CORRELATION BETWEEN BRAIN INFARCT VOLUME AND THE NEUROLOGICAL DEFICIT (STROKE SEVERITY) IN PATIENTS WITH ACUTE EPISODE OF STROKE AT MUHIMBILI NATIONAL HOSPITAL.

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By
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A dissertation submitted in partial fulfillment of the Requirements for the Degree of Master of Medicine (Radiology) of Muhimbili University of Health and Allied Science.

Muhimbili University of Health and Allied Sciences
August 2010

Certification

I, Dr. Ramadhan Kazema (The supervisor),

The undersigned certifies that I have read and hereby recommend for examination dissertation entitled, The correlation between brain infarct volume and neurological deficit (Stroke severity) in patient with acute episode of stroke at Muhimbili National Hospital. In fulfillment of the requirements for the degree of master of Medicine (Radiology) of Muhimbili University of Health and Allied science

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Date 27/11/2010

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Abstract

Backround

Stroke can affect any part of the brain and often includes multiple functional areas, making it particularly challenging to predict neurological status based on lesion characteristics. Although the location of the lesion clearly plays a role in its neurological impact, many brain functions are not anatomically distinct. Activation studies have confirmed that normal brain function often require an intact network of anatomically distinct areas working in concert. Glasgow coma scale is a valid, reproducible scale that measures one major neurological deficit. However, this is a clinical assessment. There is currently no radiological method to systematically quantify the effect of complex spatial pattern of brain injury on the severity of neurological function/ dysfunction. In the current study, the relationship between Glasgow coma scale and acute infarct volume as determined by Brain CT scan, is investigate. The aim is to see, if infarct volume can be used to assess neurological severity after an acute episode of stroke.

Objectives

To determine the correlation between brain infarct volume and the neurological deficit in patients with an acute episode of stroke in Muhimbili National Hospital between July 2009 to December 2009.

Materials and methods

This was a cross-sectional study of 74 patients with an acute episode of stroke seen at Muhimbili National Hospital Radiology department between July 2009 to December 2009, who underwent Brain CT scan examination and Glasgow coma scale within 48 hrs of stroke onset. The Glasgow coma scale was recorded prospectively by the admitting doctor at the time of acute presentation and this was used to determine neurological deficit. Acute stroke was confirmed by Brain CT scan, read by Muhimbili National Hospital Radiologist.

Stroke volume was calculated from the product of infarct diameter, the greatest perpendicular diameter to this and the thickness of the brain lesion estimated from the thickness of the CT slices. The result was then divided by two.

Correlation analysis was performed for volume scores versus Glasgow coma scale scores by computing Person correlation coefficient. $P<0.05$ was considered to be statistically significant.

Results

There was a poor correlation between infarct volume and Glasgow coma scale with a correlation coefficient of $r = -0.547$; p 0.01. This defines a weak linear association. It showed the regression t-test as $t = -5.550$ with 95% confidence interval – 1.024- -2.172 and regression correlation coefficient of $r2 = 0.300$; $p<0.001$. Hence infarct volume proved to be a poor predictor of Glasgow coma scale.

Conclusion and recommendations.

From this study, we can conclude that calculated stroke volume alone cannot be used to estimate stroke severity in patients with acute stroke. Future work with larger data sets and by incorporating knowledge of the sophisticated networks that connect different brain regions is required. Such studies in different patients cohorts would also address reproducibility and reliability of the current findings.

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List of abbreviations

BAI Berthel index of activities.

BP Blood pressure

CT Computed tomography

CVA Cerebral vascular accidents

GCS Glasgow coma scale

LACS Lacunar circulating syndrome

MNH Muhimbili national hospital

MRI Magnetic resonance imaging

NIHSSS National institute of health stroke scale score

OCSP Oxford community stroke project

TACS Total anterior circulating syndrome

TIA Transient ischemic attack

USS Ultrasound sonography

WHO World health organization

List of definitions

Brain infarct volume: It is the total amount of brain tissue deprived of sufficient oxygen long enough to cause necrosis, with no apparent cause other than vascular origin.

Neurological deficit: Clinical signs of focal or global disturbance of cerebral function. For example, decreased level of consciousness. This usually occurs secondary to disruption of blood flow to the brain which eventually leads to neurons death and hence compromises cerebral function.

Stroke severity: Assesses the extent of neurological deficit after an episode of stroke. It is measured by Glasgow coma scale.

Introduction and literature review

Stroke is a clinical term applied to any abrupt nontraumatic brain insult. Strokes are caused by either brain infarction or hemorrhage and must be distinguished from other conditions that cause abrupt neurologic deficits. Infarction is a permanent injury that occurs when tissue perfusion is decreased long enough to cause necrosis, typically as the result of occlusion of the feeding artery. Hemorrhage is seen when blood ruptures through the arterial wall, spilling into the surrounding parenchyma, subarachnoid space, or ventricles.

Stroke is the third leading cause of death in the United States and a major source of long-term disability among survivors. [1].It affects about 700,000 Americans each year.[2]

The Tanzania Stroke Incidence Project (TSIP) recorded stroke incidence in two well defined demographic surveillance sites (DSS) over a 3-year period from June, 2003. The Hai DSS (population 159 814) is rural and the Dar-es-Salaam DSS (population 56 517) is urban. Patients with stroke were identified by use of a system of community-based investigators and liaison with local hospital and medical centre staff. Patients who died from stroke before recruitment into the TSIP were identified via verbal autopsy, which was done on all those who died within the study areas.[3]

There were 636 strokes during the 3-year period (453 in Hai and 183 in Dar-es-Salaam). Overall crude yearly stroke incidence rates were 94·5 per 100 000 (95% CI 76·0—115·0) in Hai and 107·9 per 100 000 (88·1—129·8) in Dar-es-Salaam. When age-standardised to the WHO world population, yearly stroke incidence rates were 108·6 per 100 000 (95% CI 89·0—130·9) in Hai and 315·9 per 100 000 (281·6—352·3) in Dar-es-Salaam.[3]

Age-standardised stroke incidence rates in Hai were similar to those seen in developed countries. However, age-standardised incidence rates in Dar-es-Salaam were higher than seen in most studies in developed countries; this could be because of a difference in the prevalence of risk factors and emphasises the importance of health screening at a community level. Health policy makers must continue to monitor the incidence of stroke in sub-Saharan Africa and should base future funding decisions on such data.[3]

Stroke prevalence in rural South Africa is higher than previously documented in Africa but lower than in high-income countries. South Africa suffers from a huge burden of HIV/AIDS and diseases of poverty and violence and now faces the challenge of adapting its health systems to face the coming epidemic of vascular disease [4].

Assessment of patient's neurological deficit after an acute episode of stroke has many advantages and they include;-

1) Allows you to monitor patient's progress. Determining whether a patient's condition is improving or declining by comparing scores over a period of time.
2) Allows you to predict patient's outcome in terms of favourable or unfavourable.
3) Can assist you in terms of what treatment the patient's should get.

A study in Switzerland, where clinical and radiological data for 203 patients were collected prospectively: they were compromised patients with ischaemic stroke. The national institutes of health stroke scale [NIHSS], the Bamford criteria, and the trial of ORG 10172 in acute stroke treatment [TOAST] classification were used to define stroke severity, subtypes and aetiology. The clinical outcome of 198 patients was assessed using the modified Renkin scale [mRS] and categorized as favourable [score 0-1] or unfavourable [score 2-6]. In this study they concluded that the severity of the neurological deficit found on admission was a major predictor of clinical outcome. The results confirmed the relevance of the severity of the presenting neurological deficit assessed by the NIHSS as an independent predictor of unfavourable outcome, as defined by an modified Renkin scale score of 2-5. [5].

Other studies that came up with similar findings include:-

A study in Neurosurgical Department of Inselspital where Thirty-five patients under the age of 60 were admitted to the Neurosurgical Department of the Inselspital with acute supratentorial ischaemic strokes between February 1985 and June 1990. The mean delay from the onset of the symptoms until emergency room admission was 10 hours. CT scan, Doppler sonography, and angiography were done routinely at the time of admission and CT was repeated 24 hours later. A number of demographic, clinical and radiological variables were investigated for a possible prognostic significance. A grading scale was developed for each variable. They also concluded that the initial neurological deficits, aswell as the degree of motor paralysis, gaze deviation, and decreased level of consciousness correlated with an unfavourable outcome.[6]

.

