Hydrocephalus Is a Determinant of Early Mortality in Putaminal Hemorrhage

Thanh G. Phan, FRACP; Merian Koh, MBBS; Robert A. Vierkant, MAS; Eelco F.M. Wijdicks, MD

**Background and Purpose**—Previous studies have shown that the volume of intracerebral hemorrhage and Glasgow Coma Score (GCS) on admission are powerful predictors of 30-day mortality. However, the significance of hydrocephalus associated with deep cerebral hemorrhage has not been studied extensively. The purpose of this study was to determine the prognostic indicators of 30-day mortality in patients with deep cerebral hemorrhage.

**Methods**—We studied 100 consecutive patients with deep cerebral hemorrhage between 1994 and 1998. Deep cerebral hemorrhage was divided into 2 groups: putaminal hemorrhage (lateral group) and thalamic and caudate hemorrhage (medial group). Univariate and multivariate logistic regression analyses were performed to determine independent prognostic indicators of 30-day mortality.

**Results**—Hydrocephalus was present in 40 of the 100 patients. The 30-day mortality was 29%, and hydrocephalus was present in 76% of those who died. Multivariate analyses showed 2 independent prognostic indicators of 30-day mortality for putaminal hemorrhage: GCS ≤8 (P = 0.002, odds ratio [OR] 37.7, CI 3.6 to 396.9) and hydrocephalus (P = 0.005, OR 27.4, CI 2.7 to 282.6). However, only GCS ≤8 (P = 0.0002, OR 16.5, CI 3.7 to 73.4) was predictive of 30-day mortality for thalamic and caudate hemorrhage. This model (GCS ≤8 and hydrocephalus) has a sensitivity of 57% and a specificity of 91% for predicting 30-day mortality for putaminal hemorrhage. When both attributes were present in putaminal hemorrhage (GCS ≤8 and hydrocephalus), 1 (11%) of 9 patients survived, and when both attributes were missing 28 (100%) of 28 patients survived.

**Conclusions**—Obstructive hydrocephalus on admission in a comatose patient with a putaminal hemorrhage predicts 30-day mortality. (Stroke. 2000;31:2157-2162.)

**Key Words:** cerebral hemorrhage • hydrocephalus • mortality • prognosis

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**Subjects and Methods**
We reviewed the medical records and nonenhanced CT (NECT) (T.G.P., E.F.M.W.), which had been performed within 24 hours of onset, of 100 consecutive patients with deep cerebral hemorrhage between 1994 and 1998. The present study was approved by the Institutional Review Committee. One patient was excluded from the analysis, because permission to review the medical record was not granted. Reading of the NECT was by consensus, and the graders (T.G.P., E.F.M.W.) were blinded to the clinical features. Deep cerebral hemorrhage was divided into 2 groups: putaminal hemorrhage (lateral group) and thalamic and caudate hemorrhage (medial group). The volume of hemorrhage was calculated from hard copies of the NECT image by using the formula for ellipsoid mass: 4/3π×1/2Ax1/2B×1/2C.

Hydrocephalus was defined as the presence of a dilated contralateral temporal horn or a unilaterally dilated frontal and posterior horn of the lateral ventricle from deep cerebral hemorrhage.
hemorrhage. Hydrocephalus was also defined as the presence of bilateral dilated lateral ventricles with or without a dilated third ventricle resulting from obstruction by a clot in the ventricle or the mass effect of deep cerebral hemorrhage. Hydrocephalus was quantified by using the method described by Diringer et al.² This method grades each of the 8 parts of the ventricular system independently into categories as follows: normal (score 0), mild (score 1), moderate (score 2), and marked (score 3) enlargement. The frontal horn is considered to have enlarged if there is an increased radius, decreased ventricular angle, and sulcal effacement of the frontal lobe. The posterior horn is considered to have enlarged if there is rounding of the posterior horn with sulcal effacement of the parieto-occipital lobe. The temporal horn is considered to have enlarged if the width is increased. The third ventricle is enlarged if the width is increased and if there is ballooning of the anterior recess. The fourth ventricle is considered enlarged if there is bulging. The score for each ventricle is summed, and a score of ≥1 is considered hydrocephalus. A maximum score of 24 is considered marked hydrocephalus, and a score of 0 suggests no hydrocephalus.

