Stroke Mortality Outcomes in Uganda

Sam Olum, MBChB, MMed,[*,†,1] Anthony Muyingo, MBChB, MMed,[*,2] Tony L. Wilson, MD, FRCP,[*,3] Bart M. Demaerschalk, MD, MSc, FAHA, FRCP(C),[‡,4] Joseph M. Hoxworth, MD,[§,5] Nan Zhang, MS,[¶,6] Joseph G. Hentz, MS,[¶,7] Amir Abdallah, MBChB, MMed,[*,‡,8] Adrian Kayanja, MBChB, MMed,[*,9] Maria I. Aguilar, MD,[‖] and Cumara B. O'Carroll, MD, MPH[‡]

Background and Purpose: Stroke outcome data in Uganda is lacking. The objective of this study was to capture 30-day mortality outcomes in patients presenting with acute and subacute stroke to Mbarara Regional Referral Hospital (MRRH) in Uganda. *Methods:* A prospective study enrolling consecutive adults presenting to MRRH with abrupt onset of focal neurologic deficits suspicious for stroke, from August 2014 to March 2015. All patients had head computed tomography (CT) confirmation of ischemic or hemorrhagic stroke. Data was collected on mortality, morbidity, risk factors, and imaging characteristics. *Results:* Investigators screened 134 potential subjects and enrolled 108 patients. Sixty-two percent had ischemic and 38% hemorrhagic stroke. The mean age of all patients was 62.5 (SD 17.4), and 52% were female. More patients had hypertension in the hemorrhagic stroke group than in the ischemic stroke group (53% vs. 32%, $p = 0.0376$). Thirty-day mortality was 38.1% ($p = 0.0472$), and significant risk factors were National Institutes of Health Stroke Scale (NIHSS) score, female sex, anemia, and HIV infection. A one unit increase of the NIHSS on admission increased the risk of death at 30 days by 6%. Patients with hemorrhagic stroke had statistically higher NIHSS scores ($p = 0.0408$) on admission compared to patients with ischemic stroke, and also had statistically higher Modified Rankin Scale (mRS) scores at discharge ($p = 0.0063$), and mRS score change from baseline ($p = 0.04$). *Conclusions:* Our study highlights an overall 30-day stroke mortality of 38.1% in southwestern Uganda, and identifies NIHSS at admission, female sex, anemia, and HIV infection as predictors of mortality.

Key Words: Stroke—Cerebrovascular disorder—Cerebral infarction—Intracerebral hemorrhage—Sub-Saharan Africa—Outcomes

From the *Department of Medicine, Mbarara University of Science and Technology, Mbarara, Uganda; †Department of Medicine, Gulu University, Lacor, Uganda; ‡Department of Neurology, Mayo Clinic, Phoenix, Arizona; §Department of Radiology, Mayo Clinic, Phoenix, Arizona; ¶Department of Biostatistics, Mayo Clinic, Phoenix, Arizona; and ‖CHPG Penrose Neurosciences, Colorado Springs, Colorado.

Received September 13, 2020; revision received December 15, 2020; accepted February 1, 2021.

Grant Support: None

Corresponding author. E-mail: Ocarroll.cumara@mayo.edu.

[1]+256-775-978-880

[2]+256-703-896-958

[3]+256-782-225-097

[4]480-301-6640

[5]480-301-7470

[6]480-480-301-9219

[7]480-301-6010

[8]480-468-4147

[9]+256-772-382-977

1052-3057/$ - see front matter

https://doi.org/10.1016/j.jstrokecerebrovasdis.2021.105661

Introduction

Stroke is the second leading cause of death worldwide.[1–3] The largest stroke burden is carried by low and middle income countries, accounting for more than 85% of stroke mortality worldwide.[1–4] The average 30-day case fatality following first ischemic stroke is approximately 22.9% globally[5] and the 30-day case fatality rate of intracerebral hemorrhage (ICH) ranges from 42.1% in the United States[6] to 52% in the United Kingdom.[5,7] Cerebrovascular disease and ischemic heart disease also account for a significant amount of long-term morbidity and are the leading causes of overall disease burden worldwide as measured by disability-adjusted life-years lost.[8] In a systematic review of worldwide stroke incidence by *Feigin et al.* it was discovered that from 1970–1979 to 2000-2008, stroke incidence declined by 42% in high-income countries, but rose by more than 100% in low-to middle-income countries.[9,10] Unfortunately, while low and middle income countries carry most of the burden of stroke, there is very little data available to identify risk factors for stroke in these regions.

