Hydrocephalus: A Previously Unrecognized Predictor of Poor Outcome From Supratentorial Intracerebral Hemorrhage

Michael N. Diringer, MD; Dorothy F. Edwards, PhD; Allyson R. Zazulia, MD

Background and Purpose—Although several factors have been identified that predict outcome after intracerebral hemorrhage (ICH), no previous study has investigated the impact of hydrocephalus. The purpose of this study was to determine whether the presence of hydrocephalus after ICH would predict mortality and functional outcome.

Methods—Patients with spontaneous supratentorial ICH were identified in our prospectively collected database to determine the following: age, sex, race, past medical history; Glasgow Coma Scale (GCS) score and blood pressure on admission; use of mechanical ventilation, mannitol, and ventriculostomy; and medical complications. CT scans performed within 24 hours of hemorrhage were retrospectively analyzed to determine lesion size and location, pineal shift, cisternal effacement, intraventricular hemorrhage (IVH), and hydrocephalus. Outcome was determined with use of hospital disposition (dead, nursing home, rehabilitation, home) and functional outcome (Functional Independence Measure [FIM]) at 3 months. Patients with and without hydrocephalus were compared and univariate and multivariate analyses performed to determine whether hydrocephalus was an independent predictor of mortality. Data are presented as mean ± SD.

Results—Of the 81 patients studied, 40 had hydrocephalus. Those with hydrocephalus were younger (57 ± 15 versus 67 ± 15 years), had lower GCS scores (8.2 ± 4.2 versus 11 ± 2.9), were more likely to have ganglionic or thalamic hemorrhages, and were intubated more frequently (70% versus 27%). Hospital mortality was higher in patients with hydrocephalus (51% versus 2%), and fewer patients went home (21% versus 35%). Those who died had higher hydrocephalus scores (9.67 ± 7.1 versus 5.75 ± 4.5). Outcome was no different if a ventriculostomy was placed. The final logistic regression model included hydrocephalus score, gender, GCS, and pineal shift, and it correctly predicted 85% of patients as dead or alive. Multivariate analyses indicated that hydrocephalus is an independent predictor of mortality.

Conclusions—We conclude that hydrocephalus is an independent predictor of mortality after ICH. (Stroke. 1998;29:1352-1357.)

Key Words: hydrocephalus ■ intracerebral hemorrhage ■ intraventricular hemorrhage ■ stroke outcome

There has been considerable interest in predicting outcome after ICH. A number of studies have investigated the relationship among clinical and radiographic factors and outcome. Several variables have been found that predict mortality, although they are not consistently identified across studies. Clinical factors recognized include level of consciousness measured by the GCS score, blood pressure, and pulse pressure. Radiographic features include hematoma size, midline shift, and the presence of IVH. None of these studies have investigated the influence of hydrocephalus or the use of ventriculostomy on outcome.

Therapeutic options for patients with ICH are limited; the efficacy of surgical intervention has not been clearly established, and medical management, including treatment of hypertension and use of osmotic agents, remains controversial. In addition, despite its frequent use, the role of ventriculostomy in the management of hydrocephalus following ICH is not well defined.

Through the use of our prospectively collected clinical database, we sought to investigate the relationship between hydrocephalus and outcome in ICH. CT scans were retrospectively analyzed to determine lesion size and location, degree of pineal shift, cisternal effacement, IVH, and hydrocephalus. These variables were correlated with clinical features, treatment and outcome with univariate and multivariate analyses.

Subjects and Methods

We prospectively record information on all admissions to the neurology/neurosurgery ICU of a tertiary care academic hospital using a computerized database (QUiC, Space Labs Inc). Data collected include demographics, past medical history, clinical presentation, diagnoses, treatments, complications, and outcome. On a
daily basis an individual nurse collects and records data using strict guidelines. The database was searched to identify all patients admitted with a primary diagnosis of supratentorial ICH over a 20-month period. Patients were excluded if the hemorrhage was associated with trauma or subarachnoid hemorrhage or if a CT scan performed within 24 hours of the hemorrhage was not available. The study was approved by the institution’s Human Studies Committee.

