Validation of the Intracerebral Hemorrhage Score in Uganda
A Prospective Cohort Study

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Background and Purpose—Rates of intracerebral hemorrhage (ICH) are estimated to be highest globally in sub-Saharan Africa. However, outcomes of ICH are poorly described and standard prognostic markers for ICH have not been validated in the region.

Methods—We enrolled consecutive patients with computed tomography-confirmed ICH at a referral hospital in southwestern Uganda. We recorded demographic, clinical, and radiographic features of ICH, and calculated ICH scores. We fit Poisson regression models with robust variance estimation to determine predictors of case fatality at 30 days.

Results—We enrolled 73 individuals presenting with computed tomography-confirmed ICH (mean age 60 years, 45% [33/73] female, and 14% [10/73] HIV-positive). The median ICH score was 2 (interquartile range, 1–3; range, 0–5). Case fatality at 30 days was 44% (32/73; 95% CI, 33%–57%). The 30-day case fatality increased with increasing ICH score of 0, 1, and 5 from 17%, 23%, to 100%, respectively. In multivariable-adjusted models, ICH score was associated with case fatality (adjusted relative risk, 1.48; 95% CI, 1.23–1.78), as were HIV infection (adjusted relative risk, 1.92; 95% CI, 1.07–3.43) and female sex (adjusted relative risk, 2.17; 95% CI, 1.32–3.59). The ICH score moderately improved with the addition of a point each for female sex and HIV serostatus (0.81 versus 0.73).

Conclusions—ICH score at admission is a strong prognostic indicator of 30-day case fatality in Uganda. Our results support its role in guiding the care of patients presenting with ICH in the region. **(*Stroke*. 2018;49:3063-3066. DOI: 10.1161/STROKEAHA.118.022057.)**

Key Words: cerebral hemorrhage ■ HIV infections ■ mortality ■ sex ■ stroke ■ Uganda

It is estimated that low-income countries contribute 85% of the global burden of incident intracerebral hemorrhage (ICH).[1] The high regional burden of ICH has been hypothesized to be because of a high genetic predisposition to ICH among Africans,[2] an increasing prevalence of modifiable stroke risk factors[3] and a high prevalence of HIV infection, which has been associated with ICH.[4] Despite the high incidence of ICH in sub-Saharan Africa (SSA), standard prognostic tools, such as the ICH score,[5] which can be used to guide patient care has not been assessed in the region. We conducted a prospective study at a regional referral hospital in Uganda to diagnostic validity of the ICH score as a predictor of 30-day case fatality in this setting.

Methods

We enrolled subjects within 12 hours of presenting to Mbarara Regional Referral Hospital with stroke symptoms. Participants underwent a structured history, neurological examination, and clinical scoring with the Glasgow coma scale and the National Institutes of Health Stroke Scale. All patients had a confirmatory brain computed tomography scan that was read by the study radiologist (M.A.). ICH hematoma location and volume were determined with Horos software (Purview, Annapolis, MD). ICH volume was calculated using the formula ABC/2 as previously described.[6] Additional measures are listed in Appendix I in the online-only Data Supplement. The ICH score was calculated as shown in Table I in the online-only Data Supplement.[5] Participants were followed for 30 days, at which point their vital status and functional status was determined using the modified Rankin Scale. Information on reasons for early withdrawal of care for those with high scores was not available.

We fit a Poisson regression model with robust variance estimates to test the association of ICH score with 30-day case fatality, both crudely and after adjusting for sex, HIV infection, and white blood cell count. We selected covariates for inclusion in the multivariable model if they had a P value of <0.1 in univariable models. We did not consider covariates for inclusion in the multivariable model if they were related to another aggregate measure considered for inclusion. For example, we included the ICH score in the multivariable model but excluded variables, such as Glasgow coma scale score and ICH volume, because they are components of the ICH score. Finally, we