In the systematic review by *Feigin et al.* only one of the fifty-six population based studies was from sub-Saharan Africa (Nigeria).[9] There are a few published small African hospital-based studies on early stroke mortality, with in-hospital case fatality rates ranging from 15% to 44%.[11] *Walker et al.* collected prospective data (1990 to 1991) on mortality and recovery after stroke in Gambia and found 27% mortality at 1 month and 44% mortality at 6 months. In this study, 57% of deaths occurred while in the hospital. They confirmed that incontinence in the first 24 hours, sensory inattention, and impaired gag reflex on admission were significant predictors of mortality.[12] A second prospective study in Gambia completed from 2000 to 2001 also looked at mortality and morbidity after stroke and found that mortality was 41% during acute hospitalization and 62% at one year. They found National Institutes of Health Stroke Scale (NIHSS) scores to be significantly higher in women than men, with a mean NIHSS of 14 in men and 18 in women (p = 0.002). NIHSS severity on admission as well as level of consciousness were strong predictors of mortality, as were dysphagia, fever, pneumonia, and absence of aspirin.[11] In this study, as in other African studies, there was higher mortality in hemorrhagic stroke, but in much of sub-Saharan Africa without routine computed tomography (CT) scans, stroke subtypes (ischemic vs. hemorrhagic) are classified using clinical indices such as level of consciousness, blood pressure on admission, emesis, and severe headache at the time of symptom onset.[11] This may lead to over-estimation of the mortality due to hemorrhagic stroke, especially in patients dying prior to undergoing a head CT.[13] The 30-day mortality after stroke in Medunsa, South Africa was reported to be 33%, but this study did not differentiate between hemorrhagic and ischemic stroke, nor did it have extended follow-up.[14] Similarly the 30-day post-stroke mortality was 28% in an observational study conducted in a tertiary care hospital in Western Nigeria.[15] Given the paucity of stroke data in Uganda, it was our goal to collect data on 30-day mortality post stroke in patients hospitalized at one of the largest referral hospitals in the country, Mbarara Regional Referral Hospital (MRRH), as well as document the morbidity associated with stroke.

Methods

Study design and participants

Study subjects were consecutively recruited amongst patients presenting to MRRH in Mbarara, Uganda, between August 2014 and March 2015. Inclusion criteria included abrupt onset of focal neurologic deficits within 14 days of presentation and CT head confirmation of ischemic or hemorrhagic stroke. Exclusion criteria were: age < 18 years; lack of focal neurologic signs; symptom onset of greater than 14 days duration; lack of CT head; CT head with evidence of another underlying etiology as a cause for the patient's focal neurologic deficits; pregnancy; stroke evaluation occurring greater than 48 hours post admission, and absence of informed consent. Pregnant women were excluded given their classification as a vulnerable group and concern for fetal radiation exposure. We collected clinical data and demographic information from medical records and questionnaires, assessing vascular risk factors, degree of disability and premorbid functional status. All eligible patients underwent a stroke evaluation including interview, physical examination, and laboratory studies (complete blood count, lipid panel, and serum blood glucose). The physical examination included NIHSS at admission and discharge.[16,17] All patients were followed during their hospital stay, with 30-day post stroke phone interviews conducted to ascertain mortality and level of disability. All CT heads were interpreted by a neuro-radiologist (J.M.H).

The study was approved by the Institutional Review Board (IRB) at Mbarara University of Science and Technology (ID: 03/05-14) and at Mayo Clinic College of Medicine (ID: 14-005802). All patients provided written informed consent.

Outcomes

The primary endpoint was 30-day mortality in ischemic and hemorrhagic stroke patients evaluated at MRRH. Secondary endpoints were 30-day morbidity outcomes in all stroke patients with level of disability quantified by Barthel Index (BI) and Modified Rankin Scale (mRS) scores,[18–20] difference in 30-day mortality and morbidity between ischemic stroke and hemorrhagic stroke, dysphagia, and incontinence. BI and mRS scores were captured at admission, discharge, and 30 days post stroke with NIHSS scores completed at admission and discharge.

Statistical analysis

The primary outcome measure was 30-day mortality in ischemic and hemorrhagic stroke patients, and exact binomial method was used to estimate the confidence interval of the 30-day mortality. Chi-square test was utilized to compare the 30-day mortalities in the two stroke groups. The comparisons of categorical variables across the two groups were calculated using Chi-square or Fisher's exact test, and the comparisons of continuous variables across the two groups were computed using equal variance two sample t-test or unequal variance two sample t-test when appropriate. Poisson regression with a robust error variance was used to investigate the risk factors for 30-day mortality.