Clinical Data
The following historical data were included in the analysis: age, sex, race, history of hypertension, atrial fibrillation, and prior stroke. Data collected on presentation included interval from ictus to admission, GCS score, and blood pressure. The use of mechanical ventilation, mannitol, and ventriculostomy were noted, as was the presence of medical complications, including congestive heart failure, significant arrhythmias, pneumonia, and sepsis. Outcome was determined by hospital disposition (dead, nursing home, inpatient rehabilitation, home) and 3-month functional outcome as assessed by use of the telephone version of the FIM.12

Clinical Management
All patients were admitted to the neurology/neurosurgery ICU and managed concurrently by the ICU team and either the neurology or neurosurgery service. Management followed a standardized approach.13 Airway protection with endotracheal intubation was performed for patients with a GCS score of ≤8 or as needed. Mean arterial pressure was treated with labetalol, hydralazine, or intravenous nicardipine when it exceeded 135 to 150 mm Hg or if signs of end-organ dysfunction (cardiac ischemia, heart failure, renal failure) developed. Osmotic therapy with mannitol was administered to patients if there was concern for or evidence of increased intracranial pressure. Hyperventilation and barbiturates were not used. General criteria for surgical intervention included moderate-to-severe cortical hemorrhage or deterioration due to hematoma extension. The decision to insert a ventriculostomy was based on clinical rather than radiographic criteria. If hydrocephalus was thought to have contributed to deteriorating or poor clinical status a ventriculostomy catheter (Codman External Drainage System II, Codman & Shurtleff, Inc) was placed.

Decision to withdraw therapy was always made after extensive discussions with the patient’s family. Such decisions were based on the expressed wishes of the patient or a designated surrogate. The discussions were always initiated in the setting of a very poor neurological condition that was either not improving or deteriorating despite aggressive therapy.

CT Analysis
Cranial CT scans performed within 24 hours of hemorrhage were retrospectively reviewed by investigators blinded to clinical data. ICH was classified as deep (arising in the thalamus or basal ganglia) or lobar. ICH volume was calculated using the formula A×B×C/2, where A, B, and C represent the clot diameters in 3 dimensions at right angles to each other, as described by Broderick et al.14 Degree of IVH was recorded using the methods of Ruscallada and Peiro,9 in which the amount of blood visualized on CT is determined for the third, fourth, and each lateral ventricle, and the four scores are summed. The left and right ambient cisterns were scored as normal, effaced, or obliterated and given a score of 0, 1, or 2, respectively. The scores for the 2 cisterns were summed and then the total score was divided into 3 groups based on total scores of 0, 1 to 2, and 3 to 4. Pineal shift was measured (in millimeters) and corrected for magnification.

Although several scoring systems exist for grading hydrocephalus, none can be applied to situations in which a mass lesion distorts normal brain anatomy.15,16 We therefore developed a system that grades each of 8 portions of the ventricular system independently. The hydrocephalus score was determined by grading the frontal horn, atrium, and temporal horn of each lateral ventricle and the third and fourth ventricles. Each region was graded as mild or moderate or marked using the following criteria: frontal horn, rounding with increased radius, decreased ventricular angle, and sulcal effacement of the frontal lobe; atria, rounding and enlargement with sulcal effacement of the parieto-occipital lobe; temporal horns, increasing width; third ventricle, increased width with ballooning of the anterior recess; and fourth ventricle, ballooning. A score of 0 for no, 1 for mild, 2 for moderate, and 3 for marked hydrocephalus was assigned to each region and the scores summed. A total score of 0 indicates no hydrocephalus and the maximum score of 24 indicates marked hydrocephalus of all ventricles.

Statistical Analysis
Patients were divided into 2 groups: those with hydrocephalus (score of ≥1) and those without hydrocephalus. Comparisons between groups were performed with use of independent sample t tests and Fisher exact tests, as appropriate. All analyses were computed with the SAS System for Windows, version 6.12 (SAS Inc). In order to determine intrarater and interrater reliability of the hydrocephalus score 14 CT scans were selected and scored independently by two observers (M.N.D. and A.R.Z.) as well as on two separate occasions by one observer (A.R.Z.). Intraclass correlation coefficients for intrarater and interrater hydrocephalus scores were 0.83 and 0.92, respectively.

