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CLINICAL ARTICLE

# Strategies to reduce external ventricular drain–related infections: a multicenter retrospective study

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**OBJECTIVE** Various strategies have been proposed to reduce the incidence of external ventricular drain (EVD)–related infections. The authors retrospectively studied the impact of EVD care management on EVD-related infections at 3 French university hospital intensive care units.

**METHODS** Between 2010 and 2014, 462 consecutive adult patients with no evidence of a preexisting CSF infection received EVDs as part of their care at one of the following sites: Grenoble (221 patients), Saint-Etienne (130 patients), and Marseille (111 patients). Written protocols describing the EVD placement procedure, management, and removal were implemented at the 3 sites. Daily CSF sampling and intraventricular administration of antibiotics prior to EVD removal were performed at the Grenoble site only. EVD-related infection was considered for any confirmed ventriculostomy-related infection (VRI) and ventriculitis. VRI was defined as one or more positive CSF cultures or Gram stain with CSF pleocytosis and biochemical abnormalities. Ventriculitis was defined as CSF pleocytosis and biochemical abnormalities with degradation of neurological status and fever.

**RESULTS** A total of 6945 EVD days were observed in the entire population. In the Grenoble cohort, the mean cumulative incidence of EVD-related infections was significantly lower than that in the 2 other cohorts: 1.4% (95% CI 0.0%–2.9%) versus 9.2% (95% CI 4.2%–14.2%) and 7.2% (95% CI 2.4%–12.0%) at Saint-Etienne and Marseille, respectively ($p < 0.01$). Accounting for the duration of external ventricular drainage at each site, the risk for EVD-related CSF infections was significantly higher at Saint-Etienne and Marseille than at Grenoble, with ORs of 15.9 (95% CI 3.6–71.4, $p < 0.001$) and 10.0 (95% CI 2.2–45.5, $p = 0.003$), respectively.

**CONCLUSIONS** These findings indicate that it is possible to attain a low incidence of EVD-related infections, provided that an EVD care bundle, which can include routine daily CSF sampling, is implemented and strongly adhered to.

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**KEYWORDS** external ventricular drain; infection; intensive care unit; hydrocephalus

External ventricular drains (EVDs) are commonly used to monitor intracranial pressure (ICP) via the gold-standard measurement of ventricular pressure.[4] Should ICP be raised, EVDs can also provide relief by draining off CSF and should be considered in the treatment of acute hydrocephalus after subarachnoid hemorrhage or posttraumatic brain edema.[9,27] However, EVD monitoring exposes the patient to complications, including infection, hemorrhage, and malfunction or obstruction of the drainage system. According to the literature, the incidence of EVD-related CSF infection ranges from 0% to 27%, with an average cumulative rate of positive CSF cultures of 8% to 10% per patient.[2,3,6,18] In a meta-analysis of 35 studies, the overall pooled incidence of EVD-related infection was 11.4 per 1000 catheter days (95% CI 9.3–13.5).[24] Infection of the ventricles can lead to ventriculitis, a complication that markedly aggravates neurological outcome in brain-injured patients. Various risk factors for EVD-related CSF infections have been identified: duration of EVD monitoring, systemic infection, presence of intraventricular hemorrhage, basilar skull fractures with CSF leak, catheter manipulations, and leakage around the EVD

**ABBREVIATIONS** EVD = external ventricular drain; ICP = intracranial pressure; VRI = ventriculostomy-related infection; WBC = white blood cell.

