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Observational Retrospective Cohort Two Centred Study on External Ventricular Drain-Related Infections in US and Turkey

Yazile SAYIN[1], Bernice Gulay GULEK[2,3]

[1]University of Bezmialem, Faculty of Health Sciences, Department of Nursing, Division of Surgical Nursing, Istanbul, Turkey
[2]University of Washington, Harborview Medical Center, Acute Care Nurse Practitioner, Washington, USA
[3]Washington State University, Graduate School, College of Nursing, Washington, USA

Corresponding author: Yazile SAYIN ✉ yaziles@gmail.com

ABSTRACT

AIM: To compare external ventricular drain-related infection (EVD-RI) rates of two Academic Medical Centers in Turkey and the US in order to determine the key factors.

MATERIAL and METHODS: We performed an observational retrospective cohort study to compare the EVD-RI rates between two hospitals (Hospital T in Turkey; Hospital A in US). We analyzed data gathered from 736 patients (Hospital T, n=237; Hospital A, n=499), in a total of 736 EVD cases which occurred between January 1, 2013 and December 31, 2018. Electronic records of hospitals were searched according to the procedure code "external ventricular drain". The study protocol was approved by the audit and clinical governance committees of both participating hospitals

RESULTS: EVD-RI rates were 18.3 per 1000 days for a total of 3227 catheter days in Hospital T, whereas 4.0 per 1000 cases for a total of 7010 catheter days in Hospital A. The prolonged use of EVD catheter, length of stay, and frequency of number of cerebrospinal fluid sampling were associated with EVD-RI in both hospitals.

Cerebrospinal fluid culture of Hospital A was dominant for gram positive 32.6% and gram negative 46.1% rods, whereas for Hospital T, gram positive 39.0% and gram negative 33.9% rods were the main microorganisms for the EVD-RI. There was a correlation, between the duration of antibiotic use and EVD-RI in Hospital T. The nursing care facilities of the hospitals were significantly different. All-cause mortality found to be 12% versus 3.7% in Hospital A and Hospital T respectively ($p>0.05$).

CONCLUSION: In both institutions, the EVD-RI was associated with EVD characteristics rather than patients' personal characteristics. Early drain removal and patient discharge should be goals whenever medically appropriate. The wide range infection and mortality rates between Hospital A and T is most likely attributable to many factors, including the variety of populations evaluated and the use of dissimilar methodologies in the management of EDVs.

KEYWORDS: External ventricular drain, Infection control, Infection, Risk factors, Neurosurgery.

INTRODUCTION

Over the last two decades, external ventricular drain-associated infection (EVD-RI) has been among the major complications of neurosurgery, thus increasing morbidity and treatment costs (15,20,22). However, there are wide variations in the rates of EVD-RI. Previous publications have suggested that these variations may be related to the various definitions used for EVD-RI and diverse EVD-RI study methodologies (22,35).

Studies have shown that EVD duration, catheter type, cerebrospinal fluid (CSF) sampling frequency, EVD placement technique, tunnel length, and care conditions are risk factors for infection (4,13,22,35). In 2014, the International Multidisciplinary Consensus Conference on Multimodality

Yazile SAYIN : 0000-0002-5741-754X Bernice Gulay GULEK : 0000-0002-1676-2961

Monitoring adopted EVD-RI incidence as a quality metric to be followed in intensive care units (ICUs). As a result, the risk management of EVD-RI has become a current topic of discussion. At present, prospective studies examining EVD are limited due to time intensiveness and difficulties obtaining a sufficient number of cases of EVD-RI. Furthermore, previous retrospective studies have mostly been single centered (25). Such limitations prevent the development of health models as the national and international trends and practices cannot be ascertained. Nevertheless, international studies, particularly in international comparative studies, offer a large database of EVD-RI case and can assist to should be creation or revision universal standards. The findings of international comparative collaborations can generate a broader perspective on EVD-RI prevalence and its risk factors (20), accelerate improvements in EVD-RI, management strategies in institutions, and invigorate scientific advancement (18).

