### **Original Article**



# Risk factors and outcomes associated with external ventricular drain infections

Konrad W. Walek BS<sup>1</sup> (), Owen P. Leary BS<sup>1</sup> (), Rahul Sastry MD<sup>1</sup> (), Wael F. Asaad MD, PhD<sup>1,2,3</sup> (), Joan M. Walsh DNP,

APRN CNS<sup>4</sup> (D), Jean Horoho RN<sup>5</sup> and Leonard A. Mermel DO, ScM, AM (Hon), FSHEA, FIDSA, FACP<sup>6,7</sup> (D)

<sup>1</sup>Department of Neurosurgery, Warren Alpert Medical School of Medicine of Brown University, Providence, Rhode Island, USA, <sup>2</sup>Department of Neuroscience, Brown University, Providence, Rhode Island, USA, <sup>3</sup>Norman Prince Neuroscience Institute, Rhode Island Hospital, Providence, Rhode Island, USA, <sup>4</sup>Division of Critical Care, Department of Nursing, Rhode Island Hospital, Providence, Rhode Island, USA, <sup>5</sup>Department of Epidemiology and Infection Control, Rhode Island Hospital, Providence, Rhode Island, USA, <sup>6</sup>Department of Epidemiology and Infection Prevention, Lifespan Hospital System, Providence, Rhode Island, USA and <sup>7</sup>Division of Infectious Diseases, Rhode Island Hospital, Providence, Rhode Island, USA

#### Abstract

Background: Insertion of an external ventricular drain (EVD) is a common neurosurgical procedure which may lead to serious complications including infection. Some risk factors associated with EVD infection are well established. Others remain less certain, including specific indications for placement, prior neurosurgery, and prior EVD placement.

Objective: To identify risk factors for EVD infections.

Methods: We reviewed all EVD insertions at our institution from March 2015 through May 2019 following implementation of a standardized infection control protocol for EVD insertion and maintenance. Cox regression was used to identify risk factors for EVD infections.

Results: 479 EVDs placed in 409 patients met inclusion criteria, and 9 culture-positive infections were observed during the study period. The risk of infection within 30 days of EVD placement was 2.2% (2.3 infections/1,000 EVD days). Coagulase-negative staphylococci were identified in 6 of the 9 EVD infections). EVD infection led to prolonged length of stay post–EVD-placement (23 days vs 16 days; P = .045). Cox regression demonstrated increased infection risk in patients with prior brain surgery associated with cerebrospinal fluid (CSF) diversion (HR, 8.08; 95% CI, 1.7–39.4; P = .010), CSF leak around the catheter (HR, 21.0; 95% CI, 7.0–145.1; P = .0007), and insertion site dehiscence (HR, 7.53; 95% CI, 1.04–37.1; P = .0407). Duration of EVD use >7 days was not associated with infection risk (HR, 0.62; 95% CI, 0.07–5.45; P = .669).

Conclusion: Risk factors associated with EVD infection include prior brain surgery, CSF leak, and insertion site dehiscence. We found no significant association between infection risk and duration of EVD placement.

(Received 23 August 2021; accepted 24 January 2022; electronically published 26 April 2022)

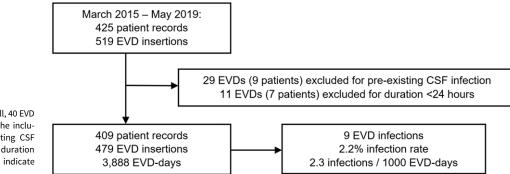
External ventricular drain (EVD) insertion may lead to serious complications including infection, which increases the risk of poor neurosurgical outcomes, increases healthcare costs, and prolongs hospital stays.<sup>1</sup> The incidence of EVD infection ranges from 0% to 45%<sup>2–21</sup>; the largest study reported that ~4% of EVDs placed resulted in infection.<sup>4</sup> Many interventions for reducing infection risk have been proposed. Factors previously associated with increased risk of EVD infection include prolonged EVD drainage, cerebrospinal fluid (CSF) leak, EVD manipulation including frequency of CSF sampling, tract hemorrhage at placement, and insufficient hair clipping.<sup>1–6,8–</sup> <sup>20,22,23</sup> Factors associated with reduced risk include perioperative and immediate postoperative antibiotics, as well as antibiotic-impregnated EVDs.<sup>21,24–29</sup> Some additional risk factors for which there has been no conclusive association with EVD infection include age, sex, Glasgow coma scale (GCS) score, elevated intracranial pressure (ICP) at time of EVD placement, systemic infection, prolonged use of postprocedural antibiotics, prolonged hospital stay prior to EVD placement, involuntary EVD disconnection, placement by a junior surgeon, or coverage of the insertion site with a dressing.<sup>1–6,8–20,22– <sup>25</sup> Controversy continues over whether specific indications for EVD placement (eg, brain trauma or intracranial hemorrhage), history of previous EVD placement, prior neurosurgery, and EVD irrigation contribute to infection risk.<sup>1–6,8–20,22–25</sup></sup>

Several institutions, including our own, have demonstrated a significant reduction in EVD infections through implementation of protocols for EVD insertion and maintenance.<sup>3,6–8,10,11,13–15,17,20,23,30</sup> In 2007, the Department of Epidemiology and Infection Control at our institution identified a high incidence of EVD infections and, in response, formed an EVD Infection Control Committee. This committee has recorded all EVD infections as they have occurred, has

Author for correspondence: Leonard A. Mermel, DO, ScM, E-mail: lmermel@lifespan. org

Cite this article: Walek KW, et al. (2022). Risk factors and outcomes associated with external ventricular drain infections. Infection Control & Hospital Epidemiology, 43: 1859–1866, https://doi.org/10.1017/ice.2022.23

<sup>©</sup> The Author(s), 2022. Published by Cambridge University Press on behalf of The Society for Healthcare Epidemiology of America. This is an Open Access article, distributed under the terms of the Creative Commons Attribution licence (https://creativecommons.org/licenses/by/4.0/), which permits unrestricted re-use, distribution, and reproduction in any medium, provided the original work is properly cited.



