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Risk factors for surgical site infections and assessment of vancomycin powder as a preventive measure in patients undergoing first-time cranioplasty

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Abstract

OBJECTIVE—Craniectomy is often performed to decrease intracranial pressure following trauma and vascular injuries. The subsequent cranioplasty procedures may be complicated by surgical site infections (SSIs) due to prior trauma, foreign implants, and multiple surgeries through a common incision. Several studies have found that intrawound vancomycin powder (VP) is associated with decreased risk of SSIs after spine operations. However, no previously published study has evaluated the effectiveness of VP in cranioplasty procedures. The purpose of this study was to determine whether intrawound VP is associated with decreased risk of SSIs, to evaluate VP's safety, and to identify risk factors for SSIs after cranioplasty among patients undergoing first-time cranioplasty.

METHODS—The authors conducted a retrospective cohort study of adult patients undergoing first-time cranioplasty for indications other than infections from January 1, 2008, to July 31, 2014, at an academic health center. Data on demographics, possible risk factors for SSIs, and treatment with VP were collected from the patients' electronic health records.

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Conception and design: Abode-Iyamah, Herwaldt, Greenlee. Acquisition of data: Abode-Iyamah, Chiang, Winslow, Park, Zanaty, Rasmussen, Herwaldt, Greenlee. Analysis and interpretation of data: all authors. Drafting the article: all authors. Critically revising the article: Abode-Iyamah, Winslow, Park, Dlouhy, Flouty, Herwaldt, Greenlee. Reviewed submitted version of manuscript: all authors. Statistical analysis: Abode-Iyamah, Herwaldt, Greenlee. Administrative/technical/material support: Abode-Iyamah, Herwaldt. Study supervision: Abode-Iyamah, Herwaldt, Greenlee.

Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

RESULTS—During the study period, 258 patients underwent first-time cranioplasties, and 15 (5.8%) of these patients acquired SSIs. Ninety-two patients (35.7%) received intrawound VP (VP group) and 166 (64.3%) did not (no-VP group). Patients in the VP group and the no-VP group were similar with respect to age, sex, smoking history, body mass index, and SSI rates (VP group 6.5%, no-VP group 5.4%, p = 0.72). Patients in the VP group were less likely than those in the no-VP group to have undergone craniectomy for tumors and were more likely to have an American Society of Anesthesiologists physical status score > 2. Intrawound VP was not associated with other postoperative complications. Risk factors for SSI from the bivariable analyses were diabetes (odds ratio [OR] 3.65, 95% CI 1.07–12.44), multiple craniotomy procedures before the cranioplasty (OR 4.39, 95% CI 1.47–13.18), prior same-side craniotomy (OR 4.73, 95% CI 1.57–14.24), and prosthetic implants (OR 4.51, 95% CI 1.40–14.59). The multivariable analysis identified prior same-side craniotomy (OR 3.37, 95% CI 1.06–10.79) and prosthetic implants (OR 3.93, 95% CI 1.15–13.40) as significant risk factors for SSIs. After adjusting for potential confounders, patients with SSIs were more likely than those without SSIs to be readmitted (OR 7.28, 95% CI 2.07–25.60).

CONCLUSIONS—In this study, intrawound VP was not associated with a decreased risk of SSIs or with an increased risk of complications. Prior same-side craniotomy and prosthetic implants were risk factors for SSI after first-time cranioplasty.

Keywords

craniotomy; complication; craniectomy; morbidity; infection

Craniectomy is a surgical procedure used for cranial vault expansion in patients who have or are likely to have intracranial hypertension from conditions such as stroke, trauma, or tumors. Weeks to months after the initial craniectomy procedure, when the brain swelling has subsided, patients undergo cranioplasty to repair the cranial defect. Cosmetic improvement previously was thought to be the primary benefit of cranioplasty. However, recent studies have found that cranioplasties may improve patients' psychological status, social performance, and neurocognitive functioning.[2,10,16,21] Nevertheless, cranioplasties can have serious complications, including infection, seizures, bone resorption, wound dehiscence, and delayed hydrocephalus. The overall complication rate from cranioplasty is fairly high, ranging from 15% to 36.5%, and infection rates range from 3.7 to 25.6%.[5,8,9,14,19,29,30,41,47,49]