A series of analyses were performed to derive a model to identify factors related to hospital mortality, which was compared to the actual outcome. Continuous variables were converted to binary variables using the following cut points: GCS score (≤8 versus >8), hematoma size (≤27 versus >27 cc), pulse pressure (≤85 versus >85), age (≤65 versus >65), cistern score (0 versus ≥1), and deep (thalamic and basal ganglia) versus lobar location. Univariate logistic regression equations were then computed for each potential predictor variable. Variables were included in the multivariate analysis if the univariate P value was ≤0.25. The first multivariate regression included non-CT variables (age, gender, race, GCS score, and pulse pressure) to allow us to explore the impact of the CT variables on the model. A backward selection procedure was used to select the subset of predictors from this group of variables. The second model was fit using the variables remaining from the first analysis and adding CT variables one at a time. A P value of <0.10 was used as the criterion for retention of each new variable in the model. The likelihood ratio was used to evaluate whether there was a significant improvement in the model as each new variable was added. The final multivariate model was fit using location and the interaction of hydrocephalus and location. Predicted probabilities of death were computed for each observation. A probability cut point of 0.50 was used to classify observations as events or nonevents. The overall accuracy of the models was determined by comparing the predicted values with the actual events.

Results
Of the 81 patients enrolled in the study, 40 had some degree of hydrocephalus. The interval from hemorrhage to admission to the ICU was 12.8±10.5 hours and did not differ between patients with and those without hydrocephalus. Those with hydrocephalus were, on average, 10 years younger than those without hydrocephalus (Table 1). The patients with hydrocephalus were more likely to have lower GCS scores and narrower pulse pressures on admission (P<0.005 and P<0.05, respectively).

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Selected Abbreviations and Acronyms

FIM = Functional Independence Measure
GCS = Glasgow Coma Scale
ICH = intracerebral hemorrhage
ICU = intensive care unit
IVH = intraventricular hemorrhage
OR = odds ratio
TABLE 1. Clinical Characteristics

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>All Subjects (n=81)</th>
<th>Hydrocephalus (n=40)</th>
<th>No Hydrocephalus (n=41)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age*</td>
<td>Mean±SD: 62.4±16.1</td>
<td>57.4±15.2</td>
<td>67.3±15.7</td>
</tr>
<tr>
<td>Range</td>
<td>18–91</td>
<td>29–88</td>
<td>18–91</td>
</tr>
<tr>
<td>Race</td>
<td>Black 46 (57%)</td>
<td>26 (65%)</td>
<td>20 (49%)</td>
</tr>
<tr>
<td></td>
<td>White 35 (43%)</td>
<td>14 (35%)</td>
<td>21 (51%)</td>
</tr>
<tr>
<td>Gender</td>
<td>Male 47 (58%)</td>
<td>25 (63%)</td>
<td>22 (54%)</td>
</tr>
<tr>
<td></td>
<td>Female 34 (42%)</td>
<td>15 (38%)</td>
<td>19 (46%)</td>
</tr>
<tr>
<td>Pulse Pressure†</td>
<td>Mean±SD: 98.7±3.9</td>
<td>8.2±4.2</td>
<td>11.0±2.9</td>
</tr>
<tr>
<td></td>
<td>Range: 3–15</td>
<td>3–15</td>
<td>4–15</td>
</tr>
<tr>
<td>MAP</td>
<td>Mean±SD: 114.6±33.8</td>
<td>114.5±32.8</td>
<td>114.8±35.2</td>
</tr>
<tr>
<td></td>
<td>Range: 32–164</td>
<td>55–164</td>
<td>32–162</td>
</tr>
</tbody>
</table>

MAP indicates mean arterial blood pressure. *P<0.0005; †P<0.05.