**Fig. 1.** Selection for study Inclusion. Overall, 40 EVD records across 16 patients did not meet the inclusion criteria for analysis due to pre-existing CSF infection (29 EVDs, 9 patients) or EVD duration <24 hours (11 EVDs, 7 patients). Arrows indicate steps in selection process.

periodically recommended changes in practice, and has assessed the impact of these interventions over time. Major elements of this protocol include minimal EVD manipulation after insertion, no routine CSF sampling, and regular cleansing of the insertion site with alcoholic chlorhexidine while the EVD is in situ.<sup>30</sup>

We undertook a retrospective review of prospectively collected data regarding EVD infections among adult or pediatric patients who received an EVD from March 2015 to May 2019 at our 719-bed, tertiary-care, academic medical center.

#### Methods

#### Data collection and outcome measures

With approval from our institutional review board (no. 1396435), clinical data were collected from the electronic medical record by one investigator (KW). EVD placement was identified in medical records utilizing billing codes (ie, Current Procedural Terminology-CPT; *International Classification of Disease, Ninth Revision*–ICD-9; and *International Classification of Disease, Tenth Revision* Procedure Coding System–ICD-10-PCS) for procedures associated with ventricular drainage via EVD that occurred during the study period. Individual charts were then reviewed to confirm the placement of an EVD and to exclude patients who had other CSF drainage procedures or miscoded procedures. Inclusion was not limited by age, sex, or indication for EVD placement. We applied the following exclusion criteria: EVD placement as part of treatment for an active CSF infection, EVD dwell time <24 hours, and pregnancy. In total, 479 EVDs placed in 409 patients were included in this study.

Our primary outcome was development of an EVD infection following EVD placement. The Center for Disease Control and Prevention National Healthcare Safety Network (CDC NHSN) has not defined EVD infections. For this study, we used the CDC NHSN definition of meningitis/ventriculitis<sup>31</sup> in patients with an EVD in situ or within 30 days of EVD removal. Secondary outcomes included EVD duration, need for EVD flushing, CSF leak, dehiscence of surgical site, total number of EVDs placed per patient, 30-day functional outcome via modified Rankin Scale (mRS) score, and total length of hospital stay. Other collected variables included age, sex, GCS at insertion, indication for insertion, comorbidities, history of brain surgery including prior EVD placement, and site of EVD placement. For patients who developed an EVD infection, additional data were collected on microbial culture results, initial and final choice of antimicrobial therapy, antimicrobial treatment duration, and number of days after insertion when EVD infection occurred.

## Treatment, procedural management, and infection control protocol

Indications for EVD placement in this patient cohort included subarachnoid hemorrhage (SAH), intracerebral hemorrhage (ICH), intraventricular hemorrhage (IVH), epidural hematoma (EDH), subdural hematoma (SDH), severe traumatic brain injury (TBI), obstructive hydrocephalus, space-occupying lesion, arteriovenous malformation, or shunt failure. EVD insertions were performed at the bedside or in the operating room. No antibiotic prophylaxis was given to the patient before the procedure or while the EVD was in place. Indications for sampling CSF from an implanted EVD were clinical or imaging suspicion of CNS infection or persistent fever. Routine sampling of CSF was not performed. The insertion site of an indwelling EVD was cleaned daily with alcoholic chlorhexidine and inspected for signs of dehiscence, CSF leak, or infection.

EVDs placed in our institution were predominantly nonantimicrobial-impregnated devices (Codman EDS3, Integra LifeSciences; Princeton, NJ). Antimicrobial-impregnated EVDs were reserved for patients with high suspicion of active CSF infection at the time of EVD placement and were thus excluded from this study.

#### Statistical analysis

Data were anonymized and exported to Microsoft Excel (Microsoft, Redmond, WA). Missing variables were assessed, and duplicate entries were removed. Continuous variables with normal and nonnormal distributions were represented as mean (± standard deviation, SD) and median (± interquartile range, IQR) respectively. Categorical data were represented as proportions with percentages. Statistical significance of comparisons between data was determined using the independent sample t test between mean values; using the nonparametric Kruskall-Wallis equality-of-populations rank test between median values; and using the  $\chi^2$  test or the Fisher exact test, as appropriate, between categorical data. Cox regression analysis was conducted to determine hazard ratios and contribution of independent risk factors to EVD infection risk. *P* < .05 was considered significant. Data analysis was conducted using Statistical Package for Social Sciences (SPSS) version 24 software (IBM, Armonk, NY) and MedCalc version 19.4 software (MedCalc Software, Belgium).