Risk factors for surgical site infections (SSIs) after cranioplasty are poorly understood. Possibilities include prior trauma, multiple operations through a common incision, foreign body placement (i.e., prosthetic implants) during cranioplasty, and general medical debilitation after significant trauma. SSIs after cranioplasty can cause significant morbidity, and treatment often involves removing the bone or prosthetic flap followed by long-term antibiotic therapy. Subsequent reoperation to correct the cranial defect is delayed several months to reduce the risk of a second infection.[15]

Given the morbidity associated with SSIs after neurosurgical and orthopedic procedures, several groups have assessed the use of intrawound vancomycin powder (VP) for preventing SSIs. Most of these studies found that this practice was associated with decreased SSI rates

after spinal operations.[6,24,33,40,43,45] During the second half of the last century, the use of intrawound VP was first introduced in patients undergoing cardiothoracic surgery.[12] Thereafter, multiple centers started using it experimentally in spinal surgery in the hope that it would reduce the number of SSIs caused by common skin flora.[22–24] This idea stemmed from the notion of achieving a high concentration in the surgical bed while minimizing the systemic effect of the antibiotic.[12] Due to lack of prospective high-quality evidence, the use of VP is still not FDA approved for cranial surgery. Although the rate of systemic absorption leading to systemic toxicity was extremely low (0.3%), in a systematic review by Ghobrial et al. there was report of systemic absorption, nephrotoxicity, and ototoxicity of intrawound VP.[12] There is also risk that the high concentration of VP could create an osmotic gradient and thereby increase the risk for seroma formation, which has also been reported.[12,13] To decrease this risk, surgeons often place wound drains when they use intrawound VP for spinal cases.

While most studies involving patients undergoing spinal operations have shown that intrawound VP application may reduce the risk of SSIs,[6,24,33,40,45] we did not identify any published studies that assessed the efficacy of VP in preventing SSI after cranioplasty. A recent study found a decreased SSI rate after craniotomy among patients treated with VP.[1] Although intravenous vancomycin does not cross the blood-brain barrier, little is known about the effect of a local high vancomycin concentration on the cerebrum.[32] Thus, we aimed to determine whether intrawound VP is associated with a decreased risk of SSI after cranioplasty, to determine if intrawound VP is associated with an increased risk of other postoperative complications and to identify risk factors for SSI after cranioplasty.

Methods

We conducted a retrospective cohort study of all adult patients (≥ 18 years old) who underwent first-time cranioplasty following a craniectomy procedure (e.g., trauma, tumor resection, vascular abnormalities, etc.) between January 1, 2008, and July 31, 2014, at University of Iowa Hospitals and Clinics. A subset of those patients had undergone numerous cranial procedures or minor procedures such as ventriculostomy, bur holes, shunt, or intracranial pressure monitor placement. The cranioplasty procedure was performed with placement of either prosthetic implants (e.g., titanium or acrylic) or native bone flaps. We excluded patients who underwent craniectomy at another institution. We also excluded patients who underwent craniectomy in the setting of infection (e.g., subdural empyema) or penetrating head injuries (e.g., gunshot wounds).

Starting in 2011 there was a departmental quality-improvement initiative in our neurosurgery department aimed at reducing cranial incision infection with the use of intrawound VP based on results of its use in spinal surgeries. The practice was initially slowly adapted, but it is now widely followed throughout the department. We collected data on demographic characteristics, comorbidities, surgical information, prophylaxis with VP (yes or no), and treatment for SSI, if applicable, from the patients' electronic health records. The Program of Hospital Epidemiology provided a list of patients who met the Centers for Disease Control and Prevention's National Healthcare Safety Network (NHSN) definition of SSI. The definition of SSI was, in short, infection within 30 to 90 days of the procedure,

involving deep soft tissues of the incision and associated with fever, local tenderness, or abscess or other evidence of infection based on anatomical or imaging test in combination with at least one of the following characteristics: purulent drainage, deep incisional dehiscence, or deliberate opening or aspiration by a surgeon.[17] Because cranioplasties involve placing implants, patients who met the SSI definition up to a year after their operations were considered to have had SSIs for purposes of this study. The University of Iowa institutional review board approved this study.

