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## Comparing External Ventricular Drains-Related Ventriculitis Surveillance Definitions

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### Abstract

**Objective**—To evaluate the agreement between the current National Healthcare Safety Network (NHSN) definition for ventriculitis and others found in the literature among patients with an external ventricular drain (EVD).

**Design**—Retrospective cohort study from January 2009 to December 2014

**Setting**—Neurology and neurosurgery intensive care unit of a large tertiary care center.

**Patients**—Patients with an EVD. Patients with an infection prior to EVD placement or a permanent ventricular shunt were excluded.

**Methods**—We reviewed the charts of patients with a positive cerebrospinal fluid (CSF) cultures and/or abnormal CSF results while they had an EVD in place and applied various ventriculitis definitions.

**Results**—We identified 48 patients with a total of 52 episodes of ventriculitis (41 CSF culture positive episodes and 11 episodes based on abnormal CSF test results) using the NHSN definition. The most common organisms causing ventriculitis were Gram positive commensals (79.2%), however 45% of these had growth of only one colony on one piece of media. About 60% of the ventriculitis episodes by NHSN definition met Honda criteria, about 56% met Gozal criteria and 23% met Citerio's definition. Honda vs. Gozal had a moderate agreement ( $K=0.528$ ,  $p<0.05$ ) whereas Honda vs Citerio ( $K=0.338$ ,  $p<0.05$ ) and Citerio vs Gozal ( $K=0.384$ ,  $p<0.05$ ) comparisons had only fair agreements.

**Conclusions**—Agreement between published VAI definitions in this cohort was moderate to fair. A VAI surveillance definition that better defines contaminants is needed for more

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homogenous application of surveillance definitions between institutions and better comparison of rates.

## Keywords

definition; surveillance; ventriculitis

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## Introduction

Ventriculostomy-associated infection (VAI) is one of the most serious complications of external ventricular drain (EVD) use. These infections can result in increased morbidity, mortality, prolonged hospital stay and higher healthcare costs.<sup>1,2</sup>

The reported incidence of VAI varies from under 1% to 45%.<sup>1,3</sup> This wide variability in the VAI incidence may be in part due to the challenge of diagnosing VAI in the presence of an abnormal cerebrospinal fluid (CSF) profile from underlying central nervous system disease, recent surgery<sup>1,4</sup> and differences between VAI definitions.<sup>5,1</sup>

The Center for Disease Control and Prevention (CDC) National Healthcare Safety Network (NHSN) has a definition for ventriculitis.<sup>6</sup> A single positive CSF culture or non-culture based microbiological test meets the NHSN ventriculitis definition. Since CSF samples for culture are generally drawn through the EVD in the course of routine care, intraluminal colonization of the device may result in a positive culture<sup>1</sup> thereby meeting the NHSN definition.

A recent study by Lewis et al compared the performance of multiple VAI definitions.<sup>3</sup> The NHSN definition was not included in the comparison and the antibiotic length of therapy was used as the gold standard for ventriculitis, which may have introduced bias due to variations in antibiotic prescribing practices.<sup>7</sup>

NHSN surveillance data is increasingly being linked to hospital reimbursement by regulatory agencies and payers, such as the Centers for Medicare and Medicaid Services, thus understanding the performance characteristics of NHSN definitions is important. The objective of our study is to compare VAIs rates using the NHSN definition versus other published definitions.

## Methods

### Study cohort

We conducted a retrospective study of patients who underwent placement of a ventricular drain (EVD) between January 2009 and December 2014 and housed in the Barnes-Jewish Hospital neurological and neurosurgical intensive care unit.

### Inclusion and exclusion criteria

A total of 965 EVDs were identified during the study period. We excluded EVDs placed in patients < 18 years old and those who had a permanent shunt, a cerebral abscess, and/or a positive CSF culture at time of EVD insertion. From the remaining EVDs, we selected only

those EVDs which satisfied the NHSN definition for ventriculitis.<sup>6</sup> These included patients having a positive CSF culture while the EVD was in place or an abnormal CSF analysis result or positive blood cultures in the presence of neurological symptoms. We considered only tests that were performed while EVD was in place and up to two days after removal.

### **NHSN CSF culture-positive episodes**

We selected all patients with a positive CSF culture. If multiple organisms grew from a single CSF culture, we considered this a polymicrobial episode. If a patient had multiple CSF cultures that grew the same organism, we considered it to be a single episode with the date of initial positive culture as the episode date. If a patient had multiple CSF cultures performed and different organisms grew from more than one culture we considered each culture as a different episode. Cultures drawn on the same day or within one calendar day were part of the inclusion criteria unless they had a pre-existing infection.

