

# **Comparison Infection Rate between Inside-Out and Outside-In Tunneling of External Ventricular Drains**

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## **Abstract**

**Background:** An external ventricular drain (EVD) is a valuable procedure in the management of temporary cerebrospinal fluid (CSF) diversion. It is associated with the well-known risk of CSF infection (range, 0% to 27%). But there has been no study which determines EVD related infections between different techniques of tunneling (inside-out vs. outside-in). In theory, we believe that the inside out tunneling reduce the infection by the fact that it does not introduce cutaneous pathogens into the ventricles.

**Objective:** To compare the infection rates between the different techniques of inside-out and outside-in tunneling of EVD.

**Methods:** All patients requiring EVD system in Ramathibodi hospital from August 2009 to August 2013 were enrolled. The outside-in group was retrospectively reviewed and prospective data collection was performed in the inside-out group. The evidence of CSF infection prior to the procedure, including meningitis, infected implant (shunt system), or ventriculitis were excluded. CSF samples for culture were collected at the time of EVD insertion and removal. For each patient we record age, sex, diagnosis, GCS at presentation, co morbidity, systemic infection, steroid use, operative time, tunnel length, position of bur hole, duration of EVD in situ, EVD access and cultured organism.

**Results:** 234 EVDs in 170 patients were included in the study. There were 12 CSF infection noted, 6 of 113 (5.3%) in the inside-out group and 6 of 121 (4.9%) in the outside-in. The infection rate was not significantly different ( $P=0.93$ ). Previous EVD insertion was found to increase the infection rate ( $P=0.01$ ) but gender, GCS, systemic infection, co morbidity, position of EVD, operating time, steroid usage, duration of EVD, SAH and IVH were not correlated.

**Conclusions:** The infection rates of inside-out and outside in tunneling of EVD were similar. Among various factors, only previous EVD insertion was found to increase infection rate.

## Background

External ventricular drains (EVDs) are commonly used to monitor intracranial pressure or to drain the cerebrospinal fluid (CSF) in patients with various etiologies of hydrocephalus. Despite the usefulness of EVDs, the placement is associated with complications, notably CSF infection. In a review from 14 studies, the CSF infection rates ranged from 0% to 27% with a mean of 8.9 %.<sup>1-3</sup> Another review that pooled 23 published reports, the infection rates ranged from 2.1% to 22% (mean, 8.8%).<sup>1,2,4</sup> In addition to being associated with a poor outcome, these infections lead to increased length of stay in the ICU and overall hospital cost.<sup>5-9</sup> Several risk factors for EVD related infection have been identified, including craniotomy, systemic infections, depressed cranial fracture, intraventricular hemorrhage (IVH), subarachnoid hemorrhage (SAH), EVD irrigation, neurosurgical intervention, and the duration of EVD in place.<sup>1,3,4,6,7,10-18</sup> There were several methods to reduce EVD-related infection such as antibiotic prophylaxis,<sup>19</sup> antibiotic coated EVD,<sup>1,3,5,20</sup> long tunnel length more than 5 cms,<sup>21,22</sup> elective revision EVD every 5-10 days.<sup>14,22</sup> However, concerning EVD surgical technique, there was no study that determines EVD-related infection between inside-out and outside-in tunneling of the EVDs. In theory, we believe that the inside out tunneling should minimize infection by the fact that it does not introduce cutaneous pathogens into the ventricles.

## Objectives

The primary objective is to compare infection rate between the different techniques of inside-out and

outside-in tunneling of EVD. The secondary objective is to find the incidence of EVD related infection in Ramathibodi hospital and risk factors of EVD related infection.

## Methods

### Inclusion and Exclusion Criteria

The outside-in group was retrospectively reviewed from August 2009-April 2011 whereas prospective data collection was performed in the inside-out group from May 2011-August 2013. All patients requiring EVD insertion due to hydrocephalus secondary to SAH, spontaneous or traumatic IVH, tumor-related hydrocephalus, intraparenchymal bleeding or cerebral edema were included to the study. The EVD system must be in situ for at least 48 hours. Our exclusion criteria were the evidence of cerebrospinal fluid infection prior to the procedure including meningitis, infected implant (shunt system), or ventriculitis. In addition, any clinical suspiciousness of CNS infection prior to the procedure such as subdural empyema or cerebral abscess were excluded.

### Data Collection

The collected data for each patient were age, sex, diagnosis, Glasgow Coma Scale at presentation (GCS), co-morbidity, systemic infection, steroid use, operative time, tunnel length, position of burr hole, duration of EVD in situ, EVD access and culture for organism growth. CSF samples for culture were collected at the time of EVD insertion and removal. The outside-in group was retrospectively reviewed whereas prospective data collection was performed in the inside-out group.

