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REVIEW ARTICLE

The Insertion and Management of External Ventricular Drains: An Evidence-Based Consensus Statement

A Statement for Healthcare Professionals from the Neurocritical Care Society

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Abstract External ventricular drains (EVDs) are commonly placed to monitor intracranial pressure and manage acute hydrocephalus in patients with a variety of intracranial pathologies. The indications for EVD insertion and their efficacy in the management of these various conditions have been previously addressed in guidelines published by the Brain Trauma Foundation, American Heart Association and combined committees of the American Association of Neurological Surgeons and the Congress of Neurological Surgeons. While it is well recognized that placement of an EVD may be a lifesaving intervention, the benefits can be offset by procedural and catheter-related complications, such as hemorrhage along the catheter tract, catheter malposition, and CSF infection. Despite their widespread use, there are a lack of high-quality data regarding the best methods for placement and management of EVDs to minimize these risks. Existing recommendations are frequently based on observational data from a single center and may be biased to the authors' view. To address the need for a comprehensive set of evidence-based guidelines for EVD management, the Neurocritical Care Society organized a committee of experts in the fields of neurosurgery, neurology, neuroinfectious disease, critical care, pharmacotherapy, and nursing. The Committee generated clinical questions relevant to EVD placement and management. They developed recommendations based on a thorough literature review using the Grading of Recommendations Assessment, Development, and Evaluation system, with emphasis placed not only on the quality of the evidence, but also on

The Neurocritical Care Society affirms the value of this consensus statement as an educational tool for clinicians.

Herbert I. Fried, Barnett R. Nathan, A. Shaun Rowe, and Joseph M. Zabramski are cochairs of Committee.

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the balance of benefits versus risks, patient values and preferences, and resource considerations.

Keywords EVD · External ventricular drain · Ventriculostomy · Ventriculostomy-related infection · Ventriculostomy associated infection · VAI · VRI · Hydrocephalus · ICP · Monitoring · CSF drainage · Hemorrhage · Antibiotics · Antibiotic coated catheter · Antimicrobial coated catheter · Antibiotic prophylaxis · DVT · Deep venous thrombosis · DVT prophylaxis · Thromboembolism · Intraventricular antibiotics

Introduction

External ventricular drains (EVDs) have been used for the relief of hydrocephalus for well over a century. EVDs use by Lundberg to study intracranial pressure in brain tumor patients demonstrated their additional value as a physiological measurement tool [1, 2]. Presently, EVDs are used for such a wide variety of indications that their insertion may be the most commonly performed cranial neurosurgical procedure [3]. For many years, EVDs were the only type of reliable ICP monitor available and were considered the gold standard for measurement of intracranial pressure. Today both EVDs and intraparenchymal ICP monitors are recommended for this purpose [4].

Acute hydrocephalus is one of the most common indications for an EVD, whether due to subarachnoid hemorrhage (SAH), intraventricular hemorrhage (IVH), intraparenchymal hemorrhage (IPH), infection, brain tumors, or shunt failure. EVDs also are included in the Brain Trauma Foundation Guidelines for the management of severe traumatic brain injury (TBI) [5].

However, despite the history and frequency of this procedure, there are concerns over the rate of complications such as infection, malposition, and hemorrhage, as well as considerable differences in EVD insertion and management techniques [3, 6–14]. Several factors may account for these significant practice variations. First, there is a paucity of high-quality evidence to support particular management practices. Most studies are observational and retrospective case series, and they describe widely variable complication rates. Further confounding the establishment of definitive practice standards is the lack of established definitions for optimal catheter placement, clinically significant procedure-related hemorrhage, and ventriculostomy-related infection (VRI). Protocols for "best practice" may meet resistance in implementation even within institutions because of the reluctance of individual practitioners to deviate from their usual practices. A recent example has been seen in the evolution of the Parkland protocol for timing of VTE prophylaxis in TBI [15]. The Neurocritical Care Society (NCS), therefore, determined that there would be benefit in developing a formal, multidisciplinary, evidence-based Consensus Statement, which it has defined as "recommendations developed using available evidence and expert opinion in areas where high quality clinical data is limited or does not exist for controversial clinical dilemmas," regarding EVD insertion and management [16].

Methods

A committee of experts in neurosurgery, neurology, neuroinfectious disease, neurocritical care, internal medicine, pharmacotherapy, and nursing was recruited from within the NCS. An organizational meeting was held in Seattle in September, 2014. The Committee generated a set of clinical questions relevant to EVD insertion and management specifying the patient group of interest, the intervention, the comparators, and the outcomes of interest (PICO format).

With the assistance of a medical librarian, the Committee undertook a comprehensive literature search of the PubMed, Embase, and Cochrane databases from 1960 to October 2014. The full search strategy is provided in the supplementary materials. The Committee did not consider articles in languages other than English, case series of five or less, primarily pediatric studies, nonhuman studies, or unpublished presentations. Pediatric studies were excluded as our group lacked the expertise to critically evaluate the pediatric literature. Abstracts of each citation were reviewed by two Committee members for relevance, and full-text articles were obtained where applicable. The Committee considered systematic reviews and meta-analyses but did not use them in evidence tables. Also included for analysis were articles identified in bibliographies and personal files which included references up to April 2015. Two experts focused on each PICO question.

The Committee utilized Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology to adjudicate the quality of evidence as high, moderate, low, or very low based on their confidence that the estimate of effect was close to the true effect. They generated recommendations only after considering quality of evidence, relative risks and benefits, patient values and preferences, and resource allocation [17]. Recommendations were made for or against an intervention, and classified as strong ("we recommend") or conditional ("we suggest"). Strong recommendations are the preferred course of action for most patients and should be adopted as policy in most situations. Conditional recommendations require further consideration within the clinical and institutional context and should be carefully evaluated by stakeholders before being implemented as policy [18].

The Committee recognized from the outset that high-quality evidence in the field of neurocritical care is seldom available. There is also growing awareness that many guidelines make strong recommendations based on low or very low-quality evidence. In some cases, these "discordant" recommendations may be inconsistent with GRADE methodology, possibly undermining clinicians' confidence in implementing the guidelines. GRADE methodologists have attempted to distinguish between recommendations based on a formal GRADE process and those better described as "good practice statements." The latter are recommendations where there is a high level of certainty in net benefit (or harm), but where published evidence is lacking, or is high quality but indirect. The Committee identified several questions where a "good practice statement" appeared more appropriate and identified them as such [19, 20]. They strove to make explicit the rationale behind each recommendation, including the weighing of risks and benefits and the basis for their level of confidence in the evidence.

A meeting of the full Committee was held on March 7–8, 2015 in Denver. Topic authors presented GRADE evidence summaries, and recommendations were arrived at after discussion by the entire panel. On July 24, 2015, the entire Committee participated in a conference call to approve the final document. The final Consensus Statement was submitted for review by experts within the Neurocritical Care Society and by reviewers from other stakeholder societies (American Association of Neurological Surgeons, Congress of Neurological Surgeons, Infectious Diseases Society of America and Society for Critical Care Medicine). Further edits were made after these reviews.

Is There an Increased Risk of Adverse Mechanical or Infectious Events in Adult Patients Undergoing EVD Insertion Outside the Operating Room?

See Evidentiary Table 1

EVDs are very frequently inserted in patients with critical illnesses and/or sudden neurologic deterioration. At times, the emergent need for EVD insertion may conflict with the availability of a sterile operating room (OR) environment. Furthermore, patients may not be medically stable for transport. For these reasons and others, placement of EVDs outside the OR has become common in neurocritical care.

In assessing whether the EVD insertion environment affects adverse mechanical events, the Committee identified only two small retrospective case series and no randomized controlled trials (RCTs). In the first, Gardner et al. retrospectively reviewed 188 EVD insertions in the OR and the ICU; the rate and size of post-procedural hemorrhages were not significantly different between the groups. However, the relatively small sample size might not allow for detection of clinically significant differences in the rates of adverse events; this study had only 37 % power to detect a doubling of the hemorrhage rate at an alpha of 0.05 and a baseline rate of 2.4 % [13]. A second retrospective study by Foreman evaluated 138 EVD placements inside or outside the OR and their association with a composite outcome of adverse events (hemorrhage, infection, or catheter malfunction) [21]. Complications in general were more frequent (21.5 vs. 6.7 %) when catheters were placed outside the OR, but of interest there was no significant difference in accuracy of placement ($p = 0.258$) or in the risk of infection (as discussed below). Other studies describe complication rates in the ICU, the OR, the Emergency Department, and the CT scan suite, but do not compare adverse mechanical events based on location of insertion [12, 22–28].

