# **PAPER**

# Presentation of intracerebral haemorrhage in a community

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**Background:** Studies on intracerebral haemorrhage (ICH) from tertiary care centres may not be an accurate representation of the true spectrum of disease presentation.

**Objective:** To describe the clinical and imaging presentation of ICH in a community devoid of the referral bias of an academic medical centre; and to investigate factors associated with lower Glasgow coma scale (GCS) score at presentation, as GCS is crucial to early clinical decision making.

**Methods:** The study formed part of the BASIC project (Brain Attack Surveillance in Corpus Christi), a population based stroke surveillance study in a bi-ethnic Texas community. Cases of first non-traumatic ICH were identified from years 2000 to 2003, using active and passive surveillance. Clinical data were collected from medical records by trained abstractors, and all computed tomography (CT) scans were reviewed by a study physician. Multivariable linear regression was used to identify clinical and CT predictors of a lower GCS score.

**Results:** 260 cases of non-traumatic ICH were identified. Median ICH volume was 11 ml (interquartile range 3 to 36) with hydrocephalus noted in 45%. Median initial GCS score was 12.5 (7 to 15). Hydrocephalus score (p = 0.0014), ambient cistern effacement (p = 0.0002), ICH volume (p = 0.014), and female sex (p = 0.024) were independently associated with lower GCS score at presentation, adjusting for other variables.

**Conclusions:** ICH has a wide range of severity at presentation. Hydrocephalus is a potentially reversible cause of a lower GCS score. Since early withdrawal of care decisions are often based on initial GCS, recognition of the important influence of hydrocephalus on GCS is warranted before withdrawal of care decisions are made.

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ntracerebral haemorrhage (ICH) has an estimated annual incidence of 12 to 15 per 100 000 in the USA.¹ Thirty day mortality estimates have been reported to be approximately 40–50%.² ³ Nearly all of the early studies describing the computed tomography (CT) features and clinical presentation of ICH were from single tertiary care centre case series, perhaps biased toward more severe cases.⁴ Population based studies, which account for all cases in a community independent of referral status, provide a more accurate estimate of the true spectrum of disease.

We assessed the clinical presentation and imaging characteristics of all ICH cases identified in a population based study conducted in a region without an academic medical centre, in order to describe the full spectrum of acute ICH presentation. A second goal was to determine the clinical and imaging characteristics associated with Glasgow coma scale (GCS) scores at presentation. The GCS is commonly used by clinicians to determine the aggressiveness of care for ICH patients. Determining potentially reversible causes of low GCS scores is important before withdrawal of care orders are considered.

#### **METHODS**

#### Case identification and clinical data

This study formed part of the BASIC project (Brain Attack Surveillance in Corpus Christi). Detailed study methods have been reported previously.<sup>7-9</sup> Briefly, active and passive surveillance were used to identify all cases of first ever non-traumatic primary ICH from 1 January 2000 to 31 December 2003 in patients older than 44 years. Cases were identified from emergency department and inpatient documentation by manually searching emergency department and inpatient logs for a set of previously validated screening

diagnostic criteria. <sup>10</sup> This active surveillance was supplemented by a review of hospital discharge records, searching for ICD-9 (*International Classification of Diseases*, ninth revision) codes for stroke, as previously described. <sup>9</sup>

Clinical variables were collected from the case notes by trained abstractors. GCS was determined as the initial value recorded in the case notes. The presence of stroke risk factors was determined from the medical records. We have previously reported a high level of agreement between patient self report and medical record risk factor data for hypertension, diabetes, atrial fibrillation, and coronary artery disease.<sup>11</sup>

Board certified neurologists validated all cases of ICH using source documentation including emergency department and hospital admission records blinded to ethnicity. ICH was defined as the acute onset of a focal neurological deficit that persisted for more than 24 hours (unless interrupted by death or a surgical procedure) and was not attributable to another disease process, together with neuroimaging evidence of a spontaneous focal collection of blood in the parenchyma or ventricle.<sup>12</sup>

