 12; 94% CI, 4.5–33;  $P < 0.001$ ).

**Conclusions:** In addition to previously reported risk factors, this study identified intraoperative administered 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,<sup>1</sup> and they lead to increased morbidity, mortality, length of hospital stay, and healthcare costs.<sup>2–4</sup> Overall, patients who develop SSI are twice as

likely to die and 60% more likely to spend time in the intensive care unit.<sup>2</sup> 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.<sup>5</sup> 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%.<sup>6</sup> These infections can lead to significant morbidity, readmission to the hospital, and additional surgeries, sometimes requiring the removal of implanted spinal hardware.<sup>7–9</sup>

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.<sup>10</sup> 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.<sup>3,4,8,11–18</sup>

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.<sup>19–27</sup> Two recent studies found that diabetes or elevated perioperative glucose levels were associated with SSI after spinal surgery.<sup>17,18</sup> 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.<sup>19–25</sup>

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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.<sup>28</sup> 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.<sup>28</sup> 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 if there is no implant and within 1 yr if an implant is in place, and have at least one of the following: purulent drainage from the deep incision, spontaneous dehiscence or deliberate opening of the incision by a surgeon when the patient has fever or localized pain (unless the culture is negative), an abscess in the deep incision, or the diagnosis of a deep 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,<sup>29</sup> McCabe disease severity score,<sup>30</sup> 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 ( $F_{iO_2}$ ) 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  $\alpha = 0.05$ , 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 between SSI 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 incisional. Missing data for study patients included race ( $n = 1$ ), ASA score ( $n = 1$ ), smoking history ( $n = 3$ ), Karnofsky and McCabe scores ( $n = 14$ ), preoperative albumin ( $n = 84$ ), intraoperative temperature ( $n = 7$ ), administered fraction of inspired nitrous oxide ( $n = 10$ ), average intraoperative infusion rate ( $n = 9$ ), and perioperative glucose ( $n = 16$ ). The mean age of subjects in the study was 55.3 yr (range, 19 to 88 yr). Patients who

developed SSI were significantly older than control patients, but they did not differ significantly from control patients with respect to gender, race, or smoking status (table 1). Univariate analysis showed that obese patients and those with cardiac disease were significantly more likely to develop SSI, as were patients with an ASA score of 3 or more and those with a Karnofsky Performance Scale of 60 or below. Routine antimicrobial prophylaxis of 1–2 g of intravenous cefazolin was administered to 171 study patients; 8 patients received vancomycin, and 29 patients received clindamycin. The majority of patients received antimicrobial prophylaxis within 60 min before surgical incision, and cases and controls did not differ significantly with regard to this variable (table 1). Patients with a perioperative glucose measurement greater than 126 mg/dl were significantly more likely to develop SSI than patients without an elevated glucose measurement (table 1). When analyzed according to the time of the elevated glucose measurement, only postoperative glucose measurements performed in the 48 h after surgery accounted for the difference between case and control patients.

Other significant risk factors on univariate analysis included a history of previous spinal surgery, emergent or urgent indications for surgery, duration of procedure greater than the 75th percentile, instrumentation, lumbar-sacral level of surgery, posterior approach, dural tear, postoperative cerebrospinal fluid leak, and perioperative blood transfusion (table 1). Intraoperative administration of a  $F_{IO_2}$  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  $F_{IO_2}$  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  $F_{IO_2}$  during surgery. There was no association between SSI and the fraction of inspired nitrous oxide or the rate of volume infusion administered during surgery.

Multivariate analysis identified independent risk factors for SSI, including duration of procedure greater than the 75th percentile, ASA score, lumbar-sacral operative level, posterior surgical approach, instrumentation, obesity, exposure to razor shaving, and intraoperative administration of a  $F_{IO_2}$  less than 50% (table 2). The final multivariate model included 99 case patients and 98 control patients. Five case patients and 6 control patients were excluded from the analysis due to missing data (ASA score [ $n = 1$ ], administered  $F_{IO_2}$  [ $n = 2$ ]) or because they had surgery by both the anterior and posterior approaches ( $n = 8$ ). Interaction testing did not reveal interactions between variables, with the exception of a potential interaction between obesity and the intraoperative administered  $F_{IO_2}$  ( $P = 0.052$  for the multiplicative interaction term). Administration of  $F_{IO_2}$  less than 50% had the strongest association with SSI, with an

