Clinical Neurology and Neurosurgery 184 (2019) 105416

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

Comparison of infection rate with tunneled vs standard external ventricular drainage: A prospective, randomized controlled trial

Yu-Jie Zhou[a,1], Jing-Nan Wu[a,1], Li-Jing Chen[b], Hong-Yang Zhao[a,*]

[a] Department of Neurosurgery, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, 430022, China
[b] Department of Rheumatology, The Affiliated ZhuZhou Hospital of XiangYa School of Medicine, Central South University, ZhuZhou 412007, Hunan Province, China

ARTICLE INFO

Keywords:
Standard external ventricular drainage
Tunneled external ventricular drainage
EVD-related infection

ABSTRACT

Objectives: A prospective, blinded, randomized trial was performed to evaluate the incidence rates of external ventricular drainage (EVD)-related infection (ERI) after tunneled EVD (T-EVD) and standard EVD (S-EVD).

Patients and methods: From February 2018 to February 2019, all adult patients admitted to the Union Hospital Neurosurgery Center for EVD placement were eligible for inclusion. After the application of strict exclusion criteria, all enrolled patients were randomly divided into two groups. The patients in Group A received S-EVD, and the remaining patients in Group B received T-EVD. A linear incision was made for T-EVD. The distal end of the catheter was inserted approximately 5 cm until cerebrospinal fluid was readily obtained, and then the catheter was tunneled approximately 4–5 cm from the insertion point. Finally, an external CSF drainage system was connected to the catheter. For the S-EVD patients, we secured the catheter at the original incision site after insertion, and an external CSF drainage system was also connected to the catheter. The rates of ERI were compared between the two patient groups. The odds ratios and χ^2 test were used to analyze the results.

Results: One hundred twenty patients were randomly divided into two groups and underwent EVD placement. Among them, 60 patients in Group A received S-EVD, and 60 patients in Group B received T-EVD. Finally, 51 patients in Group A and 50 patients in Group B met all of the study inclusion/exclusion criteria and were thus eligible for inclusion in the evaluation of ERI rates. All clinical features of the two groups were similar. A total of 12 patients' (11.9%) CSF cultures were positive for infection. Ten (19.6%) patients who underwent S-EVD had CSF-positive cultures, while only 2 (4.0%) patients who underwent T-EVD had CSF-positive cultures ($P = 0.034$). Additionally, 8 patients in Group A and 1 patient in Group B were complicated with CSF leakage ($P = 0.039$).

Conclusions: Compared to S-EVD, T-EVD, when performed according to a previously established perioperative management protocol, resulted in lower infection and CSF leakage rates. We recommend that T-EVD should be preferentially performed when surgeons determine whether a catheter can be removed within 10 days, and the catheter used for EVD should be removed as soon as permitted by the clinical circumstances.

1. Introduction

External ventricular drainage (EVD) has been universally used since the 1960s for the management of patients with acutely elevated intracranial pressure (ICP) secondary to subarachnoid hemorrhage (SAH), trauma, intraventricular hemorrhage, and brain tumors that obstruct cerebrospinal fluid (CSF) circulation [1–6]. Unfortunately, EVD implantation is associated with many serious complications, including misplacement, hemorrhage and EVD-related infection (ERI) [1–6]. ERI is a major complication [7,11–18] that can prolong hospital stays, increase exposure to systemic antibiotics, increase hospital costs, and significantly increase mortality. A number of risk factors, including an increased indwelling duration, abnormal pathology, CSF leakage, concurrent systemic infection, and increased CSF sampling frequency, are reported to be associated with an increased ERI risk [7,11–18]. The techniques and technological advances related to the EVD procedure, namely, the materials for drainage and insertion, have been significantly refined, and the indications for EVD have been expanded. A

* Corresponding author at: Department of Neurosurgery, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, 1277 Jiefang Avenue, Wuhan, 430022, China.
E-mail addresses: 741189053@qq.com (Y.-J. Zhou), jingnanwu@hust.edu.cn (J.-N. Wu), calmchen189312001@csu.edu.cn (L.-J. Chen), m201775658@hust.edu.cn (H.-Y. Zhao).
[1] These authors contributed equally to the work.

https://doi.org/10.1016/j.clineuro.2019.105416
Received 3 June 2019; Received in revised form 1 July 2019; Accepted 5 July 2019
Available online 10 July 2019

widely practiced surgical technique is standard EVD (S-EVD), which is performed by drilling a burr hole around Kocher's point, inserting the catheter into the lateral ventricle, and then securing the catheter to the skin [1,4,16,23,24]. Extraneous catheter colonization was assumed to be responsible for ERI [25,26]; therefore, various techniques have been proposed to reduce extraneous catheter colonization. Tunneled EVD (T-EVD) is one of these techniques; this technique involves insertion of a ventricular catheter that is tunneled a short distance (approximately 5 cm from the incision) distally. Although many neurosurgeons use this technique in their daily work, it has not been highlighted in the literature, and whether the technique can effectively reduce the risk of ERI remains unclear. This is a prospective observational study comparing the incidence rates of ERI after T-EVD and S-EVD. We aim to determine whether T-EVD results in lower rates of ERI than S-EVD. Furthermore, we provide supporting scientific and objective data for use in clinical practice.

