

Perioperative Means to Prevent Surgical Site Infections following Elective Craniotomies: A Single-Center Experience

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Abstract	Background Postoperative surgical site infections are a recognized complication following craniotomies with an associated increase in morbidity and mortality. Several studies have attempted to identify bundles of care to reduce the incidence of infections. Our study aims to clarify which perioperative measures play a role in reducing surgical infection rates further. Methods This study is a retrospective audit of all elective craniotomies in years 2018 to 2019. The primary endpoint was the surgical site infection rate at 30 days and 4 months after the procedure. Univariate analysis was used to identify factors predictive of postoperative infection. Results 344 patients were included in this study. Postoperative infections were observed in 5.2% of our cohort. No postoperative infections occurred within 4 months in patients receiving perioperative hair wash and intrawound vancomycin powder. In univariate analysis, craniotomy size (Fisher's exact test, $p = 0.05$), lack of perioperative hair wash, and vancomycin powder use (Fisher's exact test, $p = 0.01$) were predictive of
Keywords	postoperative infection. No complications relative to the use of intrawound vancomy-
 craniotomy 	cin were observed.
 hair wash intrawound vancomycin surgical site infection 	Conclusion Our study demonstrates that simple measures such as perioperative hair wash combined with intrawound vancomycin powder in addition to standard practice can help reducing infection rates with negligible risks and acceptable costs. Our results should be validated further in future prospective studies.

HP & PID share senior authorship of this work.

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Introduction

Postoperative surgical site infections (SSIs) are a recognized complication following craniotomy with an associated increase in morbidity and mortality, length of stay, and treatment costs. Postoperative SSIs may also worsen overall prognosis, particularly of oncological patients due to delays in further treatment such as chemotherapy and radiotherapy.¹⁻³ Postoperative SSIs include superficial skin infection, wound dehiscence, bone flap osteomyelitis, meningitis, subdural empyema, and/or brain abscess. Depending on the severity and nature of the infection, treatments include oral or intravenous antibiotics and surgical reintervention.¹ The incidence of neurosurgical postoperative infections varies between 0.8 and 7% in the published literature with several studies attempting to identify the most common risk factors.^{1,4,5} The mean infection rate for cranial neurosurgery according to a National Survey of NHS Trusts in England is 4.3%.⁶ However, it should be noted that some published studies reporting postoperative infections include both surgical and medical infections, such as pneumonia or urinary tract infections.¹ The most common organism responsible according to previous series is Staphylococcus aureus, followed by Coagulase-negative staphylococci and Propionibacterium species.⁴ Public Health England has recommended a bundle of care to reduce SSI rates; this bundle includes among other measures preoperative antibiotics within 60 minutes from skin incision and a repeat dose for prolonged procedures, intraoperative temperature monitoring, blood glucose control, and preoperative showering using soap.7

Our study aims to clarify which perioperative measures play a role in reducing surgical infection rates further.

Materials and Methods

The study was registered with our audit department and was compliant with local policy and national regulations. All data have been anonymized and no item of information that would enable the identification of any subject was recorded, hence informed consent of the participants was not sought. We retrospectively included all patients who underwent an elective craniotomy between August 2018 and August 2019. Emergency craniotomies, burr hole operations, endoscopic approaches, and spinal procedures were excluded. The primary endpoint of this retrospective observational study was the SSI rate at 30 days and 4 months after the procedure. SSIs were defined as per Section 3 of the Protocol for Surveillance of SSI published by Public Health England.⁸ This includes superficial incisional infection, deep incisional infection, and space/organ infection as per the criteria described in the guidelines. For each SSI, we determined the time from surgery to onset, the pathogen involved, if readmission was needed, the length of stay, and the treatment required including any further surgical intervention. Furthermore, we collected data regarding the surgical preparation used and use of antibiotics both at induction and, for long procedures, the use of repeated doses of antibiotics.

The craniotomy size was measured on the first postoperative magnetic resonance (MR) scan or computed tomography scan where MR was not performed, by two of the authors. Maximum dimensions were measured for height and anteroposterior diameter of the craniotomy. The larger of the two measures was taken as maximum diameter of the craniotomy (mm) for the purposes of statistical analysis.