### Description of the community

Nueces County, Texas, is a bi-ethnic community located in southeast Texas, with a population in 2000 of 313 615. <sup>14</sup> This community comprises approximately equal numbers of Mexican Americans and non-Hispanic whites. Other ethnic groups make up a small minority of the population and were therefore excluded from the study. Nueces County is predominantly an urban population with 88% of county residents residing within the city of Corpus Christi. There is

**Abbreviations:** BASIC, Brain Attack Surveillance in Corpus Christi; GCS, Glasgow coma scale; ICH, intracerebral haemorrhage

**Table 1** Demographic data and clinical characteristics (n = 260)

Characteristic	Number (%) unless specified	
Age (years)		
Mean (SD)	73 (12)	
Median (IQR)	74 (65 to 82) 129 (50%)	
Male sex (%)		
Ethnicity		
Mexican American	149 (57%)	
Non-Hispanic white	111 (43%)	
Diabetes mellitus	78 (30%)	
Hypertension	190 (73%)	
Atrial fibrillation	17 (7%) 68 (26%)	
Coronary artery disease		
Previous ischaemic stroke or TIA	75 (29%)	
Current smoker	30 (12%)	
Initial GCS (n = 192)		
Mean (SD)	11 (4.5)	
Median (IQR)	12.5 (7 to 15)	

no academic medical centre in the community, and the closest referral centres in Houston or San Antonio are approximately 150 miles away. This geographic isolation allowed complete case capture of acute neurological disease at the seven hospitals in the county which serve as the regional referral centres for the sparsely populated surrounding counties. There are 11 neurologists and four neurosurgeons in the county.

#### CT analysis

All initial head CT scans were reviewed independently by one of four study investigators (LM, DZ, NG, or PL) using a standardised protocol. Based on a 10% sample of scans, correlation coefficients for pairwise comparisons between reviewers were ≥0.87 for ICH volume, suggesting high interrater reliability.

Volume was measured using the A×B×C/2 method that has been described previously.15 The amount of midline shift of the pineal gland was measured in millimetres. Intraventricular haemorrhage (IVH) was quantified using a previously described 12 point scale, where the amount of intraventricular blood in the third, fourth, and both lateral ventricles is determined and scores from each portion are summed.16-18 Hydrocephalus and the degree of effacement of the ambient cisterns were quantified on the basis of the previously published methods of Diringer et al.16 Hydrocephalus was graded by dividing the ventricular system into eight portions (frontal horn, atrium, temporal horn of each lateral ventricle, and the third and fourth ventricle). Each portion of the ventricular system was given a score of 0 for no, 1 for mild, 2 for moderate, and 3 for marked hydrocephalus, and the scores were summed for a maximum possible score of 24. Each ambient cistern was rated as either normal, effaced, or obliterated and given a score of 0, 1, or 2, respectively. The scores from each side were then summed for a total possible score of 4. The total score was then divided into three groups based on a score of 0, 1-2, or 3-4.10 Subarachnoid haemorrhage was recorded when there was additional blood visualised in the sulci or basal cisterns, but not for isolated intraventricular haemorrhage.

#### Statistical analysis

Frequencies and percents were calculated for demographic variables, baseline clinical characteristics, and CT findings. Means with standard deviations (SD) and medians with interquartile ranges (IQR) were calculated for continuous

Characteristic	Number (%) unless specified
ICH volume (ml)	
Mean (SD)	25 (31)
Median (IQR)	11 (3 to 36)
ICH location	
Deep cerebral	142 (55%)
Lobar	87 (33%)
Brain stem	15 (6%)
Cerebellum	13 (5%)
Multifocal	3 (1%)
IVH score	
0	125 (48%)
1–4	50 (19%)
5–8	48 (18%)
9–12	37 (14%)
Mean (SD)	3 (4)
Median (IQR)	1 (0 to 6)
Hydrocephalus score	
0	144 (55%)
>= 1	116 (45%)
Mean (SD)	5 (7)
Median (IQR)	0 (0 to 7)
Pineal shift (mm) None	1.51 /509/\
None 1–5	151 (58%)
1-5 > 5	66 (25%) 43 (17%)
Mean (SD)	2 (4)
	0 (0 10 3)
	142 (42%)
3–4	55 (21%)
Median (IQR) Ambient cistern score 0 1-2	0 (0 to 3 162 (62 43 (17%

variables. Histograms showing the distribution of ICH volume and initial GCS scores were generated.

