Risk Factors for Poor Outcome in Hypertensive Intraventricular Hemorrhage Treated by External Ventricular Drainage with Intraventricular Fibrinolysis

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OBJECTIVE: **External ventricular drainage (EVD) combined with intraventricular fibrinolysis (IVF) is a commonly accepted surgical approach for some cases of hypertensive intraventricular hemorrhage (HIVH). We aimed to investigate the association between preoperative factors and outcome in patients with HIVH treated by EVD plus IVF.**

METHODS: **Records from March 2010 to March 2016 were searched for HIVH treated by EVD plus IVF. We divided this population into the favorable outcome group and the unfavorable outcome group according to the Glasgow Outcome Scale. Preoperative demographic data, radiologic findings, and clinical factors were compared in each group. Univariate and multivariable logistic regression were used to assess the relationship between factors and outcome in HIVH.**

RESULTS: **Of 267 patients included in this study, 136 had a favorable outcome and 131 had a poor outcome. Multivariate analyses showed that age (odds ratio [OR], 18.229; 95% confidence interval [CI], 1.503–221.16), Glasgow Coma Scale score (OR, 12.686; 95% CI, 1.5–107.312), blood neuron specific enolase (OR, 9.463; 95% CI, 1.178–76.012), third ventricle hematoma (OR, 15.311; 95% CI, 1.287–497.914), and fourth ventricle hematoma (OR, 25.258; 95% CI, 1.851–125.767) were associated with poor outcome of EVD in patients with HIVH.**

CONCLUSIONS: **Fourth ventricle hematoma, third ventricle hematoma, high blood neuron specific enolase value, low Glasgow Coma Scale score, and old age were risk factors for poor outcome in HIVH treated with EVD plus IVF. EVD was not suitable, particularly in patients with brainstem compression caused by fourth ventricle hemorrhage, regardless of use of IVF.**

INTRODUCTION

Primary intraventricular hemorrhage (IVH) is rare but is more commonly secondary to spontaneous intracerebral hemorrhage (ICH) and is mostly caused by hypertensive hemorrhagic stroke, with high rates of death and disability.[1-5] External ventricular drainage (EVD) has been widely applied as a rescue surgical procedure when obstructive hydrocephalus or deterioration of consciousness caused by third or fourth ventricle hematoma is present.[6-8] Recent reports have stated that EVD associated with intraventricular fibrinolysis (IVF) may be associated with better survival and functional outcomes in some patients with IVH who have a particularly poor status on admission.[6,9] However, it is unclear which subgroups obtain the greatest benefit from EVD plus IVF.[8,10,11] Thus, it is important to identify preoperative prognostic factors for EVD plus IVF for IVH, to screen for patients who are suitable for EVD. The aim of this study was to investigate the relationship between preoperative clinical characteristics and outcome in patients with hypertensive IVH (HIVH) treated by EVD plus IVF.

Key words
- External ventricular drainage
- Intraventricular fibrinolysis
- Intraventricular hemorrhage
- Outcome

Abbreviations and Acronyms
3D: Three-dimensional
bNSE: Blood neuron specific enolase
CI: Confidence interval
CT: Computed tomography
EVD: External ventricular drainage
GCS: Glasgow Coma Scale
HIVH: Hypertensive intraventricular hemorrhage
ICH: Intracerebral hemorrhage
IVF: Intraventricular fibrinolysis
IVH: Intraventricular hemorrhage
GOS: Glasgow Outcome Scale
OR: Odds ratio

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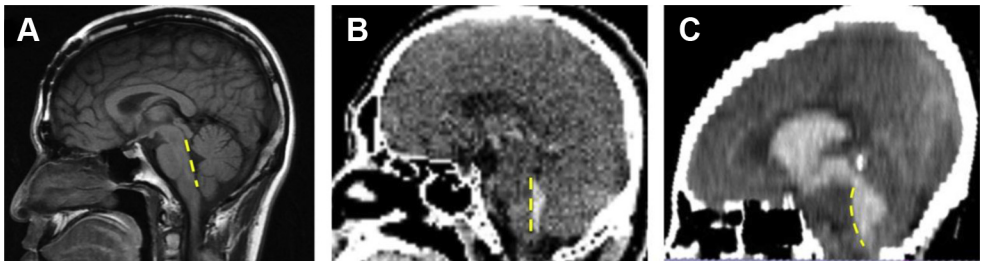

Figure 1. Magnetic resonance imaging (**A**) and computed tomography (**B**, **C**) showing different brainstem dorsal lines on sagittal images. (**A**) Normal. (**B**) Hematoma-filled fourth ventricle without brainstem compression (grade I). (**C**) Hematoma-filled fourth ventricle with brainstem compression (grade II). Yellow dotted line represents brainstem dorsal line.