#### Results

Overall, 479 EVDs inserted in 409 patients for 3,888 EVD days were included for analysis (Fig. 1). We observed a similar

distribution of sex for patients receiving EVDs, with 55% males, 45% females, an age range of 18 days to 94 years, and a median age of 54 years (Table 1). Most EVD insertions involved patients with SAH (n = 145, 30%), ICH or IVH (n = 112, 23%), and severe TBI including EDH/SDH (n = 110, 23%). At the time of EVD insertion, patients had a median GCS of 7 (IQR, 3–13); 81% were intubated. Moreover, 9 EVD infections occurred in 9 patients, for an overall infection rate of 2.2% (2.3 infections per 1,000 EVD days).

#### Effect of comorbidities on EVD infection risk

In total, 10 EVDs (2.1%) were placed in immunocompromised patients (ie, absolute neutrophil count <500/mm<sup>3</sup> and/or the use of 1 or more immunosuppressive medications). Also, 5 EVDs (1.0%) were placed in patients with type I diabetes mellitus, and 35 (7.3%) were placed in patients with type II diabetes mellitus. Although the presence of active CNS infection was an exclusion criterion, 9 EVDs (1.9%) were inserted in patients with a history of resolved CNS infection. None of these patients developed an EVD infection (Table 1).

EVDs placed in patients with a history of prior brain surgery was associated with an increased risk for EVD infection (OR, 7.8; 95% CI, 1.6–37.8; P = .0097), independent of the specific indication for brain surgery (Table 1). When further stratified by prior brain surgeries with and without concurrent or previous shunt or EVD placement, only surgeries with prior EVD or shunt placement were associated with higher EVD infection risk (OR, 5.7; 95% CI, 1.5–21.7; P = .011).

#### Effect of operative variables on EVD infection risk

Most EVDs were placed in the neurocritical care unit (NCCU; n = 268, 56%) and emergency department (n = 109, 23%) (Table 2). All 9 EVD infections occurred in the NCCU while the EVD was in place (P = .0056). The median EVD day-of-infection diagnosis was 4 days (minimum 2, maximum 11; IQR, 2–7). Most EVDs were placed by neurosurgery residents, most commonly by junior residents (n = 217, 45%). The overwhelming majority of catheters were inserted frontally at the Kocher point (n = 455; 366 right-sided and 89 left-sided). Risk of EVD infection was not influenced by training level of the primary surgeon, anatomic site of EVD insertion, total EVD indwelling time, or number of EVDs per patient.

#### EVD infection risk factors

EVD infection was associated with prolonged post-EVD-placement length of stay (23 days vs 16 days; P = .045). Upon development of an EVD infection, the device was weaned and removed promptly. If the patient continued to require CSF diversion, it was replaced with an antibiotic-impregnated catheter. Median length of treatment with antibiotics after diagnosis of EVD infection was 14 days (minimum 10, maximum 42; IQR, 14–28). The most common pathogens associated with these infections were coagulase-negative staphylococci (Table 3). Two cases were polymicrobial: one case involving *Micrococcus luteus* and *Pantoea agglomerans*, the other involving coagulase-negative staphylococci and *Cutibacterium acnes*.

Cox regression analysis adjusted for age, sex, and indication for EVD placement demonstrated increased infection risk associated with prior brain surgery involving EVD or shunt placement (HR, 8.08; 95% CI, 1.7-39.4; P = .010), development of a postoperative

CSF leak (HR, 21.0; 95% CI, 7.0–145.1; P = .0007), and dehiscence of surgical site (HR, 7.53; 95% CI, 1.04–37.1; P = .0407). Duration of EVD placement >7 days was not associated with infection risk (HR, 0.62; 95% CI, 0.07–5.45; P = .669).

#### Mortality and functional outcomes

In total, 135 (33%) deaths were observed within 30 days after EVD insertion. Of the 274 patients surviving at 30 days following EVD insertion, 48 (18%) were lost to follow-up, 134 (49%) had good functional outcomes (mRS, 0–2), and 92 (34%) had poor functional outcomes (mRS, 3–5). We detected no significant difference in mortality or mRS in patients with EVD infection when compared to those without EVD infection. Of the 2 patients with EVD infection who died, one death was due to complications of infection and the other was due to complications of shunt failure (Table 3).

#### Discussion

Previously identified risk factors for EVD infection include prolonged EVD dwell time, prior surgery, CSF leak, frequency of CSF sampling and EVD manipulation, insufficient tunneling of the EVD catheter, tract hemorrhage at placement, and insufficient hair clipping.<sup>1–6,8–20,22,23,25,32–34</sup> Previous brain surgery has been demonstrated to be an independent risk factor for EVD infection.<sup>2,3,5,6,8,15,16,18,19</sup> Our findings support these reports. Stratification by type of surgery revealed that this increased risk was specifically related to cranial surgeries with EVD or shunt placement concurrently with or before the surgery. To our knowledge, this has not been previously noted in the literature.

Prolonged EVD duration is associated with an increased risk of EVD-related infection.<sup>2,3,5,9,12-14,16-19,25,32,33</sup> Surprisingly, we did not find this to be the case. Most infections we observed occurred within 1–7 days of EVD insertion. Prolonged EVD dwell time was associated with a nonsignificant decrease in incidence of EVD infections (2.0% risk for 1–7 days, 1.9% risk for 8–14 days, 1.6% risk for >14 days). We hypothesize that this unexpected result is due to several longstanding, evidence-based infection control protocols in place at our institution, including minimal catheter manipulation after insertion, no routine CSF sampling, and regular cleansing of the insertion site with alcoholic chlorhexidine.<sup>1–3,10,14–20,22,30</sup>

Other known risk factors associated with EVD infection include CSF leak, frequency of CSF sampling, and EVD manipulation.<sup>1,3,5,11,13–15,17–19</sup> Although our institution has not routinely sampled CSF without suspicion of infection since 2008, analysis of this cohort identified a dramatically increased risk of infection with CSF leak. Indeed, CSF leak was the strongest risk factor identified in our study; although CSF leakage around the insertion site occurred in only 11 EVDs, 3 of these EVDs subsequently became infected. CSF leak has consistently been identified as a major contributor to the risk of EVD infection, and our findings further emphasize the importance of careful surgical technique during EVD catheter placement to ensure watertight wound closure and a tight seal around the catheter to mitigate risk of CSF leak and subsequent EVD infection.