A study in Wolters Kluwer heath , Camden .The aim of this prospective study was to determine whether cranial computed tomography in connection with neurological assessment was useful in prognostic evaluation of survival after acute stroke. .: Two-hundred forty-five consecutive stroke patients were included in the project during a1-year period. Each had a detailed neurological assessment 24-72 hours after stroke onset and underwent cranial computed tomography without intravenous contrast injection within the first week after admission. The lesions were divided according to neuroanatomic regions. In the statistical analyses they used a multiple logistic regression model with survival/death as the binary variable. Computed tomography showed 76% of the patients had infarcts, 11% had hemorrhages, and 13% had no acute lesion. Forty-three patients had more than one acute lesion, and 57 had one or more old infarctions. The temporal, parietal, and frontal regions and the basal ganglia were most often affected. They concluded that age, initial level of consciousness, and involvement of the temporal lobe on computed tomography were factors of prognostic significance regarding survival in the acute phase.[7]

A study in University of Carlifornia, San Francisco done between 1993-2001, investigated the effective thrombolytic treatment times for posterior circulation stroke and factors that might

help predict clinical outcome. They describe their experience treating 21 consecutive patients with either intravenous or intra-arterial thrombolytic therapy for posterior circulation ischemic stroke. Main Outcome Measures National Institutes of Health Stroke Scale, Glasgow Coma Scale, and modified Rankin Scale scores were evaluated at baseline, and the modified Rankin Scale was measured 3 months after stroke, with a good outcome being a modified Rankin Scale score of 2 or less. Nine patients received intravenous therapy; 12 patients received intra-arterial therapy. The median National Institutes of Health Stroke Scale score at onset was 20 (range, 2-39), and the median Glasgow Coma Scale score was 9 (range, 3-15). Twelve patients were treated within 8 hours of symptom onset (range, 1½ hours to 16 days). Nine patients (43%) had a modified Rankin Scale score of 2 or less at 3 months. The initial Glasgow Coma Scale score and treatment within 8 hours of symptom onset were each associated with good outcome, but the initial National Institutes of Health Stroke Scale score was not predictive. And they concluded that Thrombolytic therapy for posterior circulation stroke may be beneficial even when initiated 8 hours after symptom onset. Level of consciousness, as measured by Glasgow Coma Scale score, seems to be a more important predictor of outcome than the initial National Institutes of Health Stroke Scale score. A high presenting GCS score (≥9) was predictive of good patient outcome. [8]

Other studies that included predictors of outcome are:

Clinical stroke syndrome. [Oxford community stroke project, OCSP].

This is a simple clinical scheme to subdivide the acute strokes which was originally devised for patients with first ever life time stroke. Patients are classified using clinical criteria only. Lacunar Syndrome[LACS] include pure motor stroke, pure sensory stroke, sensorimotor stroke and ataxic hemi paresis. Patients with brain stem or cerebellum signs, and/or isolated homonymous hemianopia are classified as posterior circulating syndrome [TACS] , Those with Total anterior circulating syndrome (TACS), by definition, present with a triad of hemi paresis [or hemisensory loss] dysphasia [or other new higher cortical dysfunction] and homonymous hemianopia. Patient with partial anterior circulating syndrome [PACS] by definition, present with only two of the features of Total anterior circulating syndrome or

isolated dysphasia or parietal lobe signs. Patients are classified into syndrome after excluding intracerebral hemorrhage on brain imaging, in which case the patients are reclassified as total or partial circulating infarct [TACI or PACI,], lacunar infarcts and posterior circulalating infarct [POCI] .In this classification Total anterior circulating infarct had the worst outcome compared to the rest. [9].

Diabetes Mellitus. Hyperglycaemia predicts higher mortality and morbidity after acute stroke independently of other adverse prognostic factors such as older age, type, and severity of stroke and non reversibility of the neurological deficit. The effects of hyperglycaemia on mortality is large. The relative risk conferred by hyperglycaemia is greatest in patients with lacunar infarct. The mechanism by which hyperglycaemia might influence stroke outcome is uncertain. Both acute and chronic hyperglycaemia are associated with increased oedema and infarct size and with reduced cerebral blood flow and cerebrovascular reserve. Ischaemia leads to slowing of the oxidative glucose metabolism and an increase in anaerobic glycolysis. The concentration of lactic acid increases locally as the result. Hence intracellular pH is lowered and cells die or become dysfunctional. Hyperglycaemia exacerbates these changes. Hyperglycaemia increases lactic acid production. Such increased lactate production in the ischemic penumbra may lead to poor outcome. [10].

As stated earlier, assessment of neurological deficit after an acute episode stroke can be used to decide on how a patient should be managed. For example, there are a few randomized controlled trials on the effectiveness of surgery in the management of Intracerebral haemorrhage. In one such study, the mortality rate of patient's with surgery was similar to those managed conservatively. In patients with Glasgow coma scale scores of 11 to 14, however, the mortality in surgical group was 27% compared with 7% in the medical group. [11].In another study at the University of Texas, studied 75 patients which were retrospectively evaluated at mean time of 3 and 37 hours after intra cerebral haemorrhage to determine the factors that would predict both good and poor outcomes at the time of discharge.

Their data suggested that all patients with potentially good outcome (ie a Rankin score of 0 to 2) will have an admission Glasgow coma scale score of 11 to 15.[12]. With the possibility of such a high surgical mortality in this group of patients, it seems logical to identify and exclude from surgery these patients who would otherwise have a good outcome.

Another study in Hangang University Medical college in Korea with the aim of determining the timing of surgical intervention and prognostic factors in patients who present with acute cerebral infarction. They reviewed retrospectively 23 patients with acute cerebral infarction, who received decompressive craniectomy or conservative treatment from January 2002 to December 2004. They divided patients into two groups according to the treatment modalities (Group 1 : conservative treatment, Group 2 : decompressive craniectomy). In all patients, the outcome was quantified with Glasgow Coma Scale and Barthel Index. Of the 23 patients, 11 underwent decompressive craniectomy. With decompressive craniectomy at the time of loss of pupillary light reflex, they were able to prevent death secondary to severe brain edema in all cases. Preoperative Glasgow Coma Scale and loss of pupillary light reflex were significant to the clinical outcome statistically.[13]

Another study in Department of Neurosurgery, The General Infirmary at Leeds, England with the objective to identify easily applicable guidelines for surgical and conservative management of spontenous cerebellar haematoma. A treatment protocol was developed and prospectively applied for the management of 50 consecutive cases of cerebellar hematomas. The appearance of the fourth ventricle, adjacent to the hematoma, on computed tomographic scans was divided into three grades (normal, compressed, or completely effaced). The degree of fourth ventricular compression was correlated with the size and volume of the hematoma and the presenting Glasgow Coma Scale (GCS) score. The hematoma was surgically evacuated for all patients with Grade III compression and for patients with Grade II compression when the GCS score deteriorated in the absence of untreated hydrocephalus. Patients with Grade I or II compression were initially treated with only ventricular drainage in the presence of hydrocephalus and clinical deterioration. The degree of fourth ventricular compression was

classified as Grade I in 6 cases, Grade II in 26, and Grade III in 18. The degree of fourth ventricular compression was significantly correlated with the volume of the hematoma, hydrocephalus , the preoperative GCS score, the maximal diameter of the hematoma , and a midline location of the hematoma. Acute deterioration in GCS scores occurred for 6 (43%) of 14 patients with Grade III ventricular compression who were conscious at presentation. Thirteen patients with Grade I or II ventricular compression and stable GCS scores of more than 13 were treated conservatively. Nine patients were treated with ventricular drainage only, and 28 underwent posterior fossa craniectomy and evacuation of the hematoma with ventricular drainage. The mortality rate at 3 months was 40%. None of the patients with Grade III fourth ventricular compression and GCS scores of less than 8 at the time of treatment experienced good outcomes. Overall, 15 (60%) of 25 patients with hematomas with maximal diameters of more than 3 cm and Grade I or II compression did not require clot evacuation. So they concluded that Conscious patients with Grade III fourth ventricular compression should undergo urgent clot evacuation before deterioration. Surgical evacuation of the clot may not be required for large hematomas (>3 cm) if the fourth ventricle is not totally obliterated at the level of the clot.[14] So again this study demonstrates the importance of assessing the severity of neurological deficit after an acute episode of stroke, in this case assessed by Glasgow coma scale, in deciding what type of treatment a patient should receive.

Currently the severity of neurological deficit after stroke is mainly assessed clinically using methods such as, Glasgow coma scale, NIHSSS and Scandinavian stroke scale. There is currently no radiological method to systematically quantify the effect of complex spatial pattern of brain injury on the severity of neurological function/ dysfunction. Stroke can affect any part of the brain and often includes multiple functional areas, making it particularly challenging to predict neurological status based on lesion characteristics.

Computed tomography [CT] scan is mainly used to confirm presence of brain infarct after vascular occlusion. CT scanning is important in brain infarct classification and also CT is used

to assist in identifying the exact anatomical location of brain infarct. Stroke lesion volume as seen on CT scan has been shown to have an impact on patient's final outcome.