## Definition of CSF Infection in Patients with EVD

Ventriculitis was classified as suspected ventriculitis (that is, the patient was treated with antibiotics for ventriculitis on clinical assessment) or proven ventriculitis (that is, a positive EVD CSF culture and treated for ventriculitis). A broader definition was used because clinical presentation and laboratory findings might not, at times, correlate well.

## Standard Practice of EVD Placement

All EVDs were inserted in the operating room by attending neurosurgeons or neurosurgery residents. Hair was routinely shaved prior to 2% chlorhexidine in 70% alcohol skin preparation. The most common EVD insertion location was Kocher's point.

### 1) Outside-in Technique

Feeding tube (8 Fr, 50cm length) was uniformly utilized. By using medium size clamp, subgaleal tunnel was created from a burr hole to a posterior stab incision in order to pull the feeding tube in. This outside-in maneuver was followed by inserting the feeding tube into the ventricle via a tract established by the Cushing's needle.

### 2) Inside-out Technique

Commercialized set from Yushin Medical company (Seoul, Korea) was universally used. First, the Cushing's needle was not utilized. The EVD was directly inserted into brain cortex until CSF return which indicated entering into the ventricle was observed. Subsequently, by connecting the end of EVD to the trocar for tunneling (Figure 1), subgaleal tunnel was created from the burr hole site to the scalp by inside-out fashion. This EVD trocar-like tunneler (Figure 1) was 15 cms in length with malleability, hence, by this tun-



**Figure 1:** EVD Trocar-like Tunneler

neler, we could achieve a tunnel length greater than that by the medium size clamp.

For all cases, prophylactic antibiotics were routinely prescribed and continued to the time of their removal.

## Risk Factors

The EVD-related infection was examined by multivariate analysis for association with sex, GCS, systemic infection, co-morbidity, position of EVD, operating time, steroid use, duration of EVD in situ, previous EVD insertion, SAH and IVH. Because we were interested in studying the possible causes of EVD infection rather the sequelae of the infection, only the events that occurred before EVD removal or the diagnosis of ventriculitis were considered.

## Catheter Duration

We routinely do elective revision of EVD for 5–7 days of in situ except for few cases that their EVDs were left longer than 7 days.

## Statistic Analysis

Data were analyzed using SPSS version 18.0 (SPSS Inc, Chicago, USA). Univariate analysis was performed using chi-square test for equal proportion,

Fisher exact tests and Student t-tests. Results are presented as Odd ratio (OR), 95% Confidence interval and probability value of 0.05 indicating statistical significance.

## Results

234 EVDs in 170 patients at Ramathibodi hospital were enrolled in the study. Eighteen patients were excluded due to the pre-existing CNS infections. The evaluated patients had mean age of  $48.42 \pm 20$  years (range 1–91 years). Male patients were 54.70%. There were 113 EVDs in the inside-out group and 121 EVDs in the outside-in group. There was no different between the 2 groups with regards to age, diagnosis of IVH, SAH, GCS at present, co-morbidity, systemic infection, steroid use, EVD access, duration of EVD in

situ and previous EVD. (Table 1)

EVD-related infections rate was 6 from 113 (5.3%) in the inside-out group and 6 from 121 (4.9%) in the outside-in group. The infection rate was not different significantly ( $P=0.93$ ).

## Incidence of Infection

Our overall infection rate in this study was 5.1% somewhat below than the mean of 8.8%<sup>1,2,4</sup> from literature review.

## Microorganism Isolated in CSF Samples and Catheters

The positive CSF cultures for bacteria were documented in 12 infected patients in both groups. The organisms were listed in Table 2.

**Table 1** Characteristics in 170 Patients Undergoing EVD

Characteristic	Inside-out group	Outside-in group	P value
Number of EVDs	113(48.29%)	121(51.71%)	
Number of operations	100(47.16%)	112(52.84%)	
Number of patients	81(47.64%)	89(52.35%)	
Male patients (%)	44(54.32%)	49(55.05%)	0.7
Mean age(yr)	$48.1 \pm 20.3$	$49.4 \pm 21.2$	0.7
Systemic infection	18(15.92%)	30(24.79%)	0.1
Co-morbidity	36(31.86%)	45(37.19%)	0.5
Diagnosis IVH	35(30.97%)	43(35.53%)	0.5
Diagnosis SAH	18(15.93)	30(24.79%)	0.1
Steroid use	33(29.20)	40(33.06%)	0.7
GCS<8	27(23.89%)	34(28.10%)	0.5
Operative time > 1 hr	50(44.24%)	63(52.07%)	0.3
Duration of EVD > 7 days	54(47.79%)	58(47.93%)	0.9
Burr hole position (frontal)	90(79.64%)	96(79.34%)	0.2
Previous EVD	17(15.04%)	14(11.57%)	0.5
CSF access	55(48.67%)	70(57.85%)	0.2

IVH= intraventricular hemorrhage, SAH=subarachnoid hemorrhage, GCS= Glasgow Coma Scale

EVD= External Ventricular Drain.