To identify CT factors associated with lower GCS score, multivariable linear regression was used. Variables examined included ICH volume, pineal shift, hydrocephalus score, subarachnoid haemorrhage, ambient cistern score, age, sex, and ethnicity. All continuous variables were treated linearly. Ambient cistern score was trichotomised into the following categories: none, 0; moderate, 1–2; and severe, 3–4.16 Variables were selected in a prespecified fashion based on their known or plausible relation with presenting GCS score, or their ability to confound the other predictive variables. Intraventricular haemorrhage volume was not included in the model as it was co-linear with the hydrocephalus score. As data for GCS were not available on all cases, a

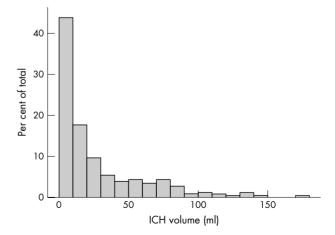


Figure 1 Distribution of haemorrhage volume (n = 260 cases). ICH, intracerebral haemorrhage.

multivariable logistic regression model was generated to identify possible predictors of missing GCS. Preselected variables included age, sex, ethnicity, ICH volume, and ICH location (lobar  $\nu$  non-lobar). Statistical analysis was carried out using S-plus 6.1 for Windows (Insightful Corporation, Seattle, 2002).

#### **Ethics**

The institutional review boards of the University of Michigan, the University of Texas at Houston, and each of the Nueces County hospitals approved this project.

#### **RESULTS**

A total of 294 cases of validated first ever ICH were identified from 2000 to 2003. Seventeen cases were excluded from the analysis as CT was not available for review, and seven cases were excluded as they were cases of recurrent ICH. An additional 10 cases were excluded after alternative diagnoses were found on CT review (eight cases of haemorrhagic transformation of ischaemic infarction, one case of ischaemic stroke, and one case of basal ganglia calcification misidentified as haemorrhage). The 10 cases that were excluded because of alternative diagnoses were agreed upon by all four reviewers. In all, 260 cases remained for analysis.

#### Clinical features

Baseline demographics and co-morbid medical conditions are given in table 1.

Previous hypertension was noted in 74% of the patients, and 30% were diabetic. A history of previous ischaemic stoke was present in 29% of patients. Data on coagulation profiles and platelet count at the time of ICH were not available.

#### CT findings

Details of CT findings are given in table 2.

Median haemorrhage volume was 11 ml (IQR 3 to 36), with a mean (SD) volume of 25 (31) ml. Just over 40% of patients had a haemorrhage volume of less than 10 ml. The distribution of haemorrhage volume is shown in fig 1. The most common site of haemorrhage, in 55% of cases, was the deep cerebral region (thalamus and basal ganglia combined). Hydrocephalus was present in 45% of cases, and intraventricular haemorrhage in 52%.

#### Glasgow coma scale

Initial GCS score was available for 192 patients. Median initial GCS score was 12.5 (IQR 7 to 15), with 27% of patients having a score of 15 at presentation. The distribution of initial

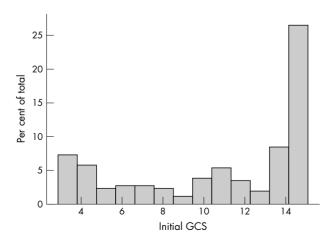


Figure 2 Distribution of initial Glasgow coma scale (GCS) scores (n = 260).

GCS scores is shown in fig 2. Multivariable linear regression revealed that hydrocephalus score (p = 0.0014), ambient cistern score of 3–4 (p = 0.0002), ICH volume (p = 0.014), and female sex (p = 0.024) were independently associated with lower GCS scores at presentation, adjusting for the other variables in the model (table 3).

Multivariable analysis to determine predictors of missing GCS showed that only increasing age was associated with missing GCS (odds ratio = 1.74 (95% CI, 1.11 to 2.73)).