Results

Investigators screened 134 potentially eligible patients between August 2014 and March 2015 and enrolled 108 subjects after assessment of eligibility criteria (Fig. 1). Patients' demographics and overall hospital measures are summarized in Table 1. Sixty-three subjects had an ischemic stroke whereas 38 had a hemorrhagic stroke, with a mean time from symptom onset to hospital presentation of 3.1 days and no significant difference in time to presentation between groups (Table 1). Fifty-two (51.5%) subjects were female. The mean age of all patients was 62.5 years, however the average age of ischemic stroke patients (mean = 65.4, SD = 17.3) was significantly higher compared to hemorrhagic stroke patients (mean = 57.6, SD = 16.8, $p = 0.0293$). The frequency of stroke type by age group is shown in Fig. 2. There was no significant difference in length of hospital stay between patients with hemorrhagic versus ischemic stroke, (mean of 5.7 days), nor was there a difference in gender, education level, or HIV infection between the 2 groups. Women of reproductive age (younger than 45 years) had 58.3% ischemic stroke and 41.7% hemorrhagic stroke, but this difference was not statistically significant ($p = 0.5637$). There were a total of 38 young patients with stroke (55 years of age or younger) and we found an equal distribution of ischemic versus hemorrhagic stroke (19 ischemic, 19 hemorrhagic) amongst them. We compared the side of the brain affected by stroke, presence of herniation, and chronic stroke prevalence between the two groups and no significant differences were found (Table 2). Ninety-two percent of patients had anterior circulation ischemic strokes and 5% had multifocal infarcts. More patients had hypertension in the hemorrhagic stroke group (52.6%) than that in the ischemic stroke group (31.7%), with the difference being statistically significant ($p = 0.0376$). Patients in the hemorrhagic stroke group had significantly higher measures of both systolic ($p = 0.0056$) and diastolic blood pressure ($p = 0.0097$) compared to patients in the ischemic stroke group, as well as more left ventricular hypertrophy than the ischemic stroke group (55.3% vs. 19.4%, $p = 0.0002$). Notably 53% of hemorrhagic strokes were in non-lobar locations (i.e., basal ganglia, thalamus), and 11% in the cerebellum, all classic locations for hypertensive hemorrhages. The prevalence of urinary incontinence in ischemic stroke patients was statistically higher than in hemorrhagic stroke patients (47.6% vs. 26.3%, $p = 0.0339$).

Table 3 displays the 30-day mortality in the overall study group and by stroke type, with the exclusion of 4 ischemic stroke patients whose 30-day survival status is missing. In the overall 104 patients (including 7 patients whose stroke type cannot be determined), 39 (37.5%) people died before or at 30 days, with a mean time to death of 9.5 days (SD 10.8) and median of 3 days (IQR 3,16). Thirty-day mortality in the overall 97 patients (excluding 7 patients with unknown stroke type) was 38.1%, with a mean time to death of 9.4 days (SD 10.8) and median of 3 days (IQR 3,13). In patients who had hemorrhagic stroke 47.4% died at 30 days, with a mean time to death of 8.6 days (SD 9.8) and median of 4 days (IQR 3,13). Lastly, 32.2% of patients with ischemic stroke died at 30 days, with a mean time to death of 10.1 days (SD 11.9) and