2. Materials and methods

From February 2018 to February 2019, a prospective, randomized, blinded study was conducted at the Union Hospital Neurosurgery Center, which is a large university teaching hospital and referral center for tertiary neurosurgery. The study evaluated the infection rate of S-EVD versus T-EVD procedures and was approved by the center's institutional review board or ethics committee. Additionally, in this study, every patient was required to provide informed consent.

2.1. Study population

All adult patients admitted to the Union Hospital Neurosurgery Center for EVD placement were eligible for inclusion. The main exclusion criteria [1–3,9,13,14,17,19–21] were (1) positive CSF culture samples taken within 24 h before EVD placement; (2) prior EVD catheter placement within the past 2 weeks; (3) the use of systemic antibiotics within a 1-2-week period before EVD placement (excluding perioperative antibiotics); and (4) sepsis, meningitis, or skin infection identified at or near the placement site. Additional exclusion criteria were an immunocompromised state, uncontrolled coagulopathy, and pregnancy.

2.2. Randomization

The patients were randomly divided into two groups.The patients in Group A received S-EVD, and the remaining patients in Group B received T-EVD. The randomization process is as follows: After sample size calculations, treatment regimens for each subject were generated by statisticians (who is not involved in subject recruitment or data collection) using a computer-generated random assignment sequence. Randomised group numbers were kept in sealed,opaque envelopes and were opened by neurosurgeons before operation. The choice of surgical procedure was determined by the neurosurgeon's envelopes, and the researchers did not influence the decision.

2.3. Surgical procedure

In accordance with the local protocol for the implantation and management of EVD, the procedure was performed under sterile conditions in a neurosurgical operating room on an operating table [25,27–33]. The incisional position of the burr hole and the EVD exit position were determined preoperatively [1–3,7,9–11,13,18–20,34]. Then, we shaved the hair at the burr hole incision site and the EVD exit position, the skin was disinfected with 1% iodine complex, and local anesthetic was administered. Depending on the attending neurosurgeon, a T-EVD or S-EVD catheter was inserted. A linear incision was made for T-EVD. The distal end of the catheter was inserted at approximately 5 cm until CSF was readily obtained, and then the catheter was tunneled approximately 4–5 cm from the insertion point [1–3,7,9–11,13,18–20,34]. Finally, an external CSF drainage system (Medtronic Inc., Minneapolis, MN, USA) was connected to the catheter. The wound was closed with interrupted sutures attached to the galea aponeurotica and the skin. For the S-EVD patients, we secured the catheter at the original incision site after insertion, and an external CSF drainage system was also connected to the catheter. The new wound was covered with a sterile, breathable dressing. When necessary, drainage blockage was eliminated by flushing the drain with 3–5 mL of 0.9% NaCl [1,17–19,22]. Postoperatively, surgical and nursing staff followed the protocols of the latest expert consensus on CSF drainage in neurosurgery.

2.4. Data collection

Following randomization, a research doctor began gathering data. Data were collected from the surgery database, clinical observations and records. A series of demographic and other significant data were recorded, including age, sex, the indications for the procedure, the time required for insertion, the number of attempts required to place the catheter, the time to infection, cultured microorganisms, the duration of systemic antibiotic use, the amount of antibiotics, complications, intensive care unit stay duration, and hospital stay duration. Drain management includes assessing the quantity and color of the CSF discharged every hour and the condition of the exit position. Each patient was examined for nervous system function with the GCS (Glasgow coma score). Additionally, a professional nurse accurately documented swelling, inflammation, exudative blood, and CSF leakage at the exit position.

2.5. Microbiology and definitions

CSF samples were collected using an aseptic technique at the time of catheterization, 3 days after catheterization, and at the time of catheter removal [27–33]. All CSF samples were sent to the institution's microbiology laboratory for routine CSF and biochemistry tests as well as CSF culture. The laboratory staff responsible for evaluating the specimens had no knowledge of the patients in the study. The definition of CSF infection was adapted from the Infectious Diseases Society of America's (IDSA) Clinical Practice Guidelines [17]. At least one of the following criteria must have been met:

(1) An organism cultured from CSF

(2) At least 2 of the following symptoms present with no other recognized cause in patients: fever > 38 °C or headache, meningeal signs, or cranial nerve signs, or at least 2 of the following symptoms present with no other recognized cause in patients: fever > 38 °C or hypothermia < 36 °C, apnea, bradycardia, or irritability with at least 1 of the following:

