Patterns of Health Care Costs Due to External Ventricular Drain Infections

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■ BACKGROUND: **External ventricular drain (EVD) infections are a significant cause of morbidity among neurosurgical patients and have been correlated with increased length of hospital stay and longer requirements for intensive care. To date, no studies have examined the financial impact of EVD infections.**

■ METHODS: **Patients who underwent EVD placement between December 2010 and January 2016 were included in the study. Clinical records were retrospectively reviewed and health care cost data were obtained from the hospital's finance department. Clinical information included patient demographics, details from the hospital course, and outcomes. Total costs, direct/indirect, and fixed/variable costs were analyzed for every patient.**

■ RESULTS: **Over the 5-year study period, 246 EVDs were placed in 243 patients with an overall infection rate of 9.9% ($N = 24$). The median EVD duration for infected versus noninfected patients was 19 and 9 days, respectively ($P < 0.0001$). Median length of intensive care unit stay also was increased for patients with EVD infection (30 days vs. 13 days, $P < 0.0001$). Total health care costs were significantly greater for infected patients (US$ 168,692 vs. US$ 83,919, $P < 0.0001$). This trend was comparable for all other cost subtypes, including fixed-direct costs, fixed-indirect costs, variable direct costs, and variable-indirect costs.**

■ CONCLUSIONS: **EVD infection has a substantial effect on clinical morbidity and healthcare costs. These results demonstrate the imperative need to improve EVD infection prevention, particularly in the setting of a value-based health care system.**

INTRODUCTION

Given its intrinsic complexity, neurosurgical care carries a greater risk and is therefore associated with greater costs compared with other medical specialties.[1] Despite maximal preventative efforts, iatrogenic complications occur in the routine care of neurosurgical patients. Placement of external ventricular drains (EVDs) for the essential monitoring and treatment of elevated intracranial pressure requires continuous breach of the blood–brain barrier and poses a significant risk of infection. Rates of EVD-associated ventriculitis have consistently remained high, ranging between 5% and 35% in the literature. Furthermore, ventriculostomy-associated infections (VAIs) have been shown to significantly increase morbidity.[2-7] Infections often necessitate removal and reinsertion of the catheter, leading to prolonged treatment time with antibiotics and increased hospital stay.[3]

Numerous efforts have been made to decrease infection rates, such as early EVD weaning, use of antibiotic-impregnated (AI)-EVDs, and the implementation of standardized hospital protocols. A 2017 survey by the American Association of Neurological Surgeons of more than 1000 U.S. neurosurgeons found that low rates of ventricular drain–associated infections were associated with greater levels of neurosurgical training, high volumes of EVD placement, and routine administration of prophylactic antibiotics. Furthermore, the use of an evidence-based EVD insertion protocol

Key words
- Central nervous system infection
- External ventricular drain infection
- Health care cost
- Health care disparity
- Health care quality assessment
- Ventriculostomy

Abbreviations and Acronyms
AI: Antibiotic-impregnated
CCI: Charlson Comorbidity Index
CI: Confidence interval
CLABSI: Central line-associated bloodstream infections
CSF: Cerebrospinal fluid
EVD: External ventricular drain
ICU: Intensive care unit
OR: Odds ratio
VAI: Ventriculostomy-associated infections

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also has been shown to decrease infection rates, yet only 42.7% of participants reported the institutional use of a protocol for EVD placement.[8] The protective value of AI-EVDs has also been well-studied and shown to decrease infection rates and lower cost by 40%–70%.[2,7,9,10]

However, the full economic burden of VAI has yet to be determined. As the United States moves toward a quality-based health care system, the need for standardized infection prevention strategies—driven by data—is imperative. Physicians and hospitals are increasingly held accountable for the cost of care provided. Despite this push, information on the health care costs associated with EVD complications, a common neurosurgical procedure, is sparse. The aim of the present study is to investigate patterns of health care spending associated with ventricular drain–associated infections.

