Risk Factors for Pediatric Surgical Site Infection Following Neurosurgical Procedures for Hydrocephalus: A Retrospective Single-Center Cohort Study

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Abstract

Background Infection is a major complication following cerebral spinal fluid (CSF) diversion procedures for hydrocephalus. However, their pediatric risk factors for surgical site infection (SSI) are currently not well defined. Because SSI prevention bundle is increasingly introduced, the purpose of this study was to evaluate risk factors associated with SSIs following CSF diversion surgeries under SSI bundle at a single quaternary care pediatric hospital.

Methods We performed a retrospective cohort study of patients undergoing CSF diversion procedures from 2017 to 2019. SSIs were identified prospectively through continuous surveillance. We performed univariate analyses to determine an association between SSIs and patient demographics, comorbidities and perioperative factors, with subsequent multivariate logistic regression analyses to identify independent risk factors for SSI.

Results We identified a total of 561 CSF diversion procedures with an overall SSI rate of 3.6%. In univariate analyses, older age, number of previous shunt revisions and comorbid cardiac disease were significantly associated with SSI. In multivariate analyses, history of brain tumor (OR2.75, 95%CI 1.03-7.33, P=0.04) and cardiac comorbidities (OR9.47, 95%CI 2.15-41.73, P=0.003) were significantly associated with SSIs. When endoscopic third ventriculostomy was excluded, only cardiac disease was independently associated with SSI. Cardiac diseases associated with SSI included single ventricle disease with palliative repair and valvulopathy with underlying connective tissue diseases.

Conclusion This study showed that comorbid conditions (cardiac disease, brain tumor) were more important than perioperative factors as risk factors for SSI in pediatric patients undergoing CSF diversion procedures. Further investigation is needed to define the mechanisms behind these associations.

Introduction

Hydrocephalus results from a disturbance of the normal pulsatile flow of cerebrospinal fluid (CSF), resulting in its abnormal accumulation within the cerebral ventricles. This can be alleviated in the short term by insertion of a reservoir or external ventricular drain (EVD). Long term, definitive treatment is most commonly accomplished by placement of a ventriculoperitoneal shunt (VPS) or by endoscopic third ventriculostomy (ETV) with or without choroid plexus cauterization (CPC)[1]. Although the rate of surgical site infections (SSIs) after neurosurgery is generally low, the clinical and financial consequences of SSIs after CSF diversion procedures are substantial[2]. Infections following neurosurgery can lead to significant complications such as seizures, neurological deficits, and malfunction of the shunt device [3, 4]. Therefore, the prevention of infection is a priority for managing these patients, and research over the years has identified modifiable risk factors and interventions [5–8]. However, infections still persist, and greater effort needs to be directed towards understanding risk factors in order to identify new ways to lower SSI rates. To compare what has been reported with our recent experience, we conducted an

observational, retrospective study to identify factors associated with SSIs after CSF diversion procedures in a pediatric cohort in a single institution.

Materials And Methods

2.1. Study cohort and patient background

This retrospective cohort study was approved by the Institutional Review Board (IRB) at Boston Children's Hospital (BCH). The need of the informed consent was waived. All the study methods were carried out in accordance with institutional guidelines and regulations. We identified patients who underwent CSF diversion surgery (shunts, EVD, ETV) at BCH from January 2017 to September 2019. We included cases with either congenital or acquired hydrocephalus, including communicating and noncommunicating hydrocephalus. We also included patients with a history of brain tumor who subsequently needed CSF diversion, but excluded patients who underwent craniotomy for tumor resection at the time of CSF diversion surgery. Preoperatively patients received skin preparation either with chlorhexidine gluconate (CHG)-alcohol (ChloraPrep™), povidone-iodine alone, povidone-iodine plus CHG-alcohol, povidone-iodine plus alcohol, or all three antiseptics in combination. Cefazolin was the standard antibiotic for surgical prophylaxis unless patients had a previous history of bacterial infections that would direct other choices, and the dose was administered within 60 minutes prior to skin incision. When SSIs were suspected, wounds and/or CSF were cultured at the medical team and/or surgeon's discretion. SSIs associated with CSF diversion procedures were identified through ongoing prospective surveillance by the Infection Prevention and Control department using National Healthcare Safety Network (NHSN) definitions from the US Centers for Disease Control and Prevention (CDC)[9]. We extracted the information on the demographics and comorbidities of the study cohort from the electronic medical records and we obtained intraoperative information such as medications, surgical duration and American Society of Anesthesiology (ASA) physical status classifications from the Anesthesia Information Management System™ (AIMS; Cerner, MO, USA) to obtain. Comorbidities were based on the International Classification of Diseases (ICD)-9 / ICD-10 codes. Congenital cardiac diseases, great vessel malformations, and cardiomyopathies were categorized as cardiac diseases. There were a total of 10 surgeons.