1) Increased white cells, elevated protein, and decreased glucose in CSF
2) Positive nonculture diagnostic laboratory test from CSF, blood, or urine
3) An organism cultured from blood

2.6. Statistical analysis

The collected data were compiled in IBM SPSS version 22 (IBM Corp, Armonk, New York, USA) for statistical analysis. The factors of ERI were examined through multivariable logistic regression models. The odds ratios and χ^2 test were used to analyze the results. Kaplan-Meier survival curves were used to illustrate infection-free days until the diagnosis of infection in the study groups receiving T-EVD and S-EVD. The differences in the numbers of days in the intensive care unit (ICU), days with implanted EVDs, days receiving systemic antibiotics, and days in the hospital were analyzed using frequencies, the medians,

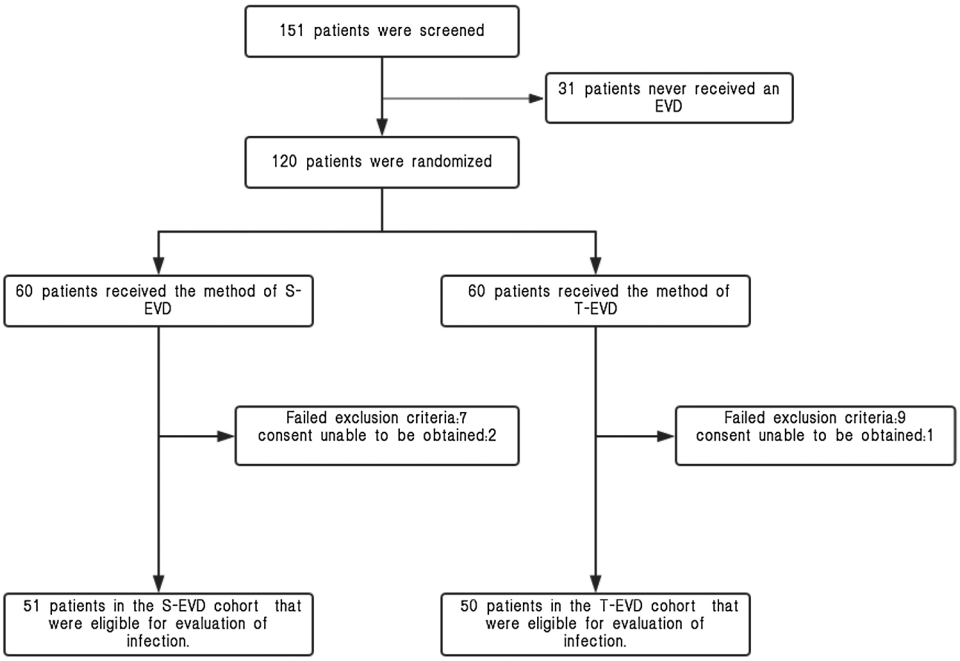

Fig. 1. Flow chart of the patients receiving EVD at the Union Hospital Neurosciences Center during the study period. EVD, external ventricular drainage; S-EVD, Standard external ventricular drainage; T-EVD, Tunneled external ventricular drainage.

and standard deviations. Finally, the significance level was set to 0.05.

3. Results

3.1. Study population

In this study, one hundred fifty-one patients were screened for inclusion (Fig. 1). Because catheter implantation was not clinically suggested, thirty-one patients did not receive EVD. One hundred twenty patients were randomly divided into two groups. Of these patients, 60 patients in Group A received S-EVD, and the remaining 60 patients in Group B received T-EVD. After the application of strict exclusion and inclusion criteria, 51 patients in the S-EVD group and 50 patients in the T-EVD group met the conditions for the evaluation of ERI.

In the final analysis, 9 patients, including 6 males and 3 females, were not included in the S-EVD group because a CSF sample was not collected (n = 2) or they met at least one of the exclusion criteria: an inability to provide consent (n = 2), pregnancy (n = 1), aplastic anemia (n = 1) and a positive CSF sample before EVD placement (n = 3). In these patients, EVD was indicated for SAH (n = 2), spontaneous intracranial hemorrhage (SIH) (n = 3), hydrocephalus (n = 2), and traumatic brain injury (TBI) (n = 2).

In the final analysis, 10 patients, including 6 males and 3 females, were not included in the T-EVD group because a CSF sample was not collected (n = 3) or they met at least one of the exclusion criteria: an inability to provide consent (n = 1), reluctancy to participate in the study (n = 1), systemic antibiotic use within a 1-2-week period before EVD placement (excluding perioperative antibiotics) (n = 2), skin infection (n = 1) and a positive CSF sample before EVD placement (n = 2). In these patients, EVD was indicated for SAH (n = 3), SIH (n = 4), hydrocephalus (n = 2), and TBI (n = 1).