### **NHSN CSF culture-negative episodes**

Patients with at least one CSF glucose measurement  $<50\text{mg/dl}$  were selected. Patients with all of the additional three criteria: CSF protein  $> 50\text{mg/dl}$ , CSF nucleated cells  $> 5\text{ cells/mm}^3$  and fever  $>38^\circ\text{C}$ , were included for further review.

CSF analysis data (protein, nucleated cells, glucose) obtained contemporaneously with CSF culture were considered. If no CSF analysis was obtained when the culture specimen was obtained, we then considered the temporally closest CSF analysis performed to the CSF culture while the EVD was in place.

If patients did not meet either the positive CSF culture or the abnormal CSF criteria, we then conducted a chart review of all patients with a positive blood culture(s) while the EVD was in place. If there was suspicion for a central nervous system infectious source, then they were included for further evaluation.

### **Other definitions**

We applied three other published VAI definitions (Honda, Gozal and Citerio) to our cohort (Table 1)<sup>6,8-10</sup>. All of these definitions required growth of an organism from CSF culture; therefore, all patients who met these definitions were a subset of the patients who met the NHSN VAI definition by virtue of a positive CSF culture.

### **Data collection**

Patient demographics, CSF testing, culture and blood culture data was abstracted from the hospital medical informatics database. We collected the following data from the charts: date of EVD insertion and removal (extracted from the per shift nursing assessment), EVD indication for placement, clinical information (maximal temperature, new meningeal or cranial nerve signs within 72 hours of CSF testing), and systemic antibiotic therapy while EVD was in placed was recorded.

We defined treatment as receiving an antibiotic with activity against the organism(s) detected in CSF cultures, based upon susceptibilities. In the case of common commensals

with no susceptibilities reported, agents with activity against methicillin-resistant bacteria were considered to be active. We defined 14 days to be an appropriate length of antibiotic therapy for ventriculitis. Of note, prior to May 2012 all EVD patients in our study received either cefazolin or vancomycin prior to EVD placement and then as long as catheter remained in place. After May 2012 patients received only peri-procedural antibiotics.

### Statistical analysis

SPSS version 22 (IBM; Armonk, NY) was used for analysis. Percentage agreement of the Honda, Gozal and Citerio definitions with NHS definition was calculated. The unweighted Kappa statistic was used to assess the agreement between Honda, Gozal and Citerio definitions.

This study was approved by the Washington University Human Research Protection Office.

### Results

After exclusions, our cohort included 49 EVDs (from 48 patients) with 52 episodes of ventriculitis, which included 41 culture-positive and 11 culture-negative episodes (Figure 1). The median age of the patients was 54 years (interquartile range (IQR) 47–64 years) and 58.3% were female (n=28). EVD characteristics are described in Table 2.

#### CSF culture-positive episodes

Thirty-seven patients with 38 EVDs contributed to 41 CSF culture-positive episodes. The median time from EVD insertion to first positive culture was 8 days (IQR 4–12 days). Two of the 41 CSF culture-positive samples were not sent for CSF analysis. The median number of nucleated cells in the remaining 39 samples was 60 cells/mm<sup>3</sup> (range 0–8440). Thirty samples (76.9%) had 5 nucleated cells/mm<sup>3</sup>. The median concentration of protein was 48mg/dl (IQR 27–87); 19 (48.7%) had a protein level > 50mg/dl. The median glucose was 74mg/dl (IQR 66–90). Only three (7.6%) had a glucose level <50mg/dl.

The microbiology of CSF cultures is shown in Table 3. Of note, 20 (49%) of 41 culture-positive episodes had an annotation of “one colony on one piece of media” for an organism. The organisms growing only a single colony in culture were: coagulase-negative *Staphylococcus* spp (11 cultures), *Micrococcus* spp (4), *Corynebacterium* spp (2), *Bacillus* spp, *Propionibacterium* spp, and unidentified yeast.

Forty (97.6%) positive-culture CSF episodes received some antibiotic therapy. Twenty-two (53.6%) received appropriate antibiotic for the organisms cultured. The median length of antibiotic use was 5 days (IQR 3–11 days). Five patients received treatment for 14 days (four with Gram negative bacteria; one with *Candida parapsilosis*). From the 20 cultures that had the annotation of “one colony on one piece of media” seven (35%) received an antibiotic with activity against the isolated organism; none received antibiotics for 14 days.