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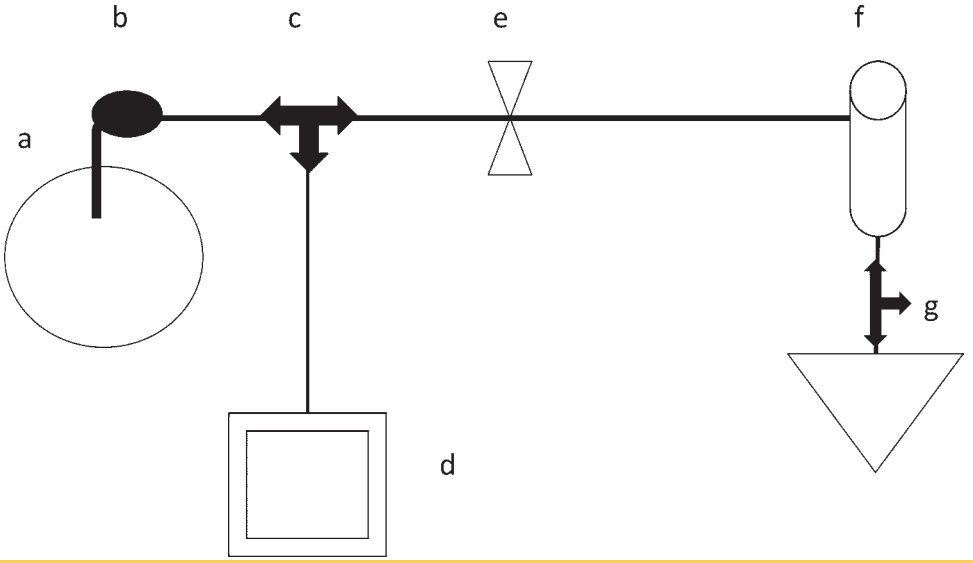


**FIG. 1.** Schematic representation of the EVD system at the Grenoble site. Intraventricular catheter (a), proximal injection site, no CSF sampling (b), 3-way tap to measure ICP and to drain CSF (c), ICP sensor (d), clamp to measure ICP (e), CSF collector (f), and CSF sample site and collection bag (g).

catheter.[8,12,18,21,26] However, the diagnosis of such EVD-related infections is often delayed due to the nonspecificity of clinical signs and/or CSF laboratory parameters and the lack of a standardized treatment of nosocomial CSF infections.[2,28] Collectively, the aforementioned extent and seriousness of issues raised with EVD-related infections underline the importance of any attempt to reduce their risk.

Various strategies have been proposed to reduce the incidence of EVD-related infections, which were recently evaluated in an evidence-based consensus statement.[11] Among the recommendations, guidelines promote the use of antimicrobial-impregnated catheters and the avoidance of routine CSF sampling.[11] More recently, the Infectious Diseases Society of America (IDSA) Practice Guidelines Committee suggested using procedural prophylactic administration of antibiotics for patients undergoing placement of an EVD.[28] As the panel of experts mentioned, many recommendations are based on expert opinion due to the lack of rigorous clinical data. In this study, we retrospectively analyzed the occurrence of ventriculostomy-related infection (VRI) and ventriculitis at 3 French university hospital ICUs regarding 2 aspects of EVD care management: daily CSF sampling and intraventricular administration of antibiotics prior to EVD removal. Although the 3 sites had written protocols describing the EVD placement procedure, management, and removal, these 2 procedures were implemented at only 1 site, and the 2 other sites served as controls. Our hypothesis was that daily CSF sampling with close monitoring of CSF parameters could allow timely decisions to be made prior to the development of an EVD-related CSF infection.

# Methods

## Study Population

This multicenter, retrospective study was conducted between January 2010 and April 2014 at 3 French university hospital ICUs in Grenoble, Marseille, and Saint-Etienne, with 9 ICU beds and 4 intermediate care beds, 20 ICU beds and 12 intermediate care beds, and 24 ICU beds, respectively. All sites have a large amount of experience in managing patients with EVDs. Only EVD patients staying longer than 24 hours in the ICU were included in this study, so that the total number of patients and patient-days could be calculated. Patients were excluded from the analysis if they received an EVD as part of a treatment for a preexisting CSF infection or an antimicrobial-impregnated EVD catheter. Electronic database access was granted by the French data protection authority (National Commission on Informatics and Liberty, CNIL). Therefore, no patient consent was sought in this retrospective study.