No statistically significant differences were noted in age or sex, and similar indications for catheterization were recorded in the patients in the two groups. SIH and SAH were the leading indications for EVD (59%; SIH in 27% of the patients and SAH in 32% of the patients), followed by TBI (18.8%), hydrocephalus (9.9%), tumor (8.9%), and other (3.4%) (Table 1).

Table 1
Baseline Characteristics of Patients undergoing T-EVD and S-EVD.

Characteristics	T-EVD (n = 50)	S-EVD (n = 51)	P value
No. of patients	50	51	–
Male patients, n(%)	24(49%)	25(51%)	.918
Mean age in years (SD)	52.76(7.000)	52.55(7.444)	.884
Indication for catheter placement			.710
Other	0	3	
Tumor	5	4	
Hydrocephalus	6	4	
Traumatic brain injury	9	10	
SIH	12	15	
SAH	18	15	

S-EVD, Standard external ventricular drainage; T-EVD, Tunneled external ventricular drainage.

3.2. CSF infection

We evaluated the incidence rates of ERI in patients undergoing S-EVD versus those undergoing T-EVD in the final analysis. A total of 12 patients (11.9%) had positive CSF cultures for infection. Among the patients receiving S-EVD treatment, 10 (19.6%) had a positive CSF culture, while 2 (4.0%) had a positive CSF culture in the T-EVD group, P = 0.034.

The Kaplan-Meier survival curves were different between the two groups (Fig. 2), and the difference was statistically significant (P = 0.015). In the logistic regression analysis, the factors that were significantly correlated with an increased incidence of ERI were hospital stay (regression coefficient: 3.775 [95% confidence interval: 1.528–9.327]) and ICU stay (regression coefficient: 2.447 [95% confidence interval: 1.325–4.520]). Notably, when we adjusted the P value to < 0.1, the EVD method was incorporated into the regression model (regression coefficient: 0.056 [95% CI: 0.002–1.470] P = 0.084). No other predictor variables, including gender, age, the number of catheter insertion attempts, implant duration, poor wound healing, subcutaneous hydrops, catheter displacement, and catheter replacement, were correlated with an increased incidence of ERI.

Table 3 shows all of the isolated microorganisms. The most frequently isolated microorganisms were *Staphylococcus epidermidis*

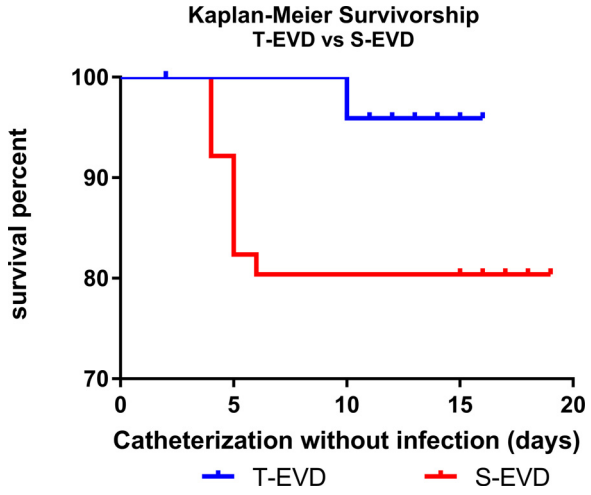

Fig. 2. Kaplan-Meier survival curves illustrating infection-free days until the diagnosis of infection in the study groups receiving T-EVD and S-EVD. S-EVD, Standard external ventricular drainage; T-EVD, Tunneled external ventricular drainage.

(n = 6, 50.0%), *Staphylococcus aureus* (n = 2, 16.7%), *Acinetobacter baumannii* (n = 2, 16.7%), Viridans streptococci (n = 1, 8.3%), and *Escherichia coli* (n = 1, 8.3%).

3.3. Days of treatment

ICU stays and the overall hospital treatment times varied based on the different methods (Table 2). The mean times in the ICU were 6.26 days (SD 2.039) for the T-EVD cohort versus 10.27 days (SD 2.201 days) for the S- EVD cohort ($P < 0.05$). The mean times in the hospital were 12.20 days (SD 2.650) for the T-EVD cohort versus 17.18 days (SD 1.493 days) for the S-EVD cohort ($P < 0.01$). Additionally, the difference in the duration of catheter placement between the two groups was statistically significant. The total cumulative implant duration of all patients was 841 days. The cumulative implant duration in the T-EVD cohort was 377 days, whereas the cumulative implant duration in the S-EVD cohort was 464 days. The mean implant durations were 7.54 days (SD 2.052) for the T-EVD cohort and 9.10 days (SD 1.781 days) for the S- EVD cohort ($P < 0.05$).

3.4. Complications

Seven (6.9%) patients, including 4 patients in the S-EVD group and 3 patients in the T-EVD group, exhibited poor wound healing, but the difference between the groups was not statistically significant

Table 2
Outcome Parameters Between the Groups undergoing T-EVD and S-EVD.