Among the 38 EVDs with one or more positive CSF cultures, 9 (23.6%) were removed and 3 (7.9%) were exchanged within 48 hours of the positive culture.

### CSF culture-negative episodes

There were 11 patients with 11 EVDs that contributed to 11 CSF culture-negative episodes (Figure 1). The median number of nucleated cells was 375 cells/mm<sup>3</sup> (IQR 100–2067). The median concentration of protein was 113 mg/dl (IQR 71–332). The median glucose was 45 mg/dl (IQR 27–48).

All 11 patients received intravenous antibiotics, but none completed 14 days of therapy. Two (18%) EVDs were removed within 48 hours of the abnormal CSF test results. The remaining 9 (81.8%) were neither removed nor exchanged.

### Comparison of ventriculitis rates

There were 52 episodes of ventriculitis by NHSN definition: 41 episodes based on a positive CSF culture and 11 episodes based upon abnormal CSF test results. Thirty-one of these episodes (59.6%), met ventriculitis criteria by the Honda definition, 29 (55.8%) by the Gozal definition and 12 (23.1%) by the Citerio definition. The ventriculitis rate varied widely by definition (6.7, 4.0, 3.7 and 1.5 per 1000 EVD-days for NHSN, Honda, Gozal and Citerio, respectively). No episodes were identified by other three definitions, but not identified by NHSN.

Comparing the agreement between the definitions, we found the Honda and Gozal definitions had a moderate agreement ( $K=0.528$ ,  $p<0.05$ ). The other comparisons had only fair agreements: Honda vs Citerio ( $K=0.338$ ,  $p<0.05$ ) and Citerio vs Gozal ( $K=0.384$ ,  $p<0.05$ ).

## Discussion

Ventriculitis rates in our study varied widely by the definition applied. Compared to three culture-based definitions in the literature, the NHSN definition resulted in substantially more episodes of VAI being identified. This is most likely due to the NHSN definition defining any growth on CSF culture, no matter the organism, the number of abnormal CSF cultures or the degree of growth on media as infection. This definition also classified episodes as VAI based upon CSF abnormalities plus neurological symptoms, irrespective of culture findings.

In our study, Gram positive commensals were the predominant organisms recovered from the CSF cultures (79.3%). These organisms are the most commonly implicated as a cause of VAIs,<sup>5,1</sup> but also are a frequent cause of culture contamination or catheter colonization. We found that 45% of the common commensals had an annotation by the laboratory of “one colony on one piece of media”; calling into question their significance as a pathogen. Of the other VAIs definitions available in the literature<sup>3,9,1</sup> only one used quantification of colony forming units and none required more than one positive culture.<sup>3</sup> Therefore, most definitions may identify either catheter colonization or contamination during collection as a VAI.

The NHSN definition also includes the presence of new cranial nerve signs, meningeal signs or headache. Given their underlying pathology, the neurosurgical patients may have these signs and symptoms, regardless of infection. Other infection surveillance definitions relying on clinical signs and symptoms have been reported to miss cases. A study examining chart-

documented signs and symptoms of catheter associated urinary tract infections found that only 9.5% of cases had documented dysuria, frequency or urgency and 4.1% had suprapubic tenderness or costovertebral angle pain.<sup>11</sup> In our cohort, we found only 9 (17.3%) patients with new or worsening cranial nerve signs and none for new or worsening meningeal signs.

A surveillance definition that cannot adequately discern VAIs from culture contamination may lead to a misinterpretation of clinical practice patterns. In our cohort, only 53.6% of NHSN-defined VAI cases received organism-specific antibiotic therapy, and only five patients received treatment for 14 days. Among “one colony on one piece of media” episodes, we found a significantly lower proportion of associated CSF protein > 50mg/dl and CSF glucose <50mg/dl versus other episodes (data not shown). Among the NHSN-defined VAI cases that grew one colony on one piece of culture media, only 35% received organism-specific antibiotic therapy, and in all these cases, treatment was <9 days. Analogous to central line-associated bloodstream infections, EVD removal is recommended in VAI.<sup>12</sup> However, among the EVDs in our cohort with a positive CSF culture, 9 (23.6%) were removed and 3 (7.8%) exchanged. Among VAIs with negative CSF cultures, only 2 (18%) EVDs were removed and none exchanged.