METHODS

Data Collection

Clinical and socioeconomic data were retrospectively collected from the medical records of patients older than 18 years of age who underwent EVD placement or were admitted with an EVD between December 2010 and January 2016. Institutional review board exemption was granted, given the study's quality improvement focus and the informed patient consent requirement was waived. Zip code was used to determine mean household income via the U.S. Census Bureau Online (https://factfinder.census.gov/faces/nav/jsf/pages/community_facts.xhtml) for all patients who were not homeless and lived in the United States. Insurance status (private, Medicare, Medicaid, and none) at the time of EVD placement also was collected.

Procedure-specific characteristics were obtained and recorded from the electronic medical record. Such factors included indication for EVD placement, anatomical location of EVD insertion, and site of procedure (operating room, intensive care unit, emergency department, radiology department, or outside hospital). Presence of bilateral EVDs also was noted. EVDs were placed according to a standardized hospital protocol. Initially, prophylactic periprocedural antibiotics (i.e., cefuroxime 1.5 g, cefazolin 1 g, or vancomycin 1 g) were given in every case, but in 2014 (3 years into the study period) we transitioned to the use of AI catheters in place of prophylactic oral or intravenous antibiotics.

Clinical comorbidities were controlled for using the Charlson Comorbidity Index (CCI), a weighted scale that accounts for age and history of myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic obstructive pulmonary disease, mild liver disease, controlled diabetes, hemiplegia, renal disease, diabetes with end organ damage, tumor without metastasis, leukemia or lymphoma, moderate or severe liver disease, AIDS, and tumor with metastasis.[11]

Outcomes measures included the need for EVD replacement, overall hospital length of stay, intensive care unit (ICU) length of stay, discharge modified Rankin Scale score, and infection. In the present study, ventriculostomy-associated ventriculitis was defined as a positive cerebrospinal fluid (CSF) gram stain plus the isolation of CSF culture with concurrent clinical symptoms of fever, seizure, or altered mental status. Total hospital cost for each individual patient was obtained from the hospital's billing department and consists of Diagnosis-Related Group codes and provider fees based on Current Procedural Terminology codes. Costs were classified as fixed direct, fixed indirect, variable direct, and variable indirect. Variable costs accounted for items like supplies and medications that vary with productivity or output; fixed costs, in contrast, do not vary with output and account for equipment, salaried labor, and other unalterable entities.[12] Direct costs are those that are associated with resource use directly attributable to a patient's care, whereas indirect costs represent standardized costs to the hospital that are theoretically divided among all patients (colloquially referred to as "overhead costs")

Statistical Analysis

All statistical analyses were performed on Statistical Analysis Software version 9.4 (SAS Institute; Cary, North Carolina, USA). Patients who developed VAIs were compared with those who did not develop a VAI. Nonparametric Wilcoxon tests were used to perform unadjusted analysis between the infected and noninfected cohorts on a variety of continuous and categorical variables. Univariate and multivariate linear regression models were created, assessing the effects of various factors on total costs, while controlling for age, sex, and the patient's CCI score.

RESULTS

Two-hundred forty-three patients with 246 EVDs were evaluated in the 5-year study period. The most common indication for EVD placement was subarachnoid hemorrhage (47.2%), followed by intracerebral hemorrhage (24.4%). Twenty-four patients developed EVD-associated ventriculitis (9.9%), 15 (62.5%) of which were gram positive and 9 (37.5%) of which were gram negative. Coagulase-negative *Staphylococcus* was the most common gram-positive organism cultured ($n = 8$) and *Klebsiella* pneumonia was the most common gram-negative organism seen ($n = 3$). Fifteen (62.5%) of the infected patients were on systemic antibiotics at the time of infection for unrelated conditions. There were no significant differences between those not infected versus those infected in age (51 vs. 57, $P = 0.31$) or sex (37.5% of females were infected vs. 47.75% who were not, $P = 0.34$). CCI score was associated with a greater risk of infection, with an average score of 2 in noninfected patients and 1 in infected patients, ($P = 0.04$; **Table 1**).

The overall median EVD duration was 10 days. The median EVD duration for patients who developed infections was 19 days compared with 9 days in patients without infections ($P < 0.0001$; **Table 1**). The median total hospital stay for patients with or without a VAI was 35.5 and 18 days, respectively ($P < 0.0001$; **Table 2**). Patients with VAIs also had a statistically longer median ICU length of stay compared with patients without infection (30 days vs. 13 days; $P < 0.0001$; **Table 2**).