Outcome Parameters	T-EVD (n = 50)	S-EVD (n = 51)	P value
Complication			
Poor wound healing	3	4	.715
Subcutaneous hydrops	8	1	.033
CSF leakage	1	8	.039
Catheter displacement	2	8	.103
No. of attempts to place the catheter (SD)	1.34(0.479)	1.24(0.425)	.249
The duration of catheter placement (SD)	7.54(2.052)	9.10(1.781)	.000
ICU stay duration (SD)	6.26(2.039)	10.27(2.201)	.000
Hospital stay duration (SD)	12.20(2.650)	17.18(1.493)	.000
The duration of systemic antibiotic use (SD)	9.44(2.082)	12.45(1.665)	.002
The amount of antibiotics (SD)	2.62(1.067)	2.67(1.125)	.831

ICU, intensive care unit; SD, standard deviation.

Table 3
List of all the isolated microbiological organisms.

Cultured organisms	No.	%
Staphylococcus epidermidis	6	50.0
Staphylococcus aureus	2	16.7
Acinetobacter baumannii	2	16.7
Streptococcus viridans	1	8.3
Escherichia coli	1	8.3

($P = 0.715$). Nine (8.9%) patients, including 1 patient in the S-EVD group and 8 patients in the T-EVD group, presented subcutaneous hydrops ($P = 0.033$). Eight patients in the S-EVD group and 1 patient in the T-EVD group experienced CSF leakage ($P = 0.039$). Additionally, the number of patients with catheter displacement was higher in the S-EVD group than that in the T-EVD group, although the difference was not statistically significant ($P = 0.103$) (Table 2).

4. Discussion

The EVD procedure continues to be a very useful and important tool for patients with acute ICP elevation [1,3,5–7,9,12,16,17,19,21,34,35]. Nevertheless, ERI is still a relatively universal problem and can result in serious morbidity. Claude-Nicholas Le Cat [1] performed the first EVD procedure in 1744. Since then, many advances in technology, materials, and indications for surgery have been achieved. The purpose of developing the T-EVD procedure was to reduce the occurrence of ERI and its related complications. Friedman and Vries [1] first detailed the T-EVD technique in 1980. They used percutaneous tunneled EVD and reported no infections after 100 ventriculostomy procedures [24]. However, limited by previous experimental statistical methods and different definitions of infection, this conclusion is not necessarily suitable for the present era. However, in this prospective, blinded, randomized trial, ten (19.6%) patients who underwent S-EVD and 2 (4.0%) patients who underwent T-EVD had positive CSF bacterial cultures ($P = 0.034$). Thus, twelve patients had positive CSF cultures, resulting in an overall infection rate of 11.9%, which is essentially consistent with the rate of ERIs reported in previous studies. Lozier et al [3] noted that the accumulated rate of positive CSF cultures was 8.8% in a systematic and critical review of the literature on ERI.

The overall ERI rates were relatively low in this study, particularly with the T-EVD method, which may reflect improvements in catheterization and nursing techniques as well as the timely use of systemic antibiotics. All patients underwent EVD placement under sterile conditions, and EVD insertions outside the hospital were excluded in this trial. Most of patients were placed in the ICU after undergoing EVD placement. Drain management includes assessing the quantity and color of the CSF discharged every hour and the condition of the exit position [1,2,10,11,17,19,20,24,35]. Each patient's nervous system function was assessed with the GCS. Additionally, a professional nurse accurately documented swelling, inflammation, exudative blood, and cerebrospinal fluid leakage at the exit position and immediately reported such observations to the attending physician. A high number of patients (90.4%) received systemic antibiotics within 24–48 hours of EVD placement, and 80.2% of the patients received multiple antibiotic agents during the duration of EVD placement. In accordance with most previous studies, the definition of infection was adapted from the IDSA [17]. In previous studies, many authors define infection as a positive CSF culture after EVD placement [1–3,5,8–11,14,18–21,34,35]. However, the definition in this trial included not only the presence of organisms in CSF cultures but also relevant parameters (fever, headache, decreased muscle force, neck stiffness, and abnormal conscious states, as well as CSF cell counts [5,7,8,11,16–18,20]) that we used to determine the need for clinical and laboratory tests. CSF culture is vital for the diagnosis of ERI, but several days may be required for incubation, and negative results do not rule out the possibility of bacterial infection

in the final diagnosis. Notably, CSF cultures are suggested for the identification of low-activity pathogens within at least 10 days, such as *Propionibacterium acne s* [31,32,36,37]. ERI is related to increased mortality; therefore, treatment should be administered promptly. Medical staff should intervene early in these situations to avoid irreversible consequences. Additionally, Ian Pople et al [3] reported that low infection rates may also be associated with low-risk populations, including only a small number of patients with TBI or SIH. In fact, the patient populations in the two groups were similar in this study (Table 2).

