Published in final edited form as:

Neurology. 2008 March 11; 70(11): 848–852. doi:10.1212/01.wnl.0000304930.47751.75.

Intraventricular hemorrhage:

Anatomic relationships and clinical implications

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Abstract

Background: Spontaneous intracerebral hemorrhage (ICH) is frequently associated with intraventricular hemorrhage (IVH), which is an independent predictor of poor outcome. The purpose of this study was to examine the relationship between ICH volume and anatomic location to IVH, and to determine if ICH decompression into the ventricle is truly beneficial.

Methods: We retrospectively analyzed the CT scans and charts of all patients with ICH admitted to our stroke center over a 3-year period. Outcome data were collected using our prospective stroke registry.

Results: We identified 406 patients with ICH. A total of 45% had IVH. Thalamic and caudate locations had the highest IVH frequency (69% and 100%). ICH volume and ICH location were predictors of IVH ($p < 0.001$). Within each location, decompression ranges (specific volume ranges where ventricular rupture tends to occur) were established. Patients with IVH were twice as likely to have a poor outcome (discharge modified Rankin scale of 4 to 6) (OR 2.25, $p = 0.001$) when compared to patients without IVH. Caudate location was associated with a good outcome despite 100% incidence of IVH. Spontaneous ventricular decompression was not associated with better outcome, regardless of parenchymal volume reduction ($p = 0.72$).

Conclusions: Intraventricular hemorrhage (IVH) occurs in nearly half of patients with spontaneous intracerebral hemorrhage (ICH) and is related to ICH volume and location. IVH is likely to occur within the “decompression ranges” that take into account both ICH location and volume. Further, spontaneous ventricular decompression does not translate to better clinical outcome. This information may prove useful for future ICH trials, and to the clinician communicating with patients and families.

Spontaneous intracerebral hemorrhage (ICH) accounts for one fifth of all strokes. It is a devastating illness with 30% mortality and a high rate of morbidity among survivors.¹⁻⁵ Most cases are attributed to hypertension or amyloid angiopathy.^{2,5,6} ICH occurs most frequently in the putamen (35 to 50%), followed by lobar (30%), thalamus (10 to 15%), pons (5 to 12%), caudate (7%), and the cerebellum (5%).⁷⁻¹⁵

Intraventricular extension of the hematoma (IVH) is an independent predictor of poor outcome in patients with ICH.^{1,16-21} Several articles addressed the importance of IVH in outcome

prediction and development of hydrocephalus.^{3,16,18,20} Others have correlated the total volume (both ICH and IVH) with outcome with a “lethal volume” of IVH greater than 20 mL.²² Most recently, the dynamic nature of IVH was studied in a subanalysis of activated factor VII phase II trial,²³ showing a relation between thalamic location and the frequency of IVH. Most studies used sophisticated volumetric analysis methods for IVH volume determination.²⁴

The purpose of this study was to further characterize the phenomenon of IVH, its relationship to ICH volume, and anatomic location. We hypothesized that IVH frequency was a function of both location and size of the hematoma: the larger the ICH and the closer the ICH is to the ventricle, the more likely IVH is to occur. We further hypothesized that for any given location there is a range of parenchymal volume in which the ICH tends to decompress into the ventricles (decompression range). Theoretically below this volume the rate of IVH is very low and above it IVH becomes universal. Finally, we explored the hypothesis that spontaneous “decompression” of ICH into the ventricles may actually be beneficial.

METHODS

We retrospectively reviewed the charts of all patients admitted to our stroke center between April 2003 and June 2006 with the diagnosis of ICH, identified in our prospective stroke registry. Patients were included if they had spontaneous non-traumatic ICH. Patients were excluded from the analysis if they had primary IVH, were treated with activated Factor VII, had ICH secondary to vascular malformations or tumor, or if they experienced hemorrhagic conversion of an infarct. Patients with coagulopathy (defined as international normalized ratio of more than 1.5) or low platelet count (defined as platelet count less than 50,000) were included.

