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Computed tomography scanning and stroke mortality in an urban medical unit in Cameroon

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ABSTRACT

Background: Despite the increasing availability of head computerized tomography (CT) in resource-limited settings, it is unclear if brain-imaging-based diagnosis of stroke affects the outcomes in the absence of dedicated structures for acute stroke management.
Objectives: In a major referral hospital in the capital city of Cameroon, we compared in-hospital mortality rates in patients with a WHO-based diagnosis of stroke between participants with and without brain imaging on admission.
Methods: Stroke patients with and without admission brain imaging were compared for demographic characteristics, risk factors, clinical and laboratory characteristic, and in-hospital mortality. Heterogeneities in mortality rates (CT vs. No CT) across major subgroups were investigated via interaction tests, and logistic regressions used to adjust for extraneous factors such as age, sex, year of study, residency, history of diabetes and hypertension, history of stroke, Glasgow coma scale, and delay between stroke symptoms onset and hospital admission.
Results: Of the 1688 participants included in the final analysis, 1048 (62.1%) had brain imaging. The median age of the non-CT vs. CT groups was 65 vs. 62 years (p-value < 0.0001%). The death rate of non-CT vs. CT groups was 27.5% vs. 16.4% (p < 0.0001). This difference was mostly similar across major subgroups, and robust to the adjustments for confounders (in spite of substantial attenuation), with excess deaths in those with CT ranging from 65% to 149%.
Conclusion: In this resource-limited environment, the absence of brain imaging on admission was associated with high in-hospital death from stroke, which was only partially explained by delayed hospitalization with severe disease. These results stressed the importance of scaling up acute stroke management in low- and middle-income countries.

1. Introduction

Stroke is a major health issue, representing the second cause of disability and mortality worldwide [1]. The burden of stroke is however unevenly distributed with more than 80% of deaths occurring in low- and middle-income countries [2]. In an effort to align with international standards of stroke care, low- and middle-income countries have been striving to implement pre-hospital care, stroke units, and post-stroke rehabilitation and follow-up, with however limited successes [3]. Acute stroke care seems to be the less developed aspect of stroke care in these settings. Obtaining brain imaging is the next step after a clinical assessment of suspected cases of stroke. In the struggle to align with acute stroke care standards as set up in developed countries, the number of patients initially screened with brain imaging has increased over recent years with CT being the most widely available and affordable imaging modality. While the current trends may herald better care to come, it is unclear if obtaining a head CT in the specific context of limited access and availability of dedicated stroke unit would translate into a better outcome and more specifically a lower mortality. Using data from the largest hospital of the capital city of Cameroon in central Africa over a period of 14 years, we hypothesized that

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among patient with a clinical diagnosis of stroke, mortality is lower in participants who obtained a CT head on admission than in those who did not.

2. Methods

2.1. Study setting

The Yaoundé Central Hospital is the largest hospital in the capital city of Cameroon, with a catchment population of about two million individuals. At the end of the year 2012, the department of medicine of this hospital was staffed with 29 specialist physicians (including three neurologists), working in collaboration with four emergency physicians, two intensivists, three neuro-radiologists and two neurosurgeons, twelve general practitioners, and junior specialist physicians in training. Patients admitted to the units were referred from the emergency department, other departments, outpatients clinics, and other hospitals. For each patient, upon discharge or in the event of in-hospital death, both the initial diagnosis and the final diagnosis were recorded in the registers. Recorded diagnoses were usually expanded to include serious comorbidities. The study was approved by the administrative authorities of the hospital acting as the local ethic committee.

2.2. Recruitments and data collection

Hospital registers were surveyed for the period from January 1999 through December 2012 to identify patients with stroke. The standardized medical record has the advantage of reducing the likelihood of missing data and improving standardization of medical information. Briefly, the standardized medical record includes a section filled by the emergency department nurse and physician that summarize patient's demographic, chief complaints, vital signs, arrival time, brief clinical exam, and disposition. The second section of the standardize medical record which is filled by the resident under the supervision of an attending physician while the patient is on the floor includes a detailed history of the chief complaint, physical examination, summary of significant laboratory, and imaging investigations as well initial and final diagnoses. Final diagnosis as reported in chart is made by the attending physician. Medical records of all patients with a diagnosis of stroke were reviewed. The diagnosis of stroke was retained if patients met the World Health Organization (WHO) definition of stroke and both recurrent and first-in-lifetime strokes were included, supplemented where available by a brain computerized tomography (CT). For each eligible patients, data were recorded on the age, sex, length of stay, place of residency (urban vs. rural), history of stroke, hypertension, current smoking, diabetes mellitus, admission systolic and diastolic blood pressure (BP), level of consciousness, stroke subtype (ischemic vs. hemorrhagic stroke), and vital status upon discharge. Vital status (deceased or alive) is part of the disposition section of the standardized medical records. This information is systematically entered in the medical records at the time of discharge or death by the medical staff and double-checked by the attending physician on service.