Perioperative Measures

All patients received antibiotic prophylaxis, as per trust policy, consisting of a single dose of intravenous cefuroxime 1.5 g 30 minutes before the skin incision. Patients allergic to penicillin received teicoplanin 400 mg intravenously. According to our local guidelines, a repeat dose of cefuroxime should be administered every 4 hours during long procedures.

Perioperative Hair Wash with Chlorhexidine Gluconate 4%

Hair wash and skin antiseptic techniques varied across the cohort and depended on the preference of the operating surgeon. Patients who received perioperative hair wash, underwent hair wash with chlorhexidine gluconate 4% and lukewarm sterile water in the anesthetic room postintubation or sedation in case of awake craniotomies. The hair was washed twice over a 5 minutes period using the above technique, until visibly clean with no scalp debris. Skin preparation involved the use of alcoholic chlorhexidine, alcoholic povidone–iodine, or both depending on the operating consultant.

Vancomycin Powder

When vancomycin was used intraoperatively, at the end of the procedure, following copious irrigation, the bone flap and subgaleal space were dusted with 1 g or 500 mg vancomycin powder depending on the craniotomy size. This subgroup of patients had their sutures removed 10 days postoperatively to minimize the risk of wound break down in view of the known osmotic effect of vancomycin.

Local side effects known to be related to vancomycin use such as aseptic wound breakdown, seromas, seizures, ototoxicity, nephrotoxicity together with systemic side effects such as cardiovascular compromise on administration of the antibiotic were recorded.⁹

Patients who had the incision site shaved perioperatively, had a non-adherent dressing applied as well as head bandage, whereas patients who had hair sparing procedures had their hair washed with chlorhexidine gluconate and dried with clean towels and no dressing or bandages were applied. Standard sutures (Vicryl, Ethilon, Prolene, surgical clips) were used for closures in all procedures depending on surgeon preference. Sutures were removed on average 10 days postoperatively. No wound drains were placed as a previous audit in our department showed an increased risk of infection in craniotomy patients when a wound drain was inserted. Postoperative hair wash with either chlorhexidine gluconate or warm saline was performed depending on surgeon's preference.

Table 1	Patient	characteristics
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Patient characteristics	
Age (years)	
Median	56
Range	17–87
Gender	
Male	181 (53%)
Female	163 (47%)
Surgery type	
Primary	283 (82%)
Redo	61 (18%)
Approach	
Supratentorial	285 (83%)
Skull base	32 (9%)
Posterior fossa	27 (8%)
Risk factors	
Diabetes mellitus	10 (3%)
Smoking	181 (53%)
Overweight or obese (BMI \geq 25)	186/333 (56%)
Laterality of surgery	
Left	183 (53%)
Right	135 (39%)
Midline	25 (7%)
Bilateral	1 (<1%)
Duration of surgery	
Median	3 hours 13 minutes
Range	39 minutes – 13 hours, 55 minutes
Maximum diameter of craniotomy (mm)	
Median	46
Range	15–200
Pathology	
Low-grade glioma	40 (12%)
High-grade glioma	116 (34%)
Meningioma	49 (14%)
Metastasis	73 (21%)
Schwannoma	22 (6%)
Other neoplasm ^a	22 (6%)
Other ^b	22 (6%)

Abbreviation: BMI, body mass index.

^aOther neoplasms included lymphoma, medulloblastoma, choroid plexus papilloma, hemangioblastoma, xanthogranuloma, gliosarcoma, neurocytoma, pituitary tumors, pineal tumors, spindle cell tumor, chondrosarcoma, and rhabdoid tumor.

^bThe other group included colloid cyst, arachnoid cyst, radiation necrosis, epidermoid cyst, cortical dysplasia, gliosis/inflammation, dermoid cyst, textiloma, aneurysmal bone cyst, tegmen defect, displaced bone flap, Rosai Dorfman, inconclusive, cavernoma, and arteriovenous malformation.

Statistical Analysis

Statistical analysis was performed using SPSS version 25. Patient characteristics were described using descriptive statistics. Factors predictive of postoperative infection (any time point) were evaluated in univariate analysis with Fisher's exact and chi-squared tests. Multivariate regression analysis could not be performed given the low number of infective events.