Two of the authors (H.H. and A.B.) who were blinded to clinical outcomes reviewed all CT scans to verify ICH location, ICH volume, and IVH presence and volume. ICH location was determined by the anatomic structure that contained the majority of the hematoma. ICH volume was determined using the ABC/2 method.²⁵ To facilitate clinical use of these data we chose to avoid volumetric analysis of IVH. Instead, we used a scoring system developed by Hijdra et al. that we termed “IVH score.” The score involves grading the amount of blood in each ventricle as 0, no blood; 1, sedimentation of blood in the posterior part; 2, partly filled with blood; or 3, completely filled with blood. The total amount of intraventricular blood (the IVH score) was the total of the four scores and ranged from 0 (no IVH) to 12 (all four ventricles completely filled with blood). This grading system is very easy and fast to obtain and has been shown to have an excellent interobserver agreement.²⁶ All medical charts were reviewed for baseline demographics, clinical presentation, laboratory values, surgical interventions such as external ventricular drainage (EVD), and outcome measures. Clinical outcome was assessed on discharge from the acute care hospital, using the modified Rankin Scale (mRS). Poor outcome was defined as mRS > 3. The study was approved by the Institutional Review Board.

Statistical analysis

Statistical analysis was carried out using SPSS for Windows, Version 15 (SPSS Inc., Chicago, IL). Volume data were logarithmically transformed to obtain normality. Continuous data were presented as either mean (95% CI for mean) or median (minimum–maximum) and compared using independent-samples Student *t* test or Mann-Whitney *U* test where appropriate. ICH volume in the different locations was compared using analysis of variance (ANOVA) with post hoc tests using Tukey honestly significant differences (HSD) method. Bivariate logistic regression was used to determine the independent effect of IVH on outcome. Categorical data were presented as frequencies and compared using the Pearson χ^2 or Fisher exact test. For the inter-rater reliability measurements we used the interclass correlation coefficient (ICC) for ICH

volume and IVH score and Kappa statistic for ICH location. A p value of <0.05 was considered statistically significant.

Decompression ranges

To determine the decompression range for each location we analyzed the normalized volume data to detect the range below which almost no IVH occurs (less than 10% of IVH cases) and above which IVH is universal (less than 10% of no-IVH cases). To achieve that we used a z score of 1.28 (mean +1.28 standard deviations) which corresponds to the upper 10% “tail” of the normal distribution of the non-IVH group as the upper limit and z score of -1.28 (mean, 1.28 SD, the lower 10% “tail” of the normal distribution) of the IVH group as the lower limit.

RESULTS

A total of 406 patients with spontaneous ICH were identified in our prospective stroke registry and included in the final analysis. The inter-rater reliability was excellent for ICH volume (ICC = 0.905, $p < 0.001$) and IVH score (ICC = 0.903, $p < 0.001$) and good for ICH location (kappa = 0.78, $p < 0.001$). There were 10 patients with a low platelet count and 31 patients with coagulopathy on admission. IVH was present in 183 patients (45.1%). The mean age was 61 years in the IVH group and 62.8 years in the non-IVH group (t test $p = 0.23$ for the difference in age); the median NIHSS was 18 (1 to 36) for the IVH group and 9 (1 to 36) for the non-IVH group (Mann-Whitney U test $p < 0.001$ for the difference in NIHSS); and the mean ICH volume was 25.2 mL for the IVH group and 11.5 mL for the non-IVH group (t test $p < 0.001$ for the difference in volume). No association was found between coagulopathy or low platelet count and IVH ($\chi^2 p = 0.3$). IVH frequency in the different locations is shown in table 1.

Location and volume analysis

Larger ICH volume was correlated with the presence of IVH ($r = 0.34$, $p < 0.0001$). The ICH decompression ranges are shown in table 1 and the figure. Cerebellar location had too few IVH cases to calculate a decompression range. All 12 cases of caudate head ICH were associated with IVH (mean volume 6 mL) so no decompression range could be determined.