**Table 1. Selected Unadjusted Risk Factors for SSI after Spinal Surgery**

Patient Characteristic/Risk Factor	Cases (n = 104)*	Controls (n = 104)*	Unadjusted OR (95% CI)	P Value
Median age, years (SD)	59.4 (15.8)	50.6 (14.0)		0.04
Female gender	53 (51%)	54 (52%)	0.96 (0.56–1.7)	0.89
European descent	90 (87%)	80 (77%)	1.9 (0.93–4.0)	0.08
Smoking	21/101 (21%)	25 (24%)	0.84 (0.41–1.7)	0.63
Diabetes	17 (16%)	11 (11%)	1.7 (0.73–3.7)	0.23
Cardiac disease	29 (28%)	13 (13%)	2.7 (1.3–5.6)	< 0.01
Obesity	46 (44%)	18 (17%)	3.8 (2.0–7.2)	< 0.001
ASA score ≥ 3	75 (72%)	31 (30%)	6.0 (3.3–11)	< 0.001
Karnofsky score ≤ 60	49 (47%)	26 (25%)	2.6 (1.4–4.9)	< 0.01
Previous spinal surgery	72 (69%)	46 (44%)	2.8 (1.6–5.0)	< 0.001
Emergent/urgent surgery	10 (10%)	1 (1%)	11(1.4–87)	0.02
Razor shaving before surgery	27 (26%)	14 (13%)	2.3 (1.1–4.6)	0.03
Antimicrobial prophylaxis within 1 h before surgery	87(84%)	75 (72%)	0.45 (0.11–1.7)	0.25
Intraoperative nitrous oxide administration†	61/99 (62%)	78/99 (79%)	0.88 (0.49–1.6)	0.66
FiO <sub>2</sub> < 50%†	70 (68%)	35 (34%)	4.1 (2.3–7.4)	< 0.001
Perioperative glucose > 126 mg/dl	82/98 (84%)	58/94 (62%)	3.2 (1.6–6.3)	0.001
Mean lowest intraoperative temperature, °C (SD) [range]	35.5 (0.75) [34.0–38.5]	35.4 (0.77) [33.1–37.1]		0.33
Mean intraoperative infusion rate, ml/min (SD) [range]	14.3 (6.5) [–4.3 to 41.5]	13.6 (5.5) [1.1–33.8]		0.37
Procedure duration > 75th percentile‡	40 (38%)	13 (13%)	4.4 (2.2–8.8)	< 0.001
Instrumentation	79 (76%)	55 (53%)	2.8 (1.6–5.1)	0.001
Lumbar-sacral level of surgery	79 (76%)	56 (54%)	2.6 (1.4–4.9)	< 0.001
Posterior surgical approach	87 (87%)	62 (62%)	4.1 (2.0–8.3)	< 0.001
Dural tear	22 (21%)	11 (11%)	2.3 (1.0–5.0)	0.04
Postoperative CSF leak	12 (12%)	3 (3%)	4.4 (1.2–16)	0.03
Transfusion§	67 (64%)	22 (21%)	6.7 (3.6–13)	< 0.001

\* Denominator is 104 patients unless another value is noted within the table. † Administered for the majority of the intraoperative period. ‡ 75th percentile duration of procedure for the study patients was 352 minutes. § Transfusion given preoperatively, intraoperatively, or postoperatively.

ASA = American Society of Anesthesiologists; CI = confidence interval; CSF = cerebral spinal fluid; FiO<sub>2</sub> = fraction of inspired oxygen; OR = odds ratio; SD = standard deviation.