Trials related to the risk of VRI, when an EVD is placed inside the OR versus outside of it, are limited to retrospective studies, and the results conflict with regard to which locale has a higher rate of VRI. Trick et al. evaluated potential causes of *Pseudomonas aeruginosa* ventriculitis in neurosurgical intensive care unit patients [29]. The authors found that those who had EVDs placed in the neurosurgical OR were more likely to develop *Pseudomonas aeruginosa* ventriculitis than those who had EVDs placed in the ICU or emergency department (8 patients [33 %] vs. 0 patients [0 %], $p = 0.004$). The authors concluded that the high infection rate observed in the OR was related to a single health care worker and potentially the lack of a sterile occlusive dressing rather than the OR setting. A second trial by Schodel et al. compared placement of EVDs in the OR with placement of EVDs at the bedside in the ICU using a cranial bolt kit [30]. As compared to the cranial bolt kit group, patients in the OR group developed more ventricular infections (6 [4.9 %] vs. 13 [6.8 %], $p = 0.034$). After controlling for age, drainage time, and multiple punctures, those patients who had an EVD placed with a cranial bolt kit in the ICU still had a lower infection rate ($p = 0.032$). However, this study did neither describe the multivariate analysis methodology nor did it control for severity of illness or EVD indication, which may have confounded the results. Arabi et al. also evaluated the effect of OR placement on VRI infection rates [31]. Although patients who had an EVD placed outside of the OR had more VRIs (odds ratio 3.21; 95 % CI 0.92–11.28), this difference did not reach statistical significance. In Foreman's retrospective review, 93 EVDs (67 %) were placed at the beside in the ICU and 45 (33 %) were inserted in the OR [21]. There was a nonstatistical increase in VRIs when EVDs were placed in the ICU instead of the OR (4 vs. 0 %, $p = 0.303$). Confounding this non-significant difference was the fact that only 10 % of the ICU patients received a periprocedural antimicrobial, as opposed to 100 % of the OR cases.

Based on the conflicting and low-quality results and with the many potential confounders of these studies, the Committee found no convincing evidence that placement of an EVD outside of the OR leads to an increased risk of mechanical or infectious complications.

Recommendation:

We suggest that the location of EVD insertion (Operating Room or bedside) should be dictated by patient characteristics and clinical circumstances

(Conditional recommendation; low-quality evidence)

In making this recommendation, the Committee acknowledges that there is a lack of conclusive evidence demonstrating equivalence of EVD insertion within and outside the OR, but the available data suggest that EVD insertion outside the OR is associated with a sufficiently low rate of complications that it is an acceptable option depending on the clinical situation and OR availability. A standardized protocol can minimize risks of complications regardless of where the procedure is performed. The importance of evidence-based protocol for the insertion and management of EVDs is covered later in these guidelines

In Adult Patients Undergoing EVD Insertion, Does the Risk of Adverse Events Vary Depending on the Training, Procedural Experience, or Specialty of the Clinician Performing the Procedure?

See Evidentiary Table 2

Although EVD placement is consistently regarded as a low-risk procedure, complications such as hemorrhage, infection, and malposition can be associated with significant morbidity and mortality. Given that neurosurgery residents most frequently perform these procedures in academic centers, the level of training and experience of the operator has been suggested as a possible variable affecting complication rates [8, 32, 33]. Furthermore, with the recent expansion of Neurocritical Care services and the shortage of neurosurgeons in some underserved areas, an increasing number of reports on bedside placement of EVD and ICP monitors by neurointensivists has been published [8, 23, 34, 35].

Increasing regionalization of healthcare, changes to the structure of medical training, and the implementation of work hour restrictions all potentially threaten the surgical procedural volume of trainees. To provide adequate procedural training, surgical simulation has emerged as an alternative to achieve and maintain competency and certification [36–40]. The Committee sought to assess the impact of operator experience, operator specialty, and virtual training methodologies on the accuracy of EVD insertion.

Very limited data exist comparing the rate of adverse events with the level of experience and training of the operator. O'Neill et al. surveyed 932 practicing neurosurgeons and 100 neurosurgery residents; both practicing neurosurgeons and senior neurosurgery residents self-reported that they required a lower number of attempts to achieve successful cannulation of the ventricle as compared to junior neurosurgery residents [8]. Kakarla et al. reported on 346 patients who underwent EVD insertions mostly by neurosurgery residents at different stages of training under a mentoring system based on resident seniority. The authors did not find a significant difference in EVD placement accuracy based on operator experience [12]. In total, the existing data suggest that even if insertion accuracy increases with experience, EVD insertion by less experienced trainees is reasonably accurate if carefully supervised by more experienced operators.

The literature is also limited regarding EVD insertion by non-neurosurgeons. Ehtisham et al. reported on 29 EVD insertions by neurointensivists and found similar complication rates as in published reports of EVD placement by neurosurgeons (34). No other studies describing EVD insertions by non-neurosurgeons were identified.

A number of simulation models have been developed to train neurosurgery residents on procedures such as EVD insertion. However, the heterogeneity of the models reported precludes an assessment of the added efficacy of these training adjuncts [36–42]. Based on the preliminary evidence reviewed, the Committee suggests that procedural simulation training for EVD insertion may be a useful educational adjunct.

Good practice statement:

We suggest that practitioners planning to place EVDs follow formal institutional protocols for training, mentoring, and quality assurance. The Committee suggests that neurosurgeons participate in development of the institutional protocol and credentialing, and that neurosurgical backup availability be assured

The Committee found no evidence that type of training, experience, or specialty affect the risk of complications during EVD insertion

What is the Risk of Hemorrhage with EVD Insertion? Are There Modifiable Factors That can Reduce This Risk?

See Evidentiary Table 3

Several publications have addressed the incidence of bleeding related to insertion of an EVD [3, 6, 7, 10–12, 43]. All but two were observational studies that often primarily

addressed other outcomes [43, 44]. Two recent meta-analyses and a systematic review have highlighted the wide variation among estimates of bleeding risk; rates have been reported to be as low as 0 %, or as high as 41 % [43, 45, 46]. This wide range is attributable to the varying design and execution of the included studies.

Obtaining a true estimate of the risk of hemorrhage requires, at a minimum, routine performance of a CT scan within a specified interval after EVD insertion together with a standardized definition of hemorrhage. Six studies met this standard. Kakarla et al. evaluated 346 patients receiving an EVD at a new surgical site and obtained an immediate post-procedure CT scan [12]. Although the study did not report on the dimensions of the hematomas, 3.8 % of these scans showed tract hemorrhages, and 1.5 % were found to have extra-axial or intraventricular hemorrhages. Two out of the 13 tract hemorrhages resulted in neurologic deterioration not requiring surgery, and two of the four patients with extra-axial hematomas subsequently died. The overall hemorrhage rate in this series was 5 %.

A second study by Ehtisham described 29 EVD placements by a neurointensivist, with follow-up CT scans done between three and 12 h post-procedure [35]. There were six instances of bleeding along the drain tract. Hematoma volumes were measured as between less than 1–5 cm^3. None subsequently enlarged or produced a detectable neurological deficit.

Maniker reported on 160 patients requiring EVD insertion, all of whom received pre- and post-insertion CT scans [11]. As in the Kakarla study, residents placed all of the EVDs. Most CT scans were acquired within eight hours, and none were acquired after 24 h. New hemorrhages in immediate proximity to the catheter were considered to be EVD related. Hemorrhage was seen in 33 % of the patients. Of the 160 patients, 28 % had "typically" small (up to 4 cm^3) or punctate intraparenchymal hemorrhages, and the volumes of the remaining hematomas (which included subdural and intraventricular hemorrhage) were not recorded.

Gardner evaluated 188 EVD insertions; most underwent neuroimaging (including gradient echo MRI scans) within 48 h [13]. Of these, 41 % ($n = 77$) had new hemorrhage, including 13 that were seen only after catheter removal. About half (51.9 %) of these new hemorrhages were described as "insignificant, punctate intraparenchymal, or trace SAHs." Larger hemorrhages were observed in 19.7 % ($n = 37$) patients, and of these 16 were less than 15 mL, 20 were greater than 15 mL, and one was a subdural hematoma. None of the new hemorrhages noted after catheter removal was larger than punctate, as in the Maniker study.