Several prior studies have demonstrated SAH and IVH as independent risk factors for EVD infection.<sup>2,5,9,12,25</sup> Of 9 EVD infections we identified, 3 occurred in patients with SAH and 4 in patients with ICH or IVH. However, these 2 indications for EVD placement comprised most cases requiring EVD insertion

#### Table 1. Patient Demographics

| Sex, male:female<br>Age at procedure, mean y (SD)<br>GCS at insertion (SD)<br>Age group<br>0–17 y<br>18–39 y<br>40–69 y<br>70+<br>Intubation status<br>Intubated<br>Not intubated<br>Primary diagnosis<br>SAH | 7:2<br>55 (±16)<br>8.0 (±4.7)<br>0<br>2<br>6<br>1<br>7<br>2<br>2<br>2 | 256:214<br>49 (±22)<br>7.9 (±4.4)<br>49<br>88<br>272<br>81<br>379<br>91 | .195<br>.230<br>NS<br>NS<br>NS<br>NS<br>NS |
|---|---|---|--|
| GCS at insertion (SD)<br>Age group<br>0-17 y<br>18-39 y<br>40-69 y<br>70+<br>Intubation status<br>Intubated<br>Not intubated<br>Primary diagnosis   | 8.0 (±4.7)<br>0<br>2<br>6<br>1<br>7<br>2                              | 7.9 (±4.4)<br>49<br>88<br>272<br>81<br>379                              | NS<br>NS<br>NS<br>NS                       |
| Age group<br>0-17 y<br>18-39 y<br>40-69 y<br>70+<br>Intubation status<br>Intubated<br>Not intubated<br>Primary diagnosis  | 0<br>2<br>6<br>1<br>7<br>2  | 49<br>88<br>272<br>81<br>379  | NS<br>NS<br>NS<br>NS                       |
| 0-17 y<br>18-39 y<br>40-69 y<br>70+<br>Intubation status<br>Intubated<br>Not intubated<br>Primary diagnosis   | 2<br>6<br>1<br>7<br>2   | 88<br>272<br>81<br>379  | NS<br>NS<br>NS                             |
| 18-39 y<br>40-69 y<br>70+<br>Intubation status<br>Intubated<br>Not intubated<br>Primary diagnosis   | 2<br>6<br>1<br>7<br>2   | 88<br>272<br>81<br>379  | NS<br>NS<br>NS                             |
| 40–69 y<br>70+<br>Intubation status<br>Intubated<br>Not intubated<br>Primary diagnosis  | 6<br>1<br>7<br>2  | 272<br>81<br>379  | NS<br>NS                                   |
| 70+<br>Intubation status<br>Intubated<br>Not intubated<br>Primary diagnosis   | 1<br>7<br>2   | 81<br>379   | NS   |
| Intubation status<br>Intubated<br>Not intubated<br>Primary diagnosis  | 7<br>2  | 379   |  |
| Intubated<br>Not intubated<br>Primary diagnosis   | 2   |   | NS   |
| Not intubated Primary diagnosis   | 2   |   | NS   |
|   | 2   |   |  |
| SAH   | 2   |   |  |
|   | 3   | 142   | NS   |
| ICH with IVH  | 4   | 108   | .282                                       |
| Severe TBI (including EDH and SDH)  | 1   | 109   | NS   |
| Obstructive HCP   | 0   | 68  | NS   |
| Space-occupying lesion  | 0   | 21  | NS   |
| Arteriovenous malformation  | 0   | 12  | NS   |
| VP shunt failure  | 1   | 10  | .205                                       |
| Patient immunocompromised?  |   |   |  |
| Yes<br>No   | 0<br>9  | 10<br>460   | NS   |
| History of diabetes?  |   |   |  |
| Type I  | 0   | 5   | NS   |
| Type II   | 0   | 35  | NS   |
| None  | 9   | 430   | NS   |
| History of MRSA/VRE infection or colonization?  |   |   |  |
| Yes<br>No   | 0<br>9  | 8<br>462  | NS   |
| Prior CNS infection? <sup>a</sup>   |   |   |  |
| Yes   | 0   | 9   | NS   |
| No  | 9   | 461   |  |
| Prior brain surgery?  | 7   | 142   | .010*                                      |
| Shunt/EVD only  | 2   | 64  | .301                                       |
| TBI ± shunt/EVD   | 1   | 19  | NS   |
| Space-occupying lesion ± shunt/EVD  | 1   | 27  | NS   |
| AVM ± shunt/EVD   | 0   | 5   | NS   |
| Spontaneous hemorrhage ± shunt/EVD<br>Prior brain surgery with<br>concurrent or previous shunt/EVD placement  | 3 5   | 27<br>81  | .012*                                      |
| Shunt/EVD only  | 2   | 64  | NS   |
| TBI + shunt/EVD   | 1   | 6   | .136                                       |
| Space-occupying lesion + shunt/EVD  | 1   | 6   | .136                                       |
| AVM + shunt/EVD   | 0   | 1   | .130<br>NS                                 |
| Spontaneous hemorrhage + shunt/EVD  | 1   | 4   | .100                                       |
| Prior brain surgery without   | 2   | 61  | .100<br>NS                                 |