Results

344 patients were included in this study. The median age was 56 years (range: 17–87 years). There were approximately equal numbers of males and females (males = 181/344, 53%). More than half of patients were active or previous smokers (181/344, 53%) or overweight/obese defined by a body mass index of more than 25 or 30 (186/333, 56%). Most procedures were supratentorial (285/344, 83%) and 18% were redo procedures (61/344). Other patient characteristics, including demographic and systemic factors that may predispose to an infection, are shown in **– Table 1**.

Most procedures were performed for tumors (322/344, 94%), including gliomas (156/344, 45%) or metastases (73/344, 21%) (**-Table 1**). All patients received a first dose of antibiotics at induction. The median length of surgery was 3 hours, 13 minutes; however, a significant proportion of procedures performed was longer than 4 hours (103/344, 30%) and of these, just over half of patients (53/103, 51%) received a further dose of antibiotics.

Postoperative Infection

Postoperative infection was observed in 18 patients (5.2%). The majority (15/18, 83%) were within 30 days, while three further infections occurred within 4 months. None of the patients who had perioperative hair wash and vancomycin powder before closure suffered an SSI infection within 4 months. **►Table 2** shows factors that were predictive of postoperative infection at any time point. In univariate analysis, craniotomy size (Fisher's exact test, p = 0.05), lack of perioperative hair wash, and vancomycin powder use (Fisher's exact test, p = 0.01) were predictive of postoperative infection. Patients with a longer length of stay showed a trend toward an increased rate of infection, although this was not statistically significant.

Perioperative hair wash and vancomycin powder use were always used in conjunction such that 81 patients underwent perioperative hair wash and also received topical vancomycin powder. No complications related to the use of vancomycin powder were recorded within 4 months, including no aseptic wound breakdown and no postoperative seromas.

Subgroup Analysis

Most cases (12/18, 67%) of postoperative infection were observed within the 267 patients with supratentorial tumors. This group was, therefore, selected for subgroup analysis. The median age was 58 years (range: 17–87 years). There were approximately equally numbers of males and females (males = 138/267, 52%). More than half of patients

Table 2	Evaluation o	f factors	predictive	of postoperativ	e infection
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Factor		Incidence of infection	Univariate analysis	
Age	\leq 56 years	10/174 (5.7%)	Fisher's exact test, $p = 0.81$	
	> 56 years	8/170 (4.7%)		
Gender	Male	13/181 (7.2%)	Fisher's exact test, $p = 0.069$	
	Female	5/163 (3.1%)	7	
Approach	Supratentorial	14/285 (4.9%)	Chi-squared test= 0.38, $p = 0.83$	
	Skull base	2/27 (7.4%)	-	
	Posterior fossa	2/32 (6.3%)		
Diabetes	No	17/334 (5.1%)	Fisher's exact test, $p = 0.42$	
	Yes	1/10 (10.0%)		
Smoking	No	7/163 (4.3%)	Fisher's exact test, $p = 0.48$	
	Yes	11/181 (6.1%)		
Overweight or obese (BMI \geq 25)	No	5/147 (3.4%)	Fisher's exact test, $p = 0.22$	
	Yes	13/186 (7.0%)		
Pathology	Glioma	8/156 (5.1%)	Chi-squared test = 0.19,	
	Meningioma	4/49 (8.2%)	p = 0.67	
	Metastasis	2/73 (2.7%)		
	Other ^a	4/66 (6.1%)		
Length of stay	\leq 4 days	6/189 (3.2%)	Fisher's exact test, $p = 0.09$	
	>4 days	12/155 (7.7%)		
Redo	No	14/283 (4.9%)	Fisher's exact test, $p = 0.54$	
	Yes	4/61 (6.6%)		
Duration of surgery	< 4 hours	12/241 (5.0%)	Fisher's exact test, $p = 0.79$	
	\geq 4 hours	6/103 (5.8%)		
Maximum diameter of craniotomy	\leq 46 mm	5/181 (2.8%)	Fisher's exact test, $p = 0.05$	
	> 46 mm	13/163 (8.0%)		
Perioperative hair wash ^b and	No	18/263 (6.8%)	Fisher's exact test, $p = 0.01$	
vancomycin powder use	Yes	0/81 (0.0%)		
Prep (unknown type in one patient)	Chlorhexidine	0/81 (0.0%)	Chi-squared test= 7.17, $p = 0.07$	
	Alcoholic betadine	13/212 (6.1%)		
	Combination	5/50 (10.0%)		
Hair removal	No	6/140 (4.3%)	Fisher's exact test, $p = 0.63$	
	Yes	12/204 (5.9%)	1	
Drain	No	18/335 (5.4%)	Fisher's exact test, $p > 0.99$	
	Yes	0/9 (0.0%)	7	