Clinical findings were expressed by GCS. The mean arterial pressure on admission was determined by multiplying the diastolic blood pressure by 2, adding the result to the systolic blood pressure, and dividing by 3 to give the mean arterial pressure. A modified Rankin score was used to determine outcome. A modified Rankin score of <2 was considered good outcome, a modified Rankin score between 3 and 4 was considered moderate or poor outcome, a modified Rankin score of 5 correlated with the dependency state, and a modified Rankin score of 6 signified death. In our institution, patients were assessed in the emergency department initially by the emergency physician and were intubated if necessary for airway protection. The neurological and neurosurgical teams were consulted in all cases regarding treatment. The decision not to continue with aggressive treatment was made after a patient had failed to make improvement; it was not determined from the initial presentation.

Statistical Methods
We first assessed the univariate association of 30-day mortality with the following set of variables: sex, ventricular extension, extension of hemorrhage into midbrain, GCS, body temperature (degrees Celsius), age, location of the hematoma (putamen, thalamus, or caudate nucleus), recent anticoagulation (warfarin, streptokinase, or recombinant tissue plasminogen activator), prothrombin time, mean arterial blood pressure, heart rate, volume of the hemorrhage (in milliliters), pineal gland shift (in millimeters), serum sodium level, white blood cell count, serum glucose, and hydrocephalus (continuous and categorical values). We compared continuous variables by use of t tests. We compared categorical variables by χ² tests or, if any of the expected cell counts were <5, by the Fisher exact test.

Next, to determine appropriate functional form for subsequent model-building procedures, each continuous variable was categorized into quartiles and entered in a univariate logistic regression analysis as 3 separate indicator variables to assess its relationship with mortality. The resulting coefficients were then plotted against the ordered levels of the quartiles. All variables exhibiting a clear log-linear dose-response relationship with mortality were used in subsequent analyses as continuous variables. The following variables did not exhibit a dose-response relationship and were categorized in the following fashion: age (>65 versus ≤65 years), prothrombin time (>20 versus ≤20 seconds), mean arterial blood pressure (≥130 versus <130 mm Hg), heart rate (>85 versus ≤85 bpm), and temperature (<35.5°C or >37.5°C versus values in between). GCS score was categorized as ≤8 versus >8 to allow direct comparisons with previous studies.¹² Variables associated with mortality in the univariate analyses (P<0.10) were then included in a multivariate logistic regression analysis. A stepwise procedure was used to select the final multivariate model, with a value of P<0.10 used as the criterion for inclusion. Predicted probabilities of 30-day mortality were computed for each observation by using the final multivariate model. A probability cut point of 0.50 was used to classify observations as predicted events or nonevents. The sensitivity, specificity, and positive predictive values of the model were determined by comparing the predicted values with the actual events. All statistical tests were 2-sided, and all analyses were carried out by use of the SAS system (SAS Institute, Inc).

Results
The mean and median ages of our patients were 67 and 70 years, respectively (range 31 to 96 years). The sex distribution was 57% men and 43% women. The prevalence of hypertension was 72%, ischemic heart disease was 26%, diabetes mellitus was 15%, and history of current or previous tobacco usage was 45%. Anticoagulation with warfarin had been administered in 15 patients, and 2 patients had received intravenous streptokinase or tissue plasminogen activator for myocardial infarction.