METHODS

Patient Population and Study Design

The study was approved by the ethics committee of Hubei University of Medicine. We retrospectively reviewed 267 patients with a diagnosis of HIVH treated with EVD plus IVF who were hospitalized in the neurosurgical unit of our institution between March 2010 and March 2016. Inclusion criteria were 1) primary HIVH and 2) secondary HIVH in which the hematoma was mainly located in the ventricular system and the primary cerebral parenchymal hemorrhage was <15 mL. Exclusion criteria were 1) hemorrhage caused by aneurysms, arteriovenous malformations, or moyamoya disease; 2) coagulation disorder; 3) trauma; and 4) severe impairment of heart, lungs, liver, kidney, or other major organs.

The reasons for our choice of primary or secondary HIVH from a small spontaneous hypertensive ICH in this study were as follows:

1) A large intraparenchymal hematoma (>15 mL) could result in confounding factors for EVD performance, in that intraparenchymal hematoma size was itself a predictor of poor outcome.[12,13]
2) The cause of the IVH could influence prognosis because it is more important in predicting outcome than the volume of IVH.[14]
3) Individualized treatment strategies with preoperative factors are better understood,[3,15] because clinical characteristics of primary HIVH and HIVH secondary to a small spontaneous ICH are different from those of a cerebral parenchymal hematoma.[16]

All patients were diagnosed by computed tomography (CT) on admission and with subsequent CT angiography. An intraventricular catheter was placed in the fontal horn of the right lateral ventricle if hydrocephalus was present on admission or if clinical status deteriorated in the intensive care unit.[8] When severe casting of both lateral ventricles was present, bilateral EVD was required. The ventricular system was flushed with urokinase as described by Shin et al.[17] All patients with HIVH had received injection of urokinase 25000 international unit) in 1 mL of normal saline solution, every 12 hours. The first intraventricular catheter injection occurred from 12 hours to 24 hours after the initial bleeding episode. Injections were preceded by gentle aspiration of no more than 5 mL of cerebrospinal fluid. Injection of the urokinase was followed by a 3 mL flush with normal saline solution. After 1 hour of closure, the intraventricular catheter was reopened. Study agent injections continued every 12 hours. Because a previous study[18] concluded that no difference was found in outcome between unilateral and bilateral EVD groups, the impact of a second EVD placement was not analyzed in this research.

Collected patient data included general data (gender, age, systolic pressure, Glasgow Coma Scale [GCS] score, pupil size and light reflex, and Babinski sign), results of laboratory tests (white blood cell count, blood sugar, blood neuron specific enolase [bNSE] level), and imaging features (lateral ventricle hematoma, third ventricle hematoma, fourth ventricle hematoma, hydrocephalus, subarachnoid hemorrhage, cisterna ambiens) on admission. We divided this population into a favorable outcome group (group A) and an unfavorable outcome group (group B). Survival and functional outcomes were assessed using Glasgow Outcome Scale (GOS) scores at 6 months after surgery.[19] A GOS score of 4–5 indicated a favorable result of treatment (group A); a GOS score of 1–3 indicated an unfavorable result (group B).

Image Description

Volume calculation of blood and three-dimensional (3D) reconstruction of CT images of ventricles were processed by 3D-Slicer software as described by Xu et al.[20] Lateral ventricles: grade I, less than one third of ventricle filled with blood; grade II, more than one third and less than two thirds of ventricle filled with blood; grade III, more than two thirds of ventricle filled with blood. Third ventricle: grade I, blood present, ventricle size normal; grade II, ventricle filled with blood and expanded. Ventricular enlargement was graded using a semiquantitative scale,[21] and recorded as present or absent. Fourth ventricle: grade I, blood present without brainstem compression; grade II, blood-filled ventricle with brainstem compression.

We defined a brainstem dorsal line curved to the ventral side as brainstem compression, for the following reason. To investigate whether the brainstem was compressed by a fourth ventricle hematoma, we reconstructed sagittal images of the fourth ventricles of healthy adults and patients using 3D-Slicer software. We found