The T-EVD technique involves the creation of a subcutaneous channel between the puncture point and the exit position of the catheter and was developed based on the theory that the design of indwelling intravenous catheters prevents ascending infection [1,4,7,18,24,35]. Most authors have reported that CSF leakage is strongly associated with the risk of infection [25–27,29–33,38]. By increasing the distance from the puncture point to the exit position of the catheter, the flow of CSF outside the catheter can be reduced, thus reducing CSF leakage. G K C Wong et al [8] reported that contamination during catheterization resulted in ERI. Clearly, as the catheter was tunneled approximately 4–5 cm from the insertion point, T-EVD should delay external colonization of the catheter. Omar et al [8] found that using a 5-cm subcutaneous channel can effectively reduce the rate of ERI from 62.9% to 11.5%. Because we secured the catheter at the original incision site to prevent displacement and the wound was covered with a sterile, breathable dressing, the rate of catheter displacement was low and highly significant. Collins et al [8] reported that long subcutaneous EVD (LTEVD) reduces infection rates. However, the lumen is difficult to flush when the LTEVD technique is used, and the sutures may shrink the lumen and enhance the additional risk of mechanical compression, leading to unnecessary surgery (EVD removal). Silver-coated and antibiotic-impregnated catheters were reported to be sufficient for decreasing the risk of ERI [25,27–29,31,32]; however, this conclusion is controversial and warrants further research. Reported evidence demonstrates that overuse of antibiotics can result in the growth of antimicrobial-resistant microorganisms and enhance the risk of *Clostridium difficile* colitis. Notably, silver-coated and antibiotic-impregnated catheters cost 4-5-times more than normal catheters. Arguably, considering patient safety and cost, the most effective and simple procedure was T-EVD.

The duration of catheter placement was positively related with the risk of ERI. However, whether the risk is linear and causal remains unclear. Holloway et al [25,27–29,31,32] reported nonlinear relationships between the duration of ventricular catheter placement and the incidence of ventriculitis in 584 patients with severe head injury. The risk of ERI gradually increased within the first 10 days, but then the incidence of ERI stabilized. Kaplan-Meier curves (Fig. 2) show that the time before infection is longer with T-EVD than that with S-EVD, and the difference was significant. In a retrospective review of the literature, Leung et al [34] noted that most ERIs occurred within the first 5 days of drainage in 114 patients receiving EVD treatment. Two patients in the T-EVD group presented infection after the 10th day of monitoring. Ten patients in the S-EVD group presented infection on the 5th-7th days of drainage. These outcomes demonstrate that T-EVD can reduce the risk of ERI, especially within the first 10 days of drainage. Some studies observed the ERI rate per catheter day and reported that the catheter was in place for a greater number of days in patients with ERI [34]. Notably, T-EVD did not reduce the overall incidence of ERI; thus, T-EVD only delays potential infections without having any impact on the real incidence of ERI.

This study had a number of limitations. First, the definitions of ERI were inconsistent with those in some previous studies. Additionally, variations in study methodologies were present. Second, we did not perform a subgroup analysis, which may have influenced the rate of ERI. Third, suspected and colonization infection definitions were not considered. When defining suspected and colonization infection cases as true cases of ERI, the incidence of ERI may be higher. In the multivariable analysis, the P value of the EVD placement method was 0.084, which is close to statistical significance and favors the T-EVD method. However, only large, prospective, controlled multicenter trials can conclusively validate these results.

5. Conclusion

T-EVD, when performed according to previously established perioperative management protocols, results in lower infection and CSF leakage rates than those reported for S-EVD. Although our sample size was small, we recommend that T-EVD should be preferentially performed when surgeons determine whether a catheter can be removed within 10 days, and the catheter used for EVD should be removed as soon as permitted by the clinical circumstances.

Funding sources

This research did not receive any specific grants from funding agencies in the public, commercial, or not-for-profit sectors.

Conflicts of interest

None.

Acknowledgments

None.