(Continued)

#### Infection Control & Hospital Epidemiology

#### Table 1. (Continued)

| Variable                   | CSF infection<br>(n=9), No. | No Infection<br>(n=470), No. | <i>P</i><br>Value |
|----------------------------|-----------------------------|------------------------------|-------------------|
| ТВІ                        | 0                           | 13                           | NS                |
| Space-occupying lesion     | 0                           | 21                           | NS                |
| Arteriovenous malformation | 0                           | 4                            | NS                |
| Spontaneous hemorrhage     | 2                           | 23                           | .099              |

NOTE: SU, standard deviation; NS, not significant; CSF, cerebrospinal fluid; GCS, Glasgow coma scale; SAH, subarachnoid hemorrhage; ICH, intracranial hemorrhage; IVH, intraventricular hemorrhage; TBI, traumatic brain injury; EDH, epidural hemorrhage; SDH, subdural hemorrhage; HCP, hydrocephalus; VP, ventriculo-peritoneal; MRSA, methicillin-resistant *Staphylococcus aureus*; VRE, vancomycin-resistant *Enterococcus* species; CNS, central nervous system; AVM, arteriovenous malformation. <sup>a</sup>History of CNS infection, but no active infection at time of EVD insertion. \*P < .05

#### Table 2. Operative Statistics

| Variable                             | CSF<br>Infection<br>(n=9), No. | No Infection (n=470), No. | P<br>Value |
|--------------------------------------|--------------------------------|---------------------------|------------|
| Primary surgeon                      |                                |                           |            |
| Intern (PGY1)                        | 2                              | 123                       | NS         |
| Junior trainee (PGY2-3)              | 4                              | 214                       | NS         |
| Senior trainee (PGY4-7)              | 1                              | 80                        | NS         |
| Consultant or attending physician    | 2                              | 53                        | .277       |
| Anatomic site of EVD                 |                                |                           |            |
| Frontal (Kocher)                     | 9                              | 455                       | NS         |
| Right-sided                          | 8                              | 366                       | NS         |
| Left-sided                           | 1                              | 89                        | NS         |
| Parietal                             | 0                              | 11                        | NS         |
| Right-sided                          | 0                              | 8                         | NS         |
| Left-sided                           | 0                              | 3                         | NS         |
| Occipital (Frazier)                  | 0                              | 4                         | NS         |
| Right-sided                          | 0                              | 4                         | NS         |
| Hospital location where EVD inserted |                                |                           |            |
| NCCU                                 | 9                              | 259                       | .0056      |
| Emergency department                 | 0                              | 109                       | .220       |
| Pediatric ICU                        | 0                              | 40                        | NS         |
| Trauma ICU                           | 0                              | 31                        | NS         |
| Operating room                       | 0                              | 26                        | NS         |
| Medical ICU                          | 0                              | 2                         | NS         |
| Other                                | 0                              | 3                         | NS         |
| EVD duration                         |                                |                           |            |
| 1-7 d                                | 5                              | 251                       | NS         |
| 8–14 d                               | 3                              | 158                       | NS         |
| >14 d                                | 1                              | 61                        | NS         |
| No. of EVDs per patient (n=409)      |                                |                           |            |
| 1                                    | 6                              | 301                       | NS         |
| 2                                    | 3                              | 72                        | .217       |
| ≥3                                   | 0                              | 27                        | NS         |
| Did EVD require flushing?            |                                |                           |            |
| Yes                                  | 3                              | 104                       | NS         |

#### Table 2. (Continued)

|   | CSF<br>Infection |                           | Р      |
|---|------------------|---------------------------|--------|
| Variable                                  | (n=9), No.       | No Infection (n=470), No. | Value  |
| No  | 6                | 366                       |        |
| CSF leak from EVD insertion site?         |                  |                           |        |
| Yes                                       | 3                | 8                         | .0007* |
| No  | 6                | 462                       |        |
| Surgical site infection?                  |                  |                           |        |
| Yes                                       | 1                | 3                         | .0734  |
| No  | 8                | 467                       |        |
| EVD insertion site dehiscence?            |                  |                           |        |
| Yes                                       | 1                | 4                         | .0908  |
| No  | 8                | 466                       |        |
| Duration of hospital stay, median d (IQR) |                  |                           |        |
| Total duration                            | 31 (24–43)       | 19 (11–29)                | .0198* |
| Duration after EVD placement              | 23 (19–43)       | 16 (8–26)                 | .0449* |
| 30-day functional outcomes (n=409)        |                  |                           |        |
| Median modified Rankin scale score (IQR)  | 4 (4–4)          | 4 (2–6)                   | NS     |
| Mortality                                 | 22% (2/9)        | 33.3% (133/400)           | NS     |

Note. CSF, cerebrospinal fluid; PGY, postgraduate year; EVD, external ventricular drain; NCCU, neurocritical care unit; ICU, intensive care unit; IQR, interquartile range. P values calculated using  $\chi^2$  goodness of fit or Fisher exact test.

