Brief Report

Infratentorial Intracerebral Hemorrhage
Relation of Location to Outcome

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Background and Purpose—Infratentorial intracerebral hemorrhage (ICH) has a poor outcome but is rarely analyzed by cerebellar versus brain stem location. We evaluated this relationship and clinical outcomes among participants of the INTERACT 1 and 2 (Intensive Blood Pressure Reduction in Acute Cerebral Hemorrhage Trials).

Methods—Participants with brain stem and cerebellar ICH were compared. Logistic regression models were used to compare outcomes of death or major disability and quality of life.

Results—Of 195 included patients, 92 (47%) and 103 (53%) had brain stem and cerebellar ICH, respectively. Patients with brain stem ICH were younger (mean [SD] age, 59±13 versus 70±11 years), less female (28.3% versus 50.5%), with higher admission National Institutes of Health Stroke Scale scores (median [interquartile range], 6 [4–10) versus 3 [2–8]), less prior ICH (3% versus 17%), smaller ICH volumes (1.6 mL [1.0–2.8 mL] versus 5.1 mL [2.6–10.7 mL]), and less intraventricular extension (3% versus 39%) than those with cerebellar ICH. Brain stem ICH had higher mortality (odds ratio, 37.1; 95% CI, 1.99–692.27) and worse scores in the European Quality of Life Scale (EQ-5D) pain domain (odds ratio, 3.36; 95% CI, 1.38–8.20).

Conclusions—Cerebellar and brain stem ICH differ in their clinical characteristics and prognosis, with the latter being associated with higher case fatality and worse EQ-5D scores in the pain domain.

Clinical Trial Registration—URL: https://www.clinicaltrials.gov. Unique identifiers: NCT00226096 and NCT00716079.

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Key Words: brain stem ■ cerebellum ■ cerebral hemorrhage ■ clinical trial

Stroke

Spontaneous intracerebral hemorrhage (ICH) is the most serious and least treatable type of stroke,[1] with prognosis strongly associated with location in the infratentorial compartment.[2] However, studies generally group cerebellar and brain stem ICH against supratentorial ICH in analyses, rather than subtyping infratentorial ICH. We assessed clinical characteristics and outcomes for patients with infratentorial ICH who participated in the INTERACT 1 and 2 (Intensive Blood Pressure Reduction in Acute Cerebral Hemorrhage Trials).[3,4]

Methods

Data from the INTERACT studies are available upon request through a formal application to the corresponding author.

INTERACT 1 and 2 were international, multicenter, prospective, open, blinded end point, randomized controlled trials assessing the effect of intensive blood pressure lowering in ICH within 6 hours of onset.[3,4] Three thousand two hundred forty-three adult patients (INTERACT1, n=1404; INTERACT2, n=2839) with imaging-confirmed ICH were randomized. The protocols received ethics approval, and written informed consent was obtained from the patient or a surrogate.

Demographic and clinical characteristics were recorded at inclusion. Brain imaging was performed according to standardized technique; 3 neurologists centrally analyzed ICH volume, infratentorial location, and presence of intraventricular hemorrhage.

Ninety-day outcomes were death or major disability (modified Rankin Scale scores, 3–6) and health-related quality of life (HRQoL) scores on the European Quality of Life Scale (EQ-5D) questionnaire.

We compared the baseline characteristics of patients with brain stem or cerebellar ICH using the χ^2 test for categorical variables and Wilcoxon test for continuous variables and assessed the associations between infratentorial ICH and modified Rankin Scale, and poor HRQoL in each domain (2 and 3 versus 1) and poor overall HRQoL (median utility score ≤0.7) in multivariable logistic regression models, adjusted for age, sex, National Institutes for Health Stroke Scale score, baseline ICH volume, and intraventricular hemorrhage extension. A significance level of $P<0.05$ was used. Data were reported

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with odds ratios and 95% CIs. Analyses were performed using SAS software version 9.3 (SAS Institute, Cary, NC).

Results

We included 195 patients with infratentorial ICH. Table 1 describes the baseline characteristics according to brain stem (n=92) and cerebellar (n=103) location. Patients with brain stem ICH were significantly younger (59±13 versus 70±11), less female (28.3% versus 50.5%), had higher admission National Institutes for Health Stroke Scale scores (median [interquartile range], 6 [4–10) versus 3 [2–8]), less prior ICH (3% versus 17%), smaller baseline hematoma volumes (1.6 versus 5.1 mL), and less intraventricular hemorrhage (3% versus 39%) compared with cerebellar ICH.

Table 2 shows that patients with brain stem ICH had higher case fatality (odds ratio, 37.1; 95% CI, 1.99–692.27) but not disability (odds ratio, 0.93; 95% CI, 0.34–2.53). After excluding 17 patients who died or had missing EQ-5D information, 178 patients were included in HRQoL analysis. After adjustment, brain stem ICH was associated with low HRQoL in the pain domain (odds ratio, 3.36; 95% CI, 1.38–8.20). All other HRQoL scores were comparable between brain stem and cerebellar ICH.

Discussion

In this post hoc analyses of INTERACT, we found that patients with cerebellar and brain stem ICH have different clinical characteristics and prognoses, with the latter having higher case fatality and worse scores in the EQ-5D pain domain.