Surgical Technique—Cranioplasty

All cranioplasty procedures were performed in a uniform fashion in both the VP and the no-VP control group. The surgical site was prepared using povidone iodine 10% gel. A second preparation was completed using povidone iodine 10% solution. The surgical site was prepared in the usual fashion. Intravenous (IV) antibiotic prophylaxis was administered preoperatively within 1 hour of incision and continued for 24–48 hours postoperatively. Nafcillin was used as the per-operative antibiotic agent until 2011, when it was replaced with cefazolin as a hospital quality-improvement initiative. Individuals with penicillin allergy received IV vancomycin. The neurosurgical team reopened the previous craniectomy incision and dissected in the subperiosteal plane to expose the cranial defect. During the initial craniectomy, dural substitute was placed over the native dura (dural repair or DuraMatrix [Stryker], per senior surgeon preference) without watertight dural closure, and no additional treatment of this layer was required during the cranioplasty procedure. Looking back at our single-center anecdotal experience, it appears that VP can be safely administered to patients without a dural seal. This, however, is not a definitive claim, since no large prospective study has been done in this domain. The cranial defect was repaired with the patient's autologous bone flap or, if the bone flap was contaminated at the time of craniectomy, with a titanium or acrylic prosthesis, based on the attending surgeon's and the patient's preferences. Rigid fixation was used to attach the bone flap or the prosthesis, and a closed drain was placed in the subgaleal space, tunneled through the scalp, and secured. Drains were removed within 24 hours. Patients in the VP group had 500 to 2000 mg of VP applied to the subgaleal space; the dose was determined primarily by the patient's wound size. In general, once the flap was placed and hemostasis was achieved, VP was placed in the surgical bed until the entire exposed area was visually coated with the drug. Since the drug formulation in our pharmacy is stored in 2 doses, 500 and 200 mg, the surgeon based the dose decision on wound size. The powder was applied immediately prior to wound closure. The galea and skin were reapproximated in separate layers.

Statistical Analysis

We used the 2-sample t-test for normally distributed continuous variables and the Wilcoxon rank-sum test for continuous variables that were not normally distributed. We used the chi-square test or the Fisher's exact test for categorical variables, and we computed the odds ratio and p value when applicable. We used logistic regression to assess the association of specific variables with SSIs and the association of SSIs with readmission to neurosurgery. All statistical tests were 2-tailed, and the significance level was 0.05. We used SAS v9.3 (SAS Institute Inc.) to analyze the data.

Results

Two hundred fifty-eight patients underwent first-time cranioplasty from January 1, 2008 through July 31, 2014. The patients' mean age was 48.8 ± 16.1 years, and 61.6% were males. Fifteen patients (5.8%) acquired SSIs within 4–238 days (median 32 days) after cranioplasty (Table 1). Of the SSIs, 87% were deep incisional (e.g., subgaleal space) or organ/space infections (e.g., meningitis or epidural abscess), and 13% were superficial incisional. *Propioni-bacterium acnes* (53%), *Staphylococcus aureus* (40%; 13% methicillin-susceptible and 27% methicillin-resistant), and coagulase-negative staphylococci (40%) were the most common organisms causing SSIs (Table 2).

Ninety-two (35.7%) patients received intrawound VP (VP group) and 166 (64.3%) did not (no-VP group). Of patients in the VP group, 6.9% received 500 mg, 70.1% received 1000 mg, and 23.0% received 2000 mg of VP. Bivariable analyses showed that patients in the VP and no-VP groups were similar with respect to age, sex, smoking history, body mass index (BMI), prior same-side craniotomy, prior minor cranial procedures, operation duration, estimated blood loss, type of implant, and perioperative glucose level (Table 3). Patients in the VP group were less likely than those in the no-VP group to have tumor removal as the indication for their craniectomies and were more likely to have American Society of Anesthesiologists (ASA) physical status scores > 2. More patients in the VP group than in the no-VP group had diabetes, but this difference did not reach the significance level of 0.05. Six (6.5%) of 92 patients in the VP group acquired SSIs compared with 9 (5.4%) of 166 patients in the no-VP group, and this difference did not reach the significance level (Table 3). The frequencies of CSF leak, seroma, hematoma, seizures, bone resorption, and hydrocephalus were similar among patients in the VP and the no-VP groups (Table 3).