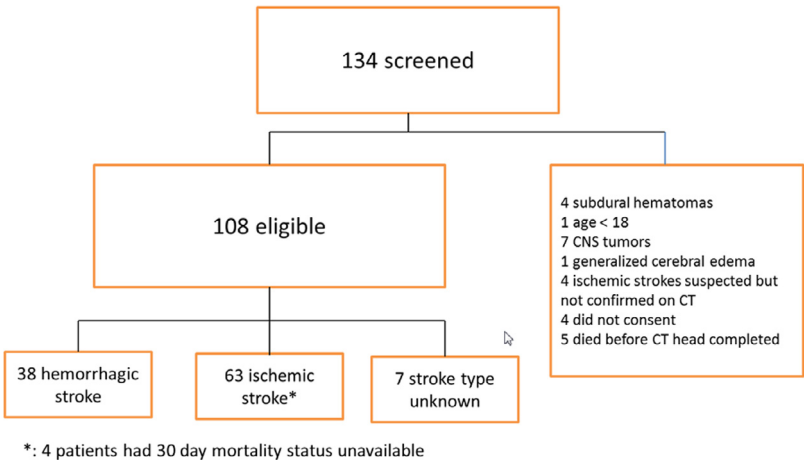

Fig. 1. *Study Flowchart.*

Table 1. *Demographics and Hospital Measures by Stroke Type*

	Hemorrhagic (N = 38)	Ischemic (N = 63)	Total (N = 101)	*p* value
Age				0.0293
Mean (SD)	57.6 (16.8)	65.4 (17.3)	62.5 (17.4)	
Median (Range)	55.0 (27.0−100.0)	70.0 (22.0−113.0)	64.0 (22.0−113.0)	
Sex				0.2919
Female	17 (44.7%)	35 (55.6%)	52 (51.5%)	
Male	21 (55.3%)	28 (44.4%)	49 (48.5%)	
Length of hospital stay(days)				0.5590
Mean (SD)	6.2 (8.2)	5.3 (5.2)	5.7 (6.5)	
Median (Range)	3.0 (0.0−44.0)	4.0 (0.0−26.0)	4.0 (0.0−44.0)	
Time from symptom onset to presentation (days)				0.2867
Mean (SD)	2.7 (3.2)	3.4 (3.3)	3.1 (3.3)	
Median (Range)	1.0 (0.0−12.0)	2.0 (0.0−13.0)	2.0 (0.0−13.0)	
Tobacco				0.8451
Yes	14 (36.8%)	22 (34.9%)	36 (35.6%)	
No	24 (63.2%)	41 (65.1%)	65 (64.4%)	
HIV status				0.1043
Negative	30 (78.9%)	57 (90.5%)	87 (86.1%)	
Positive	8 (21.1%)	6 (9.5%)	14 (13.9%)	
Hypertension				0.0376
No	18 (47.4%)	43 (68.3%)	61 (60.4%)	
Yes	20 (52.6%)	20 (31.7%)	40 (39.6%)	
Anti-hypertensive medication				0.1147
Yes	7 (18.4%)	5 (7.9%)	12 (11.9%)	
No	31 (81.6%)	58 (92.1%)	89 (88.1%)	
Dysphagia				0.0607
No	23 (60.5%)	26 (41.3%)	49 (48.5%)	
Yes	15 (39.5%)	37 (58.7%)	52 (51.5%)	
Bladder incontinence				0.0339
No	28 (73.7%)	33 (52.4%)	61 (60.4%)	
Yes	10 (26.3%)	30 (47.6%)	40 (39.6%)	
Systolic Blood Pressure				0.0056
Mean (SD)	163.3 (39.2)	143.7 (29.7)	151.1 (34.8)	
Median (Range)	159.5 (110.0−260.0)	140.0	142.0 (80.0−260.0)	
Diastolic Blood Pressure				0.0097
Mean (SD)	98.3 (25.2)	86.5 (19.5)	90.9 (22.5)	
Median (Range)	97.0 (70.0−180.0)	86.0 (50.0−150.0)	90.0 (50.0−180.0)	
LDL				0.1107
Mean (SD)	95.6 (44.3)	113.6 (64.5)	106.8 (58.1)	
Median (Range)	88.5 (5.0−187.0)	103.0 (39.0−446.0)	94.0 (5.0−446.0)	
Triglycerides				0.6008
Mean (SD)	126.4 (59.2)	135.1 (101.6)	131.8 (87.7)	
Median (Range)	123.5 (6.0−257.0)	112.0 (26.0−695.0)	116.0 (6.0−695.0)	
Hemoglobin				0.6210
Mean (SD)	13.6 (2.9)	13.9 (1.9)	13.8 (2.3)	
Median (Range)	13.7 (7.8−19.8)	14.1 (8.0−18.6)	13.9 (7.8−19.8)	
Random blood sugar				0.8733
Mean (SD)	8.3 (2.6)	8.2 (3.0)	8.2 (2.9)	
Median (Range)	7.9 (4.1−15.2)	7.0 (3.7−18.4)	7.4 (3.7−18.4)	
Left ventricular hypertrophy				0.0002
Missing	0	1	1	
No	17 (44.7%)	50 (80.6%)	67 (67.0%)	
Yes	21 (55.3%)	12 (19.4%)	33 (33.0%)	

median of 3 days (IQR 2, 20). When analyzing the 30-day mortalities in the two groups, we found they were not statistically different ($p = 0.1334$).

We compared results of mRS and BI scores (at admission, discharge and 30 days), and NIHSS score (at admission and discharge), as well as their change from

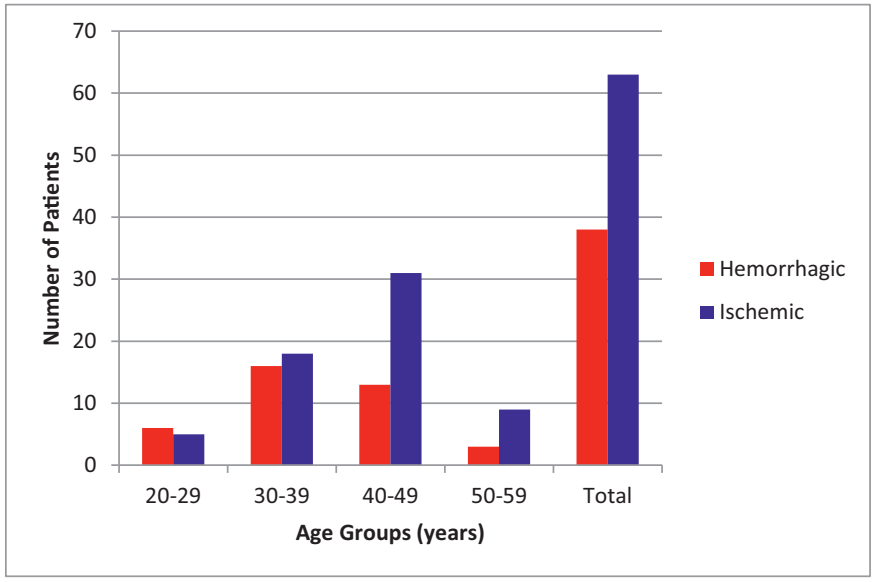

Fig. 2. *Stroke Type by Age Group.*

discharge or 30 days to baseline across the two stroke groups. For BI and NIHSS scores at discharge or 30 days, the comparison was only made among people who were alive at that time. Patients in the hemorrhagic stroke group had a statistically higher mRS score (p = 0.0475) and NIHSS score (p = 0.0408), and lower BI score (p = 0.0027) at admission compared to patients in the ischemic stroke group. Additionally, patients in the hemorrhagic stroke group also had a statistically higher mRS score at discharge (p = 0.0063) and mRS score change from baseline (p = 0.04) compared to patients in the ischemic stroke group.