Studies reporting ICH location-related outcomes usually consider infratentorial hematoma either as a single entity or grouped with deep supratentorial ICH against lobar ICH for descriptive and analytical purposes.[2,5] Sparse studies have examined brain stem and cerebellar ICH separately and, despite a small sample size,[6,7] have shown trends toward younger age, male sex, more severe neurological deficit, and smaller hematoma volume in brain stem compared with cerebellar ICH, with correspondingly worse outcomes for the former. Although some studies have included the EQ-5D in their analysis of location-related HRQoL, they have not performed domain-specific analyses.[2,8]

Our finding about pain after brain stem injury may be explained by lesions of spinothalamic pathways, olivary nuclei, periaqueductal gray, or raphe nuclei, which play important roles in the generation and transmission of allodynic impulses.[9] Also, the substantia nigra and analgesia circuit in the midbrain are involved in pain suppression and the affective component of pain[10]; injuries to these may result in decreased suppression signaling and heightened pain.

This is the largest prospective series of infratentorial ICH allowing multivariable analyses, although our trial based data is potentially influenced by selection bias based on a trial

Table 1. Baseline Characteristics of Patients With Posterior Fossa ICH, by Location

Parameter	Brain Stem (n=92)	Cerebellum (n=103)	*P* Value
Time from onset to randomization, h	3.8 (2.9–4.7)	3.8 (3.2–4.7)	0.59
Age, y	59 (13)	70 (11)	<0.0001
Female sex	26 (28.3)	52 (50.5)	0.002
Recruited from China	76 (82.6)	91 (88.4)	0.254
History of hypertension	69 (75.0)	76 (73.8)	0.846
Current use of antihypertensive drugs	48 (52.2)	48 (46.6)	0.44
Prior intracerebral hemorrhage	3 (3.3)	17 (16.5)	0.002
Prior ischemic or undifferentiated stroke	17 (18.5)	27 (26.2)	0.20
Diabetes mellitus	7 (7.6)	9 (8.7)	0.77
Use of antithrombotic agent	5 (5.4)	11 (10.7)	0.18
Systolic BP, mm Hg	181.5(18)	183.5(17)	0.37
NIHSS score*	6 (4–10)	3 (2–8)	<0.0001
GCS score†	14 (13–15)	15 (13–15)	0.63
Baseline hematoma volume, mL	1.6 (1.0–2.8)	5.1 (2.6–10.7)	<0.0001
Left hemisphere site of hematoma	35 (38.0)	49 (47.6)	0.18
Intraventricular extension of hemorrhage	3 (3.3)	39 (37.9)	<0.0001
Mean achieved BP, 1–24 h	150 (17)	148 (14)	0.70
Mean BP reduction, 1–24 h	31 (20)	36 (18)	0.25
Hematoma growth at 24 h	1.26 (–0.34 to 2.86)	–0.18 (–1.69 to 1.33)	0.20
Any surgical intervention within 7 days	1 (1.1)	4 (3.9)	0.374

Data are n (%), mean (SD), and median (interquartile range). BP indicates blood pressure; ICH, infratentorial intracerebral hemorrhage; GCS, Glasgow Coma Scale; and NIHSS, National Institutes of Health Stroke Scale.

*Scores range from 0 (normal) to 42 (coma with quadriplegia).

†Scores range from 15 (normal) to 3 (deep coma).

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Table 2. Death, Major Disability, and Health-Related Quality of Life at 90 Days After Acute Intracerebral Hemorrhage, by Location

	Brain Stem (n=92); n (%)	Cerebellum (n=103); n (%)	Crude OR (95% CI)	OR (95% CI)*	*P* Value
Death or major disability†	36 (40.0)	33 (32.7)	1.37 (0.76–2.48)	1.17 (0.44–3.11)	0.75
Death†	12 (13.0)	3 (2.9)	5.00 (1.36–18.33)	37.1 (1.99–692.27)	0.02
Major disability†	24 (30.8)	30 (30.6)	1.01 (0.53–1.92)	0.93 (0.34–2.53)	0.89
EQ-5D utility score	0.70 (0.62–0.78)	0.78 (0.72–0.84)			0.117
EQ-5D domains‡					
Mobility	47/79 (59.5)	62/99 (62.6)	0.87 (0.48–1.61)	0.81 (0.34–1.89)	0.619
Usual activity	35/79 (44.3)	52/99 (52.3)	0.72 (0.40–1.30)	0.73 (0.31–1.73)	0.475
Anxiety	23/78 (29.5)	28/99 (28.3)	1.06 (0.55–2.04)	1.31 (0.53–3.22)	0.558
Self-care	25/79 (31.7)	32/99 (32.3)	0.97 (0.51–1.83)	1.20 (0.46–3.15)	0.713
Pain	35/79 (44.3)	28/99 (28.3)	2.02 (1.08–3.76)	3.36 (1.38–8.20)	0.008

Data are n/N (%) and median (interquartile range). EQ-5D indicates European Quality of Life questionnaire; and OR, odds ratio.

*Adjusted by age, sex, National Institutes of Health Stroke Scale (NIHSS) scores, baseline hematoma volume, and intraventricular hemorrhage extension.

†Based on modified Rankin Scale: death or major disability (scores 3–6), major disability (scores 3–5), and death (score 6).

‡Data are for patients with poor health-related quality of life (scores 2 or 3 vs 1) in each domain.

population. We have not included information about withdrawal of care because of small patient numbers. The use of surgery in infratentorial ICH could be considered as a limitation but did not differ between the 2 groups.

Conclusions

In summary, patients with cerebellar and brain stem ICH have different clinical characteristics and prognosis. Although brain stem ICH tended to be smaller with less intraventricular hemorrhage, they have worse case fatality and are more likely to be associated with pain than cerebellar ICH. These findings offer practical help to caregivers in discussion with patients and families and in predicting poststroke pain.

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