We applied the WHO definition of stroke as a rapidly developing clinical sign of focal (or global) disturbance of cerebral function lasting more than 24 h (unless interrupted by death) [4]. When a CT scan was not available, stroke was judged unlikely in the presence of at least two of the following: 1) preceding fever (suggestive of abscess), 2) recent weight loss (suggestive of malignancy or chronic infection), neck rigidity, or blood in the CSF (suggestive of subarachnoid hemorrhage). Hypertension or diabetes was based on documented history, ongoing drug treatments, or a documented previous systolic (and/or diastolic) BP ≥ 140 mm Hg (90 mm Hg) for hypertension or fasting blood glucose > 126 mg/dL. Alcohol consumption and status for smoking were based on recorded history. Length of stay was estimated as the time from admission to the medical department to discharge (death or alive).

2.3. Statistical analysis

Data were analyzed with the use of SAS/STAT® v 9.1 for Windows (SAS Institute Inc., Cary, NC, USA). We have presented the results as counts and percentages, mean and standard deviation (SD), or median and 25th–75th percentiles (Q1–Q3). Differences between participants in the CT group and those in the non-CT group were analyzed via chi-square tests and equivalents (Fisher exact test and likelihood ratio chi-square test) for qualitative variables and via the Student t-test or non-parametric equivalent for quantitative variables. Mortality was compared between CT-group participants and non-CT group of participants overall, and heterogeneities across major subgroups were assessed via interaction tests. Interaction tests are appealing when considering the relationship between an outcome of interest (mortality in our case) and two or more predictors and serve to assess if the simultaneous effect of two or more predictors (status for CT scan and any of the other grouping variables in our case) on the outcome is not additive. Interactions were tested in the current study by constructing logistic regressions models to predict mortality during hospitalization and by having as predictors the main effect of 'status for CT scan,' each of our grouping variable of interest, as well as the cross-product of the later with 'status for CT scan' variable, and the p-value for the effect of this cross-product variable served to indicate whether there was a significant interaction or not. The effects of extraneous factors on the difference in death rates between the non-CT group vs. the CT group was accounted for in logistic regression analyses. Logistic regression does not account for the effect of follow-up time on the outcome occurrence, which in turn can affect the investigation of the outcome–predictor relationship. To confirm the robustness of our findings from logistic regressions, the effect of extraneous factors on the relationship of status for CT scan and mortality was also assessed using accelerated failure time regression models. A p-value of <0.05 was used to characterize statistical significance.

3. Results

3.1. General characteristics

Out of a total of 1688 participants who fulfilled the clinical diagnosis of stroke, 1048 (62.1%) had a CT of the head while 640 (37.9) did not. The overall sample, the CT group, and the non-CT group comprised 49.8%, 51.0%, and 47.8% of female, respectively (p-value = 0.210). Those who did not receive a brain CT were in generally older (median age 65 years vs. 62 years, p-value < 0.0001), had a more prolonged admission (13 days vs. 10 days, p-value < 0.0001), a shorter time from stroke onset to admission (24 h vs. 48 h, p-value < 0.0001), a higher Glasgow coma scale (p-value < 0.0001), and a lower mortality rate in the CT group compared to the non-CT group (Table 1).

3.2. Mortality in participants without CT compared to those with a CT

Of the total 348 deaths (20.6%) recorded during the hospitalization, 172 (cumulative incidence rate 16.4%) occurred in participants who had a brain CT and 176 (cumulative incidence rate 27.5%) in those who did not (p-value < 0.0001). This difference in mortality persisted within pre-specified subgroups except among participants with a history of smoking (p-value = 0.187), those with recurrent stroke (p-value = 0.465), rural participants (p-value = 0.557), and those with a shorter delay from stroke onset to admission (p-value = 0.130). However, compared with mortality pattern (CT vs. No CT) within complementary subgroups, there was no evidence of statistical interaction, with the exception of length of stay (interaction p = 0.03) for which mortality rate (CT vs. No CT) was similar at and above median length of stay (10.9% vs. 12.8%, p = 0.429), but excessively higher below median of stay for the non-CT group (23.0% vs. 39.5%, p < 0.0001) (Table 2).