## Risk Factors Associated with Infection

Of 234 EVDs, 5 of 31 (16.12%) previous EVDs had infection. Previous EVD insertion was found to increase EVD-related rate significantly (OR=5.89, P=0.01, 95%CI=1.73-20.03). Sex, GCS, systemic infection, co morbidity, position of EVD, operating time, steroid use, duration of EVD in situ, SAH and IVH were non-significant factors for CSF infection. (Table 3)

**Table 2** Incidence of EVD-associated CSF Infection in 12 EVDs

Organism	No. of Infected EVD	%
Acinetobacter	2	16.67%
Micrococcus	2	16.67%
Stenotrophomonas	2	16.67%
Enterobacter	1	8.83%
Propriionibacterium	1	8.83%
Citobacter	1	8.83%
Non lactose fermenting bacilli	1	8.83%
Not identified	2	16.67%

## Discussion

External ventricular drains (EVDs) are commonly used to monitor intracranial pressure or to drain cerebrospinal fluid (CSF) in patients with various etiologies of hydrocephalus. Despite the usefulness of EVDs, their placement is associated with EVD-related infection. In a literature review, the mean infection rate was 8.9 %<sup>1-4</sup> depending on their definitions of infection, inclusion/exclusion criteria and their prophylactic antibiotic usage. Several risk factors for EVD-related infection have been identified including craniotomy, systemic infections, depressed cranial fracture, IVH, SAH, EVD irrigation, neurosurgical intervention, and the duration of EVD in place.<sup>1,3,4,6,7,10-18</sup> There were several factors identified with reduced rate of EVD-related infection such as antibiotic prophylaxis,<sup>19</sup> antibiotic coated EVD,<sup>1,3,5,20</sup> long tunnel length > 5 cms,<sup>21,22</sup> elective revision of EVDs every 5-10 days.<sup>14,22</sup> However, concerning surgical EVD technique, there has been no study that determines related-infection between inside-out

**Table 3** Risk Factors of EVD Infection

Factors	No. infect	No. all	%	OR	p value	95%CI		
Male sex	6	93	6.45	0.70	0.70	0.22	2.28	ns
Steroid use	4	73	5.48	0.95	0.95	0.28	3.26	ns
Co morbidity	3	81	3.7	0.52	0.50	0.14	1.99	ns
Craniotomy	4	57	7.02	1.29	0.70	0.37	4.45	ns
Access of EVD	8	125	6.4	1.42	0.70	0.41	4.87	ns
<b>Previous EVD</b>	<b>5</b>	<b>29</b>	<b>17.24</b>	<b>5.89</b>	<b>0.01</b>	<b>1.73</b>	<b>20.03</b>	<b>significant</b>
IVH	5	78	6.41	1.24	0.80	0.38	4.06	ns
SAH	3	40	7.5	1.47	0.70	0.38	5.69	ns
Duration less than 7 d	4	112	3.57	0.53	0.30	0.15	1.80	ns
Duration less than 10 d	9	146	6.16	1.86	0.50	0.49	7.07	ns
GCS<8	5	116	4.35	4.57	0.95	0.52	1.75	ns
Operative time more than 1 hr	7	113	6.19	1.24	0.80	0.38	4.04	ns

NS =not significant

and outside-in tunneling of the EVDs.

We found our overall EVD-related infection rate to be 5.13%. This is somewhat less than previously reported average of 8.9%.<sup>1,2,4</sup> However, infection rates of inside-out and outside-in technique were not different (5.3% for inside-out and 4.9% for outside-in,  $P=0.93$ ). In our study, it might, perhaps, be due to a result of strict sterile technique, frequent EVD replacement, antibiotic prophylaxis and our short duration of EVD (mean=7.5 days). These variables might have prevented infection regardless of EVD technique. This may, in fact, imply that we can use both techniques safely provided the variables mentioned earlier exist.