One study was done to assess the prognostic significance of changes in lesion size of established cerebral infarcts on CT of brain. This was a retrospective study in which the size of infarct on CT brain was assessed at 2 fixed time interval points after stroke in order to investigate its influence on outcome. 220 consecutive stroke patients admitted within 24 hours after stroke onset with symptoms lasting more than 24 hours were selected. 150 displaying anterior circulating syndrome The lesion size was calculated. The patients were then divided into 4 groups according to their degree of disability at 3 months on modified rankin scale. The conclusion was that the lesion size on CT is a significant predictor of stroke outcome.[15]

A study in Netherlands investigated the relationship between stroke lesion volume and outcome. Correlations between lesion volumes (determined by conventional MRI scans in the second week post-stroke) and outcomes after one year .75 first-ever ischemic stroke survivors were investigated. They concluded that infarct volume moderately correlates with long-term motor impairment, functional outcome and quality of life of patients surviving stroke [16]

A Study in Department of Clinical Neurosciences, Western General Hospital NHS Trust, Edinburgh, UK, investigated If visible infarction on Computed Tomography associated with an adverse prognosis in acute ischemic stroke? They examined whether visible infarction was associated with a poor outcome after stroke using univariate and multivariate analyses, including easily identifiable clinical baseline variables, and adjusting for time from stroke onset to CT. All inpatients and outpatients with an acute ischemic stroke attending their hospital stroke service were examined by a stroke physician and entered into a register prospectively. The CT scan was coded prospectively for the site and size of any relevant recent visible infarct. The patients were followed up at 6 months to ascertain their functional status with the use of the modified Rankin Scale. Analyses of the effect of visible infarction on the outcomes "dead or dependent" or "dead" at 6 months were performed with adjustment for time from stroke to CT, clinical stroke type (lacunar, hemispheric, or posterior circulation), and in a

multiple logistic regression model to adjust for confounding baseline variables such as stroke severity. In 993 patients in the stroke registry, visible infarction increased the risk of being dead or dependent at 6 months or dead , both on its own and after adjustment for time from stroke to CT, stroke symptoms, and other important clinical prognostic variables. They concluded that visible infarction on CT is an adverse prognostic indicator even after adjustment for stroke severity and time lapse between the stroke and the CT scan.[17]

A study in Department of Neurological Sciences, I Chair of Neurology and Chair of Neuroradiology (S.B.), University "La Sapienza," Rome, Italy, the aims were to identify predictors of early neurological improvement in acute ischemic stroke patients, to evaluate its impact on clinical outcome, and to investigate possible mechanisms. A consecutive series of 152 first-ever ischemic hemispheric stroke patients hospitalized within 5 hours of onset underwent a first CT scan within 1 hour of hospitalization, and the initial subset of 80 patients also underwent angiography. During the first 48 hours of hospital stay, an increase or a decrease of 1 or more points in the admission Canadian Neurological Scale (CNS) score was defined as early improvement or early deterioration, respectively. Repeated CT scan or autopsy was performed 5 to 9 days after stroke. Thirty-four patients (22%) improved, 84 (56%) remained stable, and 34 (22%) deteriorated. Logistic regression, which took into account vascular risk factors, baseline clinical and CT data, and therapies administered, selected younger age, lower admission CNS score, and absence of early hypodensity at first CT as independent predictors of early improvement. Among the patients who underwent angiography, logistic regression selected arterial patency and presence of collateral blood supply as independent predictors of early improvement. At the repeated CT scan or autopsy, improving patients presented the highest frequency of small infarcts. Thirty-day case-fatality rate and disability were lower in improving patients. Variables independently associated with outcome at logistic regression were admission CNS score, early deterioration, and early improvement .They concluded that early improvement can be predicted by the absence of early CT hypodensity and is highly predictive of good outcome. Presence of collateral blood supply and presumably early spontaneous recanalization are likely to be the mechanisms underlying early improvement.[18]

A study in Department of Geriatrics, Hasharon Hospital, Golda Medical Centre Petah-Tikva, Israel, investigated the Importance of Brain Infarct Size and Location in Predicting Outcome after Stroke. Fifty-six consecutive elderly (> 65 years) patients, admitted for acute stroke to a geriatric department were included in the study and underwent CT scanning. Functional status was graded according to the modified Rankin scale. Three patients had primary intra-cerebral haemorrhage, 22 deep hemispheric infarct, 17 had anterior circulation cortical infarcts, five had posterior circulation infarcts and in nine the CT scan was normal. Stroke risk factors were equally distributed among the different CT scan groups, and all three larger groups had similar rates of non-neurological major complications including death (41%). For the normal scan group, functional recovery was intermediate. In the cortical infarct group, patients with an infarct of ⩾50 mm mean diameter (five cases) showed worse functional recovery than did eight patients with small infarcts. The mean difference between pre- and post-stroke Rankin score (DR) was 3.4 for the larger infarct patients and 1.9 for the smaller infarct group ($p = 0.027$). Pearson correlation revealed a direct relationship between the infarction size and DR ($p = 0.039$). Such a relationship was not observed for the deep hemispheric group. [19]

.Another study attempted to show the effects of infarct location on stroke severity. In this study atlases were developed consisting of location – weighted values indicating the relative importance of neurological deficit severity for every voxel of the brain. These atlases were applied to 80 first –ever ischemic stroke patients to produce estimates of the clinical deficit severity. Each patient had an MRI and National Institutes Stroke Scale [NIHSS] examination just before or soon after hospital discharge. The correlation between location based deficit predictions and measured neurological deficits (NIHSS) scores were compared. They concluded that there was a significant correlation between location and severity. [20]

So this study intends to investigate whether one can use the volume of the infarct to predict the stroke severity. Stroke severity is assessed by Glasgow coma scale. Another aspect of this study is to study the prevalence and classification of stroke cases as seen at Muhimbili National Hospital Radiology CT unit the period of July 2009 to December 2009.

A similar study done in department of neurology, division of pediatric neurology, Johns Hopkins University School of Medicine,USA. They investigated intracerebral haemorrhagic volume and neurological outcome in children. A consecutive cohort of children, including full-term newborns to those younger than 18 years of age with nontraumatic, acute ICH and head CT available for analysis were studied. Clinical information was abstracted via chart review. Hemorrhage volume was expressed as percentage of total brain volume (TBV) with large hemorrhage defined as >or=4% of TBV. Hemorrhages were manually traced on each head CT slice and volumes were calculated by multiplying by slice thickness. Location was classified as supratentorial or infratentorial. Logistic regression was used to identify predictors of poor neurological outcome, defined as a Glasgow outcome scale <or=2 (death or persistent vegetative state). Thirty children were included, median age 6 years. Median ICH volume was 20.4 cm(3) and median ICH size as a percentage of TBV was 1.9%. Only 4 of 22 children with ICH <4% of TBV had poor outcomes, vs 5 of 8 children with ICH >or=4% of TBV (P=0.03). In multivariate analysis, hemorrhage >or=4% of TBV (OR, 22.5; 95% CI, 1.4-354; P=0.03) independently predicted poor outcome 30 days after ICH. In this small sample, infratentorial hemorrhage location and the presence of intraventricular hemorrhage did not predict poor outcome. ICH volume predicts neurological outcome at 30 days in children, with worst outcome when hemorrhage is >or=4% of TBV. Location and ICH etiology may also be important. These findings identify children with ICH who are candidates for aggressive management and may influence counseling regarding prognosis.[21].There are several differences from this study to my study, despite the fact they investigated the correlation between ICH volume and Glasgow coma scale, there are several differences, and these include the fact that they only included full-term newborns to those younger than 18 years of age, where I intend to include all ages, they inco-orporated volume and location, whereas I am only

interested in volume alone, they only included stroke of Intracerebral haemorrhege type, I intend to include both ICH and infarction, timing is also different, I am looking at the acute stage < 48hrs whereas they looked at outcome at 30 days.

Another similar study in Department of Neurology, University of Cincinnati, OH, they were interested in studying measurements of acute cerebral infarction, lesion size by CT scan. They included a total of 65 patients with acute, nonhemorrhagic, cerebral infarction, computed tomographic scans of the head were obtained at 7-10 days, and 3 months. The scans were analyzed for the presence, site, size, and volume measurement of the infarction. At 7-10 days, the mean infarction volume as measured by computed tomography was 55 cm3 or about 4 x 4 x 3.5 cm (range = 0-507 cm3). At 3 months, the mean infarction volume decreased by 25% to 41 cm3. With lesion size at 7-10 days expressed as percentage of total brain volume, the mean infarction size was only 5%.The lesion volumes as measured by the 7-10-day computed tomography correlated with the neurologic examination scores on admission (Spearman's rank-order correlation = 0.78).[22].So study showed that there is a good correlation between neurological deficit examination at admission and stroke volume, but at 7-10 days, I am interested in acute stage < 48 hours.

The brain functions of the two hemispheres are slightly different. For example, language is predominately controlled by the left hemisphere, where as neglect is predominately controlled by the right hemisphere. The National Institutes of Health Stroke Scale (NIHSSS) is a valid, reproducible scale that measures neurological deficit. Of the 42 possible points, 7 points are directly related to measures language which is presumed left hemisphere function, compared with only 2 points related to neglect which is presumed to be the right hemispheric function. Taking this into account a study was done to investigate whether the relationship between acute NIHSSS scores and acute stroke volume as determined by acute diffusion and perfusion weighted MRI differs between right and left sided stroke. This was a retrospective study of 153 patients with acute stroke seen at Beth Israel Deaconess Medical Centre Between January

1995 and march 2000 who underwent an MRI examination and NIHSSS within 24 hours of stroke onset . NIHSSS score was recorded prospectively by the admitting stroke fellow at the time of acute presentation, immediately preceding imaging. Computerized volumetric analysis of the MRI lesion was performed by investigators blinded to clinical data. They concluded that patients with right sided stroke may have a low NIHSSS scores despite substantial DWI lesion volume. [23]. Another similar study was done but this time CT scan was used rather than MRI, and they concluded that for a given NIHSSS score, the median volume of right hemisphere strokes is consistently larger than the median volume of left hemisphere strokes.[24] As far as this study settings are concerned NIHSSS will not be used to assess neurological deficit, Glasgow coma scale is used instead. I use Glasgow coma scale because it is simple, valid, reliable and quick to administer. It takes approximately 2 minutes.[25].It is also used as part of several ICU scoring systems, including APACHE II, SAPS II, and SOFA.[26].So this makes it practical.