Table 1
Demographic and clinical characteristics of participants.

	CT group		Non-CT group		Overall		p-value
	1048 (62.1%)		640 (37.9%)		1688 (100%)		
	n		n		n		
Median age, years (Q1–Q3)	1048	60 [52–70]	640	65 [55–72]	1688	62 [53–70]	<0.0001
Female sex, n (%)	1046	534 (51.0)	640	306 (47.8)	1686	840 (49.8)	0.210
Length of stay, days (Q1–Q3)	1047	13 [8–19]	640	10 [6–18]	1687	12 [8–19]	<0.0001
Urban residency, n (%)	1017	830 (81.6)	607	494 (81.4)	1624	1324 (81.5)	0.947
Median delay from stroke onset to CT, hours (Q1–Q3)	313	84 [36–144]		NA	313	84 [36–144]	NA
Delay from stroke onset to admission, hours (Q1–Q3)	587	24 [12–72]	250	48 [24–96]	837	48 [24–72]	<0.0001
GCS (Q1–Q3)	1023	15 [14–15]	604	15 [13–15]	1627	15 [14–15]	<0.0001
Median SBP, mm Hg (Q1–Q3)	1038	170 [150–200]	617	173 [143–200]	1655	170 [147–200]	0.797
Median DBP, mm Hg (Q1–Q3)	1038	100 [85–110]	617	100 [85–110]	1655	100 [85–110]	0.660
Median total cholesterol, mg/dl (Q1–Q3)	503	185 [155–220]	169	177 [148–210]	672	182 [150–220]	0.032
Median LDL-C, mg/dl (Q1–Q3)	499	120 [94–152]	156	120 [95–150]	655	120 [94–151]	0.431
Median HDL-C, mg/dl (Q1–Q3)	484	40 [30–50]	153	40 [30–48]	637	40 [30–50]	0.030
Median Triglycerides, mg/dl (Q1–Q3)	495	100 [74–130]	165	90 [70–120]	660	98 [71–126]	0.030
Past stroke, n (%)	1048	144 (13.7)	630	99 (15.7)	1678	243 (14.5)	0.283
Alcohol, n (%)	1039	244 (23.5)	623	161 (25.8)	1662	405 (24.4)	0.288
Smoking, n (%)	1043	118 (11.3)	622	62 (10.0)	1665	180 (10.8)	0.415
Atrial fibrillation, n (%)	1042	17 (1.6)	623	8 (1.3)	1665	25 (1.5)	0.679
Hypertension, n (%)	1044	709 (67.9)	627	426 (67.9)	1671	1135 (67.9)	>0.999
Diabetes, n (%)	1043	128 (12.3)	624	85 (13.6)	1667	213 (12.8)	0.449
Death, n (%)	1048	172 (16.4)	640	176 (27.5)	1688	348 (20.6)	<0.0001

Legend: CT, computerized tomography; HDL-C, high-density lipoprotein cholesterol, LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure.

3.3. Adjusted effect estimates of mortality risk in participants without CT compared to those with a CT

In a basic logistic regression model comprising age, sex, year of study, and residency, the odds ratio (95% confidence interval) of in-hospital death comparing participants without to those with a CT was 2.48 (1.86–3.30) and remained at 2.49 (1.87–3.32) when history of diabetes and hypertension were added to the model, and at 2.47 (1.85–3.29) with further expansion to include history of stroke. Further adding the Glasgow coma scale to this model decreased the odd ratio to 2.04 (1.49–2.81). In a final model comprising all the above variables and delay between stroke symptoms onset and hospital admission, the odds

Table 2
Mortality in patients with and without CT scan across major subgroups.