In this study, we aimed to compare EVD-RI rates of two academic medical centers in Turkey and the United States (US) to determine the key factors related to infection risk. The research questions for the current study were as follows:

- Are there any differences in the EVD-RI rates? between Turkey and the US
- Do the risk factors for EVD-RI differ by country?
- What are the most common microorganisms encountered in EVD-RI, and do they differ by country?

MATERIAL and METHODS

Design

The comparative analyses for this observational retrospective cohort study were conducted in two private university hospitals in Istanbul in Turkey (Hospital T) and an academic medical center in Seattle in Washington State in the US (Hospital A) between January 1, 2013 and December 31, 2018.

Dependent variable: EVD-RI rate and 30 day all- cause mortality

Independent variables: Age, gender, indications for EVD, length of hospital stay (LOS), duration of EVD, EVD catheter type, length of EVD tunnel, antibiotic prophylaxis and duration, frequency of cerebrospinal fluid (CSF) sampling, CSF sampling port, type of EVD system (e.g., monoblock, multipart), existence of CSF sampling protocol.

The STROBE checklist was used as a guide in the preparation of this manuscript.

Data/Participants

The focal point of this study was EVD-RI status within the first 30 days following the hospitalization of patients with an EVD. One record was considered for each patient. The data collected between 2013 and 2018 were obtained by searching electronic health records (EHRs) according to the study protocol in collaboration with an information technologist. At the time of the study, the starting year was determined as 2013 as the data recording system in Hospital T changed in 2013, and the previous data were not complete. EHRs were searched using the procedure code "EVD 615204" in Hospital T, and "ICD-9 code 02.21" and "ICD-10 code 009630Z" in Hospital A. Once the target population had been identified from the EHRs, the Microsoft Excel spreadsheet was used to organize the variables, which had been pre-determined by the researchers based on a literature synthesis, and the data retrieved from the patients' EHRs. The data of 320 patients in Hospital T and 506 patients in Hospital A resulted in a total of 48.904 and 77.324 data points, respectively. Ninety-nine EVD patient records were excluded based on the study's inclusion and exclusion criteria. As a result, 237(32.3%) patients records were collected from Hospital T and 499 (67.7%) from Hospital A, providing a total of 736 EVD patients, which constituted the study sample.

The data storage at Hospital T is carried out by the information technology company MONAD NUCLEUS (http://www.monad.com.tr/), which was established in 1998. The EHRs are managed by the hospital's information technology department with password access. Due to electronic data privacy, the researcher was not authorized to personally search the data. However after ethics committee and institutional authorization had been provided for the study, a hospital information technology specialist was assigned by the hospital medical director to assist with the study. The data of the target audience, which had been prepared based on the variables determined by the researchers, were then shared with the researchers in a Microsoft Excel document.

The EHRs for Hospital A have been stored in the hospital's online clinical activity record system since 2003 and are managed by the hospital's information technology department. Access to the EHRs is encrypted and password protected. The data were shared with the principal investigator using an identification number in a Microsoft Excel document to protect confidentiality. The data from Hospital A were obtained based on the variables determined by the researchers and with the help of a registered nurse trained by the researchers.

The extraction of the data and the data mining took approximately one year from 2018 through 2019. Finally, the researchers determined the case and control groups by analyzing the data according to the sampling criteria and demonstrated the properties of the dependent and independent variables wia statistical tests.

The selection of the case and control groups was performed according to the guidelines of the US Centers for Disease Control and Prevention (12). Within the total sample, the patients with an EVD in place and microorganism growth in CSF cultures were defined as the "*case group",* while those who had an EVD but did not have growth in CSF cultures were idendified as the *"control group."* One EVD-RI case was matched with a minimum of two patients with an EVD without an infection in the control group.

The inclusion criteria were individuals who were 18 years or older, those who had had an EVD for least one day, and patients who had received prophylactic antibiotics.