Total health care costs were significantly increased for infected versus noninfected patients (US$ 168,629 vs. US$ 83,919, $P < 0.0001$; **Table 2**). This trend was comparable for all other cost subtypes including fixed direct (US$ 9973 vs. US$ 5079, $P < 0.001$), fixed indirect (US$ 74,473 vs. US$ 36,277, $P < 0.001$), variable direct (US$ 76,700 vs. US$ 36,870, $P < 0.001$), and variable indirect (US$ 8898 vs. US$ 4653, $P < 0.001$). The percentage cost increase for patients with infections was 96%, 105%, 108%, and 91%,

Table 1. Characteristics of a Single-Institution Population Undergoing EVD Placement With and Without Infections

	Not Infected (n = 222)	Infected (n = 24)	P Value
Age*	57 (44–66)	51 (44.5–62)	0.31
Charlson Comorbidity Index*	2 (1–4)	1 (0–2.5)	0.04
Sex (female)	106 (47.75%)	9 (37.50%)	0.34
Uninsured (yes)	80 (36.04%)	12 (50.00%)	0.18
Median household income*	$52,498 ($42,818–$70,322)	$52,168 ($44,933–$80,141)	0.72
Indication for EVD			0.7
ICH	55 (24.77%)	5 (20.83%)	
SAH	104 (46.85%)	12 (50.00%)	
Trauma	4 (1.80%)	0 (0.00%)	
Tumor	29 (13.06%)	3 (12.50%)	
Other	30 (13.51%)	4 (16.67%)	
Location of EVD placement			0.24
Emergency department	10 (4.52%)	2 (8.33%)	
Operating room	49 (22.17%)	2 (8.33%)	
Neurosurgical intensive care unit	133 (60.18%)	15 (62.50%)	
Radiology department	4 (1.81%)	1 (4.17%)	
Unknown or outside hospital	25 (11.31%)	4 (16.67%)	
Bilateral EVD placed	8 (3.60%)	7 (29.17%)	<0.0001
Prophylactic antibiotics received (yes)	175 (79.55%)	20 (86.96%)	0.4
EVD duration, days*	9 (5–14)	19 (13–29.5)	<0.0001

EVD, external ventricular drain; ICH, intracerebral hemorrhage; SAH, subarachnoid hemorrhage.
*Continuous data are presented as median (interquartile range).

respectively. There was no association between infection and median household income (US$ 52,498 for noninfected patients vs. US$ 52,168 for infected patients, $P = 0.72$) or insurance status. Of the uninsured patients, 12 (50%) developed EVD infections and 80 (36.7%) did not ($P = 0.18$; Table 1). Only EVD duration and EVD infection were significantly associated with an increased total cost $P < 0.0001$; Table 3).

DISCUSSION

A significant economic burden exists for patients, hospitals, and health care systems as a result of VAIs. In the present cost analysis, patients with VAI incurred drastically greater median total costs of hospital stay, costing on average $168,692, compared with $83,919 for patients with noninfected EVDs. Interestingly, when these values were dissected into their individual components—fixed direct, fixed indirect, variable direct and variable indirect—the proportional increase in cost between noninfected and infected cases remained the same.

The economics of infected implanted ventricular shunts for hydrocephalus has been well-studied and demonstrated a similar phenomenon: in these cases, shunt infections tend to cost up to $48,000 per patient,[4,13,14] with an estimated annual cost of $100 million in the United States.[13,15,16] Only a single previous study of cases from 1995 to 1998 by Lyke et al.[5] has indirectly estimated the total cost of an EVD infection based on hospital length of stay. In this study, EVD placement was accompanied by periprocedural antibiotic prophylaxis with mostly gram-positive coverage (typically oxacillin or cefazolin) for the duration of EVD implantation. The infected group had a mean hospital length of stay of 30.8 days versus 22.6 days in the uninfected group ($P = 0.03$), which corresponded with a mean total cost of $55,339.21 for uninfected patients and $85,674.27 for infected patients ($P = 0.009$).