Our VAI rate varied considerably, depending on the definition applied. For instance, using the Citerio definition,<sup>10</sup> there were no cases of VAI in 2012; however, using the NHSN definition, there were 12 VAI cases, a rate of 10.7 infections per 1000 EVD-days. If trying to compare rates between hospitals, this variability becomes problematic.<sup>5</sup> Currently, U.S. hospitals are mandated to report certain hospital-acquired infections as for quality of care metrics which are linked to reimbursement.<sup>13</sup> Therefore, it is increasingly important that surveillance definitions are reproducible and align well with clinical definitions. We call for refining the NHSN VAI definition, adopting a definition similar to the current NHSN central line-associated bloodstream infection definition.<sup>9</sup> This would increase definition specificity, and by removing subjective clinical criteria, allow for automated surveillance.<sup>14</sup>

The limitations of our study include being retrospective, relying on pre-existing documentation, and occurring in single center. We calculated the Cohen’s kappa coefficient between the three published definitions, but we could not directly compare them to the NHSN definition, since the ventriculitis episodes in all three definitions were a subset of NHSN-defined VAI episodes. The strengths of our study include having a large number of EVDs placed in our institution and a high number of CSF cultures to allow for comparison of various ventriculitis definitions.

The current NHSN ventriculitis definition has limitations that make difficult its use for surveillance and to compare VAI rates among institutions. Our data suggest that a modification to the current NHSN definition is needed, if such comparisons are to be made in the future.

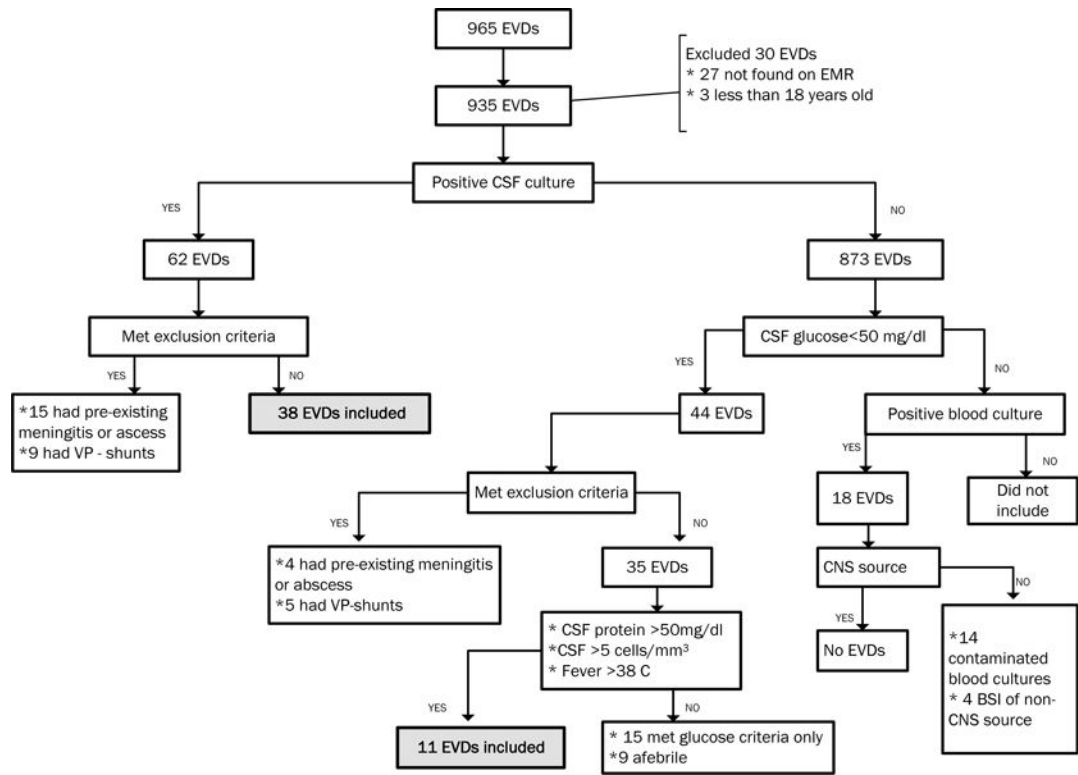
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**Figure 1. Inclusion of patients in the study**

EVDs: External ventricular drains, EMR: Electronic Medical Record, CSF: cerebrospinal fluid. CNS: Central Nervous System. BSI: bloodstream infections. VP: ventriculoperitoneal.