In the bivariable analyses, age, ASA score, additional cranial procedures before the cranioplasty, perioperative antibiotic, and operation duration were not associated with SSIs after cranioplasty. Patients with SSIs were more likely than those without SSIs to have diabetes, multiple craniotomies before the cranioplasty, prior same-side craniotomy, or prosthetic implants (Table 4). After adjusting for diabetes, ASA score > 2, prior same-side craniotomy, tumor as the indication for craniectomy, and prosthetic implants in a multivariable model, prior same-side craniotomy (OR 3.37, 95% CI 1.06–10.79 and prosthetic implants (OR 3.93, 95% CI 1.15–13.40) were associated with a significantly increased risk of SSI, but intrawound VP was not associated with a reduced risk of SSI ($p > 0.99$, Table 5).

Six patients with SSIs (40%) and 18 patients without SSIs (7.4%) were readmitted to neurosurgery after the index cranioplasty. After adjusting for diabetes, prior same-side craniotomy, indication for cranioplasty, ASA scores, and prosthetic implants, patients with SSIs were significantly more likely to be readmitted to neurosurgery (OR 7.28, 95% CI 2.07–25.6).

Discussion

This is the first study evaluating the effectiveness of intrawound VP for preventing SSI after cranioplasty. Unlike prior studies in other surgical populations, our study did not find a decreased risk of SSI among patients who received intrawound VP. In contrast, Abdullah et al.[1] reported that the infection rate among patients who did not receive VP during craniotomy procedures was significantly higher (6.7%) than that for patients who did receive VP (1.3%). Differences in the patient populations may account for this difference in results. Our study assessed the effect of intrawound VP in patients undergoing a second operation through a previous incision. In fact, some of our patients had undergone multiple procedures on the same side of the scalp and thus may have been at higher risk of SSI than patients undergoing an elective initial procedure. Of note, only 20% (30/150) of the patients in the study by Abdullah et al. had prior craniotomies, but at least 50% of the patients with SSIs had prior cranial operations.[1]

In a recent study, Lazar et al.[26] found that applying a slurry of vancomycin (2.5 g in 2 ml of normal saline) to the cut edges of the sternum was associated with lower sternal wound infection rates among patients whose blood glucose levels were maintained between 120 and 180 mg per deciliter. Their results suggest that intrawound vancomycin in conjunction with other interventions, such as intensive glucose control, might decrease the risk of SSI. Additional studies would be necessary to determine whether this approach would be successful among patients undergoing cranioplasty.

Given that gram-positive bacteria are the most common organisms causing SSIs after cranial procedures,[49] we were surprised that VP was not associated with a significant decrease in the SSI rate. However, gram-negative pathogens were isolated from 3 (20%) of the 15 SSIs in our study, and all 3 of these infections were polymicrobial. Similarly, investigators have found that gram-negative organisms caused 13.3% of cranioplasty infections and 22.5% of these infections were polymicrobial.[49] Thus, future studies should investigate interventions that could prevent gram-negative and polymicrobial SSIs after cranioplasty.

We did not measure the vancomycin concentration in the patients' wounds. Thus, we did not document whether the local vancomycin levels were adequate. However, our patients received between 500 and 2000 mg of VP in their wounds; the majority (70%) received 1000 mg, which was similar to the dose used in previous studies.[1,13,40] Abdullah et al.[1] found a tissue vancomycin concentration of 499 ± 37 μg/ml when 1000 mg of VP was applied to craniotomy wounds. In contrast to most patients in that study, all of our patients had undergone prior craniotomies. In theory, scar tissue from prior operations might inhibit tissue penetration of VP and might lower the vancomycin tissue concentration in patients undergoing cranioplasty, although we have no collected data to support this theory. With the exception of the study by Abdullah et al.,[1] all prior studies evaluated patients undergoing spine operations. Such patients might have higher tissue vancomycin concentrations after VP application because their wounds are larger and deeper and vancomycin might adhere better to these larger incisions than to smaller reoperation incisions in the scalp. Additionally, we used subgaleal drains that might have either lowered the intrawound

vancomycin concentration or might have increased the risk of infection, thereby, eliminating the beneficial effect of VP.

