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Predictors of extraventricular drain–associated bacterial ventriculitis ☆

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ABSTRACT

Purpose: Bacterial ventriculitis (BV) may develop in patients requiring external ventricular drains (EVDs). The purpose of this study was to determine predictors of EVD-associated BV onset.
Materials and Methods: A retrospective review of Duke University Hospital patients with EVD device placement between January 2005 and May 2010 was conducted. Subject data were captured for predefined variables. Outcomes included in-hospital mortality, length of stay, and neurologic status at discharge.
Results: In 410 subjects with 420 EVDs, the BV rate was 10.2%. Univariate analysis indicated that age, sex, positive blood culture, duration of EVD placement, and the number of cerebrospinal fluid (CSF) samples taken were associated with BV. Of these, the number of CSF samples and sex retained significance in multivariable modeling (female: odds ratio, 0.47 [confidence interval, 0.23-0.97]; CSF samples: odds ratio, 1.08 [confidence interval 1.01-1.17]; $P = .04$; c index = 0.69). In this model, each CSF sample taken expanded the likelihood of BV by 8.3%. The most common pathogens were *Staphylococcus* or proprioniobacter (n = 26). Bacterial ventriculitis was associated with an increase in hospital length of stay (33 ± 22.9 days vs 24.6 ± 20.4 days; $P = .04$) but not mortality.
Conclusion: An association exists between CSF sampling frequency and the development of EVD-associated BV. Larger prospective studies should be aimed at identifying causal relationships between these variables.

1. Introduction

External ventricular drain (EVD) placement is a common neurointensive care intervention for critically ill adult patients. Use of EVDs remains the cornerstone for monitoring and treating elevated intracranial pressure and hydrocephalus. Furthermore, EVDs have seen recent use as a therapeutic intervention for drainage of intraventricular hematomas [1]. Despite this, EVD placement and management are not without significant risk. The most obvious acute risk is resultant hemorrhage occurring immediately after EVD insertion. Other acute risks include pneumocephalus, damage to deep brain structures, and overdrainage of cerebrospinal fluid (CSF). More insidious is potential bacterial infection introduced into the CSF-filled spaces around and/or through the EVD.

Bacterial ventriculitis (BV) is inflammation of the ventricular drainage systemic due to bacterial infection of the CSF. Bacterial ventriculitis may often be linked to CSF drainage through an EVD. Published EVD-related BV rates range from 3.8% to 23.2%, with mortality rates spanning from 10% to 75% [2-4]. Further complicating this clinical picture is the introduction of antibiotic- [5] and silver-impregnated [6,7] EVD catheters. Both types of impregnated catheters have demonstrated reduced infection rates, although they fail to completely reduce the risk of infection. In addition, widespread use of these devices is still lacking because of disparity in outcome [8].

Thus, there remains controversy regarding the risk factors for EVD-related BV [9]. Although multiple factors may explain disparities in study results, duration of EVD placement, CSF sampling frequency, and contemporaneous systemic infections may affect the likelihood of EVD-related BV onset [10-12]. Although prior studies have examined risk factors and outcomes for EVD-related BV [13,14], predicting the occurrence of EVD-related BV remains difficult in individual patients.

The purpose of this study was to use the Duke University Hospital Neuroscience Critical Care Unit (NCCU) database to examine variables associated with EVD-related BV and construct a multivariate model to provide a predictive tool for this complication.

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2. Methods

2.1. Population

After Duke University Institutional Review Board approval, data were retrospectively abstracted from the Duke University Hospital NCCU database. Patients who underwent EVD placement and had at least 1 CSF sample sent for microbiological analysis while that EVD was in place were included. Subjects were identified using 2 clinical research tools: CSF sample records from the Clinical Microbiology Laboratory (CML) and procedure records from the Duke Enterprise Data Unified Content Explorer (DEDUCE), a database of clinical information from discharged patients. The CML data provided a list of all instances of CSF analysis from January 2005 through May 2010. Subjects were excluded if they had ventriculoperitoneal shunts (VPSs), lumbar CSF drains, or bacterial meningitis during the same hospitalization before EVD insertion or CSF sampling was performed only via lumbar puncture or drain. Multiple EVD placements occurring more than 48 hours apart were considered as separate EVD encounters. Subjects from this list were then crosschecked in DEDUCE to isolate subjects who had undergone EVD placement.

2.2. Data collection

Subjects identified in the CML and DEDUCE database searches were linked by medical record number to the NCCU database. Individual subject data were abstracted from the NCCU database by the primary investigator (R.A.W.) onto a spreadsheet (msExcel). All data points were independently verified for accuracy by a blinded reviewer (M.C.G.). Each subject's chart was examined for variables and in-hospital outcomes. Among others, collected variables included dates and species of bacterial cultures concurrent with EVD placement, presence of methicillin-resistant *Staphylococcus aureus* (MRSA) or vancomycin-resistant *Enterococcus* (VRE) colonization signified by the presence of bacterial ribonucleic acid by nasal or rectal swab before EVD placement, duration of EVD placement, number of CSF samples drawn while EVD was in place, demographics, weight, and comorbidities. The number of times the EVD tubing was violated (flushing, etc) for reasons other than CSF for analysis was not captured. Outcome variables included length of stay (LOS), mortality at discharge, discharge to hospice, modified Rankin Score (mRS) at discharge, and Glasgow Outcome Score (GOS) at discharge.

