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Clinical Study

Intracerebral hemorrhage with intraventricular extension and no hydrocephalus may not increase mortality or severe disability

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ABSTRACT

This paper aimed to test the hypothesis that intraventricular extension of spontaneous intracerebral hemorrhage (ICH) in the absence of hydrocephalus is not associated with increased mortality or severe disability. We performed a retrospective consecutive cohort study of patients with primary spontaneous ICH who were admitted to a single institution. Multivariate logistic regression analysis was used to assess the association of each variable with functional outcome as measured by the modified Rankin Scale (mRS). A total of 164 patients met our inclusion criteria and were included in the study. Only hydrocephalus ($p = 0.002$) and hematoma volume ($p = 0.006$) were significantly associated with mortality or poor functional outcome (mRS of 3 to 6). In contrast, the presence of intraventricular hematoma was not independently associated with poor functional outcome. The presence of intraventricular extension of ICH in the absence of hydrocephalus may not increase mortality or disability.

1. Introduction

Spontaneous intracerebral hemorrhage (ICH) comprises 10 to 15% of all strokes with an incidence of 15 to 40 in 100,000 people per year. ICH is associated with high morbidity and mortality. The estimated mortality rate after 30 days of admission has been reported to be 35–52% and 1 year mortality surpasses 50% [1–3]. The current ICH scoring system, which was initially introduced in 2001, has been widely used as a simple and fairly consistent model to predict 30 day mortality [4]. The main factors in this system include patient age, hematoma volume, presence of intraventricular extension, location (supra-tentorial *versus* infra-tentorial) and Glasgow Coma Scale (GCS) at the time of admission. The presence of intraventricular hemorrhage (IVH), which happens in about 45% of ICH patients at presentation, [5] has been considered a poor prognostic factor in various studies, [4–8]. On the other hand, Diringer et al. proposed that hydrocephalus is an independent poor prognostic indicator in patients with ICH [9]. Based on current literature, the presence of IVH regardless of the presence or absence of hydrocephalus is considered a poor prognostic factor [4,8,10]. However, the interplay between IVH and hydrocephalus in regards to outcome after ICH remains unclear. We hypothesized that IVH related poor prognosis is mainly derived from development of hydrocephalus rather than presence of blood in the ventricular system per se.

2. Methods and materials

2.1. Study design and patient population

This was a retrospective cohort study of patients with ICH who were admitted to the Neuroscience Intensive Care Unit at a tertiary referral center from 2008 to 2010. Approval was obtained from the Temple University School of Medicine institutional review board. Medical records including imaging data and outpatient follow-up were retrieved. All demographic data; initial GCS score; CT scan findings including volume of hematoma, intraventricular extension, and presence or absence of hydrocephalus at the time of admission; placement of external ventricular drain (EVD); any history of anti-platelet use at the time of admission; and modified Rankin Scale (mRS) as the main indicator of clinical outcome which was assessed based on neurology or physical therapy assessment notes at the time of most recent follow-up visit or discharge were carefully analyzed. The presence or absence of hydrocephalus was determined by experienced neuroradiologists based on dilatation or change in configuration of the ventricular apparatus with special focus on the temporal horns and third ventricle. In case of a second

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cerebrovascular event either ischemic or hemorrhagic, the most recent mRS prior to that event was counted. The follow-up data for about 70% of patients who survived were available ranging from 3 months to 7 years. For the patients with no follow-up, mRS values at the time of discharge were counted. Poor outcome was arbitrarily defined as mRS of 3 (moderate disability requiring some assistance) to 6 (death). We included patients with primarily spontaneous intra-parenchymal hematoma without any obvious radiographic evidence of underlying vascular malformation or neoplastic lesion. These patients were classified as "hypertensive" bleed or ICH with undetermined etiology in the medical records. The exclusion criteria consisted of primary epidural or subdural hematomas, aneurysmal subarachnoid hemorrhages, ischemic infarcts with hemorrhagic conversions, any underlying neoplastic lesions or vascular malformations, because pathophysiology is different in each category.

2.2. Measurements

The hematoma volume as a continuous variable was calculated based on the $A \times B \times C/2$ formula (where A = maximum transverse diameter, B = diameter perpendicular to A, and C = number of slices). The radiographic evidence of hydrocephalus was judged based on the presence of any of the following: [1] dilation or ballooning of the third ventricle; [2] dilatation of the temporal horns; and [3] any dilatation or alteration in configuration of the ventricular system due to the mass effect of hematoma. The initial neurologic examination in the first 24 hours of admission was assessed based on the GCS score. The main locations of intraparenchymal hematoma were labeled as thalamus, putamen, lobar, pons or cerebellum.