The effect size associated with VP use appears to be small, and our SSI rates were relatively low. Our study of 258 patients (92 in the VP group and 166 in the no-VP group) may have been underpowered to detect a significant difference in SSI rates. In addition, unmeasured factors could have confounded the association between VP use and SSI. A multicenter clinical trial could avoid some limitations of retrospective observational studies, but a large number of patients would be required to detect a significant decrease in the SSI rate after cranioplasty. For example, to detect a 50% decrease in SSI rate in the VP group given an SSI rate of 5.4% in the no-VP group, a clinical trial would need 1000 patients in the VP group and 1000 patients in the no-VP group.

The rates of noninfectious complications, such as hydrocephalus, seroma, and bone resorption, were similar in the VP and no-VP groups. Our study may not have had adequate power to detect rare but serious complications related to intrawound VP. However, our noninfectious complication rate was similar to rates reported in the literature.[5,9,29,47–49] In theory, VP could inhibit wound healing or could lead to other complications. For example, VP in the subgaleal space could contact the dura directly or could enter the subarachnoid space if the dura were violated. The VP crystals could incite an inflammatory response, which if occurring intradurally, could block the subarachnoid space and lead to delayed hydrocephalus.

We found that prior same-side craniotomy and prosthetic implants were associated with significantly increased SSI risk after first-time cranioplasty. Lee et al.[28] also found that prior same-side intracranial or calvarial surgery increased the risk SSI. Unlike Tsang et al.,[42] we did not find an association between prior minor cranial procedures, such as ventriculostomy and shunt placement, and SSI in our study. Our definition of prior minor procedure was broader than that used by Piedra et al.[35] and by Tsang et al.,[42] who included only shunt placement in this category. The different definitions may explain, in part, the different findings with respect to the effect of prior minor procedures on the risk of SSI after cranioplasty. Neither our study nor the published studies established whether the proximate risk factor for SSIs after cranioplasty is the prior cranial procedures themselves, the implanted hardware, or both. Moreover, prior studies assessing whether the timing of the cranioplasty affects the risk of SSI have had conflicting results.[4,9,34,35,39,46,47] Our study did not evaluate whether the timing of the cranioplasty was a risk factor for SSI. However, our results suggest that additional studies should assess whether the timing of prior cranial procedures with respect to the timing of the cranioplasty procedure is associated with the risk of SSI.

We found that prosthetic flaps were associated with an increased risk of SSI. Results of prior studies have varied.[34] Mollman and Haines found increased rates of SSI associated with foreign body placement, but the increase was not significant.[31] Similarly, Matsuno et al., and Moll-man and Haines found higher SSI rates among patients with polymethylmethacrylate (PMMA) flaps than among those with autologous flaps, but the difference did not reach statistical significance.[30,31] Chang et al. found that the SSI rates varied by the type of

implant with patients receiving autoclaved autologous flaps or PMMA flaps having higher SSI rates than those who received titanium plates.[5,30, 31,36] Several groups have not found an association between the type of flap and SSI rates.[25,44,48] Yadla et al.[47] conducted a systematic review of 14 retrospective studies published from 1966 through 2010. They found no difference in infection rates for autograft and allograft materials (pooled OR 0.81, 95% CI 0.40–1.66). The definitions of SSI used in the studies evaluated by Yadla et al. varied, and most of the studies did not use the NHSN definition, which may explain, in part, the difference between the results of our study and those of the systematic review.

Of note some of our patients received prosthetic flaps because their bone flaps were contaminated (i.e., bone flap surveillance cultures obtained during craniectomy were positive). We previously found that cultures from most contaminated flaps grew low levels of relatively avirulent skin organisms.[8] Additionally, reimplantation of autologous flaps with low-level contamination was not a risk factor for subsequent SSI.[8] Thus, given our current results and the results of our prior study,[8] using the patient's bone flap, whenever possible, could decrease the risk of SSI.

Like Zanaty et al.,[48] Walcott et al.,[44] and Abdullah et al.,[1] we found in our bivariable analysis that diabetes was associated with an increased risk of SSI after cranioplasty, but this variable did not remain significant in the multivariable analysis in our study. Diabetes and high blood glucose levels have been associated with increased risk of SSI after other surgical procedures,[7,18,20,46] and control of blood glucose levels has been associated with decreased risk after some surgical procedures.[3,11] Given that blood glucose levels are modifiable and interventions to control blood glucose levels have been associated with decreased SSI rates after other surgical procedures, the relationship between diabetes, blood glucose levels and SSIs after cranioplasty should be studied further.