#### **DISCUSSION**

The GCS is often used in models predicting outcome in ICH.<sup>2 3</sup> However, the factors associated with a lower GCS score in ICH have not been investigated previously. If the factors associated with a lower GCS score can be identified, important approaches to the ICH patient and targets for treatment may be suggested. Our analysis showed that hydrocephalus, effacement of the cisterns, ICH volume, and female sex are associated with lower GCS scores at presentation. Of these factors, hydrocephalus is potentially amenable to treatment by external ventricular drainage.

Hydrocephalus has previously been shown to be associated with poor outcome. <sup>16</sup> <sup>19</sup> <sup>20</sup> Predicting poor outcome for ICH patients early in their treatment course may lead to withdrawal of support and subsequent death in those with an initially low GCS score. While there is significant early mortality in ICH, survivors can have good outcomes. <sup>21</sup> It is not known whether hydrocephalus itself leads to severe irrecoverable neurological damage, or whether the development of hydrocephalus (and therefore a low GCS score) leads to withdrawal of aggressive support and subsequent death.

While it may seem intuitive that all patients with ICH and hydrocephalus should be offered ventriculostomy, published reports show that many patients with hydrocephalus are not being treated with ventriculostomy. In the study by Diringer et al, 16 ventricular drainage was undertaken in 30% of patients with hydrocephalus and was not associated with improved outcome. However, the use of ventriculostomy was not randomised, and 20% of the subjects in this study had aggressive care withdrawn. In a small study of 36 patients with isolated caudate haemorrhage, eight of 20 patients (40%) who underwent external ventricular drainage for acute hydrocephalus were functionally independent at six months. 19 While these numbers are small, they suggest that aggressive care of patients with ICH can lead to good functional recovery. Further study is needed to determine the role of aggressive treatment of hydrocephalus in patients with ICH. In the meantime, early withdrawal of care without a trial of hydrocephalus treatment may be premature.

We also found that female sex was associated with lower GCS scores at presentation. The reasons for this sex difference are unclear. The association between female sex and a lower GCS score may be partially explained by sex differences in access to acute stroke care.<sup>22 23</sup> Studies of pooled ischaemic and haemorrhagic stroke have shown that women had delayed time to hospital presentation after symptom onset compared with men. Women with strokes have also been found to present more often than men with non-traditional stroke symptoms.<sup>22</sup> Delays in presentation, evaluation, diagnosis, and treatment of women with ICH may have contributed to the association between female sex and lower GCS scores in our study.

This study shows the wide range of disease severity in ICH. We found that over 40% of the haemorrhages had a volume of less than 10 ml, with a mean (SD) volume of 25 (31) ml (median 11 ml). A study in the Greater Cincinnati area reported a much larger mean haemorrhage volume of 50 (31) ml in patients who underwent surgery, and 37 (38) ml for patients not undergoing surgery.<sup>24</sup> A study from Izumo City,

Table 3 Predictors of a lower initial Glasgow coma scale score

Characteristic	β* (SE)	p Value
Age	0.01 (0.02)	0.58
Female sex	-1.17 (0.51)	0.024
Ethnicity†	-0.31 (0.52)	0.55
ICH volume	-0.03 (0.01)	0.01
Subarachnoid haemorrhage	0.31 (0.82)	0.71
Ambient cistern score severe (3-4) v low (0)	-3.87 (1.00)	0.0002
Ambient cistern score moderate (1-2) v low (0)	-1.16 (0.74)	0.12
Pineal shift	-0.08 (0.10)	0.41
Hydrocephalus score	-0.15 (0.05)	0.001

\*Note that a negative  $\beta$  indicates a lower Glasgow coma scale score with increasing value of each variable. †Ethnicity: referent group for Mexican Americans was non-Hispanic whites.

Japan, reported a mean haemorrhage volume similar to that seen in our population (20 (28) ml), with 35% of haemorrhages having a volume less than 5 ml.<sup>25</sup> The smaller haemorrhages seen in our study and the Japanese study may reflect population differences, racial or ethnic differences in disease, or different time periods studied. As this Texas community does not have an academic medical centre, cases in the current study should not be subject to referral bias and may be a more accurate representation of the true spectrum of this disease.