\**P* < .05.

| Table 3. | Outcomes | of EVD | Infections |
|----------|----------|--------|------------|
|----------|----------|--------|------------|

| Age and<br>Sex | EVD<br>Indication | Drainage Duration,<br>Days | Infection Onset,<br>Day | Organism(s)                    | Antibiotic(s)                 | Antibiotic Duration,<br>Days | 30-Day Outcome,<br>mRS |
|----------------|-------------------|----------------------------|-------------------------|--------------------------------|-------------------------------|------------------------------|------------------------|
| 71M            | Shunt failure     | 2                          | 1                       | CoNS                           | Vancomycin                    | 10                           | 6ª                     |
| 66M            | IVH               | 6                          | 5                       | MSSA                           | Nafcillin                     | 42                           | 4                      |
| 34M            | IVH               | 11                         | 9                       | CoNS                           | Vancomycin                    | 28                           | 3                      |
| 59M            | SAH               | 10                         | 9                       | CoNS                           | Vancomycin                    | 14                           | 4                      |
| 66M            | SAH               | 2                          | 2                       | C. acnes<br>CoNS               | Meropenem                     | 10                           | 4                      |
| 58M            | IVH               | 6                          | 5                       | CoNS                           | Vancomycin                    | 14                           | 4                      |
| 65F            | TBI, SDH          | 3                          | 3                       | C. koseri                      | Gentamicin IT<br>Meropenem IV | 42                           | 6 <sup>a</sup>         |
| 25M            | IVH               | 12                         | 11                      | P.<br>agglomerans<br>M. luteum | Cefepime,<br>vancomycin       | 14                           | 4                      |
| 45M            | SAH               | 18                         | 16                      | CoNS                           | Vancomycin                    | 14                           | 3                      |

Note. EVD, external ventricular drain; IVH, intraventricular hemorrhage; SAH, subarachnoid hemorrhage; TBI, traumatic brain injury; SDH, subdural hematoma; CoNS, coagulase-negative staphylococci; MSSA, methicillin-sensitive *Staphylococcus aureus; C. acnes, Cutibacterium acnes; C. koseri, Citrobacter koseri; P. agglomerans, Pantoea* agglomerans; *M. luteus, Micrococcus* luteum; IT, intrathecal; IV, intravenous; mRS, modified Rankin Scale score (3=moderate disability, 4=severe disability, 6=death). <sup>a</sup>Pateint died.

in our study, and the incidende of infection was not significantly higher in either group.

## Comparison to incidence and mortality in other reported studies

As demonstrated in previous studies, the most common pathogens associated with EVD infections are coagulase-negative staphylococci.<sup>5–8,10–12,14–17,19,22,32,33</sup> Other common pathogens include *Staphylococcus aureus*, *Cutibacterium acnes*, and *Citrobacter koseri*,<sup>5,7,8,10–12,14–19,22,32,33</sup> and infections with these pathogens were identified in our study patients.

Our overall infection rate was 2.2% and the incidence density was 2.3 infections per 1,000 EVD days which compares favorably with prior studies,  $^{1,2,5-19,22,24,33}$  including those that also used the CDC NHSN surveillance definition of meningitis/ventriculitis (Table 4).<sup>5-19</sup> Additionally, our infection rate is comparable to,

Table 4. Incidence and Risk Factors Associated With EVD Infection in Previous Literature

| Study                               | No. of Patients | Infection Rate (%) | Predisposing Risk Factors for EVD Infection  |  |
|-------------------------------------|-----------------|--------------------|--|--|
| Walek et al, 2021 <sup>30</sup>     | 409             | 2.2                | Prior brain surgery<br>CSF leakage   |  |
| Kim et al, 2020 <sup>5</sup>        | 247             | 10.1               | Multiple EVD insertions<br>Duration of EVD drainage  |  |
| Flint et al, 2017 <sup>6</sup>      | 308             | 0.3                | Diabetes mellitus  |  |
| Talibi et al, 2016 <sup>7</sup>     | 66              | 6.1                | Not using antibiotic-impregnated catheter  |  |
| Phan et al, 2016 <sup>8</sup>       | 110             | 11.5               | Multiple drains (EVD replacement)<br>Not using perioperative systemic antibiotics<br>Not stopping antibiotics within 24 hours of EVD placement       |  |
| dos Santos et al, 2016 <sup>9</sup> | 94              | 5.3                | Duration of EVD drainage >10 days  |  |
| Kubilay et al, 2013 <sup>10</sup>   | 2928            | 1.5                | Not using prophylactic antibiotics<br>Lack of anti-microbial impregnated catheter  |  |
| Camacho et al, 2013 <sup>11</sup>   | 178             | 4.8                | Lack of educational intervention<br>Lack of strict adherence to aseptic protocol   |  |
| Kim et al, 2012 <sup>12</sup>       | 343             | 3.5                | Duration of EVD drainage<br>Concurrent systemic infection  |  |
| Kitchen et al, 2011 <sup>13</sup>   | 39              | 10.2               | Lack of strict aseptic technique during EVD management<br>Lack of care bundles for EVD management  |  |
| Hoefnagel et al, 2008 <sup>14</sup> | 228             | 23.2               | Duration of EVD drainage >11 days<br>CSF sampling frequency  |  |
| Dasic et al, 2006 <sup>15</sup>     | 59              | 11.9               | EVD insertion outside of operating room<br>Lack of prophylactic antibiotics<br>Insufficient tunneling distance of catheter<br>CSF sampling frequency |  |
| Bota et al, 2005 <sup>16</sup>      | 638             | 9.1                | Duration of EVD drainage<br>SAH or IVH<br>Craniotomy<br>Coinfection  |  |
| Korinek et al, 2004 <sup>17</sup>   | 175             | 5.7                | CSF leakage<br>CSF sampling frequency<br>EVD manipulation<br>Duration of EVD drainage >5 days  |  |
| Lyke et al, 2001 <sup>18</sup>      | 196             | 5.6                | Duration of EVD drainage<br>CSF leakage  |  |
| Mayhall et al, 1984 <sup>19</sup>   | 172             | 11.0               | ICH with IVH<br>Prior neurosurgery<br>ICP >20 mmHg<br>Irrigation of EVD  |  |