S. aureus was the most common virulent organism causing SSIs in our study population, which is consistent with other reports.[27,48] Our prior meta-analysis[37] and our prior quasi-experimental study[38] demonstrated that screening patients undergoing cardiac operations or total hip or knee arthroplasties for *S. aureus* nasal colonization, decolonizing nasal carriers with intranasal mupirocin, chlorhexidine bathing, and giving methicillin-resistant *S. aureus* carriers cefazolin and vancomycin as perioperative prophylaxis significantly reduced the risk of *S. aureus* SSIs, particularly complex SSIs. To date, no published studies have assessed the efficacy of this intervention in neurosurgical patients. Given the frequency of *S. aureus* SSIs and the severity of these infections, this intervention could have an important role in decreasing SSIs in this patient population.

Conclusions

Intrawound VP did not reduce the SSI rate and was not associated with increased risk of wound complications. Prior same-side craniotomy and prosthetic implants were risk factors for SSI after first-time cranioplasty. Large prospective studies of VP are necessary to adequately assess whether VP prevents SSIs and whether its use could increase the risk of other postoperative complications after cranioplasty. Moreover, additional studies are needed

to identify effective methods for decreasing the risk of SSI after cranioplasty given the physical, financial, and psychological burdens associated with these infections.

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ABBREVIATIONS

ASA	American Society of Anesthesiologists
BMI	body mass index
IV	intravenous
NHSN	National Healthcare Safety Network
OR	odds ratio
SSI	surgical site infection
VP	vancomycin powder

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TABLE 1.

Descriptive epidemiology: summary of 15 SSIs in a cohort of 258 patients undergoing first-time cranioplasty

Characteristic	Value
No. of SSIs	15
Days to onset of SSI	
Median	32
Range	4–238
Readmission to neurosurgery	6 (40.0)
SSI depth	
Superficial incisional	2 (13.3)
Deep incisional	9 (60.0)
Organ/space	4 (26.7)

Data are number of cases (%) unless otherwise indicated.

TABLE 2.

Descriptive epidemiology: organisms and sensitivity in 15 SSIs

Organism	No. of Cases (%)	Antibiotic Sensitivity*
Not cultured	1 (6.7)	NA
MSSA	2 (13.3)	1st case: daptomycin ≤1; gentamicin ≤1; linezolid 2; rifampin ≤0.5; tetracycline ≤0.5; TMP-SMZ ≤0.5/9.5; vancomycin 1 2nd case: clindamycin ≤0.5; erythromycin ≤0.5; gentamicin ≤1; oxacillin ≤0.25; rifampin ≤0.5; tetracycline ≤0.5; TMP-SMZ ≤0.5/9.5; vancomycin ≤0.5
MRSA	2 (13.3)	1st case: daptomycin ≤1; gentamicin ≤1; linezolid 2; rifampin ≤0.5; tetracycline ≤0.5; trimethoprim/SMZ ≤0.5/9.5; vancomycin 1 2nd case: daptomycin ≤1; gentamicin ≤1; linezolid 2; rifampin ≤0.5; tetracycline ≤0.5; TMP-SMZ ≤0.5/9.5; vancomycin 1
MRSA & *P. acnes*	1 (6.7)	Daptomycin ≤1; gentamicin ≤1; linezolid 2; rifampin ≤0.5; tetracycline ≤0.5; TMP-SMZ ≤0.5/9.5; vancomycin 1
MRSA, *P. acnes*, & *En-terobacter cloacae*	1 (6.7)	*Enterobacter*: ceftriaxone ≤2; ciprofloxacin ≤0.5; ertapenem ≤0.5; gentamicin ≤2; piperacillin/tazobactam ≤2/4; TMP-SMZ <0.5/9.5 MRSA: daptomycin ≤1; gentamicin ≤1; linezolid 2; rifampin ≤0.5; tetracycline ≤0.5; TMP-SMZ ≤0.5/9.5; vancomycin 1
CoNS	1 (6.7)	Daptomycin ≤1; linezolid 2; rifampin ≤0.5; vancomycin ≤0.5
P. acnes	1 (6.7)	No sensitivity testing performed
CoNS & *P. acnes*	3 (20.0)	1st case: daptomycin ≤1; linezolid 2; rifampin <0.5; vancomycin 1 2nd case: daptomycin ≤1; linezolid 2; rifampin ≤0.5; vancomycin 2 3rd case: erythromycin ≤0.5; oxacillin ≤0.25; rifampin ≤0.1; vancomycin 1
CoNS, *P. acnes*, & *Pseudomonas aeruginosa*	1 (6.7)	CoNS: daptomycin ≤1; erythromycin ≤0.5; linezolid 2; rifampin ≤0.5; vancomycin 2 *P. aeruginosa:* amikacin <8; cefepime ≤4; ciprofloxacin ≤0.5; meropenem ≤1; piperacillin/tazobactam ≤16
CoNS, *Candida parap-silosis*, & *Serratia marcescens*	1 (6.7)	*C. parapsilosis:* caspofungin 0.5; fluconazole 0.25 CoNS: daptomycin 1; linezolid 2; rifampin ≤0.5; vancomycin 2 S. *marcescens:* ceftriaxone ≤2; ciprofloxacin ≤0.5; ertapenem ≤0.5; gentamicin ≤2; piperacillin/tazobactam ≤4/4
P. acnes & *C. albicans*	1 (6.7)	No sensitivity testing performed