In the present study, the median ICU length of stay for patients with an infection was 30 days, compared with 13 days in uninfected patients ($P < 0.0001$). The increased ICU stay (and thus total hospital length of stay) for infected patients corresponded to an increased median total cost. These results roughly correspond with the results from Lyke et al. when adjusted for inflation. This suggests that there has been minimal improvement in cost-reduction and prevention of EVD-associated infections in the past 2 decades.

Recently there have been numerous efforts to assess infection-reduction strategies, leading to updates in the guidelines for EVD management. The 2017 Infectious Diseases Society of America's "Clinical Practice Guidelines of Healthcare-Associated

Table 2. Outcomes of a Single-Institution Population Undergoing EVD Placement With and Without Infections

	Not Infected (n = 222)	Infected (n = 24)	P Value
Modified Rankin Scale at discharge			0.55
0	17 (7.69%)	2 (8.33%)	
1	21 (9.50%)	2 (8.33%)	
2	7 (3.17%)	0 (0.00%)	
3	14 (6.33%)	3 (12.50%)	
4	42 (19.00%)	4 (16.67%)	
5	55 (24.89%)	9 (37.50%)	
6	65 (29.41%)	4 (16.67%)	
ICU length of stay*	13 (8–20)	30 (18.5–51.5)	<0.0001
Total length of stay*	18 (12–27)	35.5 (24.5–64)	<0.0001
Total cost*	$83,919 ($48,457–$120,682)	$168,629 ($106,849–$273,449)	<0.0001
Fixed direct costs*†	$5079 ($3128–$7455)	$9963 ($6647–$16,085)	<0.0001
Fixed indirect costs*†	$36,277 ($20,561–$51,252)	$74,473 ($43,837–$124,348)	<0.0001
Variable direct costs*†	$36,870 ($21,820–$54,289)	$76,700 ($52,657–$119,220)	<0.0001
Variable indirect costs*†	$4653 ($2802–$6618)	$8898 ($5871–$17,026)	<0.0001

EVD, external ventricular drain; ICU, intensive care unit.
*Continuous data are presented as median (interquartile range).
†Number for the not-infected group equals 217.

Ventriculitis and Meningitis" now strongly recommends periprocedural antibiotic prophylaxis, the use of AI-EVDs, and the development of a standardized protocol. They further advise against prolonged antimicrobial prophylaxis for the duration of the EVD drain and fixed interval exchange of the shunts.[17] In our institution, we standardized the use of AI catheters in place of prophylactic oral or intravenous antibiotics starting in 2014 (3 years into our study period).

Current Infection-Prevention and Cost-Reduction Strategies: Systemic Antibiotics and AI-EVDs

A majority of published studies demonstrate no marked reduction in VAI with the use of systemic antibiotics. In a recent analysis of patients who received long-term systemic antibiotics, Murphy et al.[18] report no decrease in the incidence of EVD infection. Instead, they showed an increased rate of nosocomial infections (defined as bloodstream infection and ventilator-associated

Table 3. Univariate and Multivariable Linear Regression Analysis of Predictors of Total Costs

	Unadjusted		Adjusted	
	Parameter Estimate (95% CI)	P Value	Parameter Estimate (95% CI)	P Value
Age	−384 (−1283 to 515)	0.40	Covariates in multivariable model	
Sex (male)	−11,665 (−38,236 to 14,906)	0.39		
CCI	−2840 (−8772 to 3092)	0.35		
Median household income	−0.26 (−0.79 to 0.27)	0.33	−0.23 (−0.76 to 0.30)	0.39
EVD duration	6885 (5529–8241)	<0.0001	6929 (5543–8314)	<0.0001
EVD infection	120,092 (78,380–161,806)	<0.0001	118,295 (76,012–60,578)	<0.0001
Insurance status (no)	5975 (−33,498 to 21,549)	0.67	−1943 (−30,297 to 26,412)	0.89

CCI, Charlson Comorbidity Index; EVD, external ventricular drain.

pneumonia) at an increased overall cost. Patients receiving systemic antibiotics had 2% rate of nosocomial infections compared with patients who only received periprocedural antibiotics during EVD placement ($P = 0.026$). Furthermore, the authors report corresponding cost-savings of $162,516 in the cohort receiving one-time antibiotic treatment due to the cost of systemic antibiotics and treatment of nosocomial infections.