References

[1] V.M. Srinivasan, B.R. O'Neill, D. Jho, D.M. Whiting, M.Y. Oh, The history of external ventricular drainage, J. Neurosurg. 120 (2014) 228.
[2] M.A. Omar, M.S. Mohd Haspani, The risk factors of external ventricular drainage-related infection at hospital kuala lumpur: an observational study, Malays. J. Med. Sci. 17 (2010) 48–54.
[3] A.P. Lozier, R.R. Sciacca, M.F. Romagnoli, E.S.J. Connolly, Ventriculostomy-related infections: a critical review of the literature, Neurosurgery 51 (170-181) (2002) 181–182.
[4] R.K. Khanna, M.L. Rosenblum, J.P. Rock, G.M. Malik, Prolonged external ventricular drainage with percutaneous long-tunnel ventriculostomies, J. Neurosurg. 83 (1995) 791–794.
[5] S.J. Gillow, B. Ouyang, V.H. Lee, S. John, Factors associated with fever in intracerebral hemorrhage, J. Stroke Cerebrovasc. Dis. 26 (2017) 1204–1208.
[6] C.G. Mayhall, N.H. Archer, V.A. Lamb, A.C. Spadora, J.W. Baggett, J.D. Ward, R.K. Narayan, Ventriculostomy-related infections. A prospective epidemiologic study, N. Engl. J. Med. 310 (1984) 553–559.
[7] J. Kim, N.S. Desai, J. Ricci, P.E. Stieg, A.J. Rosengart, R. Hartl, J.F. Fraser, Factors contributing to ventriculostomy infection, World Neurosurg. 77 (2012) 135–140.
[8] G.K.C. Wong, W.S. Poon, S. Wai, Lyon D. Yu LM, J.M.K. Lam, Failure of regular external ventricular drain exchange to reduce cerebrospinal fluid infection: result of a randomised controlled trial, J. Neurol. Neurosurg. Psychiatr. 73 (2002) 759–761.
[9] R.E. Gilbert, M. Harden, Effectiveness of impregnated central venous catheters for catheter related blood stream infection: a systematic review, Curr. Opin. Infect. Dis. 21 (2008) 235–245.
[10] E.A. Stevens, E. Palavecino, R.J. Sherertz, Z. Shihabi, D.E. Couture, Effects of antibiotic-impregnated external ventricular drains on bacterial culture results: an in vitro analysis, J. Neurosurg. 113 (2010) 86–92.
[11] N.C.H. Keong, D.O. Bulters, H.K. Richards, M. Farrington, O.C. Sparrow, J.D. Pickard, P.J. Hutchinson, P.J. Kirkpatrick, The SILVER (Silver Impregnated Line Versus EVD Randomized trial): a double-blind, prospective, randomized, controlled trial of an intervention to reduce the rate of external ventricular drain infection, Neurosurgery 71 (394-403) (2012) 403–404.
[12] M. Ramanan, J. Lipman, A. Shorr, A. Shankar, A meta-analysis of ventriculostomy-associated cerebrospinal fluid infections, BMC Infect. Dis. 15 (2015) 3.
[13] A.C. Flint, V.A. Rao, N.C. Renda, B.S. Faigeles, T.E. Lasman, W. Sheridan, A simple protocol to prevent external ventricular drain infections, Neurosurgery 72 (993-999) (2013) 999.
[14] D. Dasic, S.J. Hanna, S. Bojanic, R.S.C. Kerr, External ventricular drain infection: the effect of a strict protocol on infection rates and a review of the literature, Brit. J. Neurosurg. 20 (2006) 296–300.
[15] A. Berger, M. Weninger, A. Reinprecht, N. Haschke, C. Kohlhauser, A. Pollak, Long-term experience with subcutaneously tunneled external ventricular drainage in preterm infants, Child's Nervous Syst. 16 (103-109) (2000) 110.
[16] A.P. Lozier, R.R. Sciacca, M.F. Romagnoli, E.S.J. Connolly, Ventriculostomy-related infections: a critical review of the literature, Neurosurgery 62 (Suppl 2) (2008)