CoNS = coagulase-negative staphylococci; MRSA = methicillin-resistant *S. aureus*; MSSA = methicillin-susceptible *S. aureus*; NA = not applicable; TMP-SMZ = trimethoprim-sulfamethoxazole.

*Values for antibiotic sensitivity represent numbers of bacterial colonies after treatment.

TABLE 3.

Patient characteristics, procedure characteristics, and postoperative complications: bivariable analysis by treatment group

Variable	VP Group	No-VP Group	p Value	OR (95% CI)
Total no. of patients	92	166		
Patient factors				
Age in yrs, mean	49.3 ± 16.1	48.5 ± 16.1	0.69	—
Male	59 (64.1)	100 (60.2)	0.54	1.18 (0.70–2.00)
Smoking history	43 (46.7)	75 (45.2)	0.81	1.06 (0.64–1.78)
Diabetes	13 (14.1)	13 (7.8)	0.11	1.94 (0.86–4.38)
BMI in kg/m^2				
Median	26.7	36.2	0.50	—
Range	16.9–67.7	14.8–46.8		
Multiple craniotomy procedures	13 (14.1)	25 (15.1)	0.84	0.93 (0.45–1.92)
Prior same-side craniotomy	13 (14.1)	23 (13.9)	0.95	1.02 (0.49–2.13)
Prior minor procedures	22 (23.9)	35 (21.1)	0.60	1.18 (0.64–2.16)
Procedure factors				
Indication for craniectomy				
Hemorrhage	41 (44.6)	58 (34.9)	0.13	1.50 (0.89–2.52)
Trauma	48 (52.2)	91 (54.8)	0.68	0.90 (0.54–1.50)
Tumor	2 (2.2)	19 (11.1)	0.02	0.19 (0.04–0.86)
Other	1 (1.1)	1 (0.6)	0.65	1.88 (0.12–30.4)
ASA score >2	57 (62.0)	73 (45.9)	0.02	1.92 (1.14–3.24)
Op duration in mins, mean	137.9 ± 56.5	143.8 ± 57.5	0.44	—
EBL in ml				
Median	100	100	0.77	—
Range	10–650	15–600		
Native implant	52 (56.5)	103 (62.1)	0.39	0.80 (0.47–1.33)
Prosthetic (acrylic or titanium) implant	40 (43.5)	63 (38.0)	0.39	1.26 (0.75–2.11)
Postop complications				
SSI	6 (6.5)	9 (5.4)	0.72	1.22 (0.42–3.53)

Variable	VP Group	No-VP Group	p Value	OR (95% CI)
Seizures	16 (17.4)	38 (22.9)	0.30	0.71 (0.37–1.36)
Delayed hydrocephalus	4 (4.4)	9 (5.4)	0.78	0.79 (0.24–2.65)
Bone resorption	4 (4.4)	13 (7.8)	0.28	0.54 (0.17–1.69)
Seroma	1 (1.1)	5 (3.0)	0.43	0.35 (0.04–3.08)
Hematoma	1 (1.1)	2 (1.2)	>0.99	0.90 (0.08–10.1)

EBL = estimated blood loss; VP = vancomycin powder.