Note. EVD, external ventricular drain; CSF, cerebrospinal fluid; SAH, subarachnoid hemorrhage; IVH, intraventricular hemorrhage; ICH, intracranial hemorrhage; ICP, intracranial pressure.

and in some cases lower than, institutions using post-EVD antibiotic prophylaxis and antimicrobial-impregnated EVDs.<sup>21,24,26–29,35–39</sup> Based on a previous analysis of the effects of protocol changes at our institution,<sup>30</sup> we believe major factors that have contributed to this low infection rate include cutaneous antisepsis with alcoholic chlorhexidine, elimination of routine CSF sampling, and use of a modified tunneling technique with coiling of the catheter under the skin. We have demonstrated that EVD catheters can remain in place without contributing to EVD infection risk as long as meticulously sterile technique is used with minimal device manipulation.

Of the 9 patients who experienced an EVD infection during our study period, 2 died within 30 days of EVD placement, conferring a 30-day mortality rate of 22%. This finding is consistent with previously reported 30-day mortality rates of 17%–46%.<sup>5,9,11,12,16,19</sup>

This study had several limitations. The retrospective nature of this study leaves open the possibility of incomplete data in the medical records. However, microbiological reports were always available. Routine CSF cell counts and CSF lactate levels were not obtained throughout the course of the study; therefore, no conclusions can be drawn as to their ability to help predict or aid in the diagnosis of CSF infection associated with EVD placement. We also did not collect data on which provider manipulated the EVD once it was placed, and the number of insertion attempts per EVD was not routinely recorded. Our study may have been underpowered to identify all significant risk factors in this cohort.

In conclusion, risk of EVD infection was associated with prior brain surgery associated with EVD or shunt placement, CSF leak, and insertion site dehiscence. We did not find an association between infection risk and prolonged duration of EVD placement, which might be attributable to our institutional policies of minimal EVD manipulation after insertion, no routine CSF sampling, and regular cleansing of the insertion site with alcoholic chlorhexidine. Acknowledgments. The authors thank the Rhode Island Hospital infection control staff for their thoughtful assistance in mitigating EVD infection risk and managing data related to this project. The authors declare no conflicts of interest, and this research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Financial support. No financial support was provided relevant to this article.

**Conflicts of interest.** All authors report no conflicts of interest relevant to this article.

#### References

- Fried HI, Nathan BR, Rowe AS, et al. The insertion and management of external ventricular drains: an evidence-based consensus statement. *Neurocrit Care* 2016;24:61–81.
- Lozier AP, Sciacca RR, Romagnoli MF, Connolly ES Jr. Ventriculostomyrelated infections: a critical review of the literature. *Neurosurgery* 2002;51:170–182.
- Muralidharan R. External ventricular drains: management and complications. Surg Neurol Int 2015;6:271.
- Bischoff P, Schröder C, Gastmeier P, Geffers C. Surveillance of external ventricular drainage-associated meningitis and ventriculitis in German intensive care units. *Infect Control Hosp Epidemiol* 2020;41:452–457.
- Kim J, Lee J, Feng R, *et al.* Ventricular catheter tract hemorrhage as a risk factor for ventriculostomy-related infection. *Oper Neurosurg (Hagerstown)* 2020;18:69–74.
- Flint AC, Toossi S, Chan SL, *et al.* A simple infection control protocol durably reduces External ventricular drain infections to near-zero levels. *World Neurosurg* 2017;99:518–523.
- Talibi S, Tarnaris A, Shaw SA. Has the introduction of antibiotic-impregnated external ventricular drain catheters changed the nature of the microorganisms cultured in patients with drain-related infection? a single neurosurgical centre's experience. *Br J Neurosurg* 2016;30:560–566.
- Phan K, Schultz K, Huang C, et al. External ventricular drain infections at the Canberra Hospital: a retrospective study. J Clin Neurosci 2016;32:95–98.
- dos Santos SC, Fortes Lima TT, Lunardi LW, Stefani MA. External ventricular drain–related infection in spontaneous intracerebral hemorrhage. World Neurosurg 2017;99:580–583.
- Kubilay Z, Amini S, Fauerbach LL, *et al*. Decreasing ventricular infections through the use of a ventriculostomy placement bundle: experience at a single institution. *J Neurosurg* 2013;118:514–520.
- Camacho EF, Boszczowski Í, Freire MP, et al. Impact of an educational intervention implanted in a neurological intensive care unit on rates of infection related to external ventricular drains. PLoS One 2013;8(2):e50708.
- 12. Kim JH, Desai NS, Ricci J, *et al.* Factors contributing to ventriculostomy infection. *World Neurosurg* 2012;77:135–140.
- Kitchen WJ, Singh N, Hulme S, et al. External ventricular drain infection: improved technique can reduce infection rates. Br J Neurosurg 2011;25:632–635.
- Hoefnagel D, Dammers R, Ter Laak-Poort MP, Avezaat CJJ. Risk factors for infections related to external ventricular drainage. *Acta Neurochir (Wien)* 2008;150:209–214.
- Dasic D, Hanna SJ, Bojanic S, Kerr RSC. External ventricular drain infection: the effect of a strict protocol on infection rates and a review of the literature. Br J Neurosurg 2006;20:296–300.
- Bota DP, Lefranc F, Vilallobos HR, et al. Ventriculostomy-related infections in critically ill patients: a 6-year experience. J Neurosurg 2005;103:468–472.
- 17. Korinek AM, Reina M, Boch AL, et al. Prevention of external ventricular drain-related ventriculitis. Acta Neurochir (Wien) 2004;147:39–46.
- Lyke KE, Obasanjo OO, Williams MA, et al. Ventriculitis complicating use of intraventricular catheters in adult neurosurgical patients. *Clin Infect Dis* 2001;33:2028–2033.