We investigated risk factors for 30-day mortality with the primary predictors of interest being stroke type (hemorrhagic vs. ischemic), anemia (yes vs. no; defined as hemoglobin < 12 g/dl) and HIV status (positive vs. negative). We ran the three primary predictors in three models respectively and for every model, we adjusted for

Table 2. *CT Scan Characteristics*

	Hemorrhagic (N = 38)	Ischemic (N = 63)	Total (N = 101)	p value
Stroke side				0.0714
Left	14 (36.8%)	31 (49.2%)	45 (44.6%)	
Right	18 (47.4%)	30 (47.6%)	48 (47.5%)	
Bilateral	6 (15.8%)	2 (3.2%)	8 (7.9%)	
Herniation				0.4702
No	34 (89.5%)	59 (93.7%)	93 (92.1%)	
Yes	4 (10.5%)	4 (6.3%)	8 (7.9%)	
Chronic strokes				0.7101
No	33 (86.8%)	53 (84.1%)	86 (85.1%)	
Yes	5 (13.2%)	10 (15.9%)	15 (14.9%)	
Ischemic stroke location				
Anterior	–	58 (92.1%)	–	
Posterior	–	2 (3.2%)	–	
Multifocal	–	3 (4.8%)	–	
Hemorrhagic stroke type				
Subcortical	20 (52.6%)	–	–	
Lobar	11 (28.9%)	–	–	
Cerebellum	4 (10.5%)	–	–	
Other-Subarachnoid Hemorrhage	3 (7.9%)	–	–	
Intraventricular extension of hemorrhagic stroke				
No	20 (52.6%)	–	–	
Yes	18 (47.4%)	–	–	

Table 3. *30-day Mortality Estimates*

	Died at 30 days	Estimate (95% CI)	P value
Overall 30-day Mortality (n = 104)[1]	39	37.5% [28.2%, 47.5%]	
Overall 30-day Mortality (n = 97)[2]	37	38.1% [28.5%, 47.8%]	
Hemorrhagic stroke 30-day Mortality (n = 38)	18	47.4% [31.0%, 64.2%]	0.1334[3]
Ischemic stroke 30-day Mortality (n = 59)	19	32.2% [20.6%, 45.6%]	

[1]Including patients whose stroke type is unknown.
[2]Excluding patients whose stroke type is unknown.
[3]Hemorrhagic stroke group 30-day mortality compared to ischemic stroke group 30-day mortality.

covariates of NIHSS score at admission, age, gender, dysphagia, and urinary incontinence. The model results are shown in Table 4. Significant risk factors from this analysis were NIHSS score, gender, anemia, and HIV infection. For a given patient, a one unit increase of the NIHSS score at admission increased their chance of death at 30 days by 6% ($p < 0.0001$). Females were 1.73 (95% CI: 1.17−2.57) times more likely to die at 30 days compared to males, and patients with anemia were 1.92 (95% CI: 1.27−2.89) times more likely to die than patients without anemia. Lastly, HIV infected patients were 1.47 (95% CI: 1.01−2.14) times more likely to die at 30 days compared to patients without HIV.

Discussion

Stroke mortality is higher in sub-Saharan Africa than in the developed world,[21] an observation confirmed in our prospective study. The 30-day mortality in all stroke patients including the 7 patients with unknown stroke type was 37.5%, and the overall 30 day mortality in our population excluding the 7 patients with unknown stroke type was 38.1%. Compared to patients with ischemic stroke, patients with hemorrhagic stroke had higher NIHSS scores, higher mRS, and lower BI scores. Thirty-day mortality in the hemorrhagic stroke group was higher than the ischemic stroke group (47.4% vs. 32.2% respectively), but this was not statistically significant univariately ($p = 0.1334$), nor after adjusting for NIHSS at admission, age, gender, dysphagia, and bladder control ($p = 0.2389$).

Risk factors for 30-day mortality post-stroke in this population were NIHSS at admission, female sex, anemia, and HIV infection. NIHSS, Glasgow Coma Scale, Acute Physiology and Chronic Health Evaluation II (APACHE II), and Simplified Acute Physiology Score II (SAPS II) upon admission to hospitals have all been studied as predictors of mortality in both ischemic and hemorrhagic stroke.[22] Our study showed that a one point increase in the NIHSS score at admission increased 30-day mortality by 6%. Additionally, female sex was determined to be one of the factors associated with stroke mortality (RR 1.73, $p = 0.0059$), and this is similar to that reported in stroke studies of Nigeria and Malawi.[23,24] When we compared females to males, there was no significant difference in their admission NIHSS scores. One theory for why Ugandan women with stroke have worse outcomes compared to men is that women have higher rates of baseline malnutrition, with worsening of their nutritional status during hospitalization. While we did not specifically address nutritional status in our study, it has previously been reported that HIV-infected women in sub-Saharan Africa are susceptible to malnutrition and this affects outcomes in superimposed conditions including stroke.[25] Additionally, it is our impression that hospitalized women are less likely to have a family member caring for them throughout their hospitalization, thus receiving inferior care compared to men. Due to significant nursing shortages,