The incidence of hydrocephalus was higher in patients with deep hemorrhages (P<0.001; Table 2). Lesion size did not differ in those with and without hydrocephalus. The IVH score and degree of cisternal effacement were greater in the hydrocephalus group (P<0.004 and P<0.002, respectively);

TABLE 2. CT Characteristics

<table>
<thead>
<tr>
<th>Location</th>
<th>Hydrocephalus (n=40)</th>
<th>No Hydrocephalus (n=41)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deep</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thalamus* (n=10)</td>
<td>8 (80%)</td>
<td>2 (20%)</td>
</tr>
<tr>
<td>Basal ganglia† (n=28)</td>
<td>20 (71%)</td>
<td>8 (29%)</td>
</tr>
<tr>
<td>Lobar‡ (n=43)</td>
<td>12 (28%)</td>
<td>31 (72%)</td>
</tr>
<tr>
<td>Lesion Size</td>
<td>Mean±SD: 32.9±32.3</td>
<td>33.7±32.0</td>
</tr>
<tr>
<td></td>
<td>Range: 0–141</td>
<td>1–176</td>
</tr>
<tr>
<td>Pineal Shift†</td>
<td>Mean±SD: 1.4±2.2</td>
<td>3.4±3.4</td>
</tr>
<tr>
<td></td>
<td>Range: 0–10</td>
<td>0–10</td>
</tr>
<tr>
<td>IVH Score‡</td>
<td>Mean±SD: 5.0±3.5</td>
<td>0.8±1.6</td>
</tr>
<tr>
<td></td>
<td>Range: 0–11</td>
<td>0–6</td>
</tr>
<tr>
<td>Cisterns score†</td>
<td>0 (0)</td>
<td>21 (53%)</td>
</tr>
<tr>
<td></td>
<td>1 (1–2)</td>
<td>13 (33%)</td>
</tr>
<tr>
<td></td>
<td>2 (3–4)</td>
<td>6 (15%)</td>
</tr>
</tbody>
</table>

*P<0.05; †P<0.002; ‡P<0.005.

However, pineal shift was greater in those patients without hydrocephalus (P<0.003).

As expected, patients with hydrocephalus were significantly more likely to receive a ventriculostomy (P<0.001). Only 1 patient without hydrocephalus in the retrospective CT scan analysis had a ventriculostomy placed compared with 12 patients (30%) with hydrocephalus. Those with hydrocephalus were more frequently intubated (70% versus 27%; P<0.0001), most likely a reflection of their lower GCS scores. The incidence of congestive heart failure, seizures, and pneumonia did not differ between those with and without hydrocephalus.

Outcome differed considerably between the groups (Table 3). Over half of the patients with hydrocephalus died compared with only 2% of those without hydrocephalus. Similarly, fewer patients with hydrocephalus were discharged to home or a rehabilitation facility. Among the survivors, 3-month FIM scores were not different in those patients treated with and without hydrocephalus. A box plot of the hydrocephalus scores in those who survived and those who died is presented in the Figure.

Outcome did not differ in those patients treated with a ventriculostomy. Hematoma size tended to be smaller (19.8±22.1 versus 38.5±34.7 cc; P=0.09) and IVH score was higher (7.4±3.6 versus 3.9±2.6; P<0.004) in those treated with ventriculostomy, whereas age and GCS score did not differ. Mortality, hospital disposition, and FIM score at 3 months did not differ between those patients treated with and without a ventriculostomy.

Univariate logistic regression analyses were computed to determine the relationship between individual predictor variables and mortality. The parameter estimates, standard errors, ORs, and P values of each of these variables are presented in Table 4. Any variable in which the 95% confidence limits of the OR do not include 1 conveys significantly increased or decreased risk of mortality. The variables that emerged from the analysis as significant univariate predictors of mortality were deep hemorrhage location (P<0.04), cisternal effacement (P<0.003), pineal shift (P<0.001), IVH score (P<0.0001), GCS score (P<0.0001), and hydrocephalus (P<0.0001).
The final multivariate logistic regression model and the variables not included in the final model are presented in Table 4. GCS scores less than 8, male gender, pineal shift, and hydrocephalus are independent predictors of mortality. The odds of dying were 6.78 times greater for patients with admission GCS scores of $\leq 8$. Each 1-point increase in the hydrocephalus score was associated with a 1.64-fold increased risk of mortality. Each millimeter of pineal shift was associated with a 1.27-fold increased risk of dying. Comparison of the likelihood statistics for each model (45.54 versus 47.76) suggests that the addition of location and the interaction of location with hydrocephalus did not significantly improve the fit of the model. Thus, after accounting for the contributions of all other variables in the model, hydrocephalus was an independent predictor of mortality. The model correctly classified 85% of the patients included in the analysis as alive or dead. Ninety percent of the patients who survived were correctly classified, and 79% of the patients who died were correctly classified.