There were 47 (47%) patients with thalamic hemorrhage, 5 (5%) patients with caudate hemorrhage, and 48 (48%) patients with putaminal hemorrhage. Hydrocephalus was present in 40 (40%) patients by visual analysis and 48 (48%) of the 100 patients by the Diringer method² (Figure). After putaminal hemorrhage, hydrocephalus was present in 15 (31%) patients by visual analysis and 22 (46%) patients by the Diringer method.² After thalamic and caudate hemorrhage, hydrocephalus was present in 25 (48%) patients by visual analysis and 26 (50%) patients by the Diringer method.² There was no statistically significant difference in the frequency of hydrocephalus between the medial and lateral groups. Hydrocephalus (by visual analysis) was present in 5 (21%) of the 24 patients with small thalamic and caudate hemorrhage (<10 mL), with only one death. However, there was no hydrocephalus in 8 of the patients with small putaminal hemorrhage (<10 mL). For deep cerebral hemorrhage, the presence of hydrocephalus by both methods was associated with a GCS <8 (P<0.0001) and clinical deterioration (P<0.0001). The 30-day mortality was 29%, and hydrocephalus was present in 76% (by visual analysis) and
86% (by the Diringer method) of those who died. A statistically significant association was still present when we analyzed the relationship between hydrocephalus (by visual analysis) and 30-day mortality results for the putaminal hemorrhage group \( (P < 0.0001) \) and the thalamic and caudate hemorrhage group \( (P = 0.02) \) (Table 1).

Predictors of 30-day mortality assessed by univariate analyses include large volume of hemorrhage \( (P = 0.001) \), hydrocephalus \( (P < 0.001) \) for both continuous and categorical values), pineal shift \( (P < 0.001) \), GCS \( \leq 8 \) \( (P < 0.001) \), hemorrhage into the ventricles \( (P < 0.001) \), temperature \( (< 35.5^\circ C \text{ or } > 37.5^\circ C) \) \( (P < 0.001) \), and white cell count \( (P = 0.01) \) (Table 2). Age (continuous or categorical variable), sex, extension of hemorrhage into midbrain, anticoagulation, prothrombin time \( > 20 \text{ seconds} \), sodium, glucose, mean arterial pressure (continuous or categorical variable), and pulse rate (continuous and categorical variables) were not predictors of 30-day mortality. Multivariate analyses showed 2 independent prognostic indicators of 30-day mortality: GCS \( \leq 8 \) (odds ratio [OR] 16.7, CI 5.0 to 55.1) and hydrocephalus based on visual analysis (OR 5.5, CI 1.7 to 18.1). This model (GCS \( \leq 8 \) and hydrocephalus) has a sensitivity of 55% and a specificity of 90%. The positive predictive value and negative predictive value for the 30-day mortality were 70% and 83%, respectively. When both attributes (GCS \( \leq 8 \) and hydrocephalus) were present, 4 (20%) of 20 patients survived, and when both attributes were missing, 50 (96%) of 52 patients survived. When the categorical hydrocephalus variable was replaced in the model by the continuous measure, the resulting OR was 1.17 (CI 1.0 to 1.3), meaning that each 1-point increase in the hydrocephalus score was associated with a 17% increased odds of dying.

Next, we analyzed the results separately for putaminal hemorrhage and the medial group. By multivariate analysis, only a GCS \( \leq 8 \) is predictive of 30-day mortality in the medial group \( (P = 0.0002, OR = 16.5, CI 3.7 \text{ to } 73.4) \). Both GCS \( \leq 8 \) \( (P = 0.002, OR = 37.7, CI 3.6 \text{ to } 396.9) \) and hydrocephalus (by visual analysis) \( (P = 0.005, OR = 27.4, CI 2.7 \text{ to } 282.6) \) were predictive of 30-day mortality for the putaminal hemorrhage group. When both attributes were present in putaminal hemorrhage (GCS \( \leq 8 \) and hydrocephalus), 1 (11%) of 9 patients survived, and when both attributes were missing 28 (100%) of 28 patients survived. This model (GCS \( \leq 8 \) and hydrocephalus) has a sensitivity of 57% and a specificity of 91% for predicting 30-day mortality in the putaminal hemorrhage group. The positive predictive value and negative