There are several methodology in which stroke volume can be measured using CT scan. One study in Department of Neurology, University Medical Center Utrecht, Netherlands. Tested which of 5 different methods to measure infarct size or volume on CT scans has the highest reproducibility. Infarct volume and total intracranial volume were measured with Leica Q500 MCP image analysis software, or with a caliper, on 38 CT scans of patients who participated in the Tirilazad Efficacy Stroke Study II (TESS II). The scans were performed 8 days (±2 days) after the onset of symptoms. The 5 methods tested were based on (1) semiautomated pixel thresholding, (2) manual tracing of the perimeter, (3) a stereological counting grid, (4) measurement of the 3 largest diameters, and (5) the single largest diameter. The measurements were performed independently by 2 observers; the first observer performed all measurements twice. The single largest diameter did not correlate well with infarct volume. Of the other methods, manual tracing of the perimeter of the infarct had the lowest intraobserver and interobserver variability: coefficients of variation were 8.6% and 14.1%, respectively. For total intracranial volume, manual tracing also provided the highest

reproducibility: intraobserver and interobserver coefficients of variation were 3.3% and 4.9%, respectively. They concluded that manual tracing of the perimeter is the most reproducible method for measuring the volumes of the infarct [27]

For volume measurements, the CT scan films were placed on a transillumination base under a camera. Each image was captured and digitized. Of each scan, the images were calibrated by means of the internal calibration marks. If necessary, contrast was enhanced. Three routines were developed with Leica Q500 MCP image analysis software: **(a)** The pixel thresholding technique was based on thresholds in signal intensity for both ICV and infarct. First, each intracranial pixel with an attenuation lower than bone was assigned to the ICV. Thereafter, each pixel with a signal intensity identical to or below that of the infarct was color coded. For each slice, this threshold in signal intensity was interactively determined by the investigator and depended on the density scale settings of the CT scan and the attenuation of the infarct. After color-coded compartments other than the lesion, such as cerebrospinal fluid, had been rejected by the investigator, the computer calculated the area of the infarct in the particular slice. Infarct was distinguished from cerebrospinal fluid on the basis of anatomy and signal intensity. **(b)** In the manual tracing technique the perimeter of the area of abnormal low attenuation was traced on each CT slice showing the infarct. The same procedure was performed for the total intracranial space**. (c)** The stereological counting grid, based on the Cavalieri principle is a single-lattice square grid with an interpoint distance of 1.5 cm superimposed over the brain image. In an earlier study of infarct volume measurement, this distance was chosen on the basis of pilot studies and published nomograms. Each grid point within the intracranial space was assigned to either normal tissue or infarct. If a grid intersection fell on a boundary between 2 compartments, the point was assigned to the compartment in the lower left square. The points assigned to normal tissue or infarct were multiplied by the area of a single square. For each of the methods, all measured areas were multiplied by the slice distance to obtain the total volumes**. (d)** In the fourth method, the largest diameter (A) of the infarct and its largest perpendicular diameter (B) were measured with a caliper.The third, vertical diameter (C) was determined by summing the thicknesses of

the slices in which the lesion was visible. Infarct volume was calculated according to the formula 0.5xAxBxC **(e)** Finally, the single largest visible diameter was measured. [27]

Manual tracing of the perimeter is the most reproducible method for measuring the volume of a brain infarct and the total intracranial space in large multicenter trials of therapies for acute ischemic stroke. The method is rapid, reliable, and probably accurate, despite technical differences between the CT scans.[27].But the main disadvantages of this methodology is that it depends on the type of CT scan and also requires image analysis system.

Among the methods tested, measurement of the largest diameter of the infarct was the most rapid and reproducible. The good intraobserver and interobserver variability may well be explained by the fact that only a single, 1-dimensional measurement had to be performed. However, the relation between the largest diameter of the infarcts and their volume was insufficient. This disadvantage is overcome by the inclusion of both largest perpendicular diameters and the slice thickness in a formula to obtain infarct volume. This method has earlier been described to measure volumes of intracerebral hemorrhage. Despite its slightly lower reproducibility, the fair correlation between infarct volumes as measured according to this technique and those obtained with manual tracing makes this simple method acceptable for investigators who do not have access to an image analysis system.[27].So this is the methodology which will be used in this study. It is practical since it is just as accurate as manual tracing and does not require image analysis, so it can be performed by any CT scan and any radiologist.

A study in Departments of Emergency Medicine and Department of Surgery, University of Michigan, compared a bedside method of measuring CT ICH volume with measurements made by computer-assisted planimetric image analysis. The formula $ABC/2$ was used, where A is the greatest hemorrhage diameter by CT, B is the diameter 90° to A, and C is the approximate number of CT slices with hemorrhage multiplied by the slice thickness. The ICH volumes for 118 patients were evaluated in a mean of 38 seconds and correlated with

planimetric measurements (R^2=.96). Interrater and intrarater reliability were excellent, with an intraclass correlation of .99 for both. They conclude that ICH volume can be accurately estimated in less than 1 minute with the simple formula $ABC/2$. [28]

This method has been used in other studies and has been validated by computer measurements of volume.[29]

Statement of the problem

Stroke is a third leading cause of death in USA and a major source of long term disability among the survivors .It is a very common problem in our hospital settings. Between May and November 2008, 6.8% of admission were due to stroke in Muhimbili National Hospital.[30] The incidence of stroke in rural Tanzania, is similar to that of blacks living in New York, but in urban Tanzania, Dar-es-Salaam, the incidence is about 3 times higher than in the rural setting, suggesting that urbanization may be increasing stroke risk in the developing world .[31].More recently, community surveys undertaken in South Africa, Togo and Tanzania suggest the prevalence of stroke to be between 200 and 300 per 100,000.[32] Furthermore, it is also known that among blacks, stroke is more common, more severe, and carries a higher mortality when compared with other races. This is attributed by the fact that blacks have an increased frequency of traditional risk factors for stroke such as diabetes mellitus, hypertension, and obesity.[33]

Risk factors for stroke include:-

a) High blood pressure. Studies indicate that individuals with high blood pressure (hypertension) are four to six times more likely to have a stroke than those with normal pressure.[34]
b) Metabolic diseases .People with diabetes are more likely than non diabetic to have diseases of blood vessels such as atherosclerosis, peripheral vascular diseases, stroke, carotid artery diseases, or coronary artery diseases. [35]

Other risk factors include, heart conditions, unhealthy levels of cholesterols and trigycerides, obesity, inadequate exercises and smoking. Currently in Tanzania little is known on the magnitude of the disease in terms of common etiological factors, modes of management and treatment outcomes, but it is a well known fact that diabetes mellitus and related

cardiovascular complications are gaining more importance in sub-Saharan Africa., it is set to overtake infectious diseases in the developing world as the most common cause of death. [36] Sub-Saharan Africa is undergoing epidemiological transition. Stroke and other vascular diseases increasingly contribute to the burden of disease. Stroke mortality is as high, perhaps higher, than in high-income regions and increases with age in sub-Saharan Africa as in high-income countries, but the absolute number of stroke deaths remains low. There are no adequate community-based stroke incidence studies. Hospital-based incidence is lower than in high-income regions, but higher in young people, possibly due to hospital admission bias. There are no community-based data on case fatality, but hospital-based case fatality is higher than elsewhere. The prevalence of stroke is lower than in high-income regions, but disabling stroke is as prevalent. As the region develops economically, the incidence of stroke and other vascular diseases will increase unless interventions are implemented. [37].It is therefore concluded that stroke is common and warrants improved detection and classification using standardized criteria to improve management and its outcome focusing on morbidity and mortality.

Also the approach to treatment of ischemic stroke has been largely preventive or supportive in the past, but approval of intravenous thrombolysis for acute stroke and neuroprotective drugs development have made rapid imaging and intervention a critical part of stroke management.

The patient with haemorrhagic stroke may harbour an aneurysm, vascular malformation or other conditions and each condition involves important differences in treatment options. The Radiologist plays a critical role in the triage and evaluation of all stroke patients. Selection of proper imaging techniques, recognition of early ischemic changes, differentiation of stroke from other brain disorders and recognition of important subtypes can have a significant impact on therapy and outcome.

The outcome of stroke depends on many factors, but the strongest predictor is the severity of the neurological deficit at presentation. Glasgow Coma Scale or GCS is a neurological scale

that aims to give a reliable, objective way of recording the conscious state of a person for initial as well as subsequent assessment. A patient is assessed against the criteria of the scale, and the resulting points give a patient score between 3 (indicating deep unconsciousness) and either 14 (original scale) or 15 (the more widely used modified or revised scale).