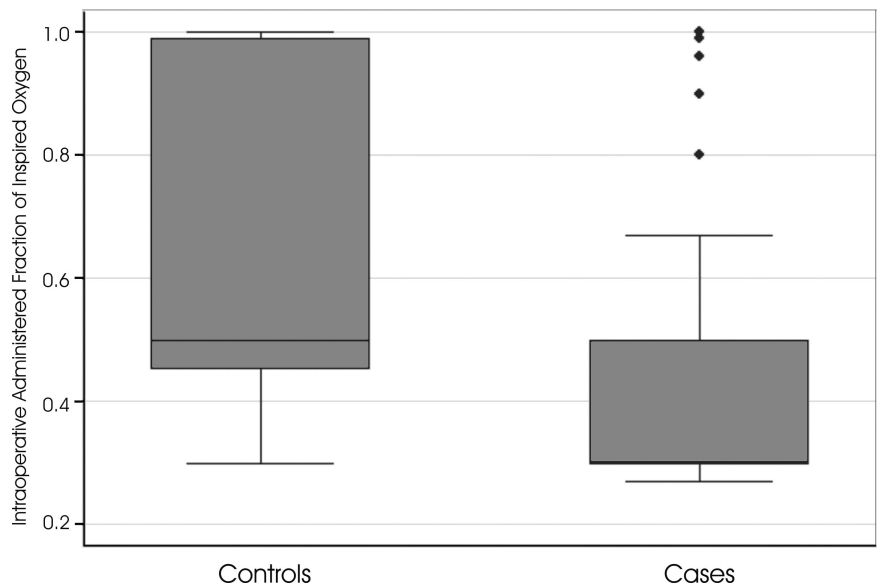
adjusted odds ratio of 12 after controlling for the other variables in the model. The final model passed the Hosmer-Lemeshow goodness-of-fit test, chi-square (9 degrees of freedom) *P* = 0.79.

**Discussion**

This is the largest study to date designed to examine risk factors for SSI after spinal surgery. The study ana-

lyzed a wide variety of risk factors, including those that were previously identified, clinically plausible, and potentially modifiable.

We found that the intraoperative administered FiO<sub>2</sub> was a significant, independent, and modifiable risk factor for SSI after spinal surgery. Patients who received less than 50% FiO<sub>2</sub> during surgery were at significantly higher risk of developing a SSI. Administered FiO<sub>2</sub> remained a strong independent risk factor after adjusting for other



**Fig. 1.** Box plot depicting the intraoperative fraction of inspired oxygen administered to control patients and case patients. Boxes, horizontal lines, whiskers, and dots represent the interquartile range, median, range of nonoutlying points, and outlying points, respectively. For case patients, the median line overlies the bottom of the shaded box.

**Table 2. Multivariable Analysis: Adjusted Risk Factors for SSI after Spinal Surgery**

Risk Factor	OR (95% CI)*	P Value
Procedure duration > 75th percentile*	4.7 (1.6–14)	< 0.001
ASA score $\geq$ 3	9.7 (3.7–25)	< 0.001
Lumbar-sacral level of surgery	2.9 (1.2–7.1)	0.02
Posterior surgical approach	3.5 (1.2–9.7)	0.02
Instrumentation	2.5 (1.1–6.0)	0.03
Obesity	4.0 (1.6–10)	< 0.01
Razor shaving before surgery	3.6 (1.2–11)	0.02
F <sub>IO<sub>2</sub></sub> < 50%	12 (4.5–33)	< 0.001

\* 75th percentile duration of procedure for the study patients was 352 minutes.

ASA = American Society of Anesthesiologists; CI = confidence interval; F<sub>IO<sub>2</sub></sub> = fraction of inspired oxygen; OR = odds ratio.

variables in the multivariate analysis. The effect was seen whether F<sub>IO<sub>2</sub></sub> was analyzed as a continuous or categorical variable, and administered F<sub>IO<sub>2</sub></sub> 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% F<sub>IO<sub>2</sub></sub> during surgery and for several hours after surgery significantly reduced the risk of SSI compared to patients who received 30% F<sub>IO<sub>2</sub></sub>.<sup>20,26,27</sup> Another randomized controlled trial by Pryor *et al.* reported the opposite result for patients undergoing a variety of abdominal surgeries.<sup>31</sup> The association between supplemental oxygen and SSI is biologically plausible because oxygen is vital to oxidative processes used for bacterial killing in leukocytes.<sup>32</sup> Studies show that the perioperative tissue oxygen tension is associated with risk of SSI.<sup>21,33</sup> 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.<sup>34,35</sup> Myles *et al.* found that nitrous oxide administration increased overall complications, including wound infection, after major surgery.<sup>34</sup> 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.<sup>35</sup> 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 fac-

tors 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.<sup>17,18</sup> 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.<sup>3,17,18</sup> Interestingly, obesity has been shown to decrease perioperative tissue oxygenation,<sup>36</sup> and we found evidence to suggest an interaction between obesity and administered F<sub>IO<sub>2</sub></sub> in this study. Recently, Hiltbrand *et al.* speculated that an inadequate volume of intraoperative fluid infusion in obese patients might contribute to reduced tissue oxygenation.<sup>37</sup> 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.<sup>38</sup> 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.<sup>4,13</sup> 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.