We have previously reported the crude three year cumulative incidence for ICH from the years 2000 to 2002 in those over 45 years of age in Nueces County, Texas—including first and recurrent ICH—as 25 per 10 000 for Mexican Americans and 19 per 10 000 for non-Hispanic whites. The age adjusted risk ratio for ICH in Mexican Americans compared with non-Hispanic whites was 1.63 (95% CI, 1.24 to 2.16).8 Ethnic differences in ICH incidence have been reported previously, with a higher incidence in both African Americans and Hispanics compared with non-Hispanic whites.26-28

Our study has limitations. We do not have data on the timing of CT in relation to symptom onset. Certain CT characteristics such as hydrocephalus or haemorrhage volume are likely to be a function of time from symptom onset. We therefore cannot evaluate whether delays in presentation may have had an effect on the clinical presentation and CT findings in this population. We also cannot be sure that the GCS recorded corresponds to the time of first CT, as patients may have had clinical fluctuations during the initial course of evaluation.

GCS was missing in 26% of subjects. Cases with missing CGS were not associated with ICH volume or ICH location, which are surrogates for ICH severity, though it was associated with increasing age. We cannot exclude the possibility that the relation between age and GCS score in our primary linear regression analysis may have been confounded by missing GCS values in older patients.

As our analysis was limited to cases over 44 years of age, we may have missed cases of ICH caused by vascular malformations. Additionally, our findings may not be applicable to ICH in younger patients. Despite these limitations, the strength of this study comes from the fact that it represents the true spectrum of disease in a population with complete case capture, and is free from the referral bias inherent in studies based at academic medical centres.

This study suggests that the presentation of ICH in a population is diverse, with a large proportion of small haemorrhages. Future efforts to improve survival in ICH should address the treatment of hydrocephalus as it is strongly associated with a lower initial GCS score, an indicator of poor prognosis. Additional studies are needed to address the influence of withdrawal of care in ICH on mortality. Further studies of aggressive ICH care within populations are also warranted.

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Competing interests: none declared

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# NEUROLOGICAL PICTURE

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## Tigroid and leopard skin pattern of dysmyelination in metachromatic leucodystrophy

3 year old female child, born of consanguineous parentage and full term normal delivery, developed psychomotor regression. When examined one year later, she exhibited no tracking of visual or auditory stimuli and optic fundi revealed mild pallor. She could produce no meaningful speech. She had drooling of saliva from the mouth, bilateral pyramidal signs, and was doubly incontinent. There was no family history of similar illness. Cranial MRI scan revealed hypointense radially oriented stripes and dots within the hyperintense cerebral white matter on T2WI (panels A and B). These dots were iso to hyperintense on T1WI (panel C). pattern of dysmyelination resembled the skin of tiger (radial stripes) and leopard (dots). A diagnosis of metachromatic leucodystrophy (MLD) was confirmed by decreased activity of arylsulfatase A in leucocytes.

Besides MLD, tigroid and leopard skin pattern of dysmyelination has also been described in Pelizaeus-Merzbacher disease and globoid cell leucodystrophy. <sup>12</sup> Recognition of this pattern could provide valuable diagnostic clue in the proper clinical context. In the MRI of present patient, the visible dots/radial stripes with shortening of both T2 and T1 values (hypointense on T2WI and hyperintense on T1WI) probably represented areas of myelin sparing or lipid storage. This observation was confirmed by MRI and histopathological correlative study of brain in MLD.<sup>2</sup>

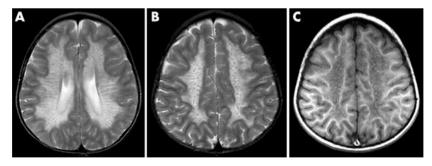
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(A) Hypointense radial stripes seen within the hyperintense cerebral white matter (resembling tiger skin) on T2 weighted axial MRI. (B) Hypointense dots resembling leopard skin seen in the same sequence at the level of centrum ovale. (C) Iso to hyperintense dots seen in the cerebral white matter on T1 weighted axial imaging.