2.3. Definition of ventriculitis, duration, and sampling

External ventricular drain–related BV was defined as positive CSF culture in a patient with a concurrent EVD. This definition is consistent with other studies reporting BV rates [12,15-17]. *Bacterial ventriculitis onset* was defined as the first date of CSF collection returning with positive CSF culture. External ventricular drain days were measured from the first EVD placement to BV onset or EVD removal for greater than 48 hours, whichever came first. Thus, EVD duration included catheter exchanges; however, patients admitted to the NCCU at Duke University Hospital do not undergo routine catheter exchange. Cerebrospinal fluid sampling was measured in number of CSF analyses performed during EVD duration. Cerebrospinal fluid sampling did not include subsequent CSF analyses after BV onset. In patients admitted to the NCCU at Duke University Hospital, routine CSF sampling is not standard practice. Rather, CSF sampling occurs when there is suspicion of CSF infection; furthermore, CSF culture occurs at a maximum frequency of every 72 hours in patients with a persistent fever and EVD.

2.4. Statistics

Univariate analysis was performed to identify covariates predictive of ventriculitis using Statistical Analysis Software (v9.3; SAS, Cary, NC). *P* values are calculated using *t* tests for continuous variables and χ^2 tests for categorical variables. Values are presented as mean ± SD. Owing to the small number of outcomes (case of BV), those variables meeting an a priori significance level of $P < .15$ in univariate analysis were used to construct a multivariate logistic regression model predicting the risk of ventriculitis. Logistic regression models were also used to determine associations between the number of days that an EVD was in place before infection, the number of CSF samples drawn from an EVD before infection, and the pathogen species of the ventriculitis. Significance was assigned at $P < .05$. Results were described using an odds ratio estimate with 95% confidence limits. *P* values for outcome measures are calculated using *t* tests for continuous variables and χ^2 tests for categorical variables.

Table 1
Univariate descriptive statistics: ventriculitis vs no ventriculitis

	No EVD-related BV (n = 377)	EVD-related BV (n = 43)	*P*
Age (y), mean (SD)	50.8 (16.6)	46.7 (14.9)	.12
Weight (kg), mean (SD)	80.4 (19.9)	79.0 (18.8)	.64
EVD days, mean (SD)	10.4 (6.8)	13.8 (10.9)	.05
Race (% white)	53.1	44.2	.27
Sex (% female)	48.5	32.6	.05
Diabetes (%)	11.7	11.6	.99
VRE colonization (%)	1.7	4.7	.23
MRSA colonization (%)	11.4	11.6	.96
Positive blood culture (%)	19.9	32.6	.05
Positive urine culture (%)	32.6	32.6	.99
Positive sputum culture (%)	62.6	67.4	.53
CSF sampling, mean (SD)	3.2 (3.9)	5.6 (4.5)	<.01

EVD days was defined as the duration in days before the first positive CSF culture or EVD removal. VRE and MRSA colonization were verified by nasal and rectal swabs for bacterial RNA. Blood, urine, and sputum cultures were considered positive if there was bacterial growth on the most recent sample before EVD insertion during the same hospitalization. Cerebrospinal fluid sampling was defined as the number of samples sent after EVD insertion and before the first positive CSF culture or EVD removal, whichever came first.
n indicates number.

3. Results

Of the 440 patients identified with EVDs over the period studied, 30 patients were excluded because of preexisting VPS (n = 24) or initial diagnosis of meningitis (n = 6). No patients were excluded for the preexisting lumbar CSF drains or CSF sampling occurring from lumbar puncture or lumbar drains only. Twenty subjects meeting the inclusion and exclusion criteria underwent more than 1 EVD placement separated by greater than 48 hours. The average number of EVDs placed in this group was 2.1 ± 0.4. For the study population of 410 subjects, a total of 420 EVD encounters were analyzed. External ventricular drain latency (time from insertion to removal or BV) lasted an average of 10.7 ± 7.3 (range, 1-64 days), and the average number of CSF samples taken from each EVD during that time was 3.4 ± 4.0 (range, 0-59). Finally, the number of EVD encounters per year over the course of study increased steadily from 54 in 2005 to 93 in 2009.

External ventricular drain encounters were categorized based on the presence (n = 43, or 10.2% of the total study population) or absence (n = 377) of EVD-related BV. The characteristics of these 2 groups are listed in Table 1. External ventricular drain encounters without EVD-related BV occurred more often in women, with less CSF sampling, concomitant positive blood cultures, and EVD days.

3.1. Ventriculitis, EVD latency, sampling frequency, and CSF culture species

To evaluate the characteristics of EVD-related BV, we used regression models were used to determine the associations between