## EVD Care Bundle

At the 3 sites, the EVD was routinely inserted under sterile conditions at the patient's bedside by a neurosurgeon, or in the operating room if needed. No antibiotics were given prophylactically during EVD placement. No antibiotic-impregnated or silver-coated catheters were used. No fixed interval exchange of EVDs was performed. Written protocols describing the EVD placement procedure, management, and removal were implemented at the 3 sites. Nurses received regular training to reach a high level of compliance with the EVD protocol of each site. Appendix 1 shows the protocol implemented at the Grenoble ICU, and differences with protocols implemented at the 2 other sites are shown in Appendix 2.

At the Grenoble site, daily samples of CSF (5–10 ml) were taken from the distal part of the EVD system, i.e., behind the collector, for white blood cell (WBC) count, protein and glucose levels, and microbiological examination (Fig. 1). On suspicion of colonization or infection of the EVD system, the distal part of the EVD system was first replaced. The rate of CSF drainage was increased

**TABLE 1. Characteristics of EVD-treated patients at the 3 sites**

| Variable | Grenoble (n = 221) | Saint-Etienne (n = 130) | Marseille (n = 111) | p Value |
|---|---|---|---|---|
| Median age (IQR), yrs | 58 (46–67) | 57 (46–65) | 59 (47–66) | 0.915 |
| Male, n (%) | 108 (49) | 72 (55) | 64 (58) | 0.250 |
| Diagnosis at admission, n (%) | | | | <0.001 |
| Subarachnoid hemorrhage | 122 (55) | 77 (59) | 43 (39) | |
| Intracerebral hemorrhage | 50 (23) | 38 (29) | 20 (18) | |
| Brain trauma | 27 (12) | 11 (9) | 7 (6) | |
| Other | 22 (10) | 4 (3) | 41 (37) | |
| Median no. of EVDs per patient, n (range) | 1 (1–5) | 1 (1–4) | 1 (1–5)* | 0.020 |
| Median duration of EV drainage per patient, days | 14 (9–23) | 13 (7–19) | 11 (5–17)† | 0.004 |

EV = external ventricular.
Median data are presented as the median (IQR) unless stated otherwise.
* $p < 0.05$ versus Saint-Etienne.
† $p < 0.05$ versus Grenoble.

whenever possible. Persistently positive CSF cultures in association with changes in serum levels of C-reactive protein and total WBC counts resulted in removal of the entire EVD system. In the event of a confirmed CSF infection or clinical degradation of neurological status with fever, intravenous antibiotics were given empirically before identification of the causative organism, which led, when necessary, to a more adapted treatment regimen. Unless stated otherwise, another specific procedure was intraventricular administration of amikacin (10 mg) with clamping the drain for 30 minutes, performed 1 hour prior to EVD removal.

At the 2 other sites (Marseille and Saint-Etienne), CSF sampling was based on clinical suspicion of EVD infection, i.e., fever, neurological degradation, and/or changes in serum levels of C-reactive protein and total WBC counts (Appendix 2). Once the CSF confirmed abnormalities of CSF cell count, glucose, and protein, the entire EVD system was removed, and intravenous antibiotics were given according to the same protocol as followed at the Grenoble ICU.

### Data Analysis

Computerized data gathered for the EVD-treated patients during the study period were patient characteristics, admitting diagnoses, surgical procedures, imaging, type of drainage, clinical and biological signs indicative of meningitis/ventriculitis, causative organism from CSF cultures and/or drain tip, resistance pattern, and antibiotic therapy. The number of EVDs and duration of drainage were also recorded during the study period.