Statistical analysis

Univariate analysis

We reported continuous variables as either means with standard deviation (SD) for normally distributed variables or medians and interquartile ranges (IQR) for variables without normal distribution. Normality of distribution was determined by Shapiro-Wilk test. Binary and categorical variables were reported using frequencies and percentages. We used Pearson chi-square tests to compare proportions for categorical variables, and t-tests or Mann–Whitney U tests to compare means or medians for continuous variables.

Multivariate analysis

To assess independent risk factors for SSIs, we performed multiple logistic regression analysis. All variables that had P-values less than 0.1 in the univariate analysis, except weight, and prematurity, were tested. All hypothesis testing had a two-sided significance level of 0.05. All statistical analyses were conducted using Stata/MP 15.0 (StataCorp, College Station, TX, USA).

Results

Among 561 CSF diversion procedures in 306 unique patients, 20 infections occurred, yielding an SSI rate of 3.6%. Characteristics of the study cohort are shown in Table 1. The median number of days from surgery to the onset of SSI was 13.5 days (IQR: 5.5, 30), with a maximum of 89 days.

Table 1
Comparison of demographics between patients with and without surgical site infection (SSI) using univariate analysis

	Total (N = 561)		Patient without SSI (N = 541)		Patient with SSI (N = 20)		P value
	n	%	N	%	n	%	
Female	227	40.5	212	39.2	9	45.0	0.64
Age (Months), median (IQR)	94	(14, 175)	88	(13, 173)	166	(131.5, 205)	0.01
Weight(kg), median (IQR)	28.0	(9.5, 51.4)	25.9	(9.4, 50.9)	46.1	(32.9, 60.7)	0.01
ASA Classification							0.72
Class ≤ II	149	26.6	143	26.4	6	30.0	
Class ≥ III	432	77.0	398	73.6	14	70.0	
Wound Class		0.0					1.00
1: Clean	554	98.8	534	98.7	20	100.0	
2: Clean-Contaminated	4	0.7	4	0.7	0	0.0	
3: Contaminated	0	0.0	0	0.0	0	0.0	
4: Dirty/Infected	3	0.5	3	0.6	0	0.0	
Comorbidity							
Brain tumor	147	26.2	138	25.5	9	45.0	0.07
Cardiac disease	22	3.9	19	3.5	3	15.0	0.04
Gastrostomy	91	16.2	85	15.7	6	30.0	0.12
Prematurity (GA < 37week)	17	3.0	17	3.1	0	0.0	1.00
Procedure							0.07
V-P shunt	306	54.5	292	54.0	14	70.0	
EVD	75	13.4	70	12.9	5	25.0	
ETV	163	29.1	162	29.9	1	5.0	

IQR, interquartile range; ASA, American Society of Anesthesiologists physical status classification; GA, gestational age; V-P, ventriculo-peritoneal; EVD, external ventricular drain; ETV, endoscopic third ventriculostomy, V-A, ventriculo-atrial; L-P, Lumbo-peritoneal; SD, standard deviation