688–700.
[17] A.R. Tunkel, R. Hasbun, A. Bhimraj, K. Byers, S.L. Kaplan, W.M. Scheld, D. van de Beek, T.P. Bleck, H.J.L. Garton, J.R. Zunt, Infectious diseases society of america's clinical practice guidelines for healthcare-associated ventriculitis and meningitis*, Clin. Infect. Dis. 2017 (64) (2017) e34–e65.
[18] K.L. Holloway, T. Barnes, S. Choi, R. Bullock, L.F. Marshall, H.M. Eisenberg, J.A. Jane, J.D. Ward, H.F. Young, A. Marmarou, Ventriculostomy infections: the effect of monitoring duration and catheter exchange in 584 patients, J. Neurosurg. 85 (1996) 419–424.
[19] A.A. Konstantelias, K.Z. Vardakas, K.A. Polyzos, G.S. Tansarli, M.E. Falagas, Antimicrobial-impregnated and -coated shunt catheters for prevention of infections in patients with hydrocephalus: a systematic review and meta-analysis, J. Neurosurg. 122 (2015) 1096–1112.
[20] R. Thomas, S. Lee, S. Patole, S. Rao, Antibiotic-impregnated catheters for the prevention of CSF shunt infections: a systematic review and meta-analysis, Brit. J. Neurosurg. 26 (2012) 175–184.
[21] K. Wright, P. Young, C. Brickman, T. Sam, N. Badjatia, M. Pereira, E.S. Connolly, M.T. Yin, Rates and determinants of ventriculostomy-related infections during a hospital transition to use of antibiotic-coated external ventricular drains, Neurosurg. Focus 34 (2013) E12.
[22] R.K. Khanna, M.L. Rosenblum, J.P. Rock, G.M. Malik, Prolonged external ventricular drainage with percutaneous long-tunnel ventriculostomies, J. Neurosurg. 83 (1995) 791.
[23] H.I. Fried, B.R. Nathan, A.S. Rowe, J.M. Zabramski, N. Andaluz, A. Bhimraj, M.M. Guanci, D.B. Seder, J.M. Singh, The Insertion and Management of External Ventricular Drains: An Evidence-Based Consensus Statement: A Statement for Healthcare Professionals from the Neurocritical Care Society, Neurocrit. Care 24 (2016) 61–81.
[24] W.A. Friedman, J.K. Vries, Percutaneous tunnel ventriculostomy. Summary of 100 procedures, J. Neurosurg. 53 (1980) 662–665.
[25] I. Pople, W. Poon, R. Assaker, D. Mathieu, M. Iantosca, E. Wang, L.W. Zhang, G. Leung, P. Chumas, P. Menei, L. Beydon, M. Hamilton, I. Kamaly, S. Lewis, W. Ning, J.T. Megerian, M.J. McGirt, J.A. Murphy, A. Michael, T. Meling, Comparison of infection rate with the use of antibiotic-impregnated vs standard extraventricular drainage devices: a prospective, randomized controlled trial, Neurosurgery 71 (2012) 6–13.
[26] R. Atkinson, L. Fikrey, A. Jones, C. Pringle, H.C. Patel, Cerebrospinal fluid infection associated with silver-impregnated external ventricular drain catheters, World Neurosurg. 89 (2016) 505–509.
[27] M. Tahir, Z. Sobani, M. Murtaza, S. Enam, Long-tunneled versus short-tunneled external ventricular drainage: prospective experience from a developing country, Asian J. Neurosurg. 11 (2016) 114.
[28] C.D.E. Collins, J.C. Hartley, A. Chakraborty, D.N.P. Thompson, Long subcutaneous tunnelling reduces infection rates in paediatric external ventricular drains, Childs Nerv. Syst. 30 (2014) 1671–1678.
[29] T.S. Jensen, J.G. Carlsen, J.C. Sørensen, F.R. Poulsen, Fewer complications with bolt-connected than tunneled external ventricular drainage, Acta Neurochir. 158 (2016) 1491–1494.
[30] J. Wiegand, L. Hickson, T.M. Merz, Indicators of external ventricular drainage-related infections—a retrospective observational study, Acta Neurochir. 158 (2016) 595–601.
[31] R.A. Atkinson, L. Fikrey, A. Vail, H.C. Patel, Silver-impregnated external-ventricular-drain-related cerebrospinal fluid infections: a meta-analysis, J. Hosp. Infect. 92 (2016) 263–272.
[32] A. Nilsson, E. Uvelius, D. Cederberg, E. Kronvall, Silver-coated ventriculostomy catheters do not reduce rates of clinically diagnosed ventriculitis, World Neurosurg. 117 (2018) e411–e416.
[33] A.A.B. Jamjoom, A.J. Joannides, M.T. Poon, A. Chari, M. Zaben, M.A.H. Abdulla, J. Roach, L.J. Glancz, A. Solth, J. Duddy, P.M. Brennan, R. Bayston, D.O. Bulters, C.L. Mallucci, M.D. Jenkinson, W.P. Gray, J. Kandasamy, P.J. Hutchinson, A.G. Kolias, A.I. Ahmed, Prospective, multicentre study of external ventricular drainage-related infections in the UK and Ireland, J. Neurol. Neurosurg. Psychiatr. 89 (2018) 120–126.
[34] G.K.K. Leung, K.B. Ng, B.B.T. Taw, Y.W. Fan, Extended subcutaneous tunnelling technique for external ventricular drainage, Brit. J. Neurosurg. 21 (2007) 359–364.
[35] F. Lundberg, L. Wady, S. Soderstrom, P. Siesjo, O. Larm, A. Ljungh, External ventricular drainage catheters: effect of surface heparinization on bacterial colonization and infection, Acta Neurochir. (Wien) 142 (2000) 1377–1383 2000;142(12):1377-83..
[36] J. Berger-Estilita, M. Passer, M. Giles, J. Wiegand, T.M. Merz, Modalities and accuracy of diagnosis of external ventricular drainage-related infections: a prospective multicentre observational cohort study, Acta Neurochir. 160 (2018) 2039–2047.
[37] R. Mounier, D. Lobo, F. Cook, M. Martin, A. Attias, B. Aït-Mamar, I. Gabriel, O. Bekaert, J. Bardon, B. Nebbad, B. Plaud, G. Dhonneur, From the skin to the brain: pathophysiology of colonization and infection of external ventricular drain, a prospective observational study, PLoS One 10 (2015) e142320.
[38] D. Hoefnagel, R. Dammers, M.P. Ter Laak-Poort, C.J.J. Avezaat, Risk factors for infections related to external ventricular drainage, Acta Neurochir. 150 (2008) 209–214.