GCS was initially used to assess level of consciousness after head injury, and the scale is now used by first aid, EMS, and doctors as being applicable to all acute medical and trauma patients. In hospitals it is also used in monitoring chronic patients in intensive care [26].Several studies have used GCS to assess neurological deficit in non-traumatic brain injury.[5,7,10,11,12].The scale was published in 1974 by Graham Teasdale and Bryan J. Jennett, professors of neurosurgery at the University of Glasgow. GCS is used as part of several ICU scoring systems, including APACHE II, SAPS II, and SOFA, to assess the status of the central nervous system.

There is a direct correlation between initial GCS score and subsequent morbidity and mortality. Stroke can effect any part of the brain and often includes multiple functional areas, making it particularly challenging to predict neurological status. There is currently no methodology to systematically quantify the effect of the complex spatial pattern of injury on the severity of neurological function./dysfunction. In this view, there is a need for a quick, reliable and simple radiological investigation that would help to do this. And this can be done through a frequently done investigation on stroke patients like CT scan. As stated earlier, stroke can effect any part of the brain and often includes multiple functional areas. In this current study, I sought to quantify the stroke volume and delineate this from Glasgow coma scale, and see if there is any correlation between stroke volume and GCS?

Study Rationale

With the bewildering and ever increasing array of examination available for imaging the brain, it seems hopeless task to decide which the best for a given clinical situation is. This is particularly problematic in the developing countries like Tanzania where resources are scarce. Plain Radiography is useless in stroke patient's management and is only of value in documentation for fracture for medical legal reasons. Nuclear medicine brain scan is useful in certain specialized settings. We still must decide between MRI, CT, USS and angiography in evaluating the acute neurological patient. Angiography is not available in Tanzania .USS is cheap and widely available but it may only be used as the first test in infants or for evaluation of carotid arteries or with intracranial techniques for evaluation of intracranial vessels. Therefore the only contenders for first test for brain imaging are CT and MRI. MRI is very expensive for most Tanzanians and not widely available .It is also not ideal to investigate an acute case, it is more appropriate for chronic and subacute cases.

As a general rule in brain imaging, CT is performed first for acute neurological illness. It is quick to perform and also cheaper compared to MRI and much more available. So in this view, CT scan will be used and see if one can assess neurological deficit using it. Among its many roles of CT in evaluating stroke patient, it would have an additional role to assess neurological severity of patients which is the most important predictor of morbidity and mortality.

I will use GCS to assess the severity of neurological deficit because is easy to use, simple, can be administered by non neurologist, valid, reliable and quick to perform, approximate time to administer is 2 minutes. [25]. It is the most widely used scoring system used in quantifying level of consciousness following brain injury, has a relatively high degree of inter observer reliability and because it correlates well with outcome following severe brain injury. Level of

consciousness, as measured by Glasgow Coma Scale score, seems to be a more important predictor of outcome than the initial National Institutes of Health Stroke Scale score.[8].It has a high sensitivity compared to NIHSSS [25].It is the scoring system commonly used in our setting to assess the severity of neurological deficit after an acute episode of stroke. So this makes it practical aswell as relevant in our setting. NIHSSS score is hardly used in our setting at all.

The formula *ABC*/2 is used to measure the infarct volume, where *A* is the greatest infarct diameter by CT, *B* is the diameter 90° to *A*, and *C* is the approximate number of CT slices with infarct multiplied by the slice thickness. This is a simple, accurate and quick method to measure infarct volume. Volume can be accurately estimated in less than 1 minute. [28].It has been previously used in other studies with no problems [12] and has been validated by computer measurements of volume.[29] Among the other methods, measurement of the largest diameter of the infarct is the most rapid and reproducible. The good intraobserver and interobserver variability may well be explained by the fact that only a single, 1-dimensional measurement is performed. However, the relation between the largest diameter of the infarcts and their volume is insufficient [27] ie, it has a poor correlation with volume. This disadvantage is overcome by the inclusion of both largest perpendicular diameters and the slice thickness in a formula to obtain infarct volume ie, ABC/2. This method has earlier been described to measure volumes of intracerebral hemorrhage. Despite its slightly lower reproducibility, the fair correlation between infarct volumes as measured according to this technique (ABC/2) and those obtained with manual tracing makes this simple method acceptable for investigators who do not have access to an image analysis system. [27]. Manual tracing of the perimeter is the most reproducible method for measuring the volumes of the infarct [27],but it depends on the type of the CT scan and the availability of image analysis system. In Radiology, when it comes to measuring volume of any sort, the most used method is to take the product of 3 dimensions and then divide it by 2 (ABC/2). So by using the method ABC/2, it will be familiar to all radiologist, something they are used to hence making it practical.

This study can further demonstrate the use of CT scanner to assess the severity of neurological deficit after a stroke by measuring the stroke volume and see if it correlates with neurological deficit and if this can then be used to predict the outcome of the patient. The study is significant in both theoretical and practical pursuit. The findings will be a challenge to neurologist as well as Radiologist who may find it necessary to study more on CT findings and see if they can correlate with clinical assessed neurological deficit.

Objectives

Broad objective

To determine the correlation between brain infarct volume and the neurological deficit in patients with an acute episode of stroke at Muhimbili National Hospital, between July 2009 to December 2010.

Specific objectives

1) To determine the prevalence of stroke on terms of sex for stroke patients at Muhimbili National Hospital
2) To determine the prevalence of different subtypes of stroke in stroke patients at Muhimbili National Hospital, between July 2009 and December 2009.
3) To determine the frequency of occurance of brain infarct in different anatomical areas of the brain in stroke patient at Muhimbili National Hospital, July 2009 to December 2009.
4) To determine the relationship between infarct volume and the patient's neurological deficit (stroke) using Glasgow coma scale at Muhimbili National Hospital, between July 2009 to December 2009.

Hypothesis

In this study, it is hypothesized that:-

1) **NULL**: there is no significant difference in using infarct volume size in estimating Glasgow coma scale of a patient after an acute episode of stroke.
2) **Alternative**:- There is a significant correlation between infarct volume size and clinical calculated Glasgow coma scale.

Methodology

Study period and study area: This study was conducted in 6 months duration, between July 2009 to December 2009 at Muhimbili National Hospital at CT unit Radiology department.

Study population: Patients who were admitted at Muhimbili National Hospital with a clinical diagnosis of first ever acute stroke and who had CT brain done within the first 48 hours of onset of ictus and who had Glasgow coma scale done were eligible for the study after all exclusion criteria have been ruled out. The description provided by World Health Organization (WHO) was used to define stroke." Rapidly developing clinical signs of focal or global disturbance of cerebral function, with symptoms lasting more than 24 hours or longer or leading to death , with no apparent cause other than vascular origin." A diagnosis of stroke was established by CT scan, reported by a Radiologist. A total of 74 patients fitted this criteria during the study period. I could have done a simple random procedure using a random number table to select the desired sample size of 44.But this sample size represents the minimum number of patients required to have a statically significance test. And since I was interested in achieving a high level of precision and power for my study, I decided to increase my sample size by including all 74 patients. Power of a study is a probability of correctly rejecting the null hypothesis when it is false. The power to identify correctly a difference of a certain size can be increased by increasing the sample size. Small samples often leads to type II error (ie there is not sufficient power to detect differences of clinical importance.)

Exclusion criteria: Patient who did not consent to participate in the study. Others include, patient presenting more than 48 hours, those with no CT scans, those with traumatic haemorrhage or haemorrhage secondary to brain tumour.

Sample size: The sample size was calculated by adopting the stroke prevalence 3% in a hospital based study done in the Nairobi Hospital, Nairobi Kenya [38].Hospital period prevalence for stroke of 3% was found in 2008[38] . Considering the study power of 95%, a randomly likely error is estimated to be 0.05. The sample size of 44 patients to be studied was estimated based Standard Sample size estimation (Kish & leslie) formular N= Z p (1- p)/ E. Where Z is the point of normal distribution corresponding to significance level 1.96, p is the prevalence 0.03, E is the maximum likely error 0.05. From this formular the sample size was calculated as follow

N= (1.96) 0.03 (1 - 0.03) / 0.05 = 44.

Research tools:-

CT scan- Philips, 4 channels, spiral, multiplanar, multidetector, imaging slices between 3-5mm and no IV contrast was used.

Digital camera

Calculator

Glasgow coma scale

SPSS version 13 for statistical analysis

Data collection: A standardized data sheet was used to record the demographic variables including age, sex, and date of admission. Diagnosis was made based on the admission CT scan. Severity of the neurological deficit was assessed by using Glasgow coma scale. The admitting doctor recorded the GCS. In this scale, three types of response are assessed. Best motor response which has a total of 6 grades, best verbal response which has total of 5 grades and last is eye opening which has a total of 4 grades. So the overall score will be 15.

CT was reported by a single MNH Radiologist whoever was reporting on that particular day and the stroke was classified by type, vascular territory,side, mass effect, ventricular enlargement, subarachnoid haemorrhage and ventricular extension if possible. Volume was calculated by myself using the formula ABC/2, where A diameter,B is the greatest perpendicular diameter to this and C is the thickness of the lesion estimated from thickness of CT slices. The result is then divided by 2.

Data analysis: Statistical analysis was carried out using SPSS 13 statistical software. A logistic regression analysis was undertaken in order to gauge the impact of infarct volume on stroke severity. $P<0.05$ was considered to be statistically significant. 95% confidence interval (CI) was used to estimate the effects.