<table>
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<th>Categorical Variable</th>
<th>Mortality</th>
<th>No Mortality</th>
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<td><strong>Medial group</strong></td>
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<td>GCS ( \leq 8 ) n (%)</td>
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<tr>
<td>No 4 (28.6) 33 (86.8)</td>
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<td>Yes 12 (46.2) 3 (11.5)</td>
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<td><strong>Lateral group</strong></td>
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<tr>
<td>GCS ( \leq 8 ) n (%)</td>
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<tr>
<td>No 3 (21.4) 31 (91.2)</td>
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<td>No 4 (26.7) 30 (90.9)</td>
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<td>Hydrocephalus,† n (%)</td>
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<tr>
<td>No 9 (40.9) 25 (96.2)</td>
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<td>( &lt;0.0001 )‡</td>
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<tr>
<td>Yes 13 (59.1) 1 (3.8)</td>
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</table>

*Visual analysis of hydrocephalus.  †Categorization of method of Diringer et al (hydrocephalus score \( \geq 1 \)).  ‡\( P \) by \( \chi^2 \) test; §\( P \) by Fisher exact test.
predictive value for 30-day mortality associated with putaminal hemorrhage were 73% and 84%, respectively.

Neurosurgical intervention was deemed necessary in 10 patients with deep cerebral hemorrhage after clinical deterioration. In the remaining patients, ventriculostomy was not performed because of a poor clinical state or because of family wishes against aggressive intervention. Eight patients had external ventricular drain insertion only (thalamic hemorrhage, 4 patients; putaminal hemorrhage, 3 patients; and caudate hemorrhage, 1 patient). Four of these patients died, and 2 patients with modified Rankin score 5, 1 patient with modified Rankin score 3, and 1 patient with modified Rankin score 1 survived. Two patients were subjected to craniotomy for evacuation of the hematoma; of these, one patient died, and the other survived (with modified Rankin score 5 at 30 days). In our series, surgical intervention (external ventricular drainage or craniotomy) in patients with GCS ≤8 was associated with poor outcome (modified Rankin score 5 or 6).

### Discussion

Hydrocephalus and not the size of the deep cerebral hemorrhage is an independent risk factor for 30-day mortality associated with deep cerebral hemorrhage. However, when we analyzed the medial and lateral groups separately, hydrocephalus remained an independent prognostic indicator only for the lateral group (putaminal hemorrhage). Remarkably, 30-day mortality was the same for the medial group (29%) and the lateral group (29%). A possible explanation for this finding is that hydrocephalus resulting from putaminal hemorrhage occurs with a larger volume of hemorrhage. There is extension of the hemorrhage laterally into the frontoparietal cortex and inferiorly into the medial temporal lobe. Extension of the hemorrhage medially into the thalamus and caudate nucleus leads to rupture into the ventricles. The mass effect from the lateral deep cerebral hemorrhage results in midline shift and obstruction at Monro’s foramen. Although a small dorsomedially located thalamic hemorrhage being adjacent to the third ventricle was sufficient to cause intraventricular hemorrhage and hydrocephalus, 30-day mortality in this group was low. This possibly suggests that hydrocephalus resulting from mass compression is a better determinant of 30-day mortality than is hydrocephalus resulting from the obstruction of Monro’s foramen by the hemorrhage.

Three studies before the study by Diringer et al analyzed the value of hydrocephalus in predicting mortality in supratentorial intracerebral hemorrhage. Kumral et al concluded that hydrocephalus was a predictor of mortality in thalamic hemorrhage. Radberg et al analyzed lobar, basal ganglia, and brain stem hemorrhage and found that dilatation of the contralateral ventricle was associated with a mortality of 67%. Multivariate analysis of this heterogeneous population to determine whether hydrocephalus was an independent predictor of mortality was not performed in either of these studies. In addition to low GCS and large volume of hematoma, it has been reported that hydrocephalus is an independent predictor of 30-day mortality in thrombolysis-related lobar hemorrhage.

Diringer et al correctly attributed the lack of inclusion of hydrocephalus in previous studies involving intracerebral hemorrhage to the difficulty of quantifying hydrocephalus. The authors developed a scoring system for identifying hydrocephalus. We used a simple method of identifying hydrocephalus (NECT) and the method of Diringer et al. At independent readings, we have obtained a similar percentage of patients with hydrocephalus. The OR (5.5) for 30-day mortality in the present study seems higher than the marginally increased OR (1.63) reported by Diringer et al; however, these ratios cannot be compared directly because we analyzed hydrocephalus as a categorical variable, and Diringer et al analyzed hydrocephalus as.
a continuous variable. When we replaced our categorical variable with the continuous variable as derived by Diringer et al, the resulting OR was 1.17.

