NEUROIMAGING PATTERNS OF ISCHEMIC STROKE AND THE DRIVERS OF DYNAMICS IN ASPECT SCORE IN RWANDA.

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Kigali, August 2022

DECLARATION AND COPYRIGHT

I, Joseph MUSABYIMANA, declare that this dissertation '**NEUROIMAGING PATTERNS OF ISCHEMIC STROKE AND THE DRIVERS OF DYNAMICS IN ASPECT SCORE IN RWANDA'** is my own original work except where specifically acknowledged. It has not been submitted for any other degree at the University of Rwanda or any other institution.

It is submitted to the University of Rwanda, College of Medicine and Health Sciences, School of Medicine and Pharmacy in partial fulfilment for the requirement of the award of a Masters of Medicine degree in Diagnostic Radiology.

MUSABYIMANA Joseph

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Signature:

DEDICATION

This research paper is dedicated to my family and friends who have been supportive and have encouraged me with their fullest and trustworthy attention to accomplish my work with fruitful achievements.

Valentine INGABIRE my wife, MUCYO Archie Joseph and MUHIZI Arnold Bonheur my children and my siblings. Your physical, financial as well as moral support pushed me to stand where I am as of now.

My friends who never stop giving of themselves in countless ways and all the people in my life who touch my heart, I dedicate this research to all of them.

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ABSTRACT

Background: Stroke is the second leading cause of death and the third leading cause of both death and disability worldwide. Clinical decision-making is supported by the use of imaging in such patients. For the purpose of determining and quantifying early ischemic changes on non-contrast brain computed tomography (CT), the Alberta Stroke Program Early CT Score (ASPECTS) was developed. ASPECT score is utilized to assist in patient selection for intra-arterial recanalization therapy and as a prognostic tool. The patients with very low ASPECT scores (0-3) are more prone to experience bleeding as a result of thrombolysis and are less likely to achieve a positive clinical result. Despite the