Table 4. *Prediction of 30-day Mortality*

Model	Effect	Level	RR (95% CI)	P value
Model 1	Stroke type	Hemorrhagic vs. Ischemic	1.28 (0.85,1.92)	0.2389
	NIHSS at admission		1.06 (1.03,1.09)	<0.0001
	Age		1.01 (1.00,1.02)	0.223
	Sex	Female vs. Male	1.73 (1.17,2.57)	0.0059
	Dysphagia	Yes vs. No	0.50 (0.23,1.09)	0.0805
	Urinary incontinence	Yes vs. No	0.57 (0.18,1.84)	0.3487
Model 2*	Anemia	Yes vs. No	1.92 (1.27,2.89)	0.0018
Model 3*	HIV status	Positive vs. Negative	1.47 (1.01,2.14)	0.0466

*Models are adjusted for age, gender, NIHSS at admission, dysphagia and urinary incontinence.

hospitalized patients in Uganda are dependent on a family member or an "attendant" to provide food, assist with feeding/hydration, administer medications, and assist with toileting, bathing, and mobilizing. We had hoped to complete subgroup analysis of women of reproductive age (younger than 45 years), but our sample size was too small to draw any meaningful conclusions.

Anemia has been associated with poor outcomes in ischemic stroke with increased risk of in-hospital mortality and death one year post stroke, as well as a strong predictor of in-hospital mortality among patients with other vascular conditions such as myocardial infarction and congestive heart failure.[26–28] Anemia may result in cerebral dysautoregulation, increased blood viscosity, and decreased oxygen-carrying capacity in areas of the brain already compromised by ischemic injury. Less is known about anemia and hemorrhagic stroke. However, a meta-analysis of 13 cohort studies concluded that anemia increases the risk of mortality in patients with stroke and included patients with hemorrhagic stroke (3 studies).[29] Additionally, there is suggestion that anemia on admission might be associated with greater ICH severity, worse functional outcome at discharge, and higher one-year mortality in hemorrhagic stroke patients.[30] In our study not only was anemia a predictor of 30-day mortality in all strokes (RR 1.92, $p = 0.0018$), it was also a predictor of mortality in hemorrhagic (RR 1.84, $p = 0.0019$) and ischemic strokes (RR 2.14, $p = 0.0332$) independently.

Stroke represents a relatively common complication in young, HAART-treated and untreated HIV positive patients. RNA viral load and CD4+ cell count < 200/uL are clinically related to stroke and its prognosis, whereas HAART therapy has shown a neutral effect.[31] In our study, HIV positive status was associated with a higher risk of 30-day mortality in patients with stroke (RR 1.47, $p = 0.0466$). However, we did not collect data on RNA viral load or treatment with HAART, and were able to collect CD4+ cell counts on only 33% of our study participants. Our results are consistent with those of a systematic review of stroke in HIV-infected individuals in sub-Saharan Africa.[32] *Abdallah et al.* found that HIV-infected patients with stroke had worse outcomes compared to HIV-negative stroke patients, with greater stroke severity (NIHSS > 13), longer hospital stays, more associated coagulopathy, and higher 30-day mortality. Additionally, a study out of Cameroon found that post-stroke infections were more frequent in HIV-infected patients than HIV-uninfected patients.[33] It is possible that HIV-infected individuals in our study had a greater risk of 30-day mortality due to higher rates of malnutrition, higher rates of opportunistic infections, higher likelihood of hospital-acquired infections, and more associated coagulopathy, but we did not specifically evaluate these factors. We must also consider that stroke is more common in untreated HIV infection and in those with low CD4+ cell counts,[34] suggesting these individuals are sicker to begin with and thus more susceptible to poor outcomes.

Ischemic strokes account for 80–85% of strokes in Western populations, with cerebral hemorrhages accounting for the remaining 15–20% of strokes,[5,35] but in our Ugandan population 38% of stroke patients had a hemorrhagic stroke. Selection bias is possible given this study was completed at a large referral hospital which might have resulted in preferential selection of hemorrhagic strokes, as these patients tend to have more severe deficits, and are thus more likely to travel longer distances in order to seek higher levels of care. The average admission NIHSS score of hemorrhagic and ischemic stroke patients was 22 and 18, respectively ($p = 0.0408$). Similarly, it is also possible that our study selected for more severe strokes in general, given an average admission NIHSS score of 20, and may not be representative of all strokes occurring in the community. The average time from symptom onset to presentation to MRRH was 3 days for all stroke patients, with 53% first seeking care at a local health clinic. There was no significant difference between females and males in time from symptom onset to presentation to MRRH. Patients with acute ischemic stroke were not treated with recombinant tissue plasminogen activator as this is not readily available at MRRH.