**Table 1**

Ventriculitis definitions used in the study

Definition name	Definition criteria	Culture criteria	Gram Stain	Clinical criteria	CSF analysis criteria	Other criteria
CDC/ NHSN <sup>6</sup>	<ul style="list-style-type: none"> <li>Culture criteria alone</li> <li>OR</li> <li>2 of 3 clinical criteria and:                             <ul style="list-style-type: none"> <li>All CSF analysis criteria</li> <li>OR</li> <li>Abnormal gram stain</li> <li>OR</li> <li>Positive blood culture</li> </ul> </li> </ul>	Any growth	Organism present	<ul style="list-style-type: none"> <li>Fever &gt;38°C</li> <li>Meningeal</li> <li>Cranial nerve signs</li> </ul>	<ul style="list-style-type: none"> <li>↑ CSF nucleated cells and ↓ CSF glucose and ↑ CSF protein</li> </ul>	
Honda <sup>8</sup>	<ul style="list-style-type: none"> <li>Culture alone</li> <li>OR</li> <li>If skin flora (*), then at least one of CSF analysis criteria must be met.</li> </ul>	Any growth	Should match culture growth		<ul style="list-style-type: none"> <li>CSF WBC 10 cells/mm<sup>3</sup></li> <li>or</li> <li>CSF glucose &lt;2.5mg/dl</li> <li>or</li> <li>CSF protein &gt;50 mg/dl</li> </ul>	Only to consider if at least 48 hours after EVD inserted.
Gozal <sup>9</sup>	<ul style="list-style-type: none"> <li>Culture and clinical criteria and CSF analysis criteria</li> </ul>	Any growth		Fever >101.5°F	<ul style="list-style-type: none"> <li>CSF glucose &lt;50mg/dl</li> <li>or</li> <li>CSF glucose/serum glucose ratio 50%</li> </ul>	Included even those in which criteria met within 72h of EVD removal
Citerio <sup>10</sup>	<ul style="list-style-type: none"> <li>Culture criteria</li> <li>And clinical criteria and CSF analysis criteria</li> </ul>	Any growth		Fever >38°C	<ul style="list-style-type: none"> <li>CSF WBC &gt; 5 cells/μL and</li> <li>CSF glucose/serum glucose ratio 50%</li> </ul>	

Note:

(\*): Common skin flora: coagulase-negative staphylococci, *Corynebacterium*, *Bacillus*, *Micrococcus*, or *Propionibacterium* spp.

**Table 2**

Characteristics of External Ventricular drains (EVDs) in study population.

Variable	EVDs (%) (n=49) *
<b>Indication for EVD placement **</b>	
Hydrocephalus	43 (87.8%)
Intracranial bleeding	42 (85.7%)
Intracranial tumor	9 (18.4%)
Trauma	3 (6.1%)
<b>Where was the EVD placed?</b>	
Neuro intensive care unit	28 (57.1%)
Operating room	13 (26.5%)
Outside hospital	5 (10.2%)
Emergency department	3 (6.1%)
<b>Neurosurgical history?</b>	
30 days before EVD placement	8 (16.3 %)
Surgery while EVD was in place	22 (44.9)

EVDs: External Ventricular drains

\* Includes 48 patients. One patient had 2 EVDs during study period.

\*\* EVDs could be placed for 1 indication.

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**Table 3**

Characteristics of CSF positive cultures

	Organisms	Frequency (n=54 <sup>*</sup> )
<b>Gram positive bacteria</b>	Coagulase negative <i>Staphylococcus spp</i>	24 (44.4%)
	<i>Micrococcus spp</i>	6 (11.1%)
	<i>Corynebacterium spp</i>	4 (7.4%)
	<i>Propionibacterium spp</i>	3 (5.6%)
	<i>Streptococcus spp</i>	3 (5.6%)
	<i>Bacillus spp</i>	2 (3.7%)
	<i>Arthrobacter spp</i>	1 (1.9%)
<b>Gram negative bacteria</b>	<i>Enterobacter spp</i>	3 (5.6%)
	<i>Neisseria spp</i>	2 (3.7%)
	<i>Moraxella spp</i>	1 (1.9%)
	<i>Klebsiella spp</i>	1 (1.9%)
	<i>Serratia spp</i>	1 (1.9%)
	<i>Brevudimonas spp</i>	1 (1.9%)
<b>Fungal</b>	<i>Candida parapsilosis</i>	1 (1.9%)
	Unidentified yeast	1 (1.9%)

Note:

\* Of 41 episodes. Four cultures were polymicrobial: Two had 2 organisms, one had 4 and another one had 9 organisms from a single culture.