Two related articles from the CLEAR investigators discuss EVD-related hemorrhage. The first by Naff et al. in 2011 was part of a dose escalation study for safety and efficacy of rtPA in the clearance of IVH [44]. This small randomized controlled trial enrolled 48 patients who had received an EVD for a non-lesional IVH. Asymptomatic bleeding was seen in 5/24 of the rtPA group and in 2/24 placebo patients; symptomatic bleeding was reported for 6/24 of the rtPA patients, and 1/24 of the placebo patients, although not all of the hemorrhages were related to the catheter.[1] Dey et al. systematically reviewed the risks of hemorrhage and infection following EVD placement together with interim results of the CLEAR III trial [43]. Stability of any prior hemorrhage on a CT scan performed at least 6 h after EVD placement was required for enrollment; a threshold of 5 mL of increased hematoma volume, or 5 mm of diameter expansion, was chosen as the upper limit of stability. CT scans were also obtained at 24 and 72 h after the last dose of drug, as well as 30 and 365 days after enrollment; hemorrhages as late as 30 days were included as complications of the procedure. The study allocation remains blinded. Of the 250 patients, 42 (16.8 %) had new or increased bleeding; six cases were symptomatic. However, only three of these six were catheter tract hemorrhages. There were also three patients with asymptomatic bleeding noted after EVD insertion but before enrollment, at which time they were judged to be stable.

Not all hemorrhages are symptomatic or lead to temporary or permanent neurological injury. In the six studies reviewed above, the clinically significant hemorrhages were only a small percentage of those detected by neuroimaging. One systematic review found an average rate of symptomatic hemorrhages of 0.7 %, and the interim CLEAR III rtPA data cite a symptomatic rate of 2.4 % [43].

It should nevertheless be noted that these studies may underestimate the true incidence of clinically important hemorrhages: the threshold for 'clinically significant' varies across studies and standard thresholds (such as a decrement of at least two points in the GCS) and may misclassify clinically relevant hemorrhages [43]. Likewise, clinical manifestations of EVD-related hemorrhages can be difficult to ascertain in critically ill patients who are sedated and ventilated. There are no long-term studies that might show subtle neurocognitive harm or persistent focal neurological deficits due to EVD-related hemorrhage.

Clearly, the literature suggests very low rates of clinically significant hemorrhage related to EVD insertion. No well-designed studies were identified that addressed potentially modifiable risk factors for procedural hemorrhage such as blood pressure at the time of insertion, coagulopathy, and the number of passes before successful cannulation.

Reversal of coagulopathy, whether due to patient disease or prior administration of anticoagulant or antithrombotic drugs, is common clinical practice before

[1] Personal communication with author.

insertion of an EVD (except in dire emergency). While there are very limited data supporting the utility of this practice, coagulopathy reversal is considered a safety issue and is therefore unlikely to be the subject of a prospective RCT. Moreover, the PTT or INR threshold for safe placement has never been standardized or validated [45]. Increasing use of novel oral anticoagulants whose effects cannot be accurately measured and new point-of-care tests lacking standardization have further complicated diagnosis and management. Similarly, no study has convincingly shown that the number of passes, surgical technique, operator experience, or underlying pathophysiology can be linked to this already quite low-symptomatic bleeding rate; nor does it appear that such a study, sufficiently powered to evaluate these variables, is feasible.

Good practice statement:

Except in dire emergencies requiring immediate ventricular decompression, coagulopathy should be corrected according to institutional protocols before insertion of an EVD

The Committee determined that no adequately powered and ethical study is likely to be performed comparing reversal of antithrombotic or anticoagulant drugs prior to the insertion of EVD. However, they felt unanimously that given the potentially devastating effect of even a small hemorrhage, taking all measures possible to minimize hemorrhagic complications is in keeping with good clinical practices

What Procedural Factors are Associated with a Decreased Risk of Catheter Malposition?

See Evidentiary Table 4

Kakarla et al. categorized the adequacy of ventricular catheter placement Grade I, optimal placement in the ipsilateral frontal horn or third ventricle; Grade 2, functional placement in the contralateral ventricle or noneloquent (parenchyma); and Grade 3, suboptimal placement in the eloquent cortex [(parenchyma) or non-target CSF space, with or without functional drainage. In their retrospective review of 346 freehand bedside placements largely by trainees, they reported 77 % Class I, 10 % Class II, and 13 % Class III catheter placements [12]. Other case series of freehand insertions report Class I/Class III placement rates of 49 %/23 %, 56 %/22.4 %, 76 %/4 %, and 79 %/7 % [47–50].

Anatomical landmarks used during freehand insertion can influence EVD insertion accuracy. One study using imaging simulation in 10 patients with normal ventricles showed that if the ipsilateral medial canthus were used to define the freehand catheter trajectory, 90 % of catheter trajectories would miss the lateral ventricle [51]. The contralateral medial canthus (10 % miss) and perpendicular to the skull (0 % miss) trajectories performed better. A second study of imaging simulation in 101 patients with normal CT scans suggested a perpendicular to the skull trajectory beginning at a point located in adults approximately 2–3 cm lateral to the midline and 11 cm posterior to the nasion but 1 cm anterior to the coronal suture ("Kocher's point") would result in 67.8 % Class I, 20.8 % Class II, and 10.4 % Class III ventriculostomy insertions. In no case did advancing the catheter to a depth $>$ 6.5 cm result in contact with the ventricle after a "miss" [52].

A small single-center trial randomized patients to receive EVD insertion either by freehand technique or using a small tripod device to direct the catheter ("Ghajar guide"). The number of passes was recorded, and placements were evaluated based on distance of the catheter tip to the Foramen of Monroe. Investigators noted fewer passes and better accuracy with the tripod device, but were unable to determine the clinical significance of the finding [53].

Use of technological adjuncts, including CT guidance [24, 27], stereotactic navigation [54], intraoperative ultrasound guidance [55], electromagnetic navigation [25, 56, 57], and ventriculostomy through a bolt [30, 48] have each been reported to improve EVD insertion accuracy, but data are of low quality, potentially conflicted, and without meaningful comparison groups. Consequently only limited inferences on effectiveness can be drawn.

Recommendation:

When ventricular anatomy is normal, we suggest using Kocher's point as entry, and a trajectory perpendicular to the skull or targeting the contralateral medial canthus to provide the highest likelihood of optimal EVD placement. The catheter should not be advanced more than 6.5 cm from the skull surface before CSF is encountered

In cases of distorted ventricular anatomy or unusually small ventricles, consider using image guidance if available

Observational clinical series and computer simulations show that the above landmarks provide the highest rates of successful placement in the frontal horn

(Conditional recommendation; low-quality evidence)

In Adult Patients Requiring EVD, What is the Optimal Method and Timing of VTE Prophylaxis?

See Evidentiary Table 5

Venous thromboembolism (VTE), which includes deep venous thrombosis (DVT) and pulmonary embolus (PE), is a major preventable cause of morbidity and mortality in

surgical patients. There are several proven approaches for thromboprophylaxis: pharmacologic (with antithrombotic agents) and mechanical (with elastic stockings, sequential compression devices, or intermittent pneumatic compression devices) [58]. Pharmacologic thromboprophylaxis is effective at decreasing the risk of VTE but may be associated with an increased risk of hemorrhage [58].

In patients undergoing EVD insertion, determining the most appropriate form of VTE prophylaxis requires consideration of the risk of VTE, the risk of harm from VTE, and the efficacy and risks of the proposed mode of prophylaxis. Also relevant are possible contraindications due to bleeding risks, and the optimal time to initiate thromboprophylaxis given these risks.

Risk of VTE in Patients Undergoing EVD Placement

Almost all patients undergoing EVD placement are at moderate to high risk of perioperative VTE. Many patients who typically require EVD placement have one or more risk factors for VTE (e.g., age > 60, immobilization, traumatic hip or long-bone fractures, critical illness and malignancy). It is noteworthy that even outpatient surgery is associated with an increased risk of VTE in patients with other such VTE risk factors [59], and that physician underestimation of VTE risk and delay in prophylaxis are associated with an increased risk of inpatient VTE [60].