ETHICAL CONSIDERATIONS

Ethical issues which are important in conducting research involving human subjects such as:-

1) Human dignity- serving as a basis for requirements of privacy, confidentiality, and medical secrecy.
2) Autonomy- serving as basis for requirements of self – determination and participation.
3) Justice- serving as a basis for requirements of equitable distribution of limited resources.
4) Beneficence and non maleficence- serving as a basis for attempts to weigh anticipated benefits against foreseeable risks

Were strictly adhered to in this study. And this was achieved in the following way. This study was done after obtaining sanction from MUHAS-IRB (Institutional Review Board) and permission to conduct the study using MNH Radiological department was obtained from the Director of Clinical Services of MNH.

The general outline of the study was carefully explained to the patient and informed consent (Written) was provided to them or their next of kin.. Such explanation include:- The purpose of the study, an outline of the study, anticipated risks and possible discomfort to be experience if any, that any personal data which either directly or indirectly identifies an individual by reference to identification number or one or more factors specific to his/her physical, psychological, mental or social identity will be kept strictly confidential, the right to with withdraw from the study or refuse to be the subject at anytime, and the fact that withdrawing will not result in a penalty or loss of benefits. The data collected will be analyzed on groups of participants, generally divided by groups and not on individual bases. All published data will be reported by group. Additionally until the data has been submitted for publication, patient will have the right to withdraw his/her consent and have

the individual data withdrawn from the group data without penalty. All information we collected was entered into computers with only the study identification number, this will help in maintaining patient's confidentiality.

Results

The study included 74 patients with mean age of 51 yrs. Males 48 (64.9%) and female 26 (35.1%). The prevalence of ischemic stroke was 56.8%, which is a total of 42 patients, while haemorrhagic stroke was 43.2%, a total of 32 patients. Majority of the patients were in the age group of 41-50 yrs which were 23 (31%) in total, followed by 21 (28.4%) patients in the age group of 51-60 yrs.15 (20.3%) patients were in the age group of 31-40 yrs, 8 (10.8%) patients were in the age group of 61-70 yrs, 5 (6.8%) patients were in the age group of more than 70yrs while only 2 (2.7%) patients were less than 30 yrs. See table 1.

Sex		Age distribution of stroke patients (yrs)						The distribution of subtypes of stroke	
M	F	<30	31-40	41-50	51-60	61-70	>70	Haemorrhagic	Ischaemic
48	26	2	15	23	21	8	5	32	42

Table 1. Shows the distribution of sex, age and subtypes of stroke in stroke patients

Glasgow coma scale scores ranged from 3 – 15 and infarct volumes from 0.3 – 52cm. For ischaemic stroke mean volume was 8.5cm .The maximum infarct volume was 43cm , while the smallest was 0.2cm . 24 patients (57.1%) of the total 42 patients had infarct volume in the range of 0-5.9 cm .There was an equal number of 6 patients (14.3%) who had infarct volumes in the range of 6-10.9 and 11-15.9 cm . 2 patients (4.8%) had volumes in the range of 21-25.9 cm , and also 2 patients (4.8%) had volumes in the range of 41-

50.9 cm .Only 1 patient (2.4%) had infarct volume in the range of 16-20.9 cm and a similar number of patients had infarct volume in the range of 36-40.9 cm .See figure 1.

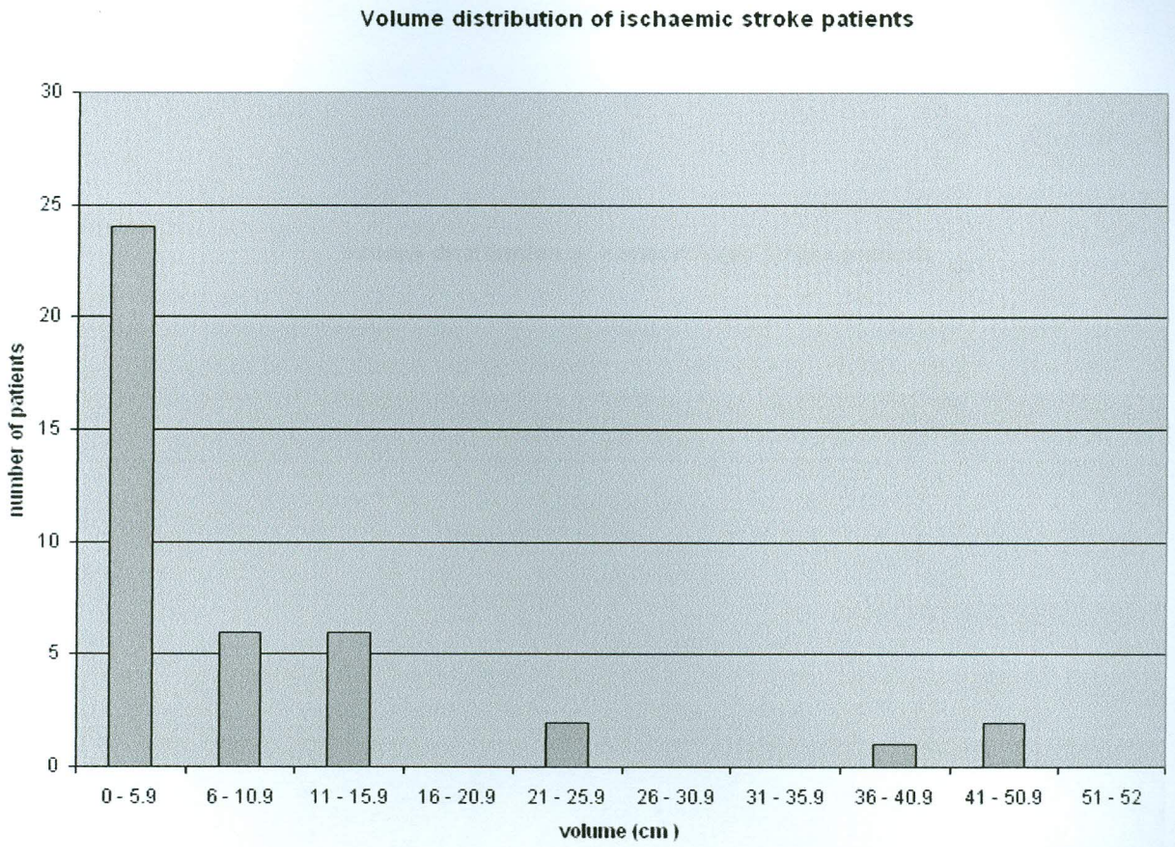


Figure 1.

As for hemorrhagic stroke, mean infarct volume was 11.1cm , slightly higher than that of ischaemic stroke. The maximum volume was 52cm , again higher than that of ischaemic stroke while the smallest volume was 0.2cm , similar to that of ischaemic type. Again majority of the patients, 20 (62.5%) of the total 32 patients had infarct volume in the range of 0-5.9 cm . 3 patients (9.4%) had volumes in the range of 11-15.9 cm , 2 patients (6.25%) had volumes in the range of 6-10.9 cm , 1 patients (3.1%) in the range of 21-25.9

cm , 2 patients (6.25%) in the range of 26-30.9 cm ,1 patient (3.1%) in the range of 36-40.9 cm , 2 patients (6.25%) in the range of 41-50.9 cm and only 1 patient (3.1%) in the range of 51-52.9 cm .See figure 2.

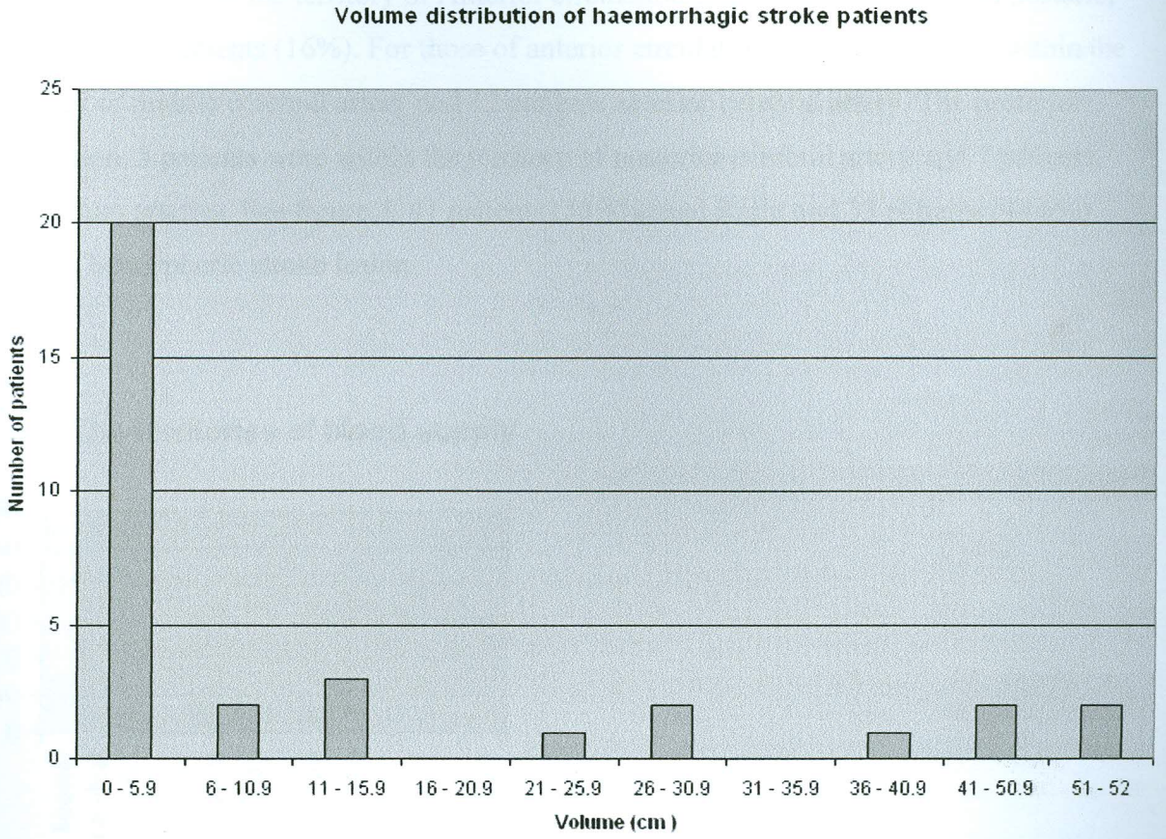


Figure 2.