The exclusion criteria were patients who had received immunosuppressive therapy, patients with a shunt, those

with a pre-existing central nervous system infection (brain abscess, meningitis, ventriculitis) prior to EVD placement, the absence of documentation regarding EVD placement or removal, patients who had an EVD placed after a shunt infection, and patients with an EVD but without CSF sample results (microbiology and cell counts).

Settings

Hospital T is a private university hospital in Istanbul, Turkey; with a capacity of 586 beds as well as, nine ICUs with 115 beds. According to 2019 data, an average of 8000 polyclinic examinations and more than 100 surgeries were performed daily in Hospital T. EVD is one of the most frequently performed surgical interventions in the neurosurgery service. During the study period, the EVD placements and replacements were performed in the operating room only by a senior neurosurgery resident or attending neurosurgeon. The subsequent care (e.g., EVD drainage, tubing care, EVD set replacement, EVD catheter care and EVD tunnel area dressing) and treatment were provided by the neurosurgeon in training. There was no advanced practice nurses (APRNs) on the neurosurgical team (this is currently not an established role in any part of the country). With regard to EVD practices, nurses only monitored intracranial pressure (ICP) and EVD drainage bag fluid. There were no nursing care protocols available for EVD care and management. In Hospital T, nurses care for 2 - 3 (sometimes 3- 4) patients in the ICUs, while in the neurosurgery wards, nurses are responsible for taking care of 5 - 10 patients (sometimes 8-15). The CSF samples in the study were taken by a neurosurgery resident predominantly only from the proximal port, and they were not obtained routinely; they were only taken if it was deemed necessary. In general, the EVD remained clamped and was only opened for drainage if the patient had an elevated ICP. Multi-piece block and standard type EVD catheters with an EVD tunnel length between 5cm and 10 cm were used in Hospital T. Intraventricular / intrathecal (IV/IT) antibiotic administration and prophylaxis were the standards of practice for Hospital T for the duration of the current study.

Hospital A is owned by the government and managed by the University of Washington. It has a capacity of 413 bed with 32-ICU bed specifically allocated for neuroscience patients. Approximately 350 patients undergo EVD placement at the hospital each year. Hospital A is a level I trauma hospital and provides treatment for neurosurgical cases in four 4 states in the region as there is no other institution have with capacity to manage aneurysmal subarachnoid hemorrhage patients. During the study period, all EVDs were managed in the ICU and considered high stakes procedures with a risk of complications. The assessment and monitoring of the EVD were performed by a trained and certified neuroscience RN. APRNs were an integral part of the team; they were order CSF lab tests, interpreted the results, initiated treatment and called infectious disease consultants in the event of complex cases and as needed. APRN training mandates doctoral level training, national certification every five years, and requires to maintain state active advance practice and registered nurse licensure in order to practice. During the study period, the neuroscience ICU had a dedicated nurse educator who held a PhD. New RNs undergo at least a 6-month hybrid orientation program (in-class and working with a designated preceptor). The care activities performed by the RNs in Hospital A for the duration of the study were as follows: monitoring and implementing EVD maintenance protocols (i.e., monitoring the time-out procedure), EVD exit site care, protecting and maintaining the EVD positions and tubing, hourly ICP transducing and recording, and hourly CSF output-recording. The RNs were responsible for the timely reporting abnormal values (ie., elevated ICP, larger volume of CSF drainage, changes observed in the neurological exam) to both neuro ICU and neurosurgery teams concurrently. The patient to RN ratios were 2:1 in some cases 1:1 depending on the clinical complexity. Hospital A has a nursing policy and procedures related to the care and management of EVDs before, during, and after procedure, and these were applied. For surveillance purposes, the CSF samples were taken twice a week from a distal port by a trained RN, with more frequent CSF samples taken if necessary, depending on the clinical situation and/or according to the recommendations of the infectious disease consult service. The EVD system consisted of a monoblock type system, and depending on the condition of the patients, and all EVDs were placed with full draping and barrier precautions either at the bedside or in the operating room by a neurosurgery resident/team only. All the EVD catheters were impregnated with antibiotic during the current study time frame. There were specific EVD orders that could only be placed by a neurosurgeon, which indicated the parameters to call (e.g., ICP, cerebral perfusion pressure), the height of the EVD measured at the level of the external auditory meatus, and the ICP values reported in centimeters of water.