There are no data on the baseline incidence of VTE in the specific population of patients with EVDs. In other populations, patients undergoing neurosurgical procedures or who have acute neurological injuries are at high risk. A retrospective study evaluating the timing of heparin prophylaxis after EVD placement reported a VTE incidence of 7.2 %, although regular surveillance was not part of the study protocol and thus the true incidence of VTE is likely underestimated [14]. Rates of proximal DVT and PE in patients undergoing neurosurgical procedures with either no VTE prophylaxis or elastic stockings alone are reported between 14 and 16 % (50) [54], although other studies have reported rates as high as 33 % (50, 51). Other studies evaluating the risk of all types of VTE report rates between 16 and 33 % in neurosurgical patients without thromboprophylaxis and only elastic stockings, although the rates of proximal DVT and PE are more consistently reported as being between 14 and 16 % [61–63]. In patients with intracerebral hemorrhage and ruptured aneurysms, the incidence of proximal DVT and PE ranges from 1 to 3.5 % [64–66]. The risk of VTE is greater in patients with primary CNS malignancies (7.5 %) and metastatic disease (17 %) [64]. Of note, one prospective study of the risk of VTE after ICH found that the only significant factor associated with thromboembolism was placement of an EVD [65]. Consequently, for the majority of patients, the question is not whether to provide thromboprophylaxis or not, but what modality should be used.

Efficacy of Prophylaxis with Unfractionated or Low-Molecular-Weight Heparin

Prophylaxis against VTE with antithrombotic medications is effective in preventing radiographic and symptomatic DVT and PE [58, 67, 68]. In the populations of patients undergoing a variety of neurosurgical procedures, pharmacological prophylaxis provides a relative risk reduction of between 30 and 50 % [61–63]. One meta-analysis found a 45 % relative risk reduction from unfractionated heparin (UFH) or low-molecular-weight heparin (LMWH) as compared to no prophylaxis [69]. A comprehensive review and guideline statement comparing thromboprophylaxis to no prophylaxis in non-orthopedic surgical patients found a decreased risk of fatal PE and nonfatal symptomatic PE with UFH (relative effect 0.53 [95 % CI 0.31–0.91] and 0.44 [95 % CI 0.31–0.63], respectively) and LMWH (relative effect 0.54 [95 % CI 0.27–1.1] and 0.31 [95 % CI 0.12–0.81], respectively) [58].

Increased Risk of Hemorrhage with Antithrombotic Therapy for Prevention of VTE

The use of antithrombotic agents for VTE prophylaxis is associated with an increase in bleeding complications. In published reviews and meta-analyses, the rate of intracranial hemorrhage caused by pharmacological VTE prophylaxis in neurosurgical patients varies between 0.35 and 1.5 % [58, 70, 71]. A comprehensive review and guideline statement found that compared with no prophylaxis, both UFH and LMWH thromboprophylaxis were associated with a significantly increased risk of nonfatal major bleeding, including intracranial hemorrhage (Relative Risk of nonfatal bleeding 1.57 [95 %CI 1.32–1.87] for UFH and 2.03 [95 %CI 1.37–3.01] for LMWH compared to no prophylaxis) [58].

One retrospective study of the timing of VTE prophylaxis (within 24 h or later) with heparin in 111 EVD placements found new hemorrhages on CT in 18.0 % of patients, although only 4.5 % were clinically significant [14]. A systematic review evaluating the risk of intracranial hemorrhage progression in patients undergoing intracranial procedures found rates of 0–5.5 % in patients who received thromboprophylaxis with heparin compared to 2.6–13 % in those who did not [72]. Another meta-analysis concluded that major bleeding rates were low; for patients receiving UFH, LMWH, or no heparin the rates were 0.82, 0.16 and 0.59/1000 patients [70]. None of these major bleeding rates

were statistically different from zero, and none of them were statistically different from one another. Similarly low rates were observed in patients with traumatic intracranial hemorrhages receiving thromboprophylaxis [72]. It should be noted, however, that the included studies often excluded patients at high risk for hematoma expansion and thus are at risk of bias and possible underestimation of the measurement of bleeding complications in patients at highest risk [72].

Efficacy of Mechanical Thromboprophylaxis

In patients undergoing craniotomy or EVD placement, there may be absolute or relative contraindications to the use of anticoagulants, even at the low doses typically used for thromboprophylaxis. Alternative options for mechanical thromboprophylaxis include Graduated Compression Elastic Stockings (ES), Intermittent Pneumatic Compression devices (IPC), and IVC filters. There are no studies evaluating the efficacy of mechanical thromboprophylaxis in patients with EVDs; however, there is potentially generalizable data from other patient populations.

Graduated Compression Elastic Stockings (ES), or elastic stockings, are commonly used in neurosurgical patients, although their efficacy when used alone is unclear [73–75]. ES were found to be inferior to pharmacologic prophylaxis in preventing VTE in neurosurgical patients, and were not found to be effective in a study of critically ill medical/surgical patients [61, 76]. Two large studies have evaluated ES in patients with acute ischemic or hemorrhagic stroke and found they are not effective at reducing proximal DVT and are associated with an increased risk of skin complications [71, 75].

Intermittent Pneumatic Compression devices (IPC) may also be used to prevent VTE. A meta-analysis evaluating thromboprophylaxis strategies in neurosurgical patients suggested that IPC devices were superior to placebo for reducing distal and proximal DVT (RR 0.41 [95 % CI 0.21–0.78]) but the reduction in proximal DVT and PE did not reach statistical significance [70]. IPC devices were found to be effective at reducing proximal DVT in immobilized patients with acute stroke, and there was a trend toward decreased all-cause mortality at 30 days for patients with IPC although this did not reach statistical significance (11 vs. 13 %; $p = 0.057$) [77].

IVC filter insertion is indicated in patients with proven VTE and either an absolute contraindication for anticoagulant therapy or a planned major surgery [78, 79]. IVC filters may also be considered in any preoperative patient with recent VTE (within 1 month) in whom anticoagulation must be interrupted. Given their use with diagnosed VTE, IVC filters have been proposed as a strategy for prophylaxis despite a lack of supporting evidence [80–82]. Indeed, there is only one randomized controlled trial evaluating IVC filter placement for the prevention of PE in patients also receiving anticoagulation, which found a decreased risk of PE in the short term that was offset by an increased risk of DVT and other complications in the long term, with no difference in long-term mortality [83]. A systematic review noted numerous adverse outcomes associated with filter placement (DVT 9.3 %, insertion site thrombosis 2.0 %, IVC thrombosis/occlusion 1.6 %, complications during insertion 1.4 %, and filter migration 0.4 %) [84]. These data suggest that IVC filters prevent PE, but cause at least as many DVTs and are associated with other complications [58]. It is also noteworthy that even when temporary IVC filters are used, the majority of these removable filters are in fact never removed [85, 86].

Weighing the Risks and Benefits of Prophylaxis Strategies

The lack of high-quality evidence to guide practice regarding thromboprophylaxis in patients undergoing EVD placement requires clinicians to carefully weigh the risk of VTE, the risks and benefits of each proposed prophylactic modality, and the clinical impact of the relevant outcomes and adverse events. In addition, clinicians must make inferences based on data from other populations when population-specific data are not available and gage their applicability to patients with EVDs.

There are few published studies directly comparing the various prophylactic modalities. One randomized pilot study comparing IPC and LMWH against IPC and UFH initiated preoperatively found no difference in postoperative hemorrhage or VTE [87]. A meta-analysis by Eppsteiner et al. examined mechanical compression versus heparin thromboprophylaxis in postoperative patients [60]. Patients receiving mechanical prophylaxis had an increased risk of DVT compared with LMWH (pooled risk ratio = 1.80 [95 % CI 1.1–2.79]), but a decreased risk of any postoperative bleeding (pooled risk ratio = 0.51 [95 % CI 0.40–0.64]). There was no significant difference in PE risk with mechanical versus heparin thromboprophylaxis (pooled risk for heparin 1.03 [95 % CI 0.48–2.22]).