Further limitations of our study include that CT was not available at all hours of the day, in addition to the inability to perform CT during power outages, which occurred routinely. Five potential study subjects died before they could have a CT head and thus they were not enrolled in our study. We can hypothesize that these patients had hemorrhagic strokes or severe ischemic strokes with malignant edema, and if this is the case it is possible that our 30-day mortality is underestimated. Due to technical difficulties incurred with the diagnostic imaging processing system, we were unable to retrieve the stored CT data on 7 patients, and thus they were labeled as having an "unknown stroke type". There were 4 patients who had clinical presentations consistent with stroke, but had no evidence of stroke on CT head. It is likely that these patients presented with small cortical or subcortical (lacunar) ischemic strokes that could have potentially been detected on MRI. However, because MRI was not available these patients were excluded from the study. While we found HIV infection to be a risk factor for 30-day mortality, we did not screen for superimposed infection, malnutrition, or associated coagulopathy possibly contributing to the higher mortality. We also did not control for HAART therapy and did not capture data on viral load, or complete data on CD4+ cell count. Importantly, HIV status is not a surrogate for immune status and having incomplete CD4+ cell counts is a limitation since we cannot reach conclusions regarding HIV control without CD4+ cell counts. Additionally, we found anemia to be a predictor of 30-day mortality, but did not screen for congestive heart failure or myocardial infarction as

potential confounders. We did not collect information on sickle cell disease, as this is more commonly seen in central and eastern Uganda. We were not able to complete vessel imaging in our stroke patients since CT angiography and carotid ultrasound were not available at MRRH, nor were we able to pursue transthoracic echocardiography, transesophageal echocardiography, or continuous hospital telemetry. Lastly, we were unable to examine patients in person at 30 days and interviews were conducted over the telephone instead. Only four patients (all ischemic) were lost to follow up at 30 days.

Our study highlights the poor outcome of stroke patients in southwestern Uganda with an overall 30-day mortality of 38.1%, and identifies NIHSS at admission, female sex, anemia, and HIV infection as predictors of mortality. Our findings confirm those of colleagues in Kampala, Uganda who reported a 30-day case fatality of 43.8% in stroke patients presenting to Mulago National Referral Hospital.[36] While there was no statistically significant difference in mortality between hemorrhagic and ischemic strokes in our study, patients with hemorrhagic stroke did have statistically higher levels of impairment on both admission and discharge from the hospital. Notably, patients in the hemorrhagic stroke group had a statistically higher mRS score at discharge, and mRS score change from baseline compared to patients in the ischemic stroke group. This is especially important given the disproportionate number of hemorrhagic strokes in our study population. This study serves as a catalyst for promoting further collection of stroke data in Uganda and sub-Saharan Africa, especially given the increasing burden of stroke in this region.

Acknowledgements

The authors thank Christine Tumuhimbise for her valuable contributions as study coordinator. This work was supported by Mayo Clinic Research, Medical Education Partnership Initiative-Medical Education for Equitable Services for All Ugandans (MEPI-MESAU), and Belgian Technical Cooperation (BTC).

Disclosures

None.

References

1. Feigin VL. Stroke in developing countries: can the epidemic be stopped and outcomes improved? Lancet Neurol 2007;6:94-97.
2. Strong K, Mathers C, Bonita R. Preventing stroke: saving lives around the world. Lancet Neurol 2007;6:182-187.
3. O'Donnell MJ, Xavier D, Liu L, et al. Risk factors for ischaemic and intracerebral haemorraghic stroke in 22 countries (the INTERSTROKE study): a case-control study. Lancet 2010;376:112-123.
4. World Health Organization. The global burden of disease—2004 update. Geneva: WHO; 2008.
5. Grysiewicz RA, Thomas K, Pandey DK. Epidemiology of ischemic and hemorrhagic stroke: incidence, prevalence, mortality, and risk factors. Neurol Clin 2008;26(4):871-895.
6. Fang MC, Coca Perraillon M, Ghosh K, Cutler DM, Rosen AB. Trends in stroke rates, risk, and outcomes in the United States, 1988 to 2008. Am J Med 2014;127(7):608-615.
7. Dennis MS, Burn JP, Sandercock PA, et al. Long-term survival after first-ever stroke: the Oxfordshire Community Stroke Project. Stroke 1993;24(6):796-800.
8. Kim AS, Johnston SC. Global variation in the relative burden of stroke and ischemic heart disease. Circulation 2011;124(3):314-323.
9. Feigin V, Lawes CMM, Bennett DA, Barker-Collo SL, Parag V. Worldwide stroke incidence and early case fatality reported in 56 population-based studies: a systematic review. Lancet Neurol 2009;8:355-369.
10. Chin JH. Stroke in sub-Saharan Africa: an urgent call for prevention. Neurology 2012;78:1007-1008.
11. Garbusinski JM, van der Sande MA, Bartholome EJ, Dramaix M, Gaye A, Coleman R, Nyan OA, Walker RW, McAdam KP, Walraven GE. Stroke presentation and outcome in developing countries: a prospective study in the Gambia. Stroke 2005;36(7):1388-1393.
12. Walker RW, Rolfe M, Kelly PJ, George MO, James OF. Mortality and recovery after stroke in the Gambia. Stroke 2003;34(7):1604-1609.
13. Rosman KD. The epidemiology of stroke in an urban black population. Stroke 1986;17(4):667-669.
14. Joubert J. The Medunsa Stroke Data Bank: an analysis of 304 patients seen between 1986 and 1987. South Afr Med J 1991;80:567-570.
15. Wahab KW, Okubadejo NU, Ojini FI, Danesi MA. Predictors of short-term intra-hospital case fatality following first-ever acute ischaemic stroke in Nigerians. J Coll Physicians Surg Pak 2008;18(12):755-758.
16. Josephson SA, Hills NK, Johnston SC. NIH Stroke Scale reliability in ratings from a large sample of clinicians. Cerebrovasc Dis 2006;22:389-395.
17. Lyden P, Raman R, Liu L, Emr M, Warren M, Marler J. National Institutes of Health Stroke Scale certification is reliable across multiple venues. Stroke. 2009;40:2507-2511.
18. Mahoney FI, Barthel D. Functional evaluation: the Barthel Index. Maryland State Med Journal 1965;14:56-61.
19. Bonita R, Beaglehole R. Modification of Rankin scale: recovery of motor function after stroke. Stroke 1988;19(12):1497-1500.
20. Van Swieten JC, Koudstaal PJ, Visser MC, Schouten HJ, van Gijn J. Interobserver agreement for the assessment of handicap in stroke patients. Stroke 1988;19(5):604-607.
21. Lemogoum D, Degaute JP, Bovet P. Stroke prevention, treatment, and rehabilitation in sub-Saharan Africa. Am J Prev Med 2005;29(5 Suppl 1):95-101.
22. Moon BH, Park SK, Jang DK, Jang KS, Kim JT, Han YM. Use of APACHE II and SAPS II to predict mortality for hemorrhagic and ischemic stroke patients. J Clin Neurosci 2015;22(1):111-115.
23. Eze CO, Kalu UA. The prognosis of acute stroke in a tertiary health centre in south-east Nigeria. Niger J Med 2014;23(4):306-310.
24. Heikinheimo T, Chimbayo D, Kumwenda JJ, Kamponderi S, Allain TJ. Stroke outcomes in Malawi, a country with high prevalence of HIV: a prospective follow-up study. PLoS One 2012;7(3):e33765. https://doi.org/10.1371/journal.pone.0033765. Epub 2012 Mar 29.