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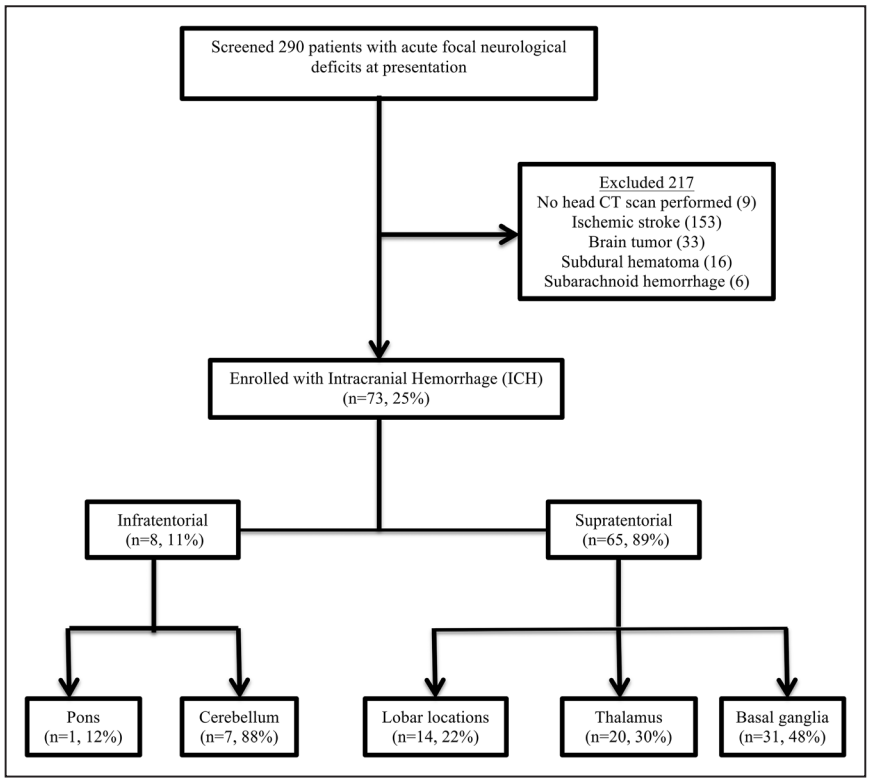

Figure. The schemata of enrollment and radiological subtypes of intracerebral hemorrhage in Uganda. We enrolled 73 out of 290 patients screened, most of whom had supratentorial intracerebral hemorrhage (ICH; 89%). CT indicates computed tomography.

fit receiver-operator curves and estimated area under the curve to assess the diagnostic validity of the standard ICH score to predict mortality for the total cohort and stratified by sex; and estimated the area under the curve after allowing an additional point each for female sex and for HIV seropositivity. The data that supports the findings of this study are available from the corresponding author on reasonable request.

The research ethics committees of Mbarara University of Science and Technology and Partners Healthcare provided approval for this study, and all participants or their caregivers gave written informed consent.

Results

Cohort Characteristics

We screened 290 patients with suspected stroke and enrolled 73 with computed tomography-confirmed ICH (Figure). The mean age at presentation was 60 years (SD 17 years, minimum age 23 years, and maximum age 100 years), 45% (33/73) were female, and 14% (10/73) had HIV infection (Table II in the online-only Data Supplement). The median ICH score was 2 (interquartile range, 1–3) with a range of 0 to 5. Supratentorial ICH was present in 89% (65/73), predominantly involving the basal ganglia (48%, 31/65), and thalamus (31%, 20/65).

ICH Morbidity, Case Fatality, and Predictors of Case Fatality

The 30-day case fatality for the entire cohort was 44% (32/73; 95% CI, 33%–57%; Table 1). The 30-day case fatality for patients with an ICH score of 0, 1, 2, 3, 4, and 5 was 17% (2/12), 23% (3/13), 47% (8/17), 48% (11/23), 100% (6/6), and 100% (5/5), respectively (Table 1). In a model adjusting for sex, HIV serostatus, and white blood cell count, we observed a 48% increase in case fatality for every 1-point increase in the ICH score, (adjusted relative risk; 1.48; 95% CI, 1.23–1.78). Other predictors of 30-day case fatality in the adjusted model included female sex (adjusted relative risk, 2.17; 95% CI, 1.32–3.59) and HIV infection (adjusted relative risk, 1.92; 95% CI, 1.07–3.43; Table 2). The area under the curve for the standard ICH score to predict mortality was 0.73 (95% CI, 0.62–0.85), and it performed similarly in men and women (0.79 versus 0.74; Table III in the online-only Data Supplement). The score appeared to improve moderately with the addition of a single point for female sex (0.78 versus 0.73) and with the addition of a point for both female sex and HIV serostatus (0.81 versus 0.73; Table IV in the online-only Data Supplement).