### Duration of the EVD in Situ

From Lo et al, multivariate analysis showed that the total duration of drainage was not a significant independent risk factor for EVD-related infection. Similarly, the amount of time each EVD remained in situ was also not a significant risk factor for infection.<sup>23</sup> In recent reviews, there was equal distribution between those who found an effect of drainage duration on EVD-associated CSF infection<sup>9,14,19,21,24-27</sup> and those who found none.<sup>3,28-32</sup> Data from the largest series by Sundborg and colleagues<sup>32,37</sup> with 1,586 patients revealed that prolonged EVD usage did not correlate with infection. Nevertheless, the clear association between the duration of drainage and the infection rate shown by Mayhall et al.<sup>14</sup> represented an astonishing contrast.

Data from our study demonstrated no evidence of a relationship between the amount of time that an EVD remained in situ (less than 7 days or less than 10 days) and the risk of EVD-related infection ( $P=0.3$ ,  $OR=0.53$ ,  $CI=0.15-1.80$  and  $P=0.5$ ,  $OR=1.86$ ,

$CI=0.49-7.07$ ).

### Microorganism Isolated in CSF Samples and catheter

The most common infectious organism in microbiological literatures<sup>3,9,14,19-21,25,26,29-36</sup> is coagulase-negative staphylococcus, accounting for 47% of cases. *Staphylococcus aureus* (14%) and *Klebsiella* (6.6%) are the next most common, with *Acinetobacter* (5.6%) representing the fourth. Our data illustrated noteworthy differences. Our most common bacterial organisms were *Acinetobacter*, *Micrococcus luteus* and *Stenotrophomonas maltophilia* which accounted for almost half of our infections. Our explanation for this occurrence is that, at one time, *Acinetobacter* was endemic in our ICU which coincided with our study period. Uncommon organism in this study may be due to partial treatment by antibiotic (mostly Cefazolin) which resulted in the more frequency of gram negative over gram positive infection.

### Previous EVD

Sundborg et al reported 60% of infections occur after an EVD revision.<sup>32</sup> Rebuck and colleagues found multiple EVDs to be a significant risk factor for infection, similar to findings from Lo et al.<sup>23</sup> From the only randomized-controlled trial in this subject, Wong et al came across higher infection rate in a group with multiple EVDs than that in another group with just one EVD. However, the differences did not reach statistical significance.<sup>20</sup> In three other studies, however, the authors did not discover multiple EVDs as significant risk factor for infection.<sup>3,9,12</sup> Our data did reveal a clear effect of previous EVDs on the infection rate ( $OR=5.89$ ,  $p=0.01$ ,  $CI1.73-20.03$ ).

### Elective Revision of EVD

The practice of electively revising EVDs, at or around 5 days after insertion, to prevent EVD-associated CSF infection was proposed by Mayhall and colleagues.<sup>14</sup> Indeed, it is only when the retrograde colonization risk predominates that this approach has merit. On the other hand, elective EVD revision increases the patient's exposure to an inoculation risk. As a result, there is doubt whether the retrograde colonization risk can be effectively modified by elective revision. Can placing a new EVD reset the clock for retrograde colonization of the CSF space along the externalized CSF column or around the outside of the EVD? Although this theoretical argument has appeal, the evidence, such as it is, does not support it. The randomized controlled trial conducted by Wong and colleagues demonstrated no benefit from elective EVD revision at Day 5.<sup>20</sup> More importantly, although not statistically significant, infections were more common in the group with elective EVD revision. An analysis of the Traumatic Coma Data Bank<sup>38</sup> revealed a higher infection rate in centers implementing a policy of elective EVD revision (16.8%) than in centers that did not (7.8%), a difference that closely approached significance ( $p = 0.054$ ).

### Tunnel Length

The study by Omar and colleague reported that the technique of subgaleal tunneling  $> 5$  cms reduced the risk of EVD-related infection.<sup>22</sup> Another Study by Khanna and colleague noted no infection during the first 16 days of catheterization with extended length of tunneling.<sup>21</sup> In our study, there was no data collection for the length of the tunnels in the outside-in group. Only 41 tunnel lengths were recorded in the inside-

out group (range 5–10 cm). In our practice, we try to maximize this length as far as possible in order to minimize risk of infection regardless of technique.

### Study Limitations

As in retrospective analysis, we must note that the review of patient data has some limitations. For example, the retrospective collection of data might have introduced a selection bias, confounding factors or unavailability of some data i.e. tunnel length. Due to the low incidence of EVD related infection, our 234 EVDs might, in fact, still be too small sample size to create any significant difference.

### Conclusions

From 234 EVDs, our infection rates of inside-out and outside-in tunneling of EVD were similar. Among various factors, only previous EVD insertion was found to increase infection rate. This may, in fact, imply that we can use both techniques safely provided the variables mentioned earlier exist.

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