Alleyne et al.[19] similarly found no relationship between VAI rates and systemic antibiotic use (4% incidence of infection in both the cohort receiving antibiotics and the cohort that did not) in a retrospective study of 208 patients. They too report savings of $80,000 directly related to minimizing drug costs. Stenager et al.[20] confirmed these results in a prospective study, with infection rates of 10% and 18% in the nonantibiotic group and antibiotic group, respectively.

Conversely, in a systematic review of 3 randomized studies and 7 observational studies, prolonged systemic antibiotics was associated with a reduced relative risk of infection of 0.32. The study had numerous limitations, however, including disparities in the definitions of ventriculitis and the types and doses of antibiotics ($I^2 = 53\%$). Despite the purported advantage of systemic antibiotics in this series, the authors warned that long-term use of broad-spectrum antibiotics can predispose patients to resistant bacterial strains, complications of antibiotic use and increased costs.[2]

Overall, there is extensive evidence demonstrating that the use of AI-EVDs significantly decreases rates of infection and treatment cost. In a prospective randomized trial, Wong et al.[21] examined the efficacy of AI-EVDs (coated with clindamycin plus rifampin) versus systemic antibiotics (intravenous ampicillin-sulbactam plus ceftriaxone) for CSF infections and found no significant difference in outcome measures such as infection, ICU length of stay, and functional outcome between the 2 groups. The authors did, however, show that AI-catheters decrease overall costs. They estimate the daily cost of prophylactic antibiotics to be $60 and the use of a Bactiseal (Codman, Johnson & Johnson, Raynham, Massachusetts, USA) catheter to be $346. Thus, it appears to be more cost-effective to use an AI-catheter only if the EVD is in place for greater than 6 days,[21] which is shorter than our cohort's overall median EVD duration of 10 days.

Large-scale studies corroborate these results. A systematic review and meta-analysis of 2 randomized control trials and 11 observational studies demonstrated a significant reduction in infection with the use of AI-EVDs (risk ratio = 0.31; $P = 0.009$).[22] Furthermore, in a pooled analysis of 2 adult randomized control trials, 2 pediatric prospective cohort series, and 2 combined adult and pediatric prospective cohort studies that compared AI-EVDs and non AI-EVDs in hydrocephalus, VAIs were decreased 75.2% with the use of AI-EVDs. The authors concluded that in 100 patients requiring EVDs, 2.7 fewer infection-related deaths would occur with 82 fewer hospital days if AI catheters were standard protocol. Moreover, they estimate $264,069 in savings per 100 AI-EVDs, based on the assumptions that the total hospital cost of infections with non-AI EVDs is $404,608, minus the $100,539 cost of infection with an AI-EVD and the $40,000 incremental cost of an AI-catheter.[4] Another meta-analysis of AI-EVD literature revealed marked protective effects and cost reduction associated with AI-EVDs compared with non AI-EVDs (risk ratio 0.31, 95% confidence interval [CI] 0.15–0.64); $P = 0.002$). Although the authors acknowledge significant heterogeneity in their pooled analysis ($I^2 = 61\%$), they also report estimated overall savings of approximately $28,100 per VAI with the use of AI-EVDs, or cost savings of $109,244–$278,239 per year if 150 AI-EVDs are placed at a given hospital annually.[7]

AI-EVDs have not appeared to alter the susceptibility of microorganisms or change the cultures from predominately gram positive to gram negative.[23] Although there also have been studies that find AI-EVDs to have no protective effect when compared to standard EVDs,[24] they do not appear to be harmful nor do they add a cost burden.