Danish et al. performed a decision analysis evaluating mechanical prophylaxis alone, mechanical prophylaxis and UFH, and mechanical prophylaxis with LMWH in patients undergoing craniotomy [71]. They found that the best management strategy was mechanical prophylaxis only; the increased efficacy of LMWH was outweighed by an increase in intracranial hemorrhage. The only variable that affected the optimal management decision was the risk of PE, where the benefits of LMWH outweighed the risk of bleeding if the estimated risk was 1.4 % or greater. It

should be noted that this threshold incidence of PE may be exceeded in patients with other risk factors for VTE and PE, including traumatic injuries, malignancy, and critical illness. For instance, a large multinational study of thromboprophylaxis in critically ill patients, which excluded neurosurgical patients, found an incidence of PE in patients receiving LMWH and UFH thromboprophylaxis of 1.3 and 2.3 %, respectively [88]. Clinicians should therefore carefully consider the risk of VTE and PE when deciding what modality of thromboprophylaxis to use, and use of UFH may be warranted in patients at high risk of VTE. Another decision analysis evaluated the question of thromboprophylaxis in the first 24 h after traumatic intracranial hemorrhage with either LMWH, IPC, or no prophylaxis at all and found that none of the choices was superior to the others [89].

Our recommendation of utilizing mechanical prophylaxis if a contraindication to anticoagulants exists recognizes the risk of perioperative VTE in patients undergoing EVD placement, while balancing the potentially devastating effects of intracranial hemorrhage, especially the progression of existing intracerebral or procedure-related hemorrhages. In making this recommendation, we are placing greater value on the avoidance of bleeding related to antithrombotic treatment (with potentially devastating disability and possible death) over the relatively small incremental risk of fatal and nonfatal pulmonary embolism if chemical thromboprophylaxis is not used over mechanical thromboprophylaxis.

For patients with additional risk factors for VTE such as malignancy, concurrent traumatic injuries, tetraplegia, or immobilization, we recommend the addition of heparin prophylaxis once contraindications to the administration of anticoagulants has resolved. Danish's decision analysis suggests that subcutaneous UFH may best balance increased VTE prevention against ICH hemorrhage risk as compared to LMWH [71], although these data are limited and consideration of LMWH may be appropriate in patients at high risk of VTE.

Timing of Initiation of Pharmacologic Prophylaxis

There is insufficient evidence available in the published literature to make a definitive recommendation regarding the timing of initiation of pharmacologic prophylaxis. There are recommendations on the timing of initiation of pharmacological prophylaxis in other populations [90, 91], which typically recommend initiation within 1–4 days after ICH or traumatic hemorrhage is stable. The existing literature on safety of early initiation is limited by small sample size [87], lack of randomized allocation [14], or lack of an appropriate comparator group [92], and thus we cannot make a strong endorsement for early initiation. However, the Committee recognizes that the risk of adverse intracranial hemorrhagic complications from EVD likely decreases over time. This potentially makes the balance between VTE prevention with heparin and the small risk of hemorrhage favor thromboprophylaxis in the days following EVD placement. As such, advancement of VTE prophylaxis may be considered when the risk of hemorrhage has been determined to be acceptably low, probably within the first 72 h (at the latest) if any existing hemorrhage is stable.

Recommendations:

In adult patients with an EVD:

We recommend VTE prophylaxis for the duration of immobilization

(Strong recommendation; low-quality evidence)

In making this recommendation, the Committee considered both the high incidence of VTE and the evidence supporting the efficacy of prophylaxis at preventing VTE in patients similar to the population in question

We recommend against the routine use of inferior vena cava filters for primary prophylaxis of VTE

(Strong recommendation; low-quality evidence)

In making this recommendation, the Committee considered the evidence suggesting possible harm and the paucity of data supporting the efficacy of IVC filters for VTE prophylaxis

We recommend the use of mechanical VTE prophylaxis (sequential compression device or intermittent pneumatic compression) in all patients with contraindications to pharmacological prophylaxis (UFH or LMWH) and without contraindications to mechanical devices

(Conditional recommendation; low-quality evidence)

In patients with additional risk factors for VTE (including, but not limited to concurrent malignancy, trauma, spinal cord injury, critical illness, and immobilization), we suggest pharmacological prophylaxis after an intracranial hemorrhage has been ruled out or is stable

(Conditional recommendation; low-quality evidence)

In making these recommendations, the Committee weighed the individualized risk of VTE, the strength of evidence showing incremental efficacy of pharmacoprophylaxis over mechanical prophylaxis, and the increased risk of major hemorrhage associated with pharmacological prophylaxis

Infection Risks, Prevention, and Management

See Evidentiary Table 6

Infection of the EVD system, otherwise known as a VRI, is a primary concern following catheter insertion. Reported infection rates range from between 0 % to 32 %; however, most typically rates of 10 % or less are described [93–95]. Although variable infection control practices undoubtedly

affect this risk, a key difficulty interpreting the EVD infection literature is the lack of a consistent definition of 'infection.' Many authors use the CDC definition which is based on positive cultures, clinical symptoms, and laboratory findings [96], while other authors use a definition of positive CSF culture only [97]. Standardizing the diagnostic criteria for VRI is challenging because organisms can colonize the catheter or contaminate the CSF without causing an infection. Further, infection is not the only cause of CSF inflammation. Hemorrhage and neurosurgery alone can cause inflammatory ventriculitis, and there is overlap of CSF parameters between infectious and chemical ventriculitis. Finally, there are no other definitive reference "gold standards" available to diagnose VRI. Without standardization, further research on VRI will continue to yield incongruent results. The Committee made no attempt at standardizing the definition of VRI across the studies it reviewed.

In Adult Patients with an EVD, Does the Risk of Infection Increase with Duration of Placement?

See Evidentiary Table 7

There is a positive association between the duration of catheter placement and the risk of infection. However, it is unclear if this risk is linear and if it represents cause and effect. In the first week after catheter placement, there is evidence of increasing risk. After 1 week, the evidence is contradictory, with various studies suggesting that the risk plateaus [98, 99], increases [97, 100–104], or decreases [31]. Part of this discrepancy arises from the inconsistent definitions of VRI. Additionally, there exists significant variation in study methodologies. Mayhall used a life table analysis, which suggested that risk of infection increases the longer the catheter is in place [97]. Other studies looked at infections per catheter days and noted that in patients with infections, the catheter was in place for a greater number of days [103, 104]. Another approach was to look at specific time points and assess whether the catheters were infected at that moment. Korinek looked at both greater than 5 days and greater than 10 days and noted no difference in infection rates between those two epochs [98].

Other investigators have also noted this positive correlation between placement duration and VRI, and have attempted routine changing of the catheter to limit infection. This practice is addressed in a subsequent section of this guideline. Although the data are inconsistent, common sense and the data that are available suggest that a foreign body like an EVD should stay in place for the minimum time necessary and be removed as early as the clinical situation allows.

Good practice statement:

External ventricular drains should be removed as early as the clinical situation allows

In making this statement, the Committee determined that there is sufficient evidence of ongoing risk of VRI to mandate removal of the EVD as soon as it is no longer indicated

In Adult Patients, Do Prophylactic Systemic Antimicrobials Reduce the Incidence of VRI? Should a Periprocedural or Duration Regimen Be Used?

See Evidentiary Table 8

Because the risk of VRI is high and the results are potentially grave, there is a clear logic in prophylactically dosing patients with antimicrobials to prevent infection. Antimicrobial prophylaxis regimens can be exclusively periprocedural (only prior to or during insertion) [97, 100, 102] or may continue for the entire duration that the EVD is in place (duration) [43, 105–108]. Most studies of VRI are prospective or retrospective large case series, and very few randomized controlled trials exist [107–109]. Most trials used a systemic antimicrobial for prophylaxis and compared periprocedural to duration treatment.

Overall, the results of these studies are inconclusive. Since there appears to be a positive (but not necessarily linear) correlation between the length of time the catheter is in place and the risk of infection, some authors have postulated that infection may be reduced by administering antimicrobials to the patient for the duration of ventricular drainage. However, in a small trial ($n = 42$), Saini randomized EVD patients between periprocedural and duration ceftazidime. The infection rate was approximately 7 % in both groups [108]. Retrospective studies by Alleyne using cefuroxime [106] and Dellit using cefazolin [105] found no significant difference in infection rates between periprocedural and duration antimicrobials. An underpowered RCT by Blomstedt using trimethoprim–sulfamethoxazole, similarly failed to detect a significant difference between the two types of regimens [110]. However, Dellit's study did note an increased rate (19 cases vs. 5 cases) of *Clostridium difficile* colitis in patients receiving antimicrobials for the duration of EVD placement ($p = 0.0036$).