Data Analysis

The data were analyzed using SPSS software version 24.0 (IBM Corporation, Armonk, NY). The descriptive statistics were presented as the mean ± standard deviation and median (min-max) values and percentiles. A Kolmogorov-Smirnov test was used to evaluate the quantitative descriptive statistic parameters for normal distribution. The difference between the quantitative parameter groups was measured using a *t* test, and significance was tested using the Mann-Whitey *U* test. The Fischer's exact test was used for the categorical parameters. The relationship between EVD-RI and the independent variables was determined by a logistic regression analysis (odds ratio: OR, confidence interval: CI). The significance level (p-value) was accepted as 0.05 in all the tests. The EVD-RI rate was calculated as follows: annual number of EVD infection cases / days of EVD usage × 1000.

Ethical Considerations

Approval was obtained from the institutional review boards of the medical centers in Turkey and the US with the codes IRB # references 18952 and STUDY00006447, respectively. For the purpose of simplicity in reporting of the results, the institutions' names were coded as Hospital T for the hospital in Turkey and Hospital A for the US hospital.

RESULTS

Demographic Characteristics and EVD-Related Characteristics

Table I demonstrates the demographics and clinical characteristics of the patients with EVD. Hospital A had more female patients (55.1% vs 44.7%), and a much longer LOS compared to Hospital T (p=0.001). The primary diagnoses for the placement of an EVD in both hospitals were similar and mostly related to various intracranial bleeds and brain tumors. However, more than half (66%) of the primary diagnoses were related to subarachnoid hemorrhage in Hospital A, where as the majority of EVD placements were due to intracranial tumors (33.6%) in Hospital T (p=0.001). The initiatives of the hospitals regarding EVD (e.g., sampling port, EVD frequency, location of the EVD placement) differed based on the respective institutional policies (p=0.001). Additionally, the EVD-RI rates were significantly higher in Hospital T compared to Hospital A. EVD-RI rates were 18.3 per 1000 days for a total of 3227 catheter days in Hospital T, whereas 4.0 per 1000 cases for a total of 7010 catheter days in Hospital A.

Table II demonstrates the relationship between the patients' sociodemographic characteristics and their characteristics related to the EVD-RI procedures. There were no statistically significant relationships between EVD-RI and age or gender. The number of CSF samples, LOS, and EVD duration were strongly associated with EVD-RI (p=0.001) at both institution, while prolonged antibiotic use and the number of EVD placements were associated with infection in Hospital T only (p=0.001). All-cause mortality found to be 10.7% versus 2.8% in Hospital A and Hospital T respectively (p>0.05). The mortality rate of the patients with EVD-RI in Hospital T were higher than those without infection; the opposite was the case in Hospital A (p>0.05).

The first choice for the treatment of EVD-RI was cephalosporins or other antibiotics, which were often combined with cephalosporins.

Microbiological Characteristics of the CSF Cultures

The CSF culture results of the patients in hospitals T and A were presented in Table III. The causative microorganisms of EVD-RI in the two hospitals were similar; however, in Hospital A, EVD-RI was dominated by gram negative (28.5%) and gram positive bacilli (25%), while gram negative bacilli (33.9%) and gram negative cocci (23.7%) were the most common cause of infection in Hospital T. Moreover, the rates of multi-organism EVD-RI were also noted as being high for both hospitals.

DISCUSSION

In this multicenter retrospective cohort study, the infection rate and risk factors of patients with EVDs in two sociodemographically different countries were investigated.