Surgical intervention (with external ventricular drainage and craniotomy) in our patients did not improve outcome. The number of patients with surgical intervention in the present study was too small to carry out further analysis. The present study cannot definitively analyze the effect of ventriculostomy at presentation or after deterioration from obstructive hydrocephalus. However, none of our 8 cases that were managed with ventriculostomy had an improved GCS. Thus, hydrocephalus in deep cerebral hemorrhage is best interpreted as a telltale sign of prognosis.

In contrast to previous studies, an increased mean arterial pressure on admission was not a predictor of mortality.5 Blood pressure on admission in our patients was the highest blood pressure in the first 24 hours. In our institution, patients with mean arterial pressure >130 mm Hg were given an antihypertensive drug, such as labetalol. Hence, blood pressure readings after admission were lower. The data in the literature reporting the importance of blood pressure in predicting mortality are conflicting.1,9–12 One study found that high blood pressure was related to increased mortality in basal ganglia hemorrhage but not in subcortical, brain stem, or cerebellar hemorrhage.13 Increased blood pressure may be a reflection of brain stem distortion and a compensating response to increased intracranial pressure and decreased cerebral perfusion pressure. Not only are treatment goals unknown, but the relationship between enlargement of the intracerebral hematoma and baseline blood pressure is controversial as well.10,14,15 There have been concerns about the rapid reduction of blood pressure in intracerebral hemorrhage, and a recent retrospective study has suggested that there is increased mortality in patients with a rapid decline in blood pressure within 24 hours of the onset of intracerebral hemorrhage.16 Although a recent study12 reported an association between fever and poor outcome, we did not find that association in the present study. This difference may be due to the different end point in both studies: death versus outcome. In addition, the earlier presence of fever may be related to the effect of the hemorrhage on the thermoregulatory centers in the hypothalamus and brain stem, whereas the presence of fever later may be an effect of both a central mechanism and infection.

Radberg et al6 found that the size of the hemorrhage was larger in patients who were anticoagulated and that a larger size was associated with increased mortality. Franke et al17 did not find a relationship between anticoagulation and mortality when the volume of the hemorrhage was taken into consideration. We were surprised to find that anticoagulation was not an independent predictor of mortality in our patients. This may be related to the small number (17 of 100) of patients with deep cerebral hemorrhage on anticoagulation; only 62.5% of those patients had a prothrombin time >20 seconds. Even when we analyzed the results with prothrombin time used as a marker of patients receiving effective anticoagulation with warfarin, a non-significant difference was found. We may have been unable to find this association because serial NECT scans were not available for all patients. The importance of demographic variables as predictors of mortality has not been confirmed in the present study. Likewise, other clinical variables within the first 24 hours, such as pulse rate, temperature, serum sodium, serum glucose, and white cell count, were eliminated after a multivariate analysis.

Advanced age was not a predictor of mortality in the present study, whether age was used as a continuous or a categorical variable (age >65 years). This was consistent with the findings in several studies.1,2,11,14 However, we acknowledge that in some studies, advanced age was found to be associated with higher mortality.19,20 Advanced age may be a factor for a systemic complication many months after the presentation of hemorrhage, but the present study was limited to outcome in the first month.

The present study confirmed the importance of the GCS and hydrocephalus as predictors of 30-day mortality in putaminal hemorrhage. Our model for predicting 30-day mortality from putaminal hemorrhage has modest sensitivity but high specificity and moderately high predictive value. Such factors may be taken into consideration when the level of care is assessed. Renewed interest has emerged in the literature concerning surgical management. The Surgical Treatment for Intracerebral Hemorrhage (STICH) study, a small pilot study, suggested the possible favorable effect of surgical treatment.21 Our results are useful in planning future surgical trials in patients with deep cerebral hemorrhage but may need to be validated prospectively.

References


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