	Overall		CT group		Non-CT group		p-value	Interaction variable*CT p
	n	N deaths (%)	n	N deaths (%)	n	N deaths (%)		
Sex								0.934
Men	846	192 (22.7%)	512	93 (18.1%)	334	99 (29.6%)	<0.0001	
Women	840	156 (18.6%)	534	79 (14.8%)	306	77 (25.2%)	0.0003	
Smoking								0.652
Yes	180	26 (14.4%)	118	14 (11.9%)	62	12 (19.3%)	0.187	
No	1485	314 (21.1%)	925	156 (16.9%)	560	158 (28.2%)	<0.0001	
Median age, years (25th–75th percentile)								0.202
Below median	852	126 (14.8%)	575	66 (11.5%)	277	60 (21.7%)	<0.0001	
At and above median	836	222 (26.6%)	473	106 (22.4%)	363	116 (32.0%)	0.002	
Residency								0.088
Rural	300	61 (20.3%)	187	36 (19.2%	113	25 (22.1%)	0.557	
Urban	1324	271 (20.5%)	830	132 (15.9%)	494	139 (28.1%)	<0.0001	
Past stroke								0.156
Yes	243	65 (26.7%)	144	36 (25.0%)	99	29 (29.3%)	0.465	
No	1435	281 (19.6%)	904	136 (15.0%)	531	145 (27.3%)	<0.0001	
Hypertension								0.813
Yes	1135	251 (22.1%)	709	127 (17.9%)	426	124 (29.1%)	<0.0001	
No	536	89 (16.6%)	335	43 (12.8%)	201	46 (22.9%)	0.004	
Diabetes mellitus								0.390
Yes	213	47 (22.1%)	128	20 (15.6%)	85	27 (31.8%)	0.007	
No	1454	293 (20.1%)	915	150 (16.4%)	539	143 (26.5%)	<0.0001	
Alcohol consumption								0.606
Yes	405	66 (16.3%)	244	32 (13.1%)	161	34 (21.1%)	0.039	
No	1257	274 (21.8%)	795	137 (17.2%)	462	137 (29.6%)	<0.0001	
Glasgow coma scale								0.469
At and above median	1120	115 (10.3)	737	63 (8.5%)	383	52 (13.6%)	0.010	
Below median	507	222 (43.8%)	286	104 (36.4%)	221	118 (53.4%)	0.0001	
Delay from stroke onset to admission, hours								0.749
Below median	416	71 (17.1%)	313	48 (15.3%)	103	23 (22.3%)	0.130	
At and above median	421	89 (21.1%)	274	49 (17.9%)	147	40 (27.2%)	0.033	
Length of stay, days								0.030
Below median	831	249 (30.0%)	479	110 (23.0%)	352	139 (39.5%)	<0.0001	
At and above median	856	99 (11.6%)	568	62 (10.9%)	288	37 (12.8%)	0.429	

Table 3
Adjusted effect estimates of mortality risk in participants with and with CT, at various levels of adjustments for confounders.

Models	Variables in the models	Effect estimates (95% CI) for No CT vs. CT	
		Odds ratios from logistic regressions	Hazard ratios from Weibul regressions
Model 1	Age, sex, year of study, residency	2.48 (1.86–3.30)	3.15 (2.40–4.13)
Model 2	Model 1 + diabetes + hypertension	2.49 (1.87–3.32)	3.14 (2.44–4.04)
Model 3	Model 2 + past stroke	2.47 (1.85–3.29)	3.10 (2.41–3.99)
Model 4	Model 3 + GCS	2.04 (1.49–2.81)	2.67 (2.07–3.45)
Model 5*	Model 4 + admission delay	1.65 (1.02–2.68)	2.27 (1.55–3.31)

* Model 5 is based on a smaller sample, considering the missing value on the admission delay in a significant number of participants.

ratio was 1.65 (1.02–2.68) (Table 3). However, this final model was based on a much smaller sample, due to missing data on the admission delay in a significant proportion of participants, hence the unstable estimate. The pattern of the association was similar when regressions were based on accelerated failure time model (Table 3).

4. Discussion

We have found that in this resource-limited setting, 1) 1 out of 5 patients with stroke will die during initial hospitalization, 2) not receiving a brain-imaging-based diagnosis on admission was associated with high death rates, which appeared to be similar across levels of most baseline characteristics, 3) the excess mortality in those who did not receive a brain imaging on admission was at least in part explained by the severity of the disease and the late admission.

