# When the Infection Hits the Wound: Matched Case-Control Study in a Neurosurgical Patient Collective Including Systematic Literature Review and Risk Factors Analysis

*Stephanie Schipmann[1], Erol Akalin[1], Justin Doods[2], Christian Ewelt[1], Walter Stummer[1], Eric Suero Molina[1]*

BACKGROUND: **To avoid surgical site infections (SSIs) by identifying patients at high risk for infectious complications, a better understanding of relevant risk factors is required. This manuscript describes a matched case-control study of patients undergoing cranial neurosurgery with postoperative surgical site infections and a systematic literature review.**

METHODS: **From January 2012 to March 2015, 70 patients (2.47%) with SSIs (out of 2819 patients) and 185 controls were identified. Statistical analyses were performed using univariate and multivariate models to identify risk factors associated with SSIs.**

RESULTS: **The time of the onset of SSIs ranged from 8 to 854 days after surgery (median: 42 days). American Society of Anesthesiologists score ($P = 0.003$), surgical drain ($P < 0.001$), number of previous operations ($P < 0.001$), and implantation of foreign material ($P < 0.001$) were significant risk factors for SSIs in multivariate analysis. In a systematic literature review, the authors identified 20 independent risk factors.**

CONCLUSIONS: **This article provides information to ease the prospective assessment of patients at risk of SSI based on preoperative and postoperative risk factors. Lowering the incidence of SSIs will improve the patient outcomes and the overall quality of the healthcare delivered. To our knowledge, this is the first systemic literature review of SSIs in cranial neurosurgery and analysis of own cases in a wide spectrum.**

## INTRODUCTION

Regardless of surgical field, surgical site infections (SSIs) play an important role when evaluating the outcome of patients. Consequently, medical costs rise, because additional complications are common and inpatient stay is prolonged, often increasing morbidity and mortality.[1] As a great source of postoperative illness, SSIs account for approximately one quarter of all nosocomial infections.[2] Because of the dense microvascular network, supplied from distinct vascular systems, wound healing problems remain rare among neurosurgical procedures.[3] Still, it is of utmost importance, as a part of risk stratification, to obtain a better understanding of risk factors to be able to identify vulnerable patients.

We aimed to investigate and identify risk factors for adult patients undergoing cranial neurosurgical procedures using a matched case-control setting and to perform a systematic literature review to assess existing data regarding risk factors.

## METHODS

### Data Collection, Patient Population, and Matching

Patients undergoing neurosurgical procedures between January 2012 and March 2015 at the Department of Neurosurgery,

**Key words**
- Craniotomy
- Neurosurgery
- Risk factors
- Surgical site infection
- Wound infection

**Abbreviations and Acronyms**
ASA: American Society of Anesthesiologists
CDC: Centers for Disease Control and Prevention
CI: Confidence interval
CSF: Cerebrospinal fluid
EVD: External ventricular drain
ICU: Intensive care unit
OR: Odds ratio
SSI: Surgical site infection

*From the [1]Department of Neurosurgery and [2]Institute of Medical Informatics, University Hospital Muenster, Muenster, Germany*

*To whom correspondence should be addressed: Stephanie Schipmann, M.D. [E-mail: stephanie.schipmann@ukmuenster.de]*

*Citation: World Neurosurg. (2016) 95:178-189.*
*http://dx.doi.org/10.1016/j.wneu.2016.07.093*

*Journal homepage: www.WORLDNEUROSURGERY.org*

*Available online: www.sciencedirect.com*

University of Muenster, were assessed retrospectively for this study. Each postoperative surgical site infection with the need for surgical intervention was recorded. Patients older than 18 years and undergoing clean or clean-contaminated cranial neurosurgery were included. Patients with single burr-hole trepanation for insertion of external ventricular drains (EVDs) and shunt operations were not included in the study.

In addition, patients with infections at the time of index surgery were excluded from the study. For classification of surgical site infections, the standard criteria from the Centers for Disease Control and Prevention (CDC) were used, classifying SSIs as superficial incisional, deep incisional, or organ space infections.

The electronic medical record from each case was reviewed. Data concerning background conditions as age, sex, American Society of Anesthesiologists (ASA) severity score, preoperative laboratory results, underlying disease, current smoking, presence of comorbid conditions, malignant tumors, diabetes mellitus, immunosuppression, medications (e.g., chemotherapy, steroids), and previous radiation were obtained. Furthermore, data regarding the surgical procedure were collected, such as duration of surgery, number of previous operations in the infected region, location and type of surgery, indication for surgery, emergency surgery, preoperative Glasgow Coma Scale score, length of preoperative stay, length of hospital stay, length of stay in the intensive care unit (ICU), the use of prophylactic antibiotics, and the use of foreign material, EVDs, and other surgical drains.