Socioeconomic Status and Increased Cost

Whether socioeconomic or insurance status contributed to the risk of EVD infection was another aim of the present study, as poor socioeconomic status has historically been associated with a general increased rate of infection and health care costs. Although this phenomenon has yet to be examined in patients with EVD, results from studies of implanted ventricular shunts demonstrate variable trends. A study by Patwardhan and Nanda[25] in 2005 found no disparity among socioeconomic status in the Nationwide Inpatient Sample database in terms of cost, yet a pediatric study of patients with hydrocephalus using the Pediatric Health Information Systems database did reveal a significant difference among insurance status and race and CSF shunt infection. Patients with public insurance were more likely to become infected (odds ratio [OR] 1.3, 95% CI 1.1–1.5), as were non-Latino black patients (OR 1.6, 95% CI 1.3–2.0) and Asian patients (OR 1.7, 95% CI 1.0–2.9).[26] An international series suggested that poor socioeconomic status correlates with latency of presentation with hydrocephalus—and thus increased rates of morbidity and mortality—but because EVD infections occur in a hospital setting, this is less relevant.[27]

Further investigation reveals that in an inpatient neurosurgical setting, risk of morbidity and mortality is associated with hospital procedural volume rather than demographic characteristics. In a study of 444,751 patients with brain tumor, using the Nationwide Inpatient Database, the authors found that hospitals with high volume had decreased rates of mortalities compared with hospitals with lower volumes.[28] Moreover, although demographic variables did not contribute directly to mortality risk, numerous studies have shown that minority patients were less likely to seek surgical care at high-volume centers.[29,30]

In the present analysis, there was no relationship found between socioeconomic status or insurance status and rates of EVD infection or cost in our series. The institution at which this study was completed is a tertiary-care teaching facility with a robust neurosurgical department, which, according to these findings, may contribute to the lack of disparity between infection and cost among socioeconomic strata in the present study.

Prevention Strategies

Although current efforts to decrease rates of VAI are promising, broader incentives to prevent infection should also be considered. The United States has begun to move toward a value-based health care system, implementing financial incentives in an effort to decrease infection rates and readmissions. Interestingly, neurosurgery has yet to be included in many of the initiatives. For example, the current Centers for Medicare and Medicaid Services policy that withholds reimbursements for hospital-acquired conditions, implemented in 2008, does not include EVD-associated infections on its list of preventable conditions (https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/HospitalAcqCond/Hospital-Acquired_Conditions.html).

Nonetheless, based on existing data for well-studied hospital-acquired conditions that were included, such as central line–associated bloodstream infections (CLABSI) and catheter-associated urinary tract infections, there is little evidence to suggest that these financial penalties had a meaningful impact on cost and infection rates. A study comparing CLABSI and catheter-associated urinary tract infections rates of infection with the rates of ventilator-associated pneumonia—a nosocomial infection that was not targeted by the Centers for Medicare and Medicaid Services policy—reported similar trends among each infection type. Rates of infection decreased prior to the implementation of the financial penalty and consistently afterward, too. This was true for centers with and without mandatory reporting of CLABSI and CAUDI infections and has been confirmed by other similar analyses.[31,32] Though analyses for these conditions did not show promising results, government incentives targeting VAI-reduction should not be overlooked.

Limitations

This study evaluated the economic impact of ventricular drain-associated infections for patients with EVDs over a 5-year period using data garnered from the institution's billing department. While these costs provide basic insight into the gravity of an EVD infection, patients may suffer additional economic consequences such as lost work or wages, decreased quality of life, or further medical costs following VAI. These societal indirect costs and consequences are beyond the scope of the current analysis and further studies are recommended to better quantify their impact. Another limitation is the use of median household income based on patient ZIP code as a surrogate for patient income. While this serves as a general approximation of patient socioeconomic status, its accuracy may be limited. Lastly, although the evolvement of our EVD placement protocol (i.e. the transition from prophylactic antibiotics to the use of AI-EVDs without systemic antibiotics in 2014) may have skewed the infection analysis, this was not the focus of the study.

CONCLUSIONS

In addition to increased clinical morbidity, both hospitals and patients incur a significant financial burden with EVD-associated infections. The cost of a hospital stay for a patient with a VAI is approximately double that of a patient without EVD-associated infection. Moreover, patients' socioeconomic levels or insurance statuses do not predispose patients to EVD infection. These results demonstrate the imperative need for continued efforts to improve EVD infection prevention, both in decreasing clinical morbidity and lowering the cost of neurosurgical care for hospitals and patients, particularly in the setting of a value-based health care system.

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