The overall death rate found is similar to those reported in other low- and middle-income countries [5–9], but higher than rates generally reported in series from high-income regions [9–11]. We have previously investigated the determinants of early and late post-stroke mortality in the study setting and found disease severity and elevated blood pressures to be major drivers of early mortality [12]. We are not aware of a previous study that looked specifically at the association between brain-imaging-acquired diagnosis on admission and in-hospital mortality for stroke in Sub-Saharan Africa. The current hypothesis-generating study will therefore contribute additional evidence to increase the awareness and refine strategies to curb the growing burden of stroke in Sub-Saharan Africa.

Our findings are in line with the observation that knowledge of stroke subtype could potentially impact stroke prognosis and fatality through a net benefit of a therapy like aspirin which is cheap and available although we cannot demonstrate that aspirin has impacted on the outcomes of patients in the present study [13]. When the proportion of acute therapy eligible patients will increase, it is anticipated that availability of imaging-guided therapies such as r-tPA or endovascular therapies will have a positive impact on stroke outcome just as demonstrated in developed countries [14–16] and in very few SSA countries [17]. It is, however, evident that a greater societal gain would be achieved through a multi-level, multi-step approach integrating stroke prevention, timely detection, and hospital admission of patients with stroke, acute stroke therapy (where obtaining a CT head will be central), and rehabilitation.

An effort to compare our findings with those from high-income countries would only be fair through data from pre tPA/thrombectomy era. Even before the advent and large-scale use of tPA in high-income countries, there have been evidence that admission to stroke units was associated with a better outcome [18,19]. It was, however, unclear which components or specific intervention within the stroke unit has the highest impact on outcomes. Patients with hemorrhagic stroke benefited as much as those with ischemic stroke but it remained unclear whether preadmission brain imaging would have any impact on the outcome. In a retrospective case control study comparing 93 patients with cerebral infarction treated before CT scanning with 92 who underwent a CT scan, the authors concluded that CT scan did not benefit stroke patients who had a clear history of acute onset, were alert, and had no findings indicating an intracranial mass [20]. The study was however conducted before implementation of stroke units.

4.1. Limitations

We are well aware of the limitations of this study. The main limitation stems from his retrospective nature which has limited our ability to control for some confounders such as the socio-economic status and stroke severity score. While it is possible that in a context where there is no universal health coverage, patients who were able to pay for a head CT may have had a better outcome, the observation that there was no interaction between residency (rural vs. urban) and mortality suggest that if any effect of socio-economic status on mortality, this would be limited. Data were missing for some participants on a key characteristic like the time from symptoms onset to hospital admission, which has affected to some extent the statistical power of our regression analyses. While the absence of CT could have included stroke mimics in our study population, results of previous studies suggest that this scenario would rather be rare just in the same line with other studies in Sub-Saharan Africa showing that only about 7% of clinical strokes were reclassified as non-stroke using CT scan [21]. We excluded participants who fulfilled the WHO definition of stroke, but had preceding fever or recent weight loss when CT scan results were not available to confirm the diagnosis. Such cases in the study setting where the prevalence of HIV is very high are more likely to be patients with brain abscess (toxoplasmosis) or metastatic tumors, which have been reported to account for about 2% of admission in specialized units in the study setting [22]. While our approach has likely excluded a few patients with true stroke, this was likely the best compromise for an acceptable specificity. Despite these limitations, our study has the merit of being one of the rare contemporary studies on the continent that have specifically addressed the question of the association between of CT and mortality using a relatively large sample. Where there are competing priorities and limited financial resources, this study provides additional data to support the needs of setting up and scaling up stroke care and stroke units.

5. Conclusion

In this resource-limited environment participant with a WHO clinical diagnosis of stroke who did not have brain imaging on admission were at high risk of in-hospital death. Some of this excess risk was explained by a delayed admission and disease severity among those who did not have brain imaging. However, both the unacceptably residual risk after accounting for these factors, just like the overall high mortality rate, support the need for additional efforts to prepare the health system to efficiently deal with the growing burden of stroke in this settings. Such efforts should include and are not restricted to

improved early recognition of stroke symptoms and timely hospital admission, improved acute stroke care including timely access to brain imaging, revascularization therapies, as well as secondary prevention therapies.

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Authors' contribution statement

AL and NC collected the data and drafted the manuscript. AD drafted the manuscript. APK performed statistical analyses and drafted the manuscript. All authors reviewed the manuscript before its final approval.

Declaration of competing interest

None for all co-authors.

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