A broad range (1%–32%) of EVD-RI risk is reported in the literature (5,11,35). The infection rate in Hospital T was similar to the findings study from Israel, which is one of the Mediterranean countries (21), while that of Hospital A was similar to the findings of a study from the US (27). Many studies have reported that the variables related to EVD-RI may play a role in these differences i.e., treatment and care facilities, differing definitions of CSF research protocols, patient population characteristics, ventriculostomy duration, protocol utilization for EVD insertion and catheter type (6,17,18,22).

In the present study, even though the rate of EVD-RI was lower in Hospital A than Hospital T, some of the risk factors related to central nervous system infections, including age and gender were determined to be independent. The age and gender of EVD-RI patients have also been shown to be independent of EVD infection in similar studies (11,16,18,21). Another risk factor that has been identified is the location in which the EVD procedure is performed (i.e., operating room, emergency department, ICU), which is controversial (27,36). However, studies have demonstrated that if strict aseptic conditions are met, the EVD procedure can be performed outside the operating room (27,29,31,36). In this study, no correlation with EVD infection was found since both institutions prefer a very high rate of the same scalp antiseptic (i.e., povidone iodine). However, a multicenter study reported the importance of chlorhexidine gluconate (CHG) in the control of surgical site infection, it was suggested that there is no significant difference between CHG and povidone-iodine (7). In addition, CHG use is not approved by a regulatory body given the absence of its safety profile in neurosurgical procedures (39). Clinicians therefore avoid using CHG whenever possible.

The CSF sampling port in relation to EVD-RI was found to be nonsignificant in this study. Each institution followed their its own protocols and policies with regard to the choice of sampling port. Previous research suggested that CSF sampling can be taken from distal or proximal port using strict aseptic techniques for surveillance or suspected CSF infection (17). Nevertheless, studies have recommended that CSF samples be taken from the distal port only to minimize the risk of infection, and such CSF samples are sufficient to diagnose an infection (18,40).

In the current study, despite the differences in EVD care and management strategies LOS, duration of EVD, and the frequency of CSF samples remained important and interrelated risk factors that were difficult to resolve. Furthermore, reports in the literature indicate that the early discharge of patients with EVD is important in preventing nosocomial infections (11,21). Prolonged LOS and/or extended gram positive antibiotic use in both hospitals may have resulted in gram negative colonization. This may explain the findings of the current study, which were in concordance with those of previous studies (10,33). In general, gram positive microorganisms that stem from skin flora (i.e., *Staphylococcus, Haemolyticus, Hominis*) are, the most common pathogens causing EVD-RI (16,28), followed by gram negative microorganisms (i.e., *Klebsiella pneumoniae, Pseudomonas aeruginosa)* (4,11,14). While the CSF culture results of Hospital A were compatible with those in the literature, the growth of the gram negative bacteria exceeded that the gram positive in CSF cultures of Hospital T, which may have been a result of the long-term use of gram positive antibiotics.

The management of patients with EVD in the ICU combined with specialized training and hig-level nursing care may