2.3. Statistical analysis

We used the Statistical Package for the Social Sciences version 22 (IBM, Armonk, NY, USA) for our statistical analysis. Multivariate logistic regression analysis was performed to compare all variables including categorical and continuous with the outcome as either good (mRS 0–2) or poor (mRS 3–6). The categorical or dichotomous variables included age ($\geqslant$80 or <80 years); hydrocephalus (present or absent); IVH (present or absent); EVD placement (present or absent); use of anti-platelets such as aspirin, clopidogrel, dipyridamole or any combinations (yes or no); location of hematoma (lobar, thalamus, putamen, cerebellum or pons); and GCS (three categories: 13–15, 5–12, 3–4). In addition, these variables were compared in three groups of patients: ICH without IVH or hydrocephalus; ICH with IVH but no hydrocephalus; and ICH with IVH and hydrocephalus. Kruskal–Wallis test for continuous variables and chi-square test for categorical variables were performed. The statistical significance for our study was defined as p value less than 0.05.

3. Results

A total of 164 patients met the inclusion criteria. These patients were divided into three sub-categories: ICH without IVH or hydrocephalus (44%); ICH with IVH but without hydrocephalus (19%); ICH with IVH and hydrocephalus (37%). The patients with IVH with no hydrocephalus at presentation did not develop hydrocephalus during the course of their hospitalization. The rate for poor outcome was 15% in ICH without IVH or hydrocephalus and 26% in ICH and IVH but no hydrocephalus groups; however, this rate was 92% in patients with ICH and IVH with hydrocephalus. The mortality rate in these groups was 1%, 3% and 52%, respectively. The overall mortality rate was 26% among all patients. The hematoma volume was significantly larger and GCS score was lower in patients with IVH and hydrocephalus compared to the other two groups. We also observed more thalamic hematoma (38%) and less lobar hemorrhage (20%) in the hydrocephalus group in comparison with the two groups without hydrocephalus (Table 1).

Multivariate logistic regression analysis revealed only hydrocephalus ($p = 0.002$) and hematoma volume ($p = 0.006$) were associated with poor outcome. The other variables including age, initial GCS, presence of IVH, location of hematoma, use of anti-platelet agents at the time of admission and placement of EVD did not meet statistical significance (Table 2). A total number of 26 patients (15.8%) presented with extremely poor neurologic examination (GCS 3–4). Only two of them (8%) had good functional outcome and the mortality rate was 69% (18/26). Delayed appearance of IVH due to hematoma extension which was not present at the time of admission was observed in only eight patients, of whom three had coagulopathy and two were on hemodialysis for end stage renal disease. These patients were classified as "no IVH" given the fact that their initial head CT scan was negative for IVH.

Of 61 patients with hydrocephalus, 42 (69%) underwent EVD placement. The remaining 19 patients (31%) did not undergo EVD placement because of either extremely poor neurologic examination at the time of admission or refusal of the family to pursue invasive procedures. The rate of poor outcome was 100% for the group with no EVD and 88% for the group with EVD, which means an absolute risk reduction of 12% for the EVD group and gives a number needed to treat of 8.3 (1/0.12). The mortality rate was 33.3% in the EVD group compared to 89% in patients with hydrocephalus without EVD, which reveals an absolute risk reduction of 55.7% with a number needed to treat of 1.8 (1/0.557). Only 11% of patients with hydrocephalus had a GCS of 13–15 at the time of presentation compared to 79% of patients without hydrocephalus.

4. Discussion

Our study demonstrates that the presence of IVH per se may not be a poor prognostic sign in the absence of hydrocephalus. A change in configuration of the ventricular system appears to be a significantly more important factor in predicting mortality or disability in ICH patients. In a recent study, Witsch et al. showed that delayed appearance of IVH is not an independent poor prognostic factor in ICH patients; however, the presence of IVH at the time of admission was associated with poor outcome [11]. Nevertheless, their findings contradict another study conducted by Mass et al. which showed delayed appearance of IVH was associated with mortality and poor functional outcome [12]. Neither of these studies properly addressed the presence or absence of hydrocephalus. There are multiple studies showing that IVH is independently associated with poor prognosis in patients with ICH [13–17]; however, hydrocephalus was never addressed as a separate issue from IVH in any of these studies. One study of 293 patients with ICH showed that the association between IVH and 30 day mortality was not significant [18].

There are various grading systems to quantify the amount of hydrocephalus and IVH which were used in the original paper showing that hydrocephalus is an independent poor prognostic factor in ICH [9]. We did not use any of these grading systems in our study mainly because quantification of hydrocephalus based on mass effect is very subjective (mild, moderate, severe) and is different from other forms of hydrocephalus, such as normal pressure hydrocephalus or aqueductal stenosis. Placement of an EVD to potentially reverse hydrocephalus was associated with less mortality; however, the functional outcome still remained poor. In other