Data are number of cases (%) unless otherwise indicated. Mean values are given with SDs. Analyses are based on 92 patients in the VP group and 166 patients in the No-VP group, with the following exceptions: for ASA score, No-VP group, n = 159; for operative duration, No-VP group, n = 150; for EBL, No-VP group, n = 155.

TABLE 4.

Risk factors and outcomes for SSIs: bivariable analysis

Variable	SSI	Uninfected	p Value	OR (95% CI)
Total no. of patients	15	243		
Patient factors				
Age in yrs, mean	50.5 ± 18.7	48.7 ± 16.0	0.67	—
Male	8 (53.3)	151 (62.1)	0.50	0.70 (0.24–1.98)
Smoking history	6 (40.0)	112 (46.1)	0.65	0.78 (0.27–2.26)
Diabetes	4 (26.7)	22 (9.1)	0.05	3.65 (1.07–12.44)
BMI in kg/m^2			0.65	—
Median	27.2	26.3		
Range	19.7–38.9	14.8–67.7		
Multiple craniotomy procedures	38 (14.7)	6 (40.0)	0.05	4.39 (1.47–13.18)
Prior same-side craniotomy	6 (40.0)	30 (12.4)	0.01	4.73 (1.57–14.24)
Prior minor procedures	3 (20.0)	54 (22.2)	>0.99	0.88 (0.24–3.21)
Procedure factors				
Indication for craniectomy				
Hemorrhage	3 (20.0)	96 (39.5)	0.17	0.38 (0.11–1.39)
Trauma	9 (60.0)	130 (53.5)	0.79	1.30 (0.45–3.78)
Tumor	2 (13.3)	17 (7.0)	0.34	1.86 (0.39–8.87)
Other	1 (6.7)	0 (0)	0.06	—
ASA score >2	8 (53.3)	122 (51.7)	0.90	1.07 (0.38–3.04)
Intrawound VP	6 (40.0)	86 (35.4)	0.72	1.22 (0.42–3.53)
Dose of intrawound VP			0.76	—
500 mg	0	6 (7.4)		
1000 mg	4 (66.7)	57 (70.4)		
2000 mg	2 (33.3)	18 (22.2)		
Prophylactic antibiotics				
Cefazolin or cefepime	5 (33.3)	119 (49.0)	0.24	0.52 (0.17–1.57)
Nafcillin	5 (33.3)	81 (33.3)	>0.99	1.00 (0.33–3.02)

Variable	SSI	Uninfected	p Value	OR (95% CI)
Vancomycin	5 (33.3)	45 (18.5)	0.18	2.20 (0.72–6.75)
Op duration in mins, mean	132.7 ± 35.9	142.1 ± 58.1	0.57	—
EBL in ml			0.10	—
Median	55	100		
Range	30–300	10–650		
Native implant	4 (26.7)	151 (62.1)	0.007	0.22 (0.07–0.72)
Prosthetic (acrylic or titanium) implant	11 (73.3)	92 (37.9)	0.007	4.51 (1.40–14.59)
Outcomes				
Postop LOS in days			0.99	—
Median	2	2		
Range	1–13	0–34		
Readmission to neurosurgery	6 (40.0)	18 (7.4)	<0.0001	8.33 (2.67–26.03)

Data are number of cases (%) unless otherwise indicated. Mean values are presented with SDs. Analyses are based on 15 patients in the SSI group and 243 patients in the uninfected group, with the following exceptions: for ASA score, uninfected group n = 236; for dose of intrawound VP, SSI group n = 6 and uninfected group n = 81; for operative duration, SSI group n = 13 and uninfected group n = 229; for EBL, SSI group n = 13 and uninfected group n = 234.

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TABLE 5.

Factors associated with SSIs: multivariable analysis

Variable	OR (95% CI)	p Value
Diabetes	3.16 (0.77–12.99)	0.11
ASA score >2	0.96 (0.28–3.29)	0.95
Prior same-side craniotomy	3.37 (1.06–10.79)	0.04
Tumor as indication for craniectomy	1.45 (0.26–8.02)	0.67
Prosthetic (acrylic or titanium) implant	3.93 (1.15–13.40)	0.03
Intrawound VP	1.00 (0.30–3.31)	>0.99

C-statistic = 0.754; Hosmer and Lemeshow Goodness-of-Fit test p = 0.59.