Data were analyzed by an independent investigator at each site to define EVD-related CSF infections according to the criteria of Lozier et al.[18] An expert in infection control (P.P.) reviewed cases of VRIs to affirm the conclusions. Suspected and confirmed CSF infections were categorized according to Lozier's criteria: 1) contamination indicated by an isolated positive CSF culture and/or positive Gram stain with normal CSF cell counts and biochemistry; 2) colonization indicated by multiple positive CSF cultures and/or positive Gram stains with normal CSF cell counts and lack of clinical symptoms other than fever; 3) suspected VRI indicated by CSF pleocytosis with absence of positive CSF cultures or Gram stains; 4) confirmed VRI indicated by one or more positive CSF cultures or Gram stains with CSF pleocytosis and biochemical abnormalities and a paucity of clinical symptoms other than fever; and 5) ventriculitis indicated by CSF pleocytosis and biochemical abnormalities with degradation of neurological status and fever. CSF pleocytosis was defined as more than 100 WBCs/mm$^3$, and biochemical abnormalities as CSF proteins of more than 0.4 g/L and a CSF glucose/serum ratio of less than 0.5. A diagnosis of EVD-related CSF infection was made for all cases of VRI and ventriculitis according to the recent guidelines.[11]

### Statistical Analysis

Descriptive statistics included frequencies and percentages for categorical variables and the median and interquartile range (25th–75th percentiles) for continuous variables. The incidence of EVD-related infection was expressed as the mean and 95% confidence interval. Odds ratios were calculated using logistic regression. Comparisons between the 3 groups were performed using nonparametric Kruskal-Wallis and Mann-Whitney tests for continuous variables and Bonferroni's correction for multiple comparisons, and the chi-square test for categorical variables (StatView SE program, SAS Institute). Statistical significance was declared at $p < 0.05$.

## Results

There were 462 consecutive adult patients with no evidence of a preexisting CSF infection who received EVDs as part of their care during the study period (Table 1). A total of 6945 EVD days were observed: 3756 in Grenoble (221 patients), 1710 in Saint-Etienne (130 patients), and 1479 in Marseille (111 patients). Patients in the Marseille group had a shorter duration of external ventricular drainage than those in the Grenoble group and more EVDs per patient than those in the Saint-Etienne group (both $p < 0.05$; Table 1).

**TABLE 2. Characteristics of the patients with positive CSF cultures and EVD-related infections at the 3 sites**

| Variable | Grenoble (n = 221) | Saint-Etienne (n = 130) | Marseille (n = 111) |
|---|---|---|---|
| No. of patients w/ positive CSF cultures (%) | 21 (9.5) | 12 (9.2) | 10 (9.0) |
| No. of patients w/ EVD-related infection (% [95% CI]) | 3 (1.4 [0–2.9]) | 12 (9.2 [4.2–14.2])* | 8 (7.2 [2.4–12.0])* |
| Median EVD-related infection rate per 1000 derivation days (95% CI) | 0.8 (0.2–1.4) | 7.0 (5.4–8.6)* | 5.4 (4.3–6.6)* |
| Causative organism | | | |
| Gram-positive cocci | | | |
| Coagulase-negative staphylococci | 15 | 5 | 3 |
| *Enterococcus faecalis* | 1 | 3 | 0 |
| Nongroupable *Streptococcus mitis* | 1 | 0 | 0 |
| Group A or B β-hemolytic streptococcus | 1 | 0 | 1 |
| MSSA | 1 | 1 | 2 |
| Gram-negative bacteria | | | |
| Enterobacteriaceae | 0 | 4 | 1 |
| *Pseudomonas* | 0 | 1 | 1 |
| *Corynebacterium* spp. | 2 | 1 | 1 |
| Undefined | 1 | 0 | 1 |

MSSA = methicillin-sensitive *Staphylococcus aureus*.
Due to polymicrobial infections, the number of microorganisms may exceed the total number of patients with positive CSF cultures. EVD-related CSF infections correspond to VRIs and ventriculitis.
* $p < 0.01$ versus Grenoble.