Hospital course and outcome on discharge

Table 2 lists the overall poor outcome and mortality rates and the rates of EVD placement in IVH and non-IVH patients. After controlling for age and ICH volume, patients with IVH were twice as likely to have a discharge mRS of 4 to 6 when compared to patients without IVH (OR 2.25, 95% CI 1.40, 3.64, $p = 0.001$). Patients with IVH were 7.4 times more likely to be treated with EVD (OR 7.4, 95% CI 3.37, 16.30, $p < 0.001$). Patients receiving EVD (with or without IVH) had increased length of stay (LOS) (21 ± 17 days vs 9.5 ± 10.4 , $p < 0.005$) and were 3.4 times more likely to experience a poor outcome compared to patients who did not require EVD (OR 3.4, 95% CI 2.21, 5.09, $p < 0.001$). Overall, 85% of IVH patients receiving EVD had a poor outcome. However, EVD was not associated with increased mortality (9/40 for IVH with EVD vs 5/16 for IVH alone, $p = 0.2$). The rates of poor outcome and mortality in the different locations are shown in table 3.

Decompression analysis

We studied the hypothesis that decompression of the hematoma into the ventricle is beneficial. Theoretically when decompression occurs, the parenchymal component may decrease in volume. To account for that we used the decompression ranges as a guide to divide supratentorial ICH into two groups arbitrarily: the decompressed group included patients with ICH volumes in the lower half of their respective decompression range and had substantial IVH (IVH score > 3). The non-decompressed group included patients with ICH volumes from

the upper half of their respective decompression range and no IVH component. Poor outcome was observed in 11/14 (78.6%) patients in the decompressed group vs 20/29 (69%) in the non-decompressed group ($p = 0.72$, Fisher exact test).

DISCUSSION

We describe the incidence, anatomic correlation, clinical course, and outcome of IVH in a large unselected cohort of patients with spontaneous nontraumatic ICH. IVH was present in nearly half of our cohort. This study is unique in presenting the percentage of IVH according to location.

As hypothesized, we found size and location of the ICH to affect the rate of IVH. Our work is in agreement with previous work²³ in regard to the high likelihood of thalamic ICH to rupture into the ventricles. This may be due to the anatomic proximity of the thalamus to the third ventricle, as well as to the tendency for blood to spread medially.⁷ We identified a unique decompression range for each location. Below this range IVH is unlikely to occur, while above it the vast majority of ICH will be accompanied by IVH. The decompression range is very narrow for thalamic and pontine ICH, probably non-measurable for caudate location and fairly wide for lobar location. The authors hypothesize that in the acute phase of ICH as the hematoma enlarges, IVH will occur in this volume range. As with previous studies,^{17-19,27} we found IVH as well as ICH volume to be independent predictors of poor outcome. Patients with IVH were twice as likely to have poor outcome and nearly three times more likely to die when compared to their non-IVH counterparts. Proposed mechanisms for this IVH-induced morbidity include development of hydrocephalus, decreased consciousness, and IVH-induced inflammation.¹⁶ Interestingly, patients with caudate hemorrhage, all of whom had IVH, did relatively well compared to other locations. This finding is in agreement with a previous report,¹³ and may reflect the low volume of the parenchymal component of caudate hemorrhage as well as its distance from the motor tracts.

Our decompression analysis provides evidence that ventricular rupture is not beneficial. In fact, despite lower parenchymal volumes the patients in the decompression group did slightly worse. This is in agreement with previous works^{21,22} that demonstrated the independent prognostic value of IVH and the importance of the combined ICH and IVH volume in determining the patient's outcome. Furthermore, IVH patients were seven times more likely to be treated by EVD; however, the rate of poor outcome for patients with EVD was alarmingly high. While this is likely due to the larger volume of IVH and hydrocephalus, EVD-related morbidity such as rebleeding and infection may contribute to the observed poor outcome in these patients,²⁸ although this has been recently debated.²⁹ The poor outcome of patients with IVH with or without EVD should encourage the development and testing of new treatments for IVH such as intraventricular instillation of thrombolytic agents.³⁰⁻³²

ICH treatment is still evolving. Recent efforts have been aimed at preventing hematoma growth³³ and reducing hematoma size (minimally invasive stereotactic surgery + tPA for ICH evacuation). The announcement of the neutral results of the phase III study of activated Factor VII treatment for ICH³⁴ underscores the need for better patient selection in ICH therapy trials. We believe that the decompression ranges identified by this work for each location may represent a patient population that is at risk for deterioration and may have the most to gain from new therapies aimed at stabilizing or reducing hematoma volume.