Discussion

In this prospective study in Uganda, we have demonstrated that the ICH score is a valid prognostic indicator of 30-day case fatality. Although this is the first assessment of the score

Table 1. Case Fatality Rates for the Entire Cohort and Stratified by ICH Score

ICH Score	n	Case Fatality at 30 d, n (%)	95% CIs
0	12	2 (17)	2.1–48.4
1	13	3 (23)	5.0–53.8
2	17	8 (47)	22.9–72.7
3	23	11 (47)	26.8–69.4
4	6	6(100)	54.7–100
5	2	2(100)	15.8–100
Entire cohort	73	32(44)	33.0–57.0

ICH indicates intracerebral hemorrhage.

Table 2. Predictors of 30-Day Mortality in the Whole Stroke Cohort

	Univariable Analysis		Multivariable Analysis	
Variable	RR (95% CI)	*P* Value	aRR (95% CI)	*P* Value
Age, per unit year increase	1.01 (0.99–1.02)	0.438		
Female sex	1.77 (1.03–3.03)	0.037	2.17 (1.32–3.59)	0.002
Systolic blood pressure, per unit increase	1.00 (0.99–1.01)	0.764		
Admission NIHSS scale, per unit increase	1.07 (1.04–1.10)	0.000		
Admission Glasgow coma scale score, per unit increase	0.84 (0.79–0.90)	0.000		
Random blood sugar, per unit increase	1.09 (0.96–1.24)	0.178		
Serum total cholesterol, per unit increase	1.00 (0.99–1.01)	0.515		
White cell count, per unit increase	1.04 (0.99- 1.10)	0.059	1.07 (0.98–1.08)	0.240
Prior history of hypertension	1.18 (1.03–1.98)	0.534		
Presence of HIV infection	1.76 (1.05–2.94)	0.029	1.92 (1.07–3.43)	0.029
Time from symptom onset to hospital presentation	1.01 (0.985–1.03)	0.500		
Intracerebral hemorrhage score	1.45 (1.22–1.74)	0.000	1.48 (1.23–1.78)	0.000

aRR indicates adjusted relative risk; and NIHSS, National Institutes of Health Stroke Scale.

in SSA, our findings are consistent with studies in multiple international settings[5,7] thus providing a critical appraisal of the ICH score in SSA where ICH patients are younger and have higher rates of hypertension and HIV infection. Strikingly, participants in our study with a score of 0 and 1 had a higher risk of case fatality compared with studies from the United States.[5,8] We hypothesize that this finding is attributable to limited access to specialized intensive care for monitoring and treatment of neurological disease available in the region,[9] which can putatively worsen outcomes especially among those with low ICH scores.

Furthermore, subjects with ICH in our cohort were considerably younger than has been seen in other parts of the world.[5] This finding suggests that ICH outcomes in the region can be possibly improved with the provision of adequate neurological care because younger patients tend to fare better after ICH.[10] Moreover, it offers the opportunity for further validation of the ICH score in broader age categories, as the current categorization of age at or >80 years might limit the performance of the ICH score in this setting.

We also found that female sex and HIV infection were associated with a higher risk of 30-day case fatality and that the addition of both variables to the ICH score slightly improved its performance. Compared with men, women had a higher case fatality at lower ICH scores. The reason for this difference is not clear, but the effect of sex on case fatality after ICH has varied in prior work, with some studies showing an increased risk of death in men while others showed no difference.[11] HIV infection has been previously associated with poor stroke outcomes in SSA, particularly among those with advanced disease and immunosuppression.[12]

Our study is limited by its conduct at a single-center, the inclusion of a small number of participants and the fact that it is only generalizable to those who present to a hospital for care. However, our study enrolled participants from the second largest hospital in Uganda and provides important preliminary data validating the ICH score in SSA.

In summary, we have demonstrated that the ICH score is a strong prognostic indicator of ICH outcomes among hospitalized patients in Uganda. The high-case fatality rates found among those with low ICH scores should prompt future work to elucidate the impact of strengthening stroke supportive therapies in those with low to intermediate ICH scores in this region. Further validation of the ICH score using lower age thresholds and the addition of criteria for sex and HIV serostatus are also warranted.

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Disclosures

None.

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