The 3 cohorts had comparable proportions of patients with positive CSF cultures (Table 2). In the Grenoble cohort, positive CSF cultures were found in 21 patients (9.5%). No gram-negative bacillus or multiresistant organisms were identified on CSF cultures and/or Gram stains. According to the categorization of suspected CSF infections, 15 patients had contamination, 4 had colonization, and 1 had suspected VRI. Diagnostic criteria for ventriculitis were met in 3 patients: 2 with positive CSF cultures and 1 with an absence of positive CSF cultures (Appendix 2). None of these 3 patients received intraventricular antibiotics prior to EVD removal. None of the patients had VRI. Based on these data, EVD-related infections had a mean cumulative incidence of 1.4% (95% CI 0%–2.9%) in the Grenoble cohort.

In the 2 other cohorts, almost all patients with positive CSF cultures developed VRI or ventriculitis (Table 2). The cumulative incidence and occurrence rate of EVD-related infections were significantly higher in these 2 cohorts than in the Grenoble cohort (both $p < 0.01$; Table 2). No significant difference was found between the Saint-Etienne and Marseille cohorts. Accounting for the duration of EVD at each site, the risk of EVD-related CSF infections was significantly higher at Saint-Etienne and Marseille than at Grenoble, with ORs of 15.9 (95% CI 3.6–71.4; $p < 0.001$) and 10.0 (95% CI 2.2–45.5; $p = 0.003$), respectively.

## Discussion

The results of this study conducted at 3 French sites show that daily CSF sampling and intraventricular administration of antibiotics prior to EVD removal were associated with a marked reduction in the occurrence rate of EVD-related CSF infections. Although the 3 sites had a comparable proportion of patients with positive CSF cultures, the incidence of EVD-related CSF infections was significantly lower at Grenoble than at the 2 control sites. The incidences at the 2 control sites were in line with data from the literature, with an average cumulative rate of 8% to 10% per patient.[2,3,6,18,26]

The diagnosis of CSF infection is challenging. Clinical features, such as changes in mental status or a new focal neurological deficit, are impossible to detect in sedated patients. Fever and Glasgow Coma Scale score might be of poor predictive value to diagnose ventriculitis.[20] Therefore, the diagnosis of CSF infection is mostly dependent on laboratory findings. In several studies, ventriculitis was defined according to the Centers for Disease Control criteria: a positive CSF culture or a combination of positive cultures, clinical symptoms, and laboratories findings, i.e., elevated cell counts and/or decreased glucose level. The results from bacteriological cultures are, however, not available for at least 48 hours. In addition, isolated positive CSF cultures may risk the inclusion of CSF contamination or colonization as EVD-related infections.[7,26] Furthermore, CSF pleocytosis may be difficult to interpret in the presence of concomitant intraventricular hemorrhage. We thus chose to categorize all suspected CSF infections according to Lozier's comprehensive criteria,[18] as has been done elsewhere.[3,32] This allowed uniform identification of infection cases across the 3 sites.

An early diagnosis of EVD-related infection is critical to permit therapeutic intervention. CSF sampling can be performed either on a daily routine basis (Grenoble) or only as needed (Saint-Etienne and Marseille). The recently published guidelines suggest avoiding routine CSF sampling on the basis of poor levels of supporting evidence, yet they recognize uncertainties over the alternatives of this strategy.[11] The risk of positive CSF culture has been reported to decrease when the frequency of CSF sampling

was lowered.[30,31] Other authors found that CSF analysis provided no additional value due to the severe CSF disturbances with intraventricular hemorrhage.[25] On the other hand, the daily calculation of leukocytes to red blood cells in CSF and in peripheral blood, i.e., the cell index, permitted an early diagnosis of EVD-related infection in patients with intraventricular hemorrhage.[22] The serial increase in the daily CSF cell count was the only laboratory parameter that correlated with positive CSF cultures.[23] The Grenoble ICU policy for daily CSF samples ensures the strict maintenance of a closed system. It should be strongly emphasized that CSF sampling was performed behind the collector (Fig. 1). By permitting close monitoring of how CSF parameters evolve over time, this strategy allows timely decisions to be made. As a result, the number of patients with CSF-positive cultures largely exceeded the number of patients with EVD-related infections in the Grenoble cohort. The 3 patients with ventriculitis in the Grenoble cohort had a pleocytosis exceeding 500 WBCs/mm$^3$, with marked changes in the 24 hours prior to the diagnosis (see Appendix 2). These results indicate that daily CSF sampling was not linked to an increased risk for CSF infection, but it might be helpful to allow for appropriate decisions to be made early.