In a randomized study of 228 patients, Poon et al. compared periprocedural and duration prophylactic regimens [107]. Patients who received antimicrobials for the duration of EVD placement developed fewer VRIs (2.6 vs. 10.6 %, $p = 0.01$). However, methodological issues may

have confounded the results; the duration arm received broader spectrum antimicrobials (ampicillin/sulbactam and aztreonam) than the periprocedural group (only ampicillin/sulbactam). Poon found that there were more resistant organisms cultured in the duration group than in the periprocedural group.

There is likely little difference in the incidence of VRI whether the antimicrobials are given only periprocedurally or for the duration that the catheter remains in the ventricle. There is evidence, however, that the use of long duration antimicrobials can lead to growth of antimicrobial-resistant organisms and to an increased incidence of *Clostridium difficile* colitis.

Recommendations:

We suggest one dose of antimicrobials prior to EVD insertion

(Conditional recommendation; low-quality evidence)

We recommend against the use of antimicrobials for the duration of EVD placement; duration regimens may increase the risk of resistant organisms and *Clostridium difficile* colitis

(Strong recommendation; low-quality evidence)

The Committee made this strong recommendation based on the potential for harm related to C. difficile diarrhea and antimicrobial-resistant organisms, as well as the lack of demonstrated efficacy of duration regimen antimicrobials

Good practice statement:

There is insufficient evidence to recommend a specific antimicrobial to be used in periprocedural prophylaxis. We recommend the use of local antibiograms to guide periprocedural antimicrobial selection

In Adult Patients with an EVD, Does the Use of Antimicrobial-Impregnated Catheters Reduce the Incidence of VRI?

See Evidentiary Table 9

Antimicrobial-impregnated catheters (including antibiotic-impregnated and silver-impregnated catheters) can potentially reduce VRI in patients requiring EVDs. The data regarding their relative efficacies were too sparse for the Committee to issue recommendations on the superiority of one over the other; however, the evidence base was robust enough for the Committee to issue recommendations comparing impregnated and non-impregnated catheters.

The Committee reviewed three randomized controlled trials [111–113], and four observational trials [114–117] comparing VRI rates using standard and antibiotic-impregnated EVD (AI-EVD) catheters. One of the RCTs was subsequently discarded [112], as it proved to be a subset of the patients reported in a subsequent report [113]. The remaining two RCTs reported conflicting results regarding the extent of benefit offered by AI-EVD catheters. The study by Zabramski et al. randomized a total of 288 patients to an AI-EVD ($n = 149$) or a standard silicon catheter ($n = 139$) [111]. The two groups were well matched with respect to all clinical characteristics, including gender, age, indication, and duration of catheter placement. Positive CSF cultures were significantly less frequent in patients with antibiotic-impregnated catheters compared with those in the control group (1.3 % compared with 9.4 %, respectively, $p = 0.002$). The second RCT by Pople et al. compared infection rates in 357 patients assigned to AI-EVD catheters ($n = 176$) or to a control group ($n = 181$) [113]. In this study, the infection rate in the control group was much lower, and as a result AI-EVD catheters were not found to have a significant effect on VRI (2.8 % controls vs. 2.3 % AI-EVD, $p = 1.0$). In this study, the infection rate in the control group was low, possibly due to the high percentage of patients receiving concomitant IV antimicrobials. Thus, as a result, AI-EVD catheters did not have a significant effect on VRI (2.8 % controls vs. 2.3 % AI-EVD, $p = 1.0$). Of interest, however, the authors noted that the mean duration to onset of infection was significantly prolonged in the antibiotic-impregnated catheter group compared to the control group (8.8 vs. 4.6 days, $p = 0.002$), a finding supported by several cohort studies [115–117].

In general, all of the cohort studies evaluating antibiotic-impregnated catheters demonstrated a significant reduction in VRI rates. Harrop et al. [114] prospectively evaluated the effect of antibiotic-impregnated catheters on the rate of VRI in 1961 EVD placements. This 5-year study included multiple distinct test periods with and without antibiotic-impregnated catheters. Of interest, the investigators noted that the introduction of an evidence-based EVD Insertion and Management Bundle alone did not change the rate of VRI (6.7 vs. 8.2 %, before and after implementation, respectively; $p = 0.44$). However, when this bundle was combined with the introduction of an antibiotic-impregnated catheter the VRI rate significantly decreased from 8.2 to 1 % ($p = 0.0005$). Technical issues led to a temporary discontinuation in the use of AI-EVD catheters, and despite the fact that there were no other changes to their institutional protocol, the VRI rate returned to 7.6 %. After a short interval, the use of AI-EVD catheters was resumed, and the VRI rate decreases again to 0.9 % ($p = 0.0001$).

Silver-impregnated EVD (SI-EVD) catheters also appear effective in reducing the risk of VRI. An RCT by Keong et al. directly compared the use of SI-EVD catheters to non-impregnated catheters in 278 patients [118]. After the results were adjusted for the duration of catheter placement and spontaneous intracranial hemorrhage,

patients with silver-impregnated catheters had a lower odds of developing VRI (OR 0.423 [95 % CI 0.026–0.820]). Three cohort studies have also compared SI-EVD catheters to non-impregnated catheters [119–121]. While all three studies noted decreased rates of VRI with the use of silver-impregnated catheters, only one was sufficiently powered to demonstrate a statistically significant effect [121].

Two small studies have compared antibiotic-impregnated and silver-impregnated catheters. Winkler et al. enrolled a total of 40 patients in a prospective, randomized, single-center pilot study and found no significant difference in VRI rates for AI-EVD (16 %) versus SI-EVD catheters (21 %) [122]. Lemcke et al. retrospectively reviewed 95 patients and obtained similar results; both the antibiotic- ($n = 31$) and silver-impregnated ($n = 32$) catheters reduced the risk of VRI when compared to the control group (6.5 vs. 9.4 % vs. 15.6, respectively) [123]. The small number of patients in both of these studies prevented any meaningful statistical analysis.

The Committee members agreed that antimicrobial-impregnated catheters, either antibiotic or silver-impregnated, may be useful for reducing the rate of VRI when used as part of a comprehensive insertion and management protocol. In addition, the Committee determined that there is not enough literature to recommend one antimicrobial-impregnated catheter over another.

The Committee recognized that the benefit of using antimicrobial-impregnated catheters is related to the baseline infection rate. For example, assuming that addition of antimicrobial-impregnated catheters would reduce the VRI rate to 2 %, the number needed to treat to prevent one infection can be readily calculated. If a center's baseline VRI rate is 3 %, then 100 patients need to be treated to prevent one infection; however, if the baseline VRI rate is 8 % only 17 patients need to be treated for the same result.

Recommendations:

We recommend using antimicrobial-impregnated catheters as part of a comprehensive management protocol to reduce the rate of VRI

(Strong recommendation; moderate-quality evidence)

In making this recommendation, the Committee felt that overwhelming evidence, though most of it retrospective, supports the use of antimicrobial-impregnated catheters as part of a regimen to reduce VRI. Additionally, the benefit: risk ratio is positive. There is insufficient evidence to compare the efficacy of antibiotic-impregnated and silver-impregnated catheters. Individual institutions and practitioners should choose catheters based on availability and cost

Are Additional Intraventricular Antimicrobials Effective for the Treatment of VRI as Compared to Intravenous Antimicrobials Alone?

See Evidentiary Table 10

Intraventricular antimicrobials might be necessary when patients do not respond to intravenous antimicrobials alone or when organisms have high-minimum inhibitory concentrations (MICs) to intravenous antimicrobials that do not achieve high cerebrospinal fluid (CSF) concentrations, especially multidrug-resistant organisms. Intraventricular antimicrobials bypass the blood-CSF barrier and achieve much higher CSF concentrations. There are no well-designed studies that compare intravenous antimicrobials to intraventricular antimicrobials alone, and no antimicrobial agent has been approved by the U.S. Food and Drug Administration for intraventricular use. However, there have been several studies on their pharmacokinetics, safety, and efficacy, especially for vancomycin, aminoglycosides, and colistin methanesulfonate [124–128]. CSF sterility and normalization of CSF parameters were achieved sooner with intraventricular and intravenous use when compared with intravenous use alone. In a prospective randomized trial examining the treatment of Staphylococcal ventriculitis, 10 patients treated with intraventricular vancomycin had much higher CSF levels as compared to intravenous therapy [129]. In a study of 34 patients with persistently positive CSF cultures despite antimicrobial treatment, those who received intraventricular or lumbar intrathecal antimicrobials achieved CSF sterilization within 24 h in 50 % and within 48 h in an additional 18 % [130]. Only three patients had adverse effects, all of which were clinically insignificant. The clinical outcome of patients as assessed by the modified Rankin Scale improved in 50 % and stayed unchanged in 29 %. In another study on infections with CSF diversion devices, 25 patients received intraventricular and systemic antimicrobials, and 23 received systemic antimicrobials alone. The mean times to CSF sterilization and normalization of CSF microscopy were significantly shorter for the intraventricular group ($p < 0.05$ and $p < 0.005$ respectively), as was duration of hospital stay ($p < 0.002$) and required length of systemic antimicrobial therapy ($p < 0.001$) [125]. The literature is not sufficiently robust to make a recommendation for a specific antimicrobial or duration of treatment.