Table I: Demographics and Clinical Characteristics of the Patients with EVD

Characteristics	Hospital A (n=499)	Hospital T (n=237)	p
	n (%)	n (%)	
Age (year/mean)*	55.60 ± 14.43	48.61 ± 16.90	**0.001**
LOS (mean ± SD)*	26.74 ± 16.51 (4-125)	13.74 ± 10.72 (1-72)	**0.001**
Service admitted			
ICU	499 (100.0)	196 (82.7)	-
Neurosurgery ward	-	41 (17.3)	
EVD Indication**			**0.001**
Brain Tumour	37 (7.4)	80 (33.6)	
Traumatic Bleed (SDH/ICH)	118 (23.6)	44 (18.6)	
aSAH/AVM	332 (66.5)	97 (41.2)	
Others	12 (2.2)	16 (6.7)	
Location of the EVD placement**			**0.001**
OR	94 (18.8)	215 (91.1)	
ICU/ED	405 (81.2)	21 (8.9)	
Scalp antiseptics **			**0.001**
Chlorhexidine	7 (1.4)	26 (11.0)	
Povidone iodine	492 (98.6)	211 (89.0)	
CSF sample port*			**0.001**
Proximal	2 (0.4)	222 (93.7)	
Distal	499 (99.6)	15 (6.3)	
EVD duration (days) ***			**0.001**
Mean	14.04 ± 7.48	13. 61 ± 10.34	
Min-max	(2-83)	(1-72)	
EVD frequency***			0.094
Mean	1.25 ± 0.57	1.45 ± 0.89	
Min-max	(1-5)	(1-6)	
Number of CSF samples***			**0.001**
Mean	4.37 ± 3.03	5.57 ± 4.54	
Min-max	(1-33)	(0-25)	
Antibiotic Ppx***			**0.001**
Mean	1.00 ± 0.04	3.43 ± 2.06	
Min-max, day	(1-2)	(1-11)	
Antibiotic Rx* (n=28; n=59)**			**0.001**
Mean	16.50 ± 7.31	28.48 ± 11.30	
Min-max, day	(7-30)	(5-52)	
EVD-RI Rate (1000 days)	4.0	18.3	**0.001**
All-cause Mortality (%)	60 (12.0)	9 (3.7)	**0.001**

EVD-RI: *External ventricular drain related infections,* ***ICU:*** *Intensive cere unit,* ***CHG:*** *Chlorhexidine gluconate,* ***ICH:*** *Intracranial haemorrhage,* ***SDH:*** *Subdural haemorrhage,* ***AVM:*** *Arteriovenous malformation,* ***CSF:*** *Cerebral Spinal Fluid,* ***aSAH:*** *aneurysmatic Subarachnoid Haemorrhage*
** Independent t test; ** Chi square; *** Mann Whitney U test*
EVD duration: hospital A; 7010 EVD duration days, hospital T; 3227 EVD duration days, some patients have more than one hospitalization.

Table II: Demographics and Certain Clinical Outcomes of Hospital A and Hospital T and External Ventricular Drain-related Infections

Characteristics	Hospital A, n=499 EVD-RI			Hospital T, n=237 EVD-RI		
	With n=28 (%)	Without n=471	Test p	With n=59 (%)	Without n=178	Test p
	(EVD-RI: 4.0)		OR (95%CI)	(EVD-RI: 18.3)		OR (95%CI)
Age			0.52			0.45
Mean	53.07	55.75	0.98 (0.93-1.03)	46.1	49.61	0.98 (0.93-1.03)
Min-max	(19-91)	(22-72)		(18-91)	(18-91)	
LOS			**0.001**			**0.001**
Mean	48.96	25.42	1.04 (1.03-1.08)	28.41	9.04	2.23 (1.59-3.14)
Min-max	(72-125)	(4-24)		(12-72)	(1-17)	
Gender						0.90
Male, n (%)	9 (32.1)	215 (45.6)		33 (55.9	98 (55.1)	0.96 (0.53-1.74)
Female, n (%)	19 (67.9)	256 (54.4)		26 (44.1)	80 (44.9)	
Location of the EVD placement						0.24
OR	5 (17.9)	89 (18.9)		56 (94.9)	160 (89.9)	0.48 (0.13-1.67)
ED/ICU	23 (82.1)	382 (81.1)		3 (5.1)	18 (10.1)	
Number of CSF samples*			**0.001**			**0.014**
Mean	11.96	3.92	2.25 (1.74-2.90)	10.13	2.73	1.66 (1.10-2.49)
Min-max	(5-33)	(1-13)		(1-25)	(1-10)	
EVD duration*			**0.001**			**0.001**
Mean	34.64	12.82	1.99 (1.36-2.91)	27.81	8.91	2.01 (1.39-2.89)
Min-max	(17-83)	(2-29)		(11-72)	(1-17)	
EVD frequency**			0.316			**0.011**
Mean	2.53 ± 0.88	1.18 ± 0.45	0.22 (0.01-4.12)	2.62 ± 0.88	1.03 ± 0.20	6.27 (1.52-25.90)
Min-max, day	(1-5)	(1-3)		(1-4)	(1-3)	
Antibiotic Ppx***						0.89
Mean	1	1		3.41	3.49	0.96 (0.60-0.54)
Min-max, day	0.0	(1-1)		(1-11)	(1-9)	
Antibiotic Rx***						**0.001**
Mean	16.59	0.0		28.45	3.78	1.79 (1.35-2.38)
Min-max, day	(7-30)	0.0		(5-52)	(1-20)	
Mortality, n (%)			0.999			0.167
	3 (10.7)	57 (12.1)	0.87 (0.25-2.97)	4 (6.8)	5 (2.8)	2.51 (0.65-9.70)