25. Hadgu TH, Worku W, Tetemke D, Berhe H. Undernutrition among HIV positive women in Humera hospital, Tigray, Ethiopia, 2013: antiretroviral therapy alone is not enough, cross sectional study. BMC Public Health 2013;13:943.
26. Sico JJ, Concato J, Wells CK, Lo AC, Nadeau SE, Williams LS, Peixoto AJ, Gorman M, Boice JL, Bravata DM. Anemia is associated with poor outcomes in patients with less severe ischemic stroke. J Stroke Cerebrovasc Dis 2013;22(3):271-278.
27. Hao Z, Wu B, Wang D, Lin S, Tao W, Liu M. A cohort study of patients with anemia on admission and fatality after acute ischemic stroke. J Clin Neurosci 2013;20(1):37-42.
28. Del Fabbro P, Luthi JC, Carrera E, Michel P, Burnier M, Burnand B. Anemia and chronic kidney disease are potential risk factors for mortality in stroke patients: a historic cohort study. BMC Nephrol 2010;11:27.
29. Li Z, Zhou T, Li Y, Chen P, Chen L. Anemia increases the mortality risk in patients with stroke: A meta-analysis of cohort studies. Sci Rep 2016;6:26636.
30. Bussière M, Gupta M, Sharma M, Dowlatshahi D, Fang J, Dhar R. Investigators of the Registry of the Canadian Stroke Network. Anaemia on admission is associated with more severe intracerebral haemorrhage and worse outcomes. Int J Stroke 2015;10(3):382-387.
31. D'Ascenzo F, Quadri G, Cerrato E, Calcagno A, Omedè P, Grosso Marra W, Abbate A, Bonora S, Biondi Zoccai G, Moretti C, Gaita F. A meta-analysis investigating incidence and features of stroke in HIV-infected patients in the highly active antiretroviral therapy era. J Cardiovasc Med (Hagerstown) 2015;16(12):839-843.
32. Abdallah A, Chang JL, O'Carroll CB, Musubire A, Chow FC, Wilson AL, Siedner MJ. Stroke in human immunodeficiency virus-infected individuals in Sub-Saharan Africa (SSA): A Systematic Review. J Stroke Cerebrovasc Dis 2018;27(7):1828-1836.
33. Mapoure YN, Mondomobe CAA, Nkouonlack C, Ayeah CM, Luma HN, Njamnshi AK. HIV infection does not influence stroke outcomes in HIV-infected patients: A prospective study. Rev Neurol (Paris) 2019;175(5):313-318.
34. Benjamin LA, Corbett EL, Connor MD, Mzinganjira H, Kampondeni S, Choko A, Hopkins M, Emsley HC, Bryer A, Faragher B, Heyderman RS, Allain TJ, Solomon T. HIV, antiretroviral treatment, hypertension, and stroke in Malawian adults: a case-control study. Neurology 2016;86(4):324-333.
35. Goldszmidt AJ, Caplan LR. Stroke Essentials. 2nd ed. Sudbury, MA: Jones & Bartlett Publishers; 2010.
36. Kwarisiima L, Mukisa R, Nakibuuka J, Matovu S, Katabira E. Thirty-day stroke mortality and associated clinical and laboratory factors among adult stroke patients admitted at Mulago Hospital (Uganda). Afr J Neurol Sci 2014;33(1):79-86.