**Discussion**

This study demonstrates for the first time the impact of hydrocephalus on outcome from ICH. Hydrocephalus was associated with a considerably higher mortality and fewer patients being discharged to home. Univariate and multivariate analyses indicate that hydrocephalus is an independent predictor of outcome. This finding, however, awaits validation with an independent data set. Outcome was no different in patients treated with a ventriculostomy.

Over the past 2 decades a large number of investigators have attempted to define factors associated with outcome from ICH. Predictors of outcome in early studies included age, ICH location, electrocardiographic abnormalities, and history of hypertension. More recent studies have also identified lesion size, level of consciousness, midline shift, blood pressure or pulse pressure, and IVH as factors related to outcome.

Review of these studies reveals considerable variability in the factors identified. Some of this variability results from the statistical techniques used, because the univariate analyses used in early studies determine only whether a single factor is related to outcome. The more recent studies applied multivariate regression analyses; these determine which of several factors, when taken together, relate to outcome. This technique has the advantage of being able to determine whether 2 factors covary and only 1 independently predicts outcome. Factors identified with multivariate techniques include age, ICH size, level of consciousness, IVH, and pulse pressure.

Despite the frequency with which it occurs in ICH patients, none of these studies included hydrocephalus in their analyses. The reason for this omission is not clear, although it may reflect the fact that a means of quantifying hydrocephalus in the setting of ICH did not exist. Previously available methods for defining hydrocephalus all relied on the relationship between ventricular size and shape and the anatomy of the surrounding tissues. In the presence of a mass lesion that distorts the normal anatomy, these methods cannot be applied. Additionally, the mass of the hematoma may compress

### Table 4. Comparison of ORs From Univariate and Multivariate Logistic Regression Models

<table>
<thead>
<tr>
<th>Variable</th>
<th>$\beta$</th>
<th>SE$\beta$</th>
<th>$P&lt; $</th>
<th>OR</th>
<th>$\beta$</th>
<th>SE$\beta$</th>
<th>$P&lt; $</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
<td>-0.78</td>
<td>0.54</td>
<td>0.15</td>
<td>2.17 (0.76–6.84)</td>
<td>1.75</td>
<td>0.89</td>
<td>0.05</td>
<td>5.73 (1.15–40.08)</td>
</tr>
<tr>
<td>Age $\geq 65$</td>
<td>0.02</td>
<td>0.51</td>
<td>0.97</td>
<td>1.02 (0.37–2.84)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulse pressure $&gt;85$ mm Hg</td>
<td>0.04</td>
<td>0.51</td>
<td>0.92</td>
<td>1.05 (0.37–2.86)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Size $&gt;27$ cc$^3$</td>
<td>0.71</td>
<td>0.38</td>
<td>0.06</td>
<td>2.02 (0.96–4.39)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cistern score</td>
<td>0.66</td>
<td>0.22</td>
<td>0.003</td>
<td>1.92 (1.27–3.11)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IVH Score</td>
<td>0.31</td>
<td>0.08</td>
<td>0.001</td>
<td>1.36 (1.17–1.61)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GCS Score $\leq 8$</td>
<td>2.54</td>
<td>0.63</td>
<td>0.0001</td>
<td>12.75 (4.0–43.9)</td>
<td>1.91</td>
<td>0.89</td>
<td>0.03</td>
<td>6.77 (1.27–46.95)</td>
</tr>
<tr>
<td>Pineal shift</td>
<td>0.28</td>
<td>0.08</td>
<td>0.001</td>
<td>1.33 (1.12–1.60)</td>
<td>0.24</td>
<td>0.13</td>
<td>0.06</td>
<td>1.28 (1.01–1.68)</td>
</tr>
<tr>
<td>Hydrocephalus</td>
<td>0.23</td>
<td>0.05</td>
<td>0.0001</td>
<td>1.26 (1.13–1.42)</td>
<td>0.28</td>
<td>0.09</td>
<td>0.001</td>
<td>1.63 (1.20–2.31)</td>
</tr>
<tr>
<td>Deep location</td>
<td>1.09</td>
<td>0.53</td>
<td>0.04</td>
<td>3.00 (1.08–8.95)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