	Type of stroke	N	Mean	Std. Deviation	Std. Error Mean
Stroke volume	infarct	42	8.543	10.7326	1.6561
	haemorrhagic	32	11.094	14.5533	2.5727

Table 2.Shows the mean stroke volume of the subtypes of stroke patients

Infarcts were within the territory of Anterior circulation in 62 patients (83%) and posterior circulation 12 patients (16%). For those of anterior circulation , 50 patients were within the territory of middle cerebral artery and 12 patients anterior cerebral artery. The posterior circulation, 5 patients were within the territory of posterior cerebral artery and 7 patients, cerebellum arteries. See figure 3. 41 patients (55.4%) had Right and 33 patients (44.6%) had left hemispheric stroke lesion.

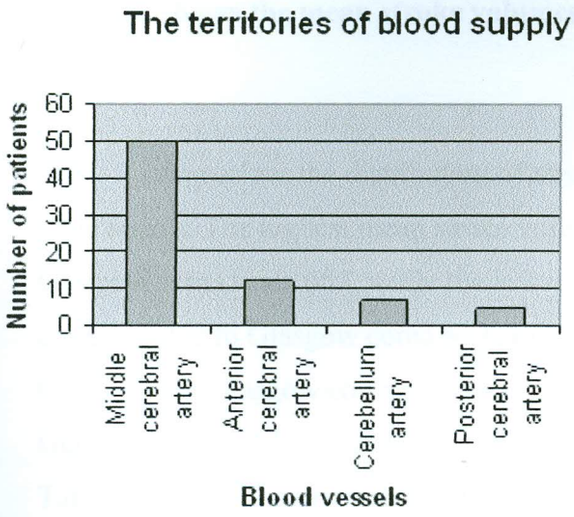


Figure 3. Shows the territories of blood supply involved in stroke patients.

Glasgow coma scale score	Mean stroke volume	N	Std. Deviation
3.0	26.643	7	22.2930
4.0	23.982	9	14.7068
5.0	7.750	2	6.1518
6.0	10.550	8	5.6435
7.0	1.100	1	.
8.0	7.367	9	4.6130
10.0	6.125	8	2.0569
11.0	1.200	4	.8124
12.0	5.100	1	.
13.0	12.500	4	11.8415
14.0	2.580	10	1.1584
15.0	.860	11	.8614
Total	9.646	74	12.5002

Table 3. Shows the mean stroke volumes of various Glasgow coma scale scores.

Table 3 summarizes the distribution of mean stroke volumes of various Glasgow coma scale scores. The highest mean stroke volume was 26.6cm , which corresponded to Glasgow coma scale of 3, while the lowest mean stroke volume was 0.860cm , which corresponded to Glasgow coma scale of 15. This shows that the bigger the stroke volume the lower the Glasgow coma scale score while the lower the stroke volume, the higher the Glasgow coma scale score. Hence the two are inversely proportional. .

Table 4 shows the correlation coefficient between infarct volume and Glasgow coma scale was r = -0.547.This defines a weak linear association.

Correlation

		Volume score	GCS score
Volume score	Pearson correlation	1	-0.547
	Sig. (2-tailed)		.000
	N	74	74
GCS Score	Pearson correlation	-0.547	1
	Sig. (2-tailed)	.000	
	N	74	74

Correlation is significant at the 0.01 level (2-tailed)

Table 4.Shows the correlation coefficient (r) between infarct volume versus Glasgow coma scale

Table 5 shows the regression coefficient of r2 = 0.300: p< 0.001.This indicates that infarct volume is a poor predictor of Glasgow coma scale.

Model summary and Parameter Estimates

Equation	Model summary					Parameter Estimate	
	R square	F	df1	df2	Sig.	Constant	b1
Linear	.300	30.805	1	72	.000	26.182	-1.598

Table 5. Summarizes the data when regression analysis was used.

Table 6 shows t-test is -5.550 with 95% confidence interval of -1.024 - -2.172

Coefficient

Model	Unstandardized coefficient		Standardized coefficient	t	Sig	95% confidence interval	
	B	Std.Error	Beta			Lower Bound	Upper Bound
1(constant)	26.182	3.153		8.303	.000	19.896	32.423
GCS score	-1.598	.288	-.547	-5.550	.000	-2.172	-1.024

Dependent Variable: Volume score

Table 6. Shows the 95% confidence interval and t value.

Figure 4 shows a regression correlation between infarct volume and Glasgow coma scale by approximating a line through the centre of a scatterplot. The graph shows that Glasgow coma scale and infarct volume are inversely related. As the GCS score increases, the infarct volume decreases. The gradient of the line is the regression coefficient (r2), which is 0.300; $p < 0.001$. r2 makes more sense when expressed as a percentage. So in this case its 30%, which means that out of the total 74 stroke patients, correlation between infarct volume and Glasgow coma scale only occurred in 30% of the patients, hence there was a correlation in 22 patients while

there was no correlation in 52 of the patients. This indicates that infarct volume is a poor predictor of Glasgow coma scale. According to the graph, there is a good correlation between infarct volume and GCS score, when the GCS scores are high, in a range of 10-15, this is where most of the scatterplot points are very close to the line. On the other hand for low GCS scores especially in a range 3-5, there is a poor correlation, the scatteplot points are very far away from the centre line.

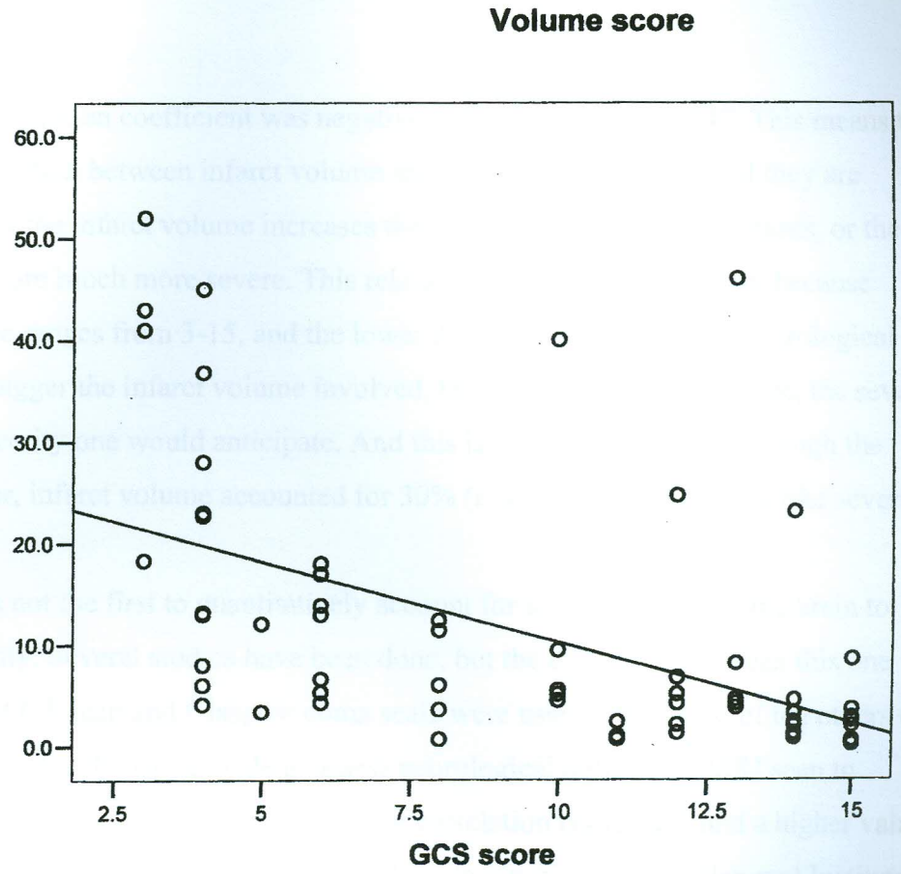


Figure 4.It shows a regression correlation between infarct volume and Glasgow scale by approximating a line through the centre of a scatterplot.

