Cell Index in the Diagnosis of External Ventricular Drain-Related Infections

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BACKGROUND: **The use of an external ventricular drain is required for the treatment of many diseases, such as traumatic brain injury and subarachnoid hemorrhage (SAH). Meningitis and ventriculitis are frequent complications arising from the use of external ventricular drain therapy. This study aimed to determine the sensitivity, specificity, and cutoff point for cell index (CI) in patients with traumatic brain injury, SAH, and hemorrhagic stroke.**

METHODS: **Our study population consisted of patients with different underlying diseases and few culture-positive cerebrospinal fluid samples. The diagnosis of infection was based on Centers of Disease Control and Prevention criteria.**

RESULTS: **Overall CI analysis showed an area under the curve (AUC) of 0.982. The cutoff of 2.9 for overall CI provided a sensitivity of 95% and a specificity of 92.9%. In patients with SAH, the AUC was 1.0 for a CI of 2.8; furthermore, sensitivity and specificity were 100%. The relative variation of the CI was also assessed. This analysis revealed an AUC of 0.882, and a 4.33-fold increase was found be indicative of infection ($P = 0.002$), findings similar to those in the literature. In addition, a heatmap analysis demonstrated that the CI is unlikely to return to normal in patients with meningitis, even after treatment.**

CONCLUSIONS: **Therefore, CI is valuable for the diagnosis of infection, but was inadequate for monitoring treatment. We hope to use the new cutoff point proposed by this study in our institution to improve patient clinical outcome.**

INTRODUCTION

The use of an external ventricular drain (EVD) may be required to control hydrocephalus and monitor intracranial pressure in many diseases, such as traumatic brain injury (TBI),[1] hemorrhagic stroke (HS), and subarachnoid hemorrhage (SAH).[2]

Complications related to the use of EVD include meningitis and ventriculitis. The incidence of these infections may vary from 5%–20%, with severe consequences, such as reduced intellectual capacity and death.[3] The occurrence of hemorrhage in cerebral ventricles makes it difficult to diagnose these infections because hemorrhage leads to additional confounding factors (e.g., increased cellularity and reduced cerebrospinal fluid [CSF] glucose concentration[4]).

Risk factors for EVD infection include duration of catheter use, SAH (especially intraventricular hemorrhage), penetrating and open brain injury, basilar skull fracture with CSF leak, and other neurosurgical procedures.[2]

Measures to avoid EVD infection are described in the literature such as surgical prophylaxis with antimicrobials, catheters coated with antimicrobials, careful aseptic insertion and manipulation of catheter. These have shown encouraging results.[1] The education of the healthcare team with regard to the required care measures, including hand hygiene, has also been found effective

Key words
- Cerebral hemorrhage
- Cerebral ventriculitis
- Craniocerebral trauma
- Diagnosis
- Meningitis
- Ventriculostomy

Abbreviations and Acronyms
AUC: Area under the curve
CDC: Centers for Disease Control and Prevention
CI: Cell index
CSF: Cerebrospinal fluid
EVD: External ventricular drain
HS: Hemorrhagic stroke
SAH: Subarachnoid hemorrhage
SD: Standard deviation
TBI: Traumatic brain injury

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in reducing infections.[5] CSF collected only when clinically required is also a protective measure against EVD infection.[6]

The establishment of more rapid, more accurate, and less expensive diagnostic methods compared with current methods may lead to an earlier and more successful treatment, as well as a more specific diagnosis and the rational use of antimicrobials.

Our objective was to determine the cell index (CI) sensitivity and specificity versus current diagnostic criteria for EVD-related meningitis/ventriculitis after TBI and to establish the most adequate cutoff points. We also investigated the use of the CI to monitor the treatment of these infections.

METHODS

This prospective cohort study (from January 2015 to December 2016) followed patients for up to 30 days after suspected meningitis. These patients were treated at Hospital Cristo Redentor, a reference hospital for the treatment of patients with TBI, cerebral tumors, and intracranial hemorrhage trauma. This hospital, whose facilities include 250 beds and a 29-bed intensive care unit (ICU), is located in southern Brazil.

Study inclusion criteria were as follows: only cases of TBI and intracranial hemorrhage, especially SAH and HS, to ensure sample homogeneity, and inpatients >18 years of age, using EVD with available results for CSF collection and complete blood count obtained on the same day. Potentially eligible patients were selected from a list of patients who used EVD during the study period (consecutive series).

The CI was calculated as follows: ratio between white blood cell count and red blood cell count in the CSF divided by the ratio between white blood cell count and red blood cell count.[7] In addition to calculating the CI, we also assessed the time elapsed from EVD placement until suspected meningitis (time from EVD insertion until suspected meningitis/ventriculitis, i.e., time until suspected infection) and total EVD time (duration of EVD placement), as well as need for changing the EVD. Patients' demographic data, such as sex and age, were also collected. All patients received surgical prophylaxis with antimicrobial agents, according to the hospital protocol for EVD placement, which comprises the use of cefazolin.

Meningitis/ventriculitis were diagnosed using criteria from the Centers of Disease Control and Prevention (CDC),[8] similar to those recommended by the Brazilian National Health Surveillance Agency (Agência Nacional de Vigilância Sanitária, ANVISA).[9] The use of lactate as a parameter for the diagnosis nosocomial meningitis has also already been described in the literature and was included in patients' assessment. The lactate cutoff point used in this study was 4 mmol/L.[10] These criteria were adopted by the infectious disease physician in the Hospital Infection Control Service, according to hospital routine. Patients with and without meningitis were grouped according to their disease status.

This study was conducted in accordance with the ethical standards established by the Declaration of Helsinki. All enrolled patients signed an informed consent form. When a patient could not sign it for any reason, the form was signed by a legal representative. The present study was approved by the hospital's Research Ethics Committee with protocol no. 14191.

Results were assessed using the Statistical Package for the Social Sciences (IBM, Chicago, Illinois, USA), version 19. Sample size was calculated using the GPower software, version 3.1.9.2 (Universitat Dusserldorf, Dusseldorf, Germany). The MatLab

Table 1. Patients' Demographic Data

Variable	Non-meningitis Group (n = 14)	Meningitis Group (n = 20)	P Value
Sex			
Female	10 (71.4)	7 (35.0)	0.081
Male	4 (28.6)	13 (65.0)	
Underlying disease			
Subarachnoid hemorrhage	6 (42.9)	14 (70.0)	0.256
Hemorrhagic stroke	3 (21.4)	3 (15.0)	
Traumatic brain injury	5 (35.7)	3 (15.0)	
Need for changing EVD catheters			
Yes	2 (16.7)	5 (25.0)	0.683
No	10 (83.3)	15 (75.0)	
Outcome			
Discharge	7 (50.0)	14 (70.0)	0.411
Death	7 (50.0)	6 (30.0)	
Age, years	54.07 (10.92)	51.70 (11.74)	0.555
Time from EVD insertion until suspected meningitis/ventriculitis, days	8 (2.59)	7.2 (2.56)	0.402
Duration of EVD placement, days	10.42 (5.48)	11.50 (4.63)	0.554

EVD, external ventricular drain.