OR indicates odds ratio with 95% confidence interval; $\beta$, beta weight. See “Subjects and Methods” for detail of analyses.
sites of communication within and between ventricles, leading to “trapped ventricles.” In an attempt to overcome these problems, we chose to analyze separate regions of each lateral ventricle as well as the third and fourth ventricles independently. The results of our intrarater and interrater reliability testing indicate that the scale can be applied in a consistent and reliable manner.

We used several approaches to determine whether hydrocephalus is an independent predictor of mortality. The OR of 1.26 (95% confidence limits, 1.13 to 1.42) in the univariate analysis indicates that hydrocephalus is a predictor of mortality. The present multivariate analysis included all potentially confounding variables identified by our univariate analyses and the literature. This model yielded an OR of 1.63 (1.20 to 2.31) for hydrocephalus, which suggests that it is an independent predictor of mortality. Surprisingly, the addition of hydrocephalus to the model resulted in some previously identified predictors of outcome (size, IVH) being forced out of the model. This suggests that size and IVH may be surrogates of the more direct predictor—hydrocephalus. Caution should be exercised in interpreting this finding, however, since these results await validation with an independent data set. This model correctly classified as alive or dead 85% of the patients, a degree of accuracy very similar to previously published models.

The relationship between hydrocephalus and outcome may vary with different hemorrhage locations. In hematomas that occur close to the ventricles, IVH and thus hydrocephalus are common. Small thalamic hemorrhages can easily cause hydrocephalus by compressing the cerebral aqueduct, whereas small ganglionic hemorrhages rarely have any impact on ventricular size. The relationship between hydrocephalus and hematoma location was explored using an interaction term; however, despite the rate of hydrocephalus differing by location, the interaction term did not improve the predictive power of the model.

The association we found between male gender and increased mortality was unexpected. Although previous studies had not identified such a relationship, few studies searched for it. Two studies report a trend toward increased mortality in males that was not statistically significant. We plan to account for it. Two studies report a trend toward increased mortality in males that was not statistically significant. We plan to account for it. Two studies report a trend toward increased mortality in males that was not statistically significant.

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The withdrawal of care must be taken into account when predictive models are developed. Ideally, to develop an accurate model, all patients should receive maximal therapy. The current ethical and social climate makes this impossible. Therefore, although not done in the vast majority of published reports on outcome from ICH, it is important to report the frequency of this occurrence to facilitate interpretation of the data.

While this study clearly demonstrates the relationship between the presence of hydrocephalus and poor outcome, the impact of treatment of hydrocephalus with ventriculostomy is much less clear. Our previous report indicated that placement of a ventriculostomy rarely led to clinical and radiographic improvement and was associated with a high mortality rate. That study, however, included only patients treated with ventriculostomy. The present study includes patients with hydrocephalus regardless of whether a ventriculostomy was placed, and there was no difference in outcome. It is important to note that patients were not randomized and that decisions to place a ventriculostomy were clinically based; thus, it is not possible to exclude the chance that those treated with a ventriculostomy might have had a worse outcome had the procedure not been performed. This question can be answered only by a prospective randomized study. In addition, the lack of an apparent response to ventriculostomy may have resulted from failure of the ventricular catheter to adequately drain cerebrospinal fluid because of obstruction by IVH. The use of thrombolytics instilled into the catheter may be helpful in this setting and should be investigated in a controlled trial.

Acknowledgments

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References


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