EVD-RI: *External ventricular drain related infections,* ***ICU:*** *Intensive cere unit,* ***CHG:*** *Chlorhexidine gluconate,* ***ICH:*** *Intracranial haemorrhage,* ***SDH:*** *Subdural haemorrhage,* ***AVM:*** *Arteriovenous malformation,* ***CSF:*** *Cerebral Spinal Fluid,* ***aSAH:*** *Aneurysmatic Subarachnoid Haemorrhage*

**-2 Log likelihood 22,71 Negelkerge; R^2: .914; Omnibus test: .001; sensitivity: 99.8, specificity: 92.8*

*** -2 Log likelihood 38.39 Negelkerge; R^2: .914, Omnibus test: .001; sensitivity: 99.4; specificity: 93.2*

ED: *Emergency department,* ***ICU:*** *Intensive care unit,* ***CSF:*** *Cerebral spinal fluid,* ***CHG:*** *Chlorhexidine gluconate*

**** As antibiotics for prophylaxis and treatment in both hospitals, the first choice was cephalosporins, the second was other drugs combined with cefalosporins.*

Table III: Class of Organism Growth in the CSF Culture

	Hospital A n=28	Hospital T n=59
	n (%)	n (%)
Gram negative		
Cocci	1 (3.6)	3 (5.1)
Bacilli	8 (28.5)	20 (33.9)
Gram positive		
Cocci	6 (21.1)	14 (23.7)
Bacilli	7 (25)	5 (10.2)
Yeast	1 (3.6)	-
Multi-Organism	5 (17.8)	16 (27.1)

Gram negative: *Staphylococcus epidermidis, Acinetobacter baumani, Moraxella, pseudomonas aeruginosa, corneabacteria, morganella morganii, etc.*
Gram positive: *Staphylococcus aureus, haemaylticus, hominis, Strept.milleri MSSA, Citrobacter freundi etc.*
Multi-Organism: *Enterobacterial (EC, Klebsiella pneum. etc) and gram positive or negative cocci/bacilli, etc.*

have played a role in the lower rate of EVD-RI in Hospital A. Prior studies have indicated that this can be considered a risk reduction approach (1,17,19). In addition, although the patients in Hospital A required a longer duration of EVD than those in Hospital T, the use of antibacterial-impregnated EVD catheters may have reduced the number of EVD-RI cases (13,24,30,37,41).

The selection of a monoblock-type EVD system in Hospital A may have influenced the EVD-RI rate. The differences between this system and the conventional system are the absence of stopcocks and the presence of an injection port for drug infusion (called an interlink) to prevent violation of the system and disconnection. The monoblock EVD system is believed to provide better asepsis as manipulation is limited, and the system is designed to prevent accidental EVD disconnections. However, in previous studies, the monoblock system did not result in significantly lower infection rates compared to the conventional system (2).

In this study, the duration of EVD in both hospitals were much longer than 4-5 days (11,31,34), which is the time that is critical for infection. Despite the longer duration of EVD and the higher number of CSF samples taken in hospital A, the use of distal port CSF samples may have played a role in the lower rate of infection. In addition, the literature suggests that with long-term catheterization, EVD retrograde microbial colonization increases and becomes one of the most important risk factors for infection (17,18,31,34). For patients with prolonged catheterization, some authors (32,38,41) have recommended the routine replacement of EVDs, while others (4,11,18,31,34) have argued against this. Routine CSF sampling in patients with EVD may lead to false-positive findings and unnecessary antibiotic administration, which could increase the risk of nosocomial infection (17,18).