The role of procedure duration highlights the need to complete surgical procedures as expediently 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 comorbid 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.<sup>3,13,13</sup>

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  $F_{iO_2}$  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 collinearity. 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  $F_{iO_2}$  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%  $F_{iO_2}$  should be tested prospectively as an intervention to prevent SSI after spinal surgery.

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## References

1. Martone WJ, Nichols RL: Recognition, prevention, surveillance, and management of surgical site infections: Introduction to the problem and symposium overview. *Clin Infect Dis* 2001; 33(Suppl 2):S67-8

2. Kirkland KB, Briggs JP, Trivette SL, Wilkinson WE, Sexton DJ: The impact of surgical-site infections in the 1990s: Attributable mortality, excess length of hospitalization, and extra costs. *Infect Control Hosp Epidemiol* 1999; 20:725-30
3. Olsen MA, Mayfield J, Lauryssen C, Polish LB, Jones M, Vest J, Fraser VJ: Risk factors for surgical site infection in spinal surgery. *J Neurosurg* 2003; 98:149-55
4. Apisarnthanarak 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
5. National Healthcare Safety Network (NHSN) Report, data summary for 2006 through 2007, issued November 2008. Edwards JR, Peterson KD, Andrus ML, Dudeck MA, Pollock DA, Horan TC; National Healthcare Safety Network Facilities. *Am J Infect Control*. 2008; 36:609-26. PMID: 18992647
6. Whitehouse JD, Friedman ND, Kirkland KB, Richardson WJ, Sexton DJ: The impact of surgical-site infections following orthopedic surgery at a community hospital and a university hospital: Adverse quality of life, excess length of stay, and extra cost. *Infect Control Hosp Epidemiol* 2002; 23:183-9
7. Cronquist AB, Jakob K, Lai L, Della LP, Larson EL: Relationship between skin microbial counts and surgical site infection after neurosurgery. *Clin Infect Dis* 2001; 33:1302-8
8. Levi AD, Dickman CA, Sonntag VK: Management of postoperative infections after spinal instrumentation. *J Neurosurg* 1997; 86:975-80
9. Calderone RR, Garland DE, Capen DA, Oster H: Cost of medical care for postoperative spinal infections. *Orthop Clin North Am* 1996; 27:171-82
10. Gaynes RP, Culver DH, Horan TC, Edwards JR, Richards C, Tolson JS: Surgical site infection (SSI) rates in the United States, 1992-1998: The National Nosocomial Infections Surveillance System basic SSI risk index. *Clin Infect Dis* 2001; 33(Suppl 2):S69-S77
11. Kramer MH, Mangram AJ, Pearson ML, Jarvis WR: Surgical-site complications associated with a morphine nerve paste used for postoperative pain control after laminectomy. *Infect Control Hosp Epidemiol* 1999; 20:183-6
12. Labbe AC, Demers AM, Rodrigues R, Arlet V, Tanguay K, Moore DL: Surgical-site infection following spinal fusion: A case-control study in a children's hospital. *Infect Control Hosp Epidemiol* 2003; 24:591-5
13. 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
14. Weinstein MA, McCabe JP, Cammisia FP Jr: Postoperative spinal wound infection: A review of 2,391 consecutive index procedures. *J Spinal Disord*. 2000; 13:422-6
15. Capen DA, Calderone RR, Green A: Perioperative risk factors for wound infections after lower back fusions. *Orthop Clin North Am* 1996; 27:83-6
16. Patir R, Mahapatra AK, Banerji AK: Risk factors in postoperative neurosurgical infection. A prospective study. *Acta Neurochir (Wien)* 1992; 119:80-4
17. Friedman ND, Sexton DJ, Connelly SM, Kaye KS: Risk factors for surgical site infection complicating laminectomy. *Infect Control Hosp Epidemiol* 2007; 28:1060-5
18. Olsen MA, Nepple JJ, Riew KD, Lenke LG, Bridwell KH, Mayfield J, Fraser VJ: Risk factors for surgical site infection following orthopaedic spinal operations. *J Bone Joint Surg Am* 2008; 90:62-9
19. Dellinger EP: Preventing surgical-site infections: The importance of timing and glucose control. *Infect Control Hosp Epidemiol* 2001; 22:604-6
20. Greif R, Akca O, Horn EP, Kurz A, Sessler DI: Supplemental perioperative oxygen to reduce the incidence of surgical-wound infection. *Outcomes Research Group. N Engl J Med* 2000; 342:161-7
21. Hopf HW, Hunt TK, West JM, Blomquist P, Goodson WH III, Jensen JA, Jonsson K, Paty PB, Rabkin JM, Upton RA, von SK, Whitney JD: Wound tissue oxygen tension predicts the risk of wound infection in surgical patients. *Arch Surg* 1997; 132:997-1004
22. Kurz A, Sessler DI, Lenhardt R: Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization. Study of Wound Infection and Temperature Group. *N Engl J Med* 1996; 334:1209-15
23. Latham R, Lancaster AD, Covington JF, Pirolo JS, Thomas CS: The association of diabetes and glucose control with surgical-site infections among cardiothoracic surgery patients. *Infect Control Hosp Epidemiol* 2001; 22:607-12
24. Melling AC, Ali B, Scott EM, Leaper DJ: Effects of preoperative warming on the incidence of wound infection after clean surgery: A randomised controlled trial. *Lancet* 2001; 358:876-80
25. Van den BG, Wouters PJ, Bouillon R, Weekers F, Verwaest C, Schetz M, Vlasselaers D, Ferdinande P, Lauwers P: Outcome benefit of intensive insulin therapy in the critically ill: Insulin dose *versus* glycemic control. *Crit Care Med* 2003; 31:359-66
26. Mayzler O, Weksler N, Domchik S, Klein M, Mizrahi S, Gurman GM: Does supplemental perioperative oxygen administration reduce the incidence of wound infection in elective colorectal surgery? *Minerva Anesthesiol* 2005; 71:21-5
27. Belda FJ, Aguilera L, García de la Asunción J, Alberti J, Vicente R, Ferrandiz L, Rodriguez R, Company R, Sessler DI, Aguilar G, Botello SG, Orti R, Spanish Reduccion de la Tasa de Infeccion Quirurgica Group: Supplemental perioperative oxygen and the risk of surgical wound infection: A randomized controlled trial. *JAMA* 2005; 294:2035-42
28. Horan TC, Gaynes RP, Martone WJ, Jarvis WR, Emori TG: CDC definitions