Abbreviation: BMI, body mass index.

Craniotomy size and lack of perioperative hair wash and lack of vancomycin powder use were predictive of postoperative infection. Variables such as age, length of stay, and craniotomy size were dichotomized by median values.

^aRefers to all other pathology (see **Table 1** for list).

^bPreoperative hair wash was performed immediately prior to proceed with surgery in the anesthetic room using chlorhexidine gluconate.

were active or previous smokers (141/267, 53%) or overweight/obese (139/257, 54%). Nineteen percent of procedures were redo procedures (50/267).

► Table 3 shows factors that were predictive of postoperative infection in this subgroup. Lack of perioperative hair wash and vancomycin powder use (Fisher's exact test, p = 0.04) was predictive of postoperative infection.

Management of Infection

Management of postoperative infection was purely medical in 8/18 (44%) patients. With 10/18 (56%) patients requiring a combination of surgical and medical treatment, seven patients (39%) required removal of their bone flap. The most common organisms were *Staphylococcus aureus* 7/18 (39%) and gram-negative organisms 4/18 (22%) such as

Factor		Incidence of infection	Univariate analysis	
Age	\leq 58 years	7/135 (5.2%)	Fisher's exact test, $p = 0.77$	
	>58 years	5/132 (3.8%)		
Gender	Male	9/138 (6.5%)	Fisher's exact test, $p = 0.14$	
	Female	3/129 (2.3%)	-	
Diabetes	No	12/259 (4.6%)	Fisher's exact test, p > 0.99	
	Yes	0/8 (0.0%)		
Smoking	No	4/126 (3.2%)	Fisher's exact test, $p = 0.39$	
	Yes	8/141 (5.7%)	-	
Overweight or obese (BMI \geq 25)	No	3/118 (2.5%)	Fisher's exact test, $p = 0.23$	
	Yes	9/139 (6.5%)	-	
Pathology	Glioma	7/149 (4.7%)	Chi-squared test= 1.28,	
	Meningioma	3/45 (6.7%)	p = 0.73	
	Metastasis	2/61 (3.3%)		
	Other ^a	0/12 (0.0%)		
Length of stay	\leq 4 days	6/152 (3.9%)	Fisher's exact test, $p = 0.78$	
	>4 days	6/115 (5.2%)		
Redo	No	10/217 (4.6%)	Fisher's exact test, p > 0.99	
	Yes	2/50 (4.0%)		
Duration of surgery	<4 hours	8/202 (4.0%)	Fisher's exact test, $p = 0.49$	
	\geq 4 hours	4/65 (6.2%)	7	
Maximum diameter of craniotomy	≤48mm	3/134 (2.2%)	Fisher's exact test, $p = 0.08$	
	>48mm	9/133 (6.8%)		
Perioperative hair wash and	No	12/196 (6.1%)	Fisher's exact test, $p = 0.04$	
vancomycin powder use	Yes	0/71 (0.0%)	7	
Prep (unknown type in one patient)	Chlorhexidine	0/71 (0.0%)	Chi-squared test= 4.85, $p = 0.1$	
	Alcoholic betadine	9/155 (5.8%)		
	Combination	3/40 (7.5%)]	
Hair removal	No	3/113 (2.7%)	Fisher's exact test, $p = 0.25$	
	Yes	9/154 (5.8%)	7	
Drain	No	12/260 (4.6%)	Fisher's exact test, $p > 0.99$	
	Yes	0/7 (0.0%)	7	

Table 3 Evaluation of factors predictive of postoperative infection in patients with supratentorial tumo	Tabl	le 3	Evaluation	of fact	ors predict	ive of po	stoperative	infection in	patients wit	n supratentoria	tumor
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Variables such as age, length of stay, and craniotomy size were dichotomized by median values. ^aRefers to all other pathology (see \sim **Table 1** for list).