Foreign material comprises cranioplasty implants, synthetic dura, brain electrodes, and stimulators. Finally, the date of the onset of surgical site infection, infection site, CDC score and results from microbiological cultures were analyzed. Follow-up time was at least 9 months.

All patients received a single-shot antibiotic prophylaxis of intravenous cefuroxime (1.5 g) 30 minutes before surgery. An additional cefuroxime dose was administered every 4 hours during surgery. When patients were allergic, clindamycin was used instead. Prolonged systemic antibiotic prophylaxis was not used.

The hair was washed with an antiseptic shampoo the morning before surgery. Skin preparation immediately before the surgical procedure was performed using antiseptic iodine and alcohol.

Each patient with an SSI was matched with controls based on 4 criteria: age (±12 months), sex, neurosurgical diagnosis based on the International Classification of Disease-10 code, period of procedure (±12 months). Three perfect matches could be found in nearly all cases. The same criteria were used and extracted from the medical records for the controls.

In case of SSIs, patients received a standardized antibiotic scheme until the antibiotics could be adapted according to resistogram. Patients with superficial SSIs were treated with cefuroxime (or clindamycin) for 10–14 days. In cases of deep SSIs without contact to the cerebrospinal fluid (CSF) compartment, piperacillin-tazobactam was used over 4 weeks. Patients with organ space infections (e.g., brain abscess, or subdural empyema) received ceftriaxone, vancomycin, and metronidazole until adaption to an antibiotic resistogram for 6 weeks.

## Statistical Analysis

Statistical analyses were performed for identifying the rate of SSIs and possible risk factors. Data were analyzed using the software IBM SPSS Statistics 23.0 (IBM, Armonk, New York, USA). To assess the association between SSIs and potential risk factors, we used univariate logistic regression modelling for quantitative factors and $\chi^2$ test or Fisher exact test for categorical variables, as appropriate. All factors with $P < 0.15$ in the bivariate analyses were put into a multivariable logistic regression model. Odds ratios (ORs) were obtained with corresponding 95% confidence intervals (CIs). A probability value less than 0.05 was considered statistically significant. Time-to-event analyses were performed using Kaplan-Meier curves and log-rank test. The time to the manifestation of SSIs was calculated from the date of the initial neurosurgical procedure to the date of the revision surgery.

## Systemic Literature Review

The systemic literature review followed the PRISMA guidelines.[4] A computerized search using the Medline/PubMed database to identify relevant articles on risk factors for SSIs after cranial neurosurgical procedures was performed. The search included only articles in English published until December 2015 with no lower date limit. The syntax used was as follows:

> site infection (abstract) AND neurosurgery (abstract), site infection (title) AND neurosurgery (title), site infection (abstract) AND neurosurgical (abstract), site infection (title) AND neurosurgical (title), site infection (abstract) AND craniotomy (abstract), site infection (title) AND craniotomy (title), wound infection (abstract) AND craniotomy (abstract), wound infection (title) AND craniotomy (abstract), wound infection (abstract) AND neurosurgery (abstract), wound infection (title) AND neurosurgery (title), wound infection (abstract) AND neurosurgical (abstract), wound infection (title) AND neurosurgical (title), MESH Wound infection AND neurosurgery, MESH wound infection AND craniotomy, MESH site infection AND neurosurgery, MESH site infection AND craniotomy.

All articles were screened regarding their titles and abstracts. Only articles about neurosurgical patients intending to identify risk factors for SSIs were included. Articles published in languages other than English and without an abstract were excluded from the study. In addition, only studies on patients older than 18 years were included. Subsequently, relevant articles were then retrieved and evaluated independently by 2 authors (S.S. and E.S.M.) using EndNote X7 software (Thompson Reuters, Carlsbad, California, USA). A cross-reference check of the citations of each included relevant literature review was done to ensure that no relevant studies were missed by the computer database search. Issues of disagreement regarding inclusion of studies were resolved by discussion and consensus agreement.

For quality assessment of the eligible studies, 2 authors (S.S., E.S.M.) independently evaluated the methodological quality using a previously designed criteria list (**Table 1**), which was adapted from Lievense et al.[5] and has been used previously in systematic review articles.[6] The criteria were adjusted to our study. Three of the 15 items were applicable only for case control studies; therefore, the maximum score for the studies varied with a maximum score of 15 for case control studies and of 12 for case series. In addition, the studies were classified into 3 quality levels (high, moderate, and low) based on their quality scores (**Table 2**).