Recommendation:

We recommend using intraventricular antimicrobials to treat ventriculostomy-related infections in patients who fail to respond to intravenous antimicrobials alone or when organisms have high MICs to antimicrobials that do not achieve high CSF concentrations, especially multidrug-resistant organisms. Strong consideration should be given to involving an Infectious Diseases expert in making this decision and choosing the appropriate antimicrobials

(Strong recommendation; moderate-quality evidence)

In making this recommendation, the Committee determined that in cases where a VRI has not responded to intravenous antimicrobials, the therapeutic alternatives are limited. Since the existing data support their safety and efficacy, the use of intraventricular antimicrobials is reasonable in this situation

EVD Management

In Adult Patients Requiring an EVD, Does Routine CSF Sampling Increase EVD-Related Infections as Compared to Maintaining a Closed System with Sampling of CSF Only When Clinically Indicated?

See Evidentiary Table 11

The diagnosis of EVD-related infections can be challenging, as clinical signs and symptoms are often masked by the primary disease process. In addition, the most common causative pathogens (i.e., staphylococci) initially provoke only a mild inflammatory response in the CSF.

To overcome these issues, some centers have adopted a policy of obtaining routine CSF samples. Other centers, citing concerns over potential contamination of the drainage system, maintain a strict closed system policy with CSF studies obtained only when clinically indicated by an unexplained change in neurologic status or a fever of unknown etiology.

While the frequency of CSF sampling is often anecdotally linked to an increased infection risk, the Committee identified only five observational studies that addressed this relationship directly. Three were underpowered, or had other methodological flaws that resulted in downgrading the level of evidence from low to very low. Two of these three down-graded studies found no difference in the rate of infection related to sampling frequency [31, 131], and one reported a decreased incidence with a daily CSF sampling protocol [132]. In this latter report, the incidence of VRI was markedly elevated when CSF sampling was performed only as needed and declined after the authors initiated a management bundle that included daily cultures (52 vs. 10.3 %, respectively). The change to daily CSF sampling was associated with adoption of a new sampling protocol that utilized "…only experienced staff using a more stringent theatre style asepsis…" The decrease in infection rate was likely a reflection of this improved attention to aseptic detail.

The remaining two observational studies were more methodologically robust. A study by Williams and colleagues in 2011 reviewed the rate of VRI in 382 patients [133]; 206 patients in the control group underwent daily cultures and 176 patients underwent cultures every 3 days. The control group consisted of historical controls from the 2 years prior to implementing sampling on every third day. The risk of culture-positive infection decreased from 10 to 3 % ($p = 0.02$) with sampling every third day. A recent study by Williamson et al. in 2014 reviewed 410 patients over a 5-year interval [134]. The authors used the results of a univariate analysis to construct a multivariate logistic regression model predicting the risk of VRI. In this model, the relative likelihood of VRI increased by 8.3 % for each CSF sample obtained.

In discussing CSF sampling, the Committee also noted that infection rates of less than 2 % have been reported at many centers since the introduction of antibiotic-impregnated EVD catheters [111, 112, 114, 135–137], making it much less likely that routine collection of CSF samples will provide clinically useful information.

Recommendation:

We suggest avoiding routine CSF sampling and obtaining CSF for analysis only when clinically indicated

The Committee recognized that there is significant uncertainty about the best estimates of benefits and harms related to the frequency of CSF sampling and that depending on local circumstances, other alternatives may be equally reasonable

(Conditional recommendation; low-quality evidence)

In Adult Patients Requiring an EVD, Do Routine Catheter Changes Decrease the Incidence of VRI Compared to No Catheter Changes?

See Evidentiary Table 12

Studies on the epidemiology of VRI began appearing in the 1980s. An influential article by Mayhall et al. published in the NEJM in 1984 reviewed a prospectively collected database of 172 patients undergoing a total of 213 EVD placements [97]. Risk factors associated with VRI included intraventricular hemorrhage ($p = 0.027$), irrigation ($p = 0.021$), and ventricular catheterization for more than 5 days ($p = 0.017$). They concluded that "Ventriculostomy-related infections may be prevented by

maintenance of a closed drainage system and early removal of the ventricular catheter. If monitoring is required for more than 5 days, the catheter should be removed and inserted at a different site." While the review included 172 patients, the analysis for risk factors associated with VRI was based on only 19 culture-positive cases, and only 38 of the 172 patients had multiple EVDs placed. The recommendation to change catheters sites was not directly tested but was based on the results of a post hoc analysis. While the results of this study were quickly challenged by other groups, the idea has persisted that changing ventriculostomy sites may reduce the risk of VRI.

The Committee's literature review identified a total of six observational studies [31, 97, 131, 138–140], and one small randomized controlled trial that met selection criteria [141]. Only Mayhall et al. recommended changing ventriculostomy sites [97]. A randomized controlled trial reported by Wong et al. was severely underpowered [141], enrolling only 103 patients; 51 patients randomized to routine change of the catheter site every 5 days and 52 to a no change group. Fewer VRIs were diagnosed in the no change group (3.8 %) versus the routine change group (7.8 %), but this difference did not reach statistical significance ($p = 0.44$). Lo et al. retrospectively reviewed 199 patients who underwent 269 EVD placements [139]. Using a multivariate logistic regression model, they identified the number of EVD placements as a statistically significant predictor of VRI. Each additional EVD increased the risk of infection more than fourfold (odds ratio = 4.6, 95 % CI 2.3–9.1, $p = 0.0001$).

While nearly all of these studies found a direct correlation between the duration of EVD placement and the risk of VRI, the majority found that the relationship was nonlinear. In general, the risk of VRI appears to be greatest in the first 7–12 days following EVD placement. The introduction of antibiotic-impregnated EVD catheters has reduced the risk of these early infections [116], and many centers are now reporting VRI rates of 2 % and lower without changing catheter sites [111, 112, 114, 135–137].

The Committee recognized that infection risk rises with increasing duration of EVD placement and recommends the removal of the EVD as soon as clinically practical. However, if continued EVD monitoring is required, there is no convincing evidence that routinely changing catheter sites reduces the risk of VRI. The lack of evidence supporting this practice, combined with the risks associated with repeated EVD placement led the Committee to make a strong recommendation against routinely changing catheter sites.

Recommendation:

We recommend against routinely changing catheter sites

(Strong recommendation; moderate-quality evidence)

In issuing this recommendation, the Committee considered the lack of evidence supporting routine catheter changes along with the demonstrated risk of VRI associated with catheter changes

In Adult Patients Requiring an EVD, Does Gradual Weaning Decrease the Incidence of Hydrocephalus and Need for VP Shunting as Compared to Immediate Clamping?

See Evidentiary Table 13

EVDs are used routinely for monitoring and treating patients with subarachnoid hemorrhage, intraventricular hemorrhage, and traumatic brain injury. In these conditions, the obstruction of CSF drainage pathways by blood leads to acute hydrocephalus and elevated ICP. EVD placement allows for temporary diversion of CSF flow during the acute period of hydrocephalus. In time, CSF flow dynamics return to normal in many of these patients, allowing the EVD to be discontinued without the need for a permanent VP shunt. In others, however, chronic hydrocephalus develops and placement of a VP shunt is necessary.

The removal of the EVD and the decision to proceed with shunting typically involve some form of weaning, which usually occurs once the patient is clinically stable. Conventional wisdom holds that gradually weaning over several days, during which the drain height is sequentially increased before clamping, minimizes the need for shunting.