Implementation of an EVD care bundle has been shown by several authors to create a "culture of safety" and minimize the risk of EVD-related infections.[1,7,10,15,19] First, extensive education of all staff, i.e., doctors, trainees, and nurses, with regard to EVD-specific care is essential.[5] Strict adherence by nurses to the written protocol is critical, with any violation of the protocol shown to affect the rate of EVD-related ventriculitis.[14] Second, interventions to prevent sources of CSF infection must be implemented, such as sterile technique, tunneling of the catheter, use of a closed system, use of a sterile dressing, and no site changes after placement. The use of prophylactic systemic antibiotics for the insertion of EVDs has insufficient supporting evidence to allow its recommendation.[11] Although promising in reducing the risk for infection,[13] the impact of antimicrobial-impregnated and silver-coated EVD catheters is probably minor in a population at low risk of EVD-related infections, as pointed out by the guidelines.[11] Because our study population did not receive treated catheters, we cannot draw conclusions about their effectiveness. In the Grenoble cohort, amikacin was administered via the intraventricular route prior to EVD removal to prevent gram-negative bacillary ventriculitis, which would be devastating in these patients.[29] According to a recent systematic review, the administration of aminoglycosides via this route appeared safe and effective for the treatment of EVD-related infections.[16] Although the prophylactic effectiveness of such action needs to be confirmed, all 3 cases of ventriculitis in the Grenoble cohort presented after EVD removal (see Appendix 2). Ventricular contamination may happen during the stripping of the drain. This may explain, in part, why EVD changes were associated with an increased risk of VRI.[17] Curiously, in the literature accidental EVD removal was not identified among risk factors for EVD-related infections.[8,11,12,18,21,26] Third, rapid interventions must be made in cases of suspected CSF infection, including replacing the distal part of the system, increasing the rate of CSF drainage wherever possible, and, if needed, removing the entire CSF system.

This study has several limitations. First, this is a retrospective observational study. We did study all patients consecutively admitted to the 3 ICUs during the study period, which should have limited any attrition bias. Second, we found a low incidence of EVD-related infections among 462 treated patients. A low incidence rate of any event would be difficult to confirm with accuracy on a limited number of exposed individuals. It is therefore more appropriate to express such incidence of CSF infections per EVD days using 95% confidence intervals to assess the precision of the measurement as done in this study. Third, we found an association between 2 procedures of EVD care management, i.e., daily CSF sampling and intraventricular antibiotics prior to EVD removal, and a reduced rate of EVD-related infections. Whether these procedures and which one may have a causative impact on CSF infections needs to be determined.

## Conclusions

It is possible to attain a low incidence of EVD-related infections, provided that an EVD care bundle, which can include routine daily CSF sampling, is implemented and strongly adhered to.

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## Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

## Author Contributions

Conception and design: Payen, Champey, Mourey. Acquisition of data: Champey, Mourey, Gergele, Manet, Velly, Bruder. Analysis and interpretation of data: all authors. Drafting the article: Payen, Champey, Mourey. Critically revising the article: Francony, Pavese, Gergele, Manet, Velly, Bruder. Reviewed submitted version of manuscript: Gay. Approved the final version of the manuscript on behalf of all authors: Payen. Statistical analysis: Champey.

## Supplemental Information

### Online-Only Content

Supplemental material is available with the online version of the article.

*Appendices 1–3*. https://thejns.org/doi/suppl/10.3171/2018.1.JNS172486.

### Previous Presentations

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