Discussion

In this study, the correlation coefficient was negative and closer to zero-0.547. This means that there is a poor correlation between infarct volume and Glasgow coma scale and they are inversely related. As the infarct volume increases the Glasgow coma scale decreases, or the neurological deficit are much more severe. This relationship is what is expected, because Glasgow coma scale ranges from 3-15, and the lower the value, the severe the neurological deficit is. And the bigger the infarct volume involved, thus the more tissue damage, the severe the neurological severity one would anticipate. And this is what is observed. Although the correlation was poor, infarct volume accounted for 30% (r2) of the variation in stroke severity.

The current study is not the first to quantitatively account for infarct volume in the brain to predict stroke severity. Several studies have been done, but the difference between this one and the others is that CT scan and Glasgow coma scale were used, while most of the others use National Institutes of Health Stroke Scale to assess neurological deficit and MRI scan to calculated infarct volume. Their findings have a +ve correlation coefficient and a higher value of r when compared to our study. This means that the relationship between National Institute of Health Stroke Scale and infarct volume is directly proportional and have a moderate correlation coefficient as compared to this study. One study [20], had a r value of 0.65, P 0.047.

The National Institutes of Health Stroke scale is a valid, reproducible scale that measures neurological deficit. There is a total of 42 points. There is 11 parts to the NIHSSS, with 13 specific tests being performed. It examines the level of consciousness, vision and gaize, facial palsy and extremity weakness, limb ataxia, sensory loss, language and dysarthria, and neglect. It is designed to be conducted over 7 minutes. A patient with a completely normal neurological exam and normal mental status will have NIHSSS score of 0. The maximum recordable score is 42. However, since acute ischemic stroke causes unilateral paralysis and blindness, the maximum score is actually 31 for stroke patients with complete hemiparesis,

hemianopia, and aphasia. Patients with an NIHSSS score greater than 15-20 are considered to have severe stroke clinically. Glasgow coma scale on the other hand gives a reliable, objectives way of recording the conscious state of a person. Three types of response are assessed, best motor, best verbal and eye opening. An overall score is made by summing the scores in the three areas assessed. Severe injury GCS<8, moderate injury 9-12, minor injury 13-15. So with NIHSSS, as the score increases, the neurological deficit becomes more severe, while with Glasgow coma scale, the neurological deficit becomes less severe with higher scores. This can explain the +ve correlation one gets for NIHSSS versus infarct volume, thus they are directly proportional, as the infarct volume increases so does the neurological deficit.

As stated earlier, the NIHSSS score assesses 11 parts which include level of consciousness, while Glasgow coma scale only assess the level of consciousness. This could help to explain as to why the correlation coefficient is higher (0.67) when you have NIHSSS score versus infarct volume as compared to Glasgow coma scale versus infarct volume(0.547), because the NIHSSS is much more sensitive to brain damage. This is for two main reasons:-

First of all out the possible 42 points awarded in NIHSSS score 7 points are directly related to measurements of language compared to 2 points related to neglect. This means that more points are rewarded for presumed Left-hemisphere function, ie language than for test of Right hemispheric function, ie neglect. 2 studies [23, 24] have confirmed that because of this difference, the NIHSSS favours left hemispheric stroke, what was found out was that for a given NIHSSS score the median volume of Right hemisphere stroke is consistently larger than the median volume of Left hemisphere stroke, so patients with R sides stroke may have a lower NIHSSS score despite substantial lesion volume. So overall NIHSSS tests more parts of the brain's functions as compared to Glasgow coma scale, which makes the NIHSSS more sensitive to neurological function/dysfunction.

Secondly, it is not uncommon to see patients with large brain lesions (infarct volume) as seen by CT scan and still be awake, the level of consciousness is not yet affected despite other

neurological deficits, and hence has a high Glasgow coma scale than one would expect. So by simply assessing the level of consciousness to determine neurological deficit is not a very sensitive test. The level of consciousness can change within hours in acute patients whose clinical signs may still be evolving.

The choice of time at which to perform structural or functional correlation is important. This study used acute time point to perform structural functional correlations because the damage pattern seen on imaging presumably closely corresponds to measured neurological deficit. The impact of this study, though lies in the ability to translate the results to the acute timeframe, in which final outcome prediction can effect treatment decision. For example, there are a few randomized controlled trials on the effectiveness of surgery in management of patients of Intracerebral haemorrhage. Some studies have shown that the mortality rate of patients with surgery was similar to those managed conservatively. In patients with Glasgow coma scale scores of 11-14, however, the mortality in surgical group was 27% compared with 7% in the medical group [11]. One study [12], suggested that all patients with potentially good outcome will have an admission Glasgow coma scale score of 11-15. With possibility of such a high surgical mortality in this group of patients, its seems logical to identify and exclude from surgery these patients who would otherwise have a good outcome. So you need a very sensitive and specific methodology to do this, and we thought structural or functional correlation would help this.

The formula *ABC*/2 was used to measure the infarct volume. This is a simple, accurate and quick method to measure infarct volume. Volume can be accurately estimated in less than 1 minute.[28].It has been previously used in other studies with no problems[12] and has been validated by computer measurements of volume.[29].

There are other methods in measuring infarct volume and these include (a) semiautomated pixel thresholding, (b) manual tracing of the perimeter, (c) a stereological counting grid, and (e) the single largest diameter.

Measuring a single largest diameter is the most rapid and reproducible. This may well be explained by the fact that only a single, 1-dimensional measurement is performed. However, the relation between the largest diameter of the infarcts and their volume is insufficient [27] ie, it has a poor correlation with volume. This disadvantage is overcome by the inclusion of both largest perpendicular diameters and the slice thickness in a formula to obtain infarct volume ie, ABC/2.

For the stereological counting grid, the largest interpoint distance that produced the minimum error has been reported to be 1.5 cm. However, with this grid size, the intraobserver and interobserver variabilities are much higher than with the other methods. In addition, up to 36% of the cases of lacunar infarct may be missed because none of the grid intersections fall on the infarct. Both problems would probably be reduced if a smaller grid size are used, but this would make the method much more time-consuming.[27]

Semiautomated pixel thresholding, Manual tracing of the perimeter and stereological counting grid have a good correlation with infarct volume [27], ie are an accurate method of measuring infarct volume, but to me their main disadvantage is that they depend on the type of CT scan which requires to have an image analysis system. The main disadvantage of using the formula ABC/2 to calculate infarct volume is that it has been shown in other studies that it has a low reproducibility. But despite its slightly lower reproducibility, the fair correlation between infarct volumes as measured according to this technique (ABC/2) and those obtained with manual tracing makes this simple method acceptable for investigators who do not have access to an image analysis system. [27].

The sex distribution in the current study was males 48 (64.9%) and female 26 (35.1%). This is consistence with other studies, in a sense that stroke is much more common in male than female [30,38].

The distribution of type of stroke was ischemic 56.8% and hemorrhagic 43.2%. Again this is consistence with other studies in a sense that ischemic stroke is much more common than hemorrhagic stroke [1].Nevertheless the proportion of haemorrhagic stroke was higher than other strokes. As a matter of fact 2 studies done in Muhimbili National Hospital,[30,39] found out that the proportion of haemorrhagic stoke was actually higher than ischaemic stroke. The reason for this difference may be due to the fact that, my the sample size was small. With a bigger sample size the results may have been different. And secondly, the current study had biased sample not represent the true population of all stroke cases seen in Muhimbili National Hospital. It only looked at those cases which had brain CT scan done and stroke within the first 48 hours, so cases which do not fit these criteria would have been missed.

The vascular distribution of stroke was , anterior circulation in 62 patients (83%) and posterior circulation 12 patients (16%). Infarcts were within the territory of the middle cerebral artery in 50, anterior cerebral artery in 12, posterior cerebral artery in 5, and cerebellum arteries in 7. This is consistence with other studies in a fact that most brain infarcts involve the anterior circulation and more specifically Middle cerebral artery. This could be due to the fact that the middle cerebral artery supply most of the brain.

Conclusion

From this study, we can conclude that calculated stroke volume alone cannot be used to estimate stroke severity in patients with acute stroke.

Other similar studies have also come up with similar conclusion, infarct volume alone cannot be used to predict neurological deficit, whether you correlate it with NIHSSS or Glasgow coma scale.

Recommendations

1) Future work with larger data sets is required. Such studies would also address reproducibility and reliability of the current findings.
2) Most patients in this study had middle cerebral infarcts, and so there was considerable less data available for brain regions outside the middle cerebral artery. So Such studies in different patients cohorts would again also address the reproducibility and reliability of the current findings.
3) To do a study, to find the prevalence of stroke in Tanzania. There is very little data available on this.

Limitations of the study

The main limitation of this study was that it only looked at those cases that presented to CT scan department, hence only those patients with brain CT scan done were included in the study, this means that the rest of the cases of stroke patients who did not have CT scan done were missed. So this means that the true prevalence of stroke cases in Muhimbili National Hospital was not recorded.

Other limitation include the fact that during literature review most of the recent studies done now world over were done using MRI rather than CT scan. So it was very challenging to find studies done using CT scan and as the result most of the articles which were referred to, MRI is the modality used.

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