An extensive literature search for weaning protocols in patients with EVDs identified only one small, randomized study comparing the outcome of gradual and rapid weaning [142]. In this study, 91 patients with aneurysmal subarachnoid hemorrhage were randomized to two groups; 40 patients to a gradual wean group and 41 to a rapid weaning protocol. All patients were arbitrarily drained at a height of 10 cm H_2O prior to weaning. Initiation of weaning was left to the discretion of the attending neurosurgeon, who was blinded to the treatment group. For gradual weaning, the drain height was raised 5 cm every 24 h to a final level of 25 cm H_2O. On day 4, the drain was closed. The drain was reopened if the ICP exceeded 20 mm Hg for more than 5 min, if the patient's neurological status deteriorated, or if

a CT scan obtained the next morning demonstrated hydrocephalus. Rapid weaning was completed in 24 h and when weaning began the EVD was closed immediately. The criteria for reopening the drain were identical to the patients undergoing gradual weaning. A VP shunt was placed in all patients that failed weaning. Failure of the weaning protocol occurred in 20 patients in the gradual and 22 patients in the rapid weaning groups. There was no difference in the incidence of hydrocephalus (need for VP shunting) in the gradual and rapid weaning groups (62.5 vs. 63.4 %, respectively, $p = 0.932$). Not surprisingly, patients in the gradual weaning group spent a mean of 2.8 more days in the ICU than patients in the rapid weaning group ($p = 0.0002$).

The Committee noted that the study population was small and that the incidence of hydrocephalus requiring shunting was higher than what is commonly reported. These limitations may have masked potential differences in outcome between the two groups. Nevertheless, the study demonstrated that rapid weaning can be accomplished safely.

Good practice statement:

EVD weaning should be accomplished as quickly as is clinically feasible so as to minimize the total duration of EVD monitoring and VRI risk

In making this statement, the Committee prioritized the early discontinuation of EVD and the resultant reduction in EVD-associated VRIs even though there is one small trial supporting the equivalence of rapid and gradual EVD weaning strategies

In Adult Patients Requiring an EVD, Does the Type of Dressing Reduce VRI?

See Evidentiary Table 14

Cranial dressings are commonly used to protect surgical sites. Maintaining these dressings is often difficult due to hair growth impairing adhesion, interference with multimodality monitoring, and patient discomfort. The dressings used in postsurgical incision management are often also used in EVD site care, but there is little evidence to guide this aspect of clinical management. Clear bio-occlusive dressings, head wrapping, chlorhexidine disks, antibiotic ointments, and no dressings are described in various studies of care bundles. However, the Committee did not find any randomized trials specifically examining dressing practices.

One retrospective review by Bookland et al. focused only on maintenance of the drain exit site, comparing a bio-occlusive dressing to the application of skin adhesive [143]. The authors reported a reduction in VRI from 15.1 to 3.54 % ($p = 0.002$). Although promising, this overall infection rate is still greater than recommended quality standards and the Committee agreed a randomized trial would be needed before this type of dressing could be recommended.

One related pediatric study examined not using dressings at all on incisional scalp wounds. Instead, the wound was cleaned daily and the hair shampooed. The authors describe a total of 702 operations with a postoperative infection rate of 0.48 %/1000 days [144]. Although ventricular drain sites were not studied, the no-dressing approach warrants further study.

Honda et al. conducted an 8-year study of a dressing protocol that included a sterile gauze dressing applied over the insertion site that was changed every 48 h [145]. This intervention resulted in a reduction of VRI from an incidence of 3.2 to 2.17/1000 catheter days. Subsequently, the introduction of an impregnated catheter with the new dressing protocol resulted in a further reduction in incidence to 0.87/1000 catheter days. The authors were not able to demonstrate statistical significance due to the sample size but report a 76 % reduction in incidence of VRI ($p = 0.066$).

Good practice statement:

Cleansing the insertion site using an antimicrobial agent at the time of EVD insertion and using a dressing as part of a management bundle is considered safe and effective practice

The lack of studies evaluating the effect of various dressing choices on VRI rates limited the Committee's ability to evaluate this issue

In Adult Patients, Does Routinely Changing the Tubing and Collection Devices Decrease the Incidence of EVD-Related Infection?

See Evidentiary Table 15

As with any invasive monitoring device, breaching the sterility of a closed EVD system increases the risk of introducing pathogens. Breaches occur when emptying or changing a cerebrospinal fluid (CSF) collection bag or when CSF sampling is desired. Changing the collection system is not routine practice but questions about a possible benefit are often raised. There is little evidence available addressing this question.

A study of 19 patients describing a change of drainage sets at 1 week vs. every 72 h demonstrated a reduction in the VRI rate; however, the small sample size limits this study's utility and the authors did not compare routine changing of drainage sets to no change [146]. An additional

study by Korinek et al. retrospectively compared VRI rates before and after implementation of a care bundle, noting any protocol violations [98]. They found that CSF sampling and drain manipulation that breached aseptic technique was the most common violations. These violations were four times higher in infected versus noninfected patients.

Several studies describing the use of "bundled" protocols that reduced VRI rates did not include routine changes of the collection device and also ensured that aseptic technique was used whenever the collection system was manipulated or cerebrospinal fluid collected [147]. Moreover, an expert consensus statement by the American Association of Neuroscience Nurses recommends against routinely changing EVD components [148]. The Center for Disease Control also recommends minimizing accessing any collection device to decrease infection risk [149].

Good practice statement:

The EVD collection system should be manipulated as little as possible

In making this statement, the Committee prioritized the prevention of VRIs. Although there are no high- or moderate-quality studies to guide decision making, the existing data suggest only potential harm from routine manipulation and no studies suggest benefit

In Adult Patients, Does Introduction of an EVD Management Bundle Reduce the Risk of EVD-Related Infections?

See Evidentiary Table 16

Care bundles are a structured way of improving the processes of care and patient outcomes. Kubilay et al. suggested the overall goal of a bundle is to create a "culture of safety" and that a bundled approach to the insertion and care of the patient with a ventricular drain is successful in reducing VRI [136]. Hospitals that have instituted a bundled approach report infection rates of less than 1 % [114, 150]. Common practices within bundles include attention to sterile technique, tunneling of the catheter, periprocedural antibiotic use only, use of an impregnated catheter, use of a closed system, no routine CSF sampling, use of a sterile dressing, and no site changes after placement [98, 151, 152].

The Committee did not identify any randomized controlled trials directly applicable to the clinical question. However, they did review studies of various designs that support the benefits a formalized guideline or bundle in promoting quality of care and reducing VRI rates.

Kubilay et al. noted that the use of a checklist and a nursing observer to monitor sterile procedure during catheter insertion decreased infection rates from 9.2 to 0.0 % [136]. A prospective observational study by Harrop et al. supported the use of an impregnated catheter as an important component of a bundle approach [114]. This 5-year study described distinct test periods, allowing the introduction or removal of variables. Of interest, the investigators noted that the introduction of an insertion and maintenance bundle alone did not change the rate of VRI but the combination of insertion, maintenance, and introduction of an antibiotic-impregnated catheter reduced the VRI rate from 6.1 to 0.2 %. Flint et al. described a protocol which included both antibiotic-impregnated catheters and dressing the catheter site with an antibiotic-impregnated disk [153]. VRI rates decreased from 6.3 to 0.8 %/1000 catheter days.

Honda demonstrated a major reduction in VRI rates using a three component bundle which included sterile technique, a standardized dressing of gauze and adhesive changed every 48 h, and the use of an antibiotic-impregnated catheter [145]. Together, these interventions resulted in a 76 % reduction in the incidence of VRI.

Recommendation:

We recommend using an EVD management bundle that includes aseptic insertion, limits manipulation of the closed system, and standardizes dressings and weaning to reduce VRI

(Strong recommendation; moderate-quality evidence)

In making this recommendation, the Committee recognized the benefit of a bundled approach to prevent VRI but could not determine which individual components would be most impactful due to the variability in study methodology

Conclusion

EVD catheters are considered an effective and generally safe method of ventricular decompression and intracranial pressure monitoring. However, estimating the true rate of clinically significant complications is confounded by incomplete and inconsistent reporting and by variability in management practices. In particular, adopting a uniform definition of VRI would greatly assist in standardizing research aimed at reducing complication rates. Given that EVD management bundles have already been shown to reduce complications significantly, further adequately powered prospective quality improvement studies may be difficult to conduct. The committee strongly supports thromboembolism prophylaxis, antimicrobial-impregnated

catheters, and institutional adherence to a bundle of EVD insertion and management techniques.

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Compliance with Ethical Standards

Conflict of interest The authors do not have any conflicts of interest to declare.

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