Enterobacter aerogenes and Klebsiella oxytoca. In the remaining cases, no organism was identified.

Discussion

In this retrospective study of patients undergoing elective craniotomies, we demonstrated that the use of multiple perioperative surgical measures can significantly reduce SSI rates. These measures include perioperative hair wash performed immediately prior to surgery combined with the use of vancomycin powder prior to wound closure. Our overall infection rate up to 4 months postcraniotomy is 5.2%, which is consistent with published literature for neurosurgical SSI.⁴

Staphylococcus aureus was the responsible organism in most SSI cases. Within the group of supratentorial tumors, 12 (6.1%) had an infection postoperatively. Perioperative hair wash with chlorhexidine and use of vancomycin powder prior to closure of the craniotomy significantly reduced the risk of infection. None of the patients who underwent hair wash and had topical vancomycin administered developed an infection within 4 months. Vancomycin is a broad-spectrum antibiotic

that provides cover for gram-positive pathogens that are usually involved in SSI. Applied as a topical agent vancomycin powder has a local bactericidal action; it is deemed to be a safe and not excessively expensive way to prevent infection mainly related to skin flora. Intrawound administration of vancomycin has been extensively described and demonstrated to be effective in spine and orthopaedic surgery.^{10–12} A systematic review and meta-analysis by Bokhari et al found an overall beneficial effect on SSI incidence with the use of intrawound vancomycin across all neurosurgical subspecialties except cranioplasty insertion. The studies reported no complications from the use of vancomycin powder and no evidence that use of vancomycin powder resulted in the emergence of vancomycin resistant microorganisms.¹² A prospective cohort study by Mallela et al compared the efficacy of 1 g of vancomycin powder sprinkled over the bone flap and in the subgaleal space after the final irrigation versus standard of care alone in craniotomy patients. They demonstrated a significant reduction in SSI in the vancomycin cohort with no side effects.¹¹ In our center, similarly to Mallela et al, we administered vancomycin powder over the bone flap and in the subgaleal space above the bone flap after final irrigation of the surgical cavity. We recorded no side effects related to use of vancomycin powder. Administration of vancomycin does not prolong the surgical procedure and is cost-effective in reducing SSI.

In our cohort, patients who received intraoperative vancomycin also underwent double hair wash just before surgery with chlorhexidine gluconate and lukewarm water. The Cochrane review by Webster and Osborne¹³ published in 2015 concluded that preoperative showering or bathing with chlorhexidine did not significantly reduce SSI rates compared with other wash products or no wash. However, this review included over 10,000 patients across multiple surgical specialties in different geographical locations. Results may not, therefore, be applicable to elective neurosurgical patients. Furthermore, studies in other specialties such as gynecology and colorectal surgery have suggested a reduced rate of infection in patients that have undergone preoperative wash with antiseptic agents.^{14,15} In our study, perioperative hair wash with chlorhexidine has been proven to be effective in reducing SSI.

Other factors that showed a nonstatistically significant trend toward reduced infection rates included small craniotomy size and shorter length of stay. These factors have been found to be associated with SSI in other studies.¹⁶ Given the small number of infections multivariate analysis was not performed, the impact of the craniotomy size on the infection rate may have been underestimated.

Limitations of this study include its retrospective nature, the relatively small sample size, and the fact that this is a single-center study. Data collection relied on the operation notes; perioperative hair wash may, therefore, have been performed but not documented in some cases. The low incidence of infections overall meant that robust multivariate analysis was not possible, though we do not feel this had a significant impact on results given the small number of variables that were significant at the univariate level.

Conclusion

This study evaluated the impact of surgical measures on SSI rates in patients undergoing elective craniotomies. We found that simple measures such as peri-operative hair wash and use of intrawound vancomycin powder in addition to standard practice can help to reduce infection rates with negligible risk to patients and acceptable costs. Our results should be validated further in future prospective studies.

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (name of institute/committee) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study, formal consent is not required.

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Conflict of Interest None declared.

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