Our study has several limitations. First, it is a retrospective analysis. As such, our observations need to be validated prospectively. Second, the length of follow-up is limited to discharge or in-hospital death. It is possible that the recovery of patients with IVH is slower than their non-IVH counterparts. A longer follow-up may thus provide a more accurate view of the outcome

distribution. Third, presumably the hematoma volume may decrease as it ruptures into the ventricles. This makes estimation of the true range of IVH-related ICH volume difficult to assess. Finally, ICH growth is an important factor in outcome prediction.³⁵ This work was not designed to address hematoma growth but this may differentially impact the outcome in patients with and without IVH.

GLOSSARY

ANOVA, analysis of variance; EVD, external ventricular drainage; HSD, honestly significant differences; ICC, interclass correlation coefficient; ICH, intracerebral hemorrhage; IVH, intraventricular hemorrhage; LOS, length of stay; mRS, modified Rankin Scale.

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Figure.

Decompression ranges: Graphic representation of the relationship between intracerebral hemorrhage (ICH) location and size in the production of intraventricular hemorrhage (IVH). The distribution of IVH in relation to ICH volume in the different locations. Gray areas represent decompression ranges (see text for details).

Table 1
Location-specific measurements of volume, intraventricular hemorrhage (IVH) score, and decompression ranges

	Thalamus (n = 72)	Putamen (n = 125)	Lobar (n = 150)	Caudate (n = 12)	Pons (n = 28)	Cerebellum (n = 19)	Total (n = 406)	p Value
Mean ICH volume, cc (95% CI)	12.2 (9.6–15.4)	20.9 (17.5–25)	23.8 (20–28.4)	5.3 (3.3–8.7)	9.7 (6.5–14.6)	5.8 (1.6–21)	16.4 (14.7–18.3)	<0.001 [*]
IVH (%)	50 (69.4)	49 (39.2)	56 (37.3)	12 (100)	12 (42)	4 (21)	183 (45.1)	<0.001 [†]
Median IVH score (range)	5.5 (1–12)	7.5 (1–12)	3 (1–12)	8 (1–11)	6.5 (1–12)	4 (2–7)	6 (1–12)	0.14 [‡]
Decompression range (cc)	7.0–12.7	14.8–43.9	15.4–70.7	—	4.3–11.2	—	—	

ICH = intracerebral hemorrhage.

^{*} Analysis of variance test.

[†] χ^2 test.

[‡] Kruskal-Wallis test.

Table 2

Clinical course and outcome measures between patients with and without intraventricular hemorrhage (IVH)

	IVH (n = 183)	No IVH (n = 223)	Statistics
Mortality (%)	56 (30.4)	28 (12.6)	OR 3, 95% CI 1.8, 5.0, $p < 0.0001$ *
Poor outcome (%)	133 (73)	50 (27.2)	OR 3.4, 95% CI 2.21, 5.09, $p < 0.0001$ *
LOS (days $\pm$ SD)	12 $\pm$ 13	7.6 $\pm$ 8	$p < 0.001$ (t test)
Ventriculostomy (%)	40 (21.7)	8 (3.6)	OR 7.4, 95% CI 3.37, 16.30, $p < 0.0001$ *
Poor outcome with ventriculostomy	34/40 (85%)	7/8 (87.5%)	$p = 0.85$ *

LOS = length of stay.

* χ^2 test.

Table 3
Poor outcome and mortality rates in the different locations

	Thalamus (n = 72)	Putamen (n = 125)	Lobar (n = 150)	Caudate (n = 12)	Pons (n = 28)	Cerebellum (n = 19)	Total (n = 406)	p Value
Poor outcome, non-IVH patients (%)	6/22 (27)	32/76 (42)	42/94 (52)	0/12 (0)	9/16 (56)	2/15 (13)	98/223 (44)	0.019*
Poor outcome, IVH patients (%)	34/50 (68)	42/49 (86)	42/55 (76)	4/13 (31)	12 (100)	1 (25)	135/183 (74)	<0.001*
Mortality, all patients (%)	12 (16.7)	32 (25.6)	28 (18.7)	1 (8)	11 (23)	0 (0)	84 (20.7)	0.055*

IVH = intraventricular hemorrhage.

* χ^2 test.