- Mayhall CG, Archer NH, et al. Ventriculostomy-related infections. N Engl J Med 1984;310:553–559.
- 20. Rahman M, Whiting JH, Fauerbach LL, *et al.* Reducing ventriculostomyrelated infections to near zero: the eliminating ventriculostomy infection study. *Jt Comm J Qual Patient Saf* 2012;38:459–464.
- 21. Sheppard JP, Ong V, Lagman C, *et al.* Systemic antimicrobial prophylaxis and antimicrobial-coated external ventricular drain catheters for preventing ventriculostomy-related infections: a meta-analysis of 5242 cases. *Neurosurgery* 2020;86:19–29.
- 22. Hader WJ, Steinbok P. The value of routine cultures of the cerebrospinal fluid in patients with external ventricular drains. *Neurosurgery* 2000;46:1149–1155.
- Hepburn-Smith M, Dynkevich I, Spektor M, et al. Establishment of an external ventricular drain best practice guideline. J Neurosci Nurs 2016;48:54–65.
- Moussa WMM, Mohamed MAA. Efficacy of postoperative antibiotic injection in and around ventriculoperitoneal shunt in reduction of shunt infection: a randomized controlled trial. *Clin Neurol Neurosurg* 2016;143:144–149.
- Trick WE, Kioski CM, Howard KM, et al. Outbreak of Pseudomonas aeruginosa ventriculitis among patients in a neurosurgical intensive care unit. Infect Control Hosp Epidemiol 2000;21:204–208.
- Wang X, Dong Y, Qi X-Q, et al. Clinical review: efficacy of antimicrobialimpregnated catheters in external ventricular drainage—a systematic review and meta-analysis. Crit Care 2013;17:234.
- Zabramski JM, Whiting D, Darouiche RO, *et al.* Efficacy of antimicrobialimpregnated external ventricular drain catheters: a prospective, randomized, controlled trial. *J Neurosurg* 2003;98:725–730.
- Winkler KML, Woernle CM, Seule M, *et al.* Antibiotic-impregnated versus silver-bearing external ventricular drainage catheters: preliminary results in a randomized controlled trial. *Neurocrit Care* 2013;18:161–165.
- 29. Wong GKC, Ip M, Poon WS, et al. Antibiotics-impregnated ventricular catheter versus systemic antibiotics for prevention of nosocomial CSF and non-CSF infections: a prospective randomised clinical trial. J Neurol Neurosurg Psychiatry 2010;81:1064–1067.
- 30. Walek KW, Leary OP, Sastry R, Asaad WF, Walsh JM, Mermel L. Decreasing external ventricular drain infection rates in the neurocritical care unit: 12-year longitudinal experience at a single institution. World Neurosurg 2021;150:e89–e101.
- 31. National Healthcare Safety Network. NHSN patient safety component manual. Centers for Disease Control and Prevention website.
- https://www.cdc.gov/nhsn/pdfs/pscmanual/pcsmanual\_current.pdf. Published January 2021. Accessed January 28, 2021.
- Zhou Y-J, Wu J-N, Chen L-J, Zhao H-Y. Comparison of infection rate with tunneled vs standard external ventricular drainage: a prospective, randomized controlled trial. *Clin Neurol Neurosurg* 2019;184:105416.
- Collins CDE, Hartley JC, Chakraborty A, Thompson DNP. Long subcutaneous tunnelling reduces infection rates in paediatric external ventricular drains. *Childs Nerv Syst* 2014;30:1671–1678.
- Sorinola A, Buki A, Sandor J, Czeiter E. Risk factors of external ventricular drain infection: proposing a model for future studies. *Front Neurol* 2019;10. doi: 10.3389/fneur.2019.00226.
- Lansdown ABG. A pharmacological and toxicological profile of silver as an antimicrobial agent in medical devices. *Adv Pharmacol Sci* 2010. doi: 10. 1155/2010/910686.
- 37. Blomstedt GC. Results of trimethoprim-sulfamethoxazole prophylaxis in ventriculostomy and shunting procedures. J Neurosurg 1985;62:694–697.
- Pople I, Poon W, Assaker R, *et al.* Comparison of infection rate with the use of antibiotic-impregnated vs standard extraventricular drainage devices. *Neurosurgery* 2012;71:6–13.
- Hong B, Apedjinou A, Heissler HE, et al. Effect of a bundle approach on external ventricular drain-related infection. Acta Neurochir (Wien) 2021;163:1135–1142.