- of nosocomial surgical site infections, 1992: A modification of CDC definitions of surgical wound infections. *Infect Control Hosp Epidemiol* 1992; 13:606-8
29. Schag CC, Heinrich RL, Ganz PA: Karnofsky performance status revisited: Reliability, validity, and guidelines. *J Clin Oncol* 1984; 2:187-93
30. McCabe W, Jackson G: Gram-Negative Bacteremia. *Arch Intern Med* 1962; 110:847-55
31. Pryor KO, Fahey TJ III, Lien CA, Goldstein PA: Surgical site infection and the routine use of perioperative hyperoxia in a general surgical population: A randomized controlled trial. *JAMA* 2004; 291:79-87
32. Babior BM: Oxygen-dependent microbial killing by phagocytes (first of two parts). *N Engl J Med* 1978; 298:659-68
33. Ives CL, Harrison DK, Stansby GS: Tissue oxygen saturation, measured by near-infrared spectroscopy, and its relationship to surgical-site infections. *Br J Surg* 2007; 94:87-91
34. Myles PS, Leslie K, Chan MT, Forbes A, Paech MJ, Peyton P, Silbert BS, Pascoe E: Avoidance of nitrous oxide for patients undergoing major surgery: A randomized controlled trial. *ANESTHESIOLOGY* 2007; 107:221-31
35. Fleischmann E, Lenhardt R, Kurz A, Herbst F, Fulesdi B, Greif R, Sessler DI, Akca O: Nitrous oxide and risk of surgical wound infection: A randomised trial. *Lancet* 2005; 366:1101-7
36. Kabon B, Nagele A, Reddy D, Eagon C, Fleshman JW, Sessler DI, Kurz A: Obesity decreases perioperative tissue oxygenation. *ANESTHESIOLOGY* 2004; 100:274-80
37. Hildebrand LB, Kaiser HA, Niedhart DJ, Pestel G, Kurz A: Subcutaneous oxygen pressure in spontaneously breathing lean and obese volunteers: A pilot study. *Obes Surg* 2008; 18:77-83
38. 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