Long-term antibiotic treatment may be related to disparities in patient care (wards vs ICU) and substantial care provided by neurosurgery residents. In Hospital T, neurosurgery residents are overloaded with additional obligations, including the management of all neurosurgery patients, the operating room, emergency department and inpatient consultations, and clinic duties, so this may have resulted in the higher rate of EVD-RI at the hospital. An important and different approach at Hospital T in relation to infection control was that IV/IT prophylaxis was used. Even though IV/IT prophylaxis antibiotic use has been reported in the literature, its prophylactic effect had not been proven (3,23). While IV/IT antibiotics are currently used as an alternative in the treatment of ventriculitis, evidence of fatal complications was reported in a meta-analysis (9). Moreover, the IV/IT use was based on poor quality evidence and the safety of IT/IVT has not been established for broader use (9). However, in this study, prolonged antibiotic use did not provide the expected results for the treatment of EVD-RI in Hospital T. Even though it was at a lower rate, prolonged antibiotic use was also noted in Hospital A. The inappropriate (e.g., under/overdosing, treatment not guided by susceptibility, misprescription) or prolonged use of antibiotics may cause changes in the mutations in the chromosomal genes of the microorganisms, subsequently leading to changes in the flora and the formation of multidrug resistant bacteria. The high rate of multi-organism EVD-RIs warrants the urgent adoption of antibiotic stewardship and the implementation of programs according to the local antibiogram, biology, and genome of the microorganisms (8,26). Kocak et al. reported that only slightly more than half (52.4%) of the providers in their study followed antimicrobial prophylaxis guidelines and 63.5% continued prophylaxis until drain removal (24).

In this study, the mortality rate was higher in Hospital A compared to Hospital T, however, the group analysis showed that the mortality rate of the patients with EVD-RI in Hospital A was lower than for those without infection, whereas the opposite results were obtained for Hospital T. These results indicate that other factors could have been at play (e.g., comorbidities, severity of disease, concurrent infections) in addition to EVD-RI in both institutions. Unfortunately, the lack of sufficient data made it difficult to clearly interpret the mortality results for both hospitals.

Finally, the wide range of infection and mortality rates between Hospital A and T were most likely attributable to many factors, including variations in the populations evaluated and the use of dissimilar methodologies in the management of EVDs.

Limitations

This study had a few limitations. First, the mortality rate reflected all-cause mortality, because 30-day mortality could not be clearly determined. Second, cooccurring infections and comorbidities were not taken into account, which may have been increased the bias in the EVD-RI rates. Third, given the retrospective design, causality could not be established.

CONCLUSION

This multicenter study revealed that the critical determinants of EVD-RI were related to clinical characteristics, namely, LOS, duration of EVD, and frequency of CSF samples, rather than patients' personal characteristics (i.e., age and gender). The difference in the EVD-RI prevalence in the two hospitals may have stemmed from institutional policies and practices as well as the available resources in each country. Although the risk factors associated with EVD-RI in both hospitals were similar, the reasons leading to these risks may have been different. Accordingly, each center should address EVD-RI according to the most likely cause of the predictors. Multi-organism EVD-RI emerged as a new finding in this research, thus further advanced the scientific knowledge on the subject. Antibiotic treatment choices and appropriate prescribing practices that are guided by susceptibility results, narrowing the antibiotics as early as possible and infectious disease consultation would be beneficial in preventing antibiotic resistance and the development of "superbugs". Multi-organism EVD-RI emerged as a new finding in this research, thus scientific knowledge on the subject should be expanded.

In addition, adopting and reinforcing strict infection control measures, the removal of EVDs as early as medically possible, and early patient discharge from hospital provide other methods of controlling EVD-RI rates.

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