	Total (N = 561)		Patient without SSI (N = 541)		Patient with SSI (N = 20)		P value
	n	%	N	%	n	%	
V-A shunt	7	1.2	7	1.3	0	0.0	
L-P shunt	10	1.8	10	1.8	0	0.0	
Number of shunt revision, mean (SD)	2.4	(2.98)	2.3	(2.9)	3.9	(4.6)	0.02
Emergent surgery	309	55.1	297	55.6	12	60.0	0.82
IQR, interquartile range; ASA, American Society of Anesthesiologists physical status classification; GA, gestational age; V-P, ventriculo-peritoneal; EVD, external ventricular drain; ETV, endoscopic third ventriculostomy, V-A, ventriculo-atrial; L-P, Lumbo-peritoneal; SD, standard deviation							

Table 1 also shows all available variables and their unadjusted association with SSIs. In univariate analyses, factors that were significantly associated with infection included older age, higher weight, comorbid cardiac disease and increased number of shunt revisions. The results of univariate analysis for perioperative drugs, procedures and other variables are presented in **Supplemental Table 1.** None of the perioperative factors, including the duration of procedure, surgeon, type of skin preparation agent, and prophylactic antibiotic administration were associated with SSIs.

Next, all variables other than weight that were found to have a univariate association with SSIs at P-value < 0.1 were included in multivariate analyses (Table 2). Of note, the data regarding gestational age at birth were missing in 348 cases (62%). Brain tumor (odds ratio [10], 2.79; 95% confidence interval [10], 1.05–7.44) and comorbid cardiac disease (OR,8.50 ;95% CI, 1.98–36.56) were independent risk factors for SSIs.

Table 2
Independent risk factors for surgical site infection in multivariate analysis

Surgical site infection			
	Odds Ratio	95 % CI	P value
Age (year)	1.00	0.999−1.01	0.10
Number of shunt revisions	1.11	0.980−1.25	0.10
Brain tumor	2.75	1.03−7.33	0.04
Cardiac disease	9.47	2.14−41.73	0.003
Procedure			
V-P shunt	(base)		
EVD	1.17	0.35−3.91	0.79
ETV	0.17	0.02−1.42	0.10
CI, confidence interval; V-P, ventriculo-peritoneal; EVD, external ventricular drain; ETV, endoscopic third ventriculostomy			

CSF diversion procedures can be with or without device implantation. To identify risk factors for SSIs for hydrocephalus surgery without device implantation, we evaluated ETV cases alone in a secondary analysis. Out of 163 ETV cases, one SSI (0.6%) occurred (in a patient with a brain tumor). 28 (17.3%) and 10 (6.1%) patients had a history of brain tumor and cardiac disease, respectively. In addition, the patients who underwent ETV had a median age of 13 months (IQR: 5,109). Congenital cerebral cyst was significantly more common in cases that underwent ETV compared to patients who received device implantation (13.5% vs 4%). There were 27 ETV cases (16.6%) in which the shunt had been revised more than twice in the past. When the analysis for risk factors for SSI was limited to shunting with device implantation (for which SSI incidence was 4.9%), only comorbid cardiac disease was independently associated with SSIs (OR = 11.0 [95%CI: 2.5−48.7], P = 0.002) (Table 3).

Table 3
Risk factors for surgical site infection when endoscopic third ventriculostomy (ETV) procedures are excluded

	Patient without SSI (N = 379)		Patient with SSI (N = 19)		Univariate	Multivariate		
	n	%	n	%	P-value	Odds ratio	95% CI	P-value
Female	153	40.4	9	47.4	0.63			
Age (Months), median (IQR)	127	(31, 195)	166	(118, 207)	0.18	1.0	1.00-1.01	0.17
ASA Classification					0.47			
Class ≤ II	87	23.0	3	15.8				
Class ≥ III	292	77.0	16	84.2				
Wound Class (1; Clean)	372	98.2	19	100.0	1.0			
Comorbidity								
Brain tumor	111	29.3	8	42.1	0.30	2.4	0.86–6.59	0.09
Cardiac disease	9	2.4	3	15.8	0.02	12.0	2.59–54.85	0.001
Gastrostomy status	70	18.5	6	31.6	0.23			
Prematurity (GA < 37week)	8	2.1	0	0.0	1.00			
Procedure*					0.81			
Number of shunt revision, mean (SD)	2.9	(3.1)	4.1	(4.7)	0.15	1.1	0.98–1.26	0.09
Duration of surgery(min), median (IQR)	73	(51, 104)	69	(55, 93)	0.85			

IQR, interquartile range; SD, standard deviation; ASA, American Society of Anesthesiologists physical status classification; GA, gestational age; CI, confidence interval

* V-P Shunt, V-A shunt, L-P shunt and EVD

Table 4 presents the CSF culture results for patients with SSIs. *Staphylococcus epidermidis* (15%) and *Cutibacterium acnes* (formerly *Propionibacterium acnes*) (15%) were detected most frequently. Of the 20 samples, 15 different bacterial and fungal species were detected.

Table 4
Microorganisms identified in
cerebrospinal fluid (CSF) cultures sent
from pediatric surgical site infection
(SSI) after shunt surgery

CSF culture N = 20	
Result	n
Cutibacterium acnes	3
Staphylococcus epidermidis	3
Staphylococcus capitis	2
Staphylococcus aureus	1
Streptococcus viridans	1
Corynebacterium coyleae	1
Enterococcus avium	1
Microbacterium	1
Propionibacterium sp. CL1305	1
Rothia aeria	1
Serratia marcescens	1
Acinetobacter sp.	1
Caulobacter segnis	1
Stenotrophomonas maltophilia	1
Trichosporon asahii	1
CSF, cerebrospinal fluid	

Discussion

In this study, we investigated risk factors for pediatric SSIs after CSF diversion surgery at a single quaternary care pediatric center. We found that comorbid cardiac disease and the presence of a brain tumor were independent risk factors for SSI. In patients who underwent shunt procedures, comorbid cardiac disease was the only independent risk factor for SSI.

In our study, the incidence of SSI in combined CSF diversion surgery was 3.6%, while SSI rates for shunt surgery and ETV were 4.9% and 0.5%, respectively. ETV is an important procedure for hydrocephalus that serves as an alternative to shunt device implantation. The success rate of ETV and its use in various ages and background diseases vary across reports [11]. ETV can be done with or without CPC. In our

institution, CPC is generally done together with ETV. In general, the SSI rate of ETV is lower than that of a shunt device implantation procedure, but the post-ETV SSI rate depends on background and age [12]. In our institution, ETV was often performed for hydrocephalus due to congenital diseases in infancy, but it was also performed in cases of repeated shunting and brain tumor complications.

There is no previous study showing that a history of brain tumor is an independent risk factor in pediatric SSI after CSF diversion surgery, but a number of studies have examined the rate of infection and prognosis after brain tumor surgery [13–15]. The cohort in our study had a higher rate (26.2%) of infection in patients with a diagnosis of brain tumor than found in previous studies investigating risk factors for shunt malfunction and infection (8% [16] and 17% [17]). Although results may vary depending on the distribution of causative diseases of hydrocephalus in each center as well as the chemotherapy regimens, our result was somewhat novel. The association of cardiac disease with shunt infection was previously described in a study of children who underwent shunt surgery within the first year of life [18]. Our study consisting of older children also demonstrated that comorbid cardiac disease was associated with an increased risk of shunt SSI. Although not directly related to infection, cardiac anomalies were associated with shunt failure in the prospective study of children from six Hydrocephalus Clinical Research Network Centers [16]. The authors suggested that this finding may be related to repeated hospitalizations and surgeries or immunodeficiencies, but they did not formally analyze these exposures. Immunological profiles for patients with a history of brain tumor and cardiac disease who present for CSF diversion procedures are not known, and could be a topic of future investigation.

The association between age and SSIs varies across studies. While some studies have identified younger age, particularly infancy, as a risk factor for SSI [19–22], other studies have demonstrated that age is not a risk factor for shunt failure or infection [23, 24]. In our cohort, older patients tended to have a higher SSI rate in univariate analysis. Most of the patients in our cohort were beyond infancy. Post- intraventricular hemorrhage (IVH) hydrocephalus secondary to prematurity occurs in infants, but most of the tumor-related hydrocephalus occurs in older children. However, age was not an independent risk factor in the multivariate analysis after the adjustment for comorbidities and the number of shunt revisions. The effects of residual tumor, chemotherapy and radiation should also be considered in future studies.

The risk of shunt failure or infection generally increases with each subsequent shunt replacement, resulting in a rising cumulative risk of SSIs [17, 22, 25]. However, in the present study, the number of shunt revisions was not an independent risk factor for SSIs in multivariate analysis, although there was a significant difference in univariate analysis. Previously, other investigators found that the presence of a gastrostomy tube was associated with infection risk in the larger study [17], but this did not substantially contribute to infections in this study. Some studies showed that lower gestational age (GA) at the time of procedures and prematurity were significant risk factors for infection after shunt surgery [21, 26]. In our study cohort, there was no incidence of SSIs in patients with a history of preterm birth, although a number of patients did not have detailed perinatal information available. Although it is difficult to determine the association between GA at birth and SSIs, GA was not a risk factor for SSI in our study. Further investigation is needed to clarify why our result differs from the previous reports.

Research on modifiable perioperative risk factors and interventions to reduce the risk of shunt infection has been done for many years. Traditional risk factors include the duration of surgery [27], the experience of the surgeon [28], hair shaving [29], prophylactic systemic antibiotics [8], antibiotic-impregnated sutures [30] and skin preparation [5, 6]. In our cohort, surgeon, prophylactic antibiotics, duration of surgery, and skin preparation agent were not associated with SSIs. In addition, our institution routinely utilizes antibiotic-impregnated shunt tubing (Bactiseal tubing) [10, 31]. In our cohort, patient factors were suggested to be more relevant as risk factors for SSIs than perioperative factors. Among the perioperative factors other than those mentioned above, there have been no reports that have examined the type and dose of anesthetics and the amount of oxygen administered in shunt surgery. Intraoperative factors such as oxygen dosage, and temperature control are known to play a role in SSI following adult general surgery [32–34]. The effect of volatile anesthetics on immune function have been reported previously [35–41]. In our previous work using a preclinical model, a long exposure (6-hour) of volatile anesthetics was associated with increased infection, while a short exposure (2-hour) was not [42]. In a study at our institution, we previously showed that higher volatile anesthetic dose was an independent risk factor for SSI in pediatric gastrointestinal surgery [43]. Anesthetic drugs and oxygen dosage also had no impact on the incidence of SSIs. The operative duration was less than 80 minutes for the groups with and without SSIs. Our result was in line with the finding in our preclinical study. In the present study, the median number of days to the date of SSI onset after surgery was 13.5 days, but more than 75% of the patients with SSI had a postoperative period of more than 30 days. In previous reports, the risk of infection was shown to be highest in the first eight weeks after a shunt procedure, and the risk decreased substantially after six months [44]. Because of relatively late onset of SSI postoperatively and the short surgical duration, it is perhaps not surprising that the impact of intraoperative drugs and oxygen dose on immune function was less after CSF diversion surgery.

The most common bacteria detected in our cohort were *Staphylococcus epidermidis* and *Cutibacterium acnes*, generally consistent with previous reports [19, 20, 45, 46]. *Staphylococcus aureus* was detected in a smaller proportion of cases. While the effectiveness of antimicrobial-impregnated and -coated shunts (AIS) has been described [46, 47], there are concerns including the emergence of methicillin-resistant Staphylococcus aureus (MRSA) and resistant gram negative rods (GNR) with repeated use [45, 46]. Although we routinely use antimicrobial impregnated shunting, MRSA was not detected in our cohort.

Our study has several limitations. First, it was limited as a single-center study and was retrospective. Second, the low SSI rate and small sample size may impair statistical power to find associations. Third, we did not examine the type of device implanted, when the brain tumor or cardiac diseases were diagnosed, or the history of treatment.

In conclusion, we have shown that comorbidities of cardiac disease and brain tumor are independent risk factors for SSIs in children undergoing CSF diversion procedures. In the presence of routine evidence-based bundles of SSI prevention measures, patient-level factors remain important predictors; future research should evaluate the mechanism underlying these associations, including the investigation of underlying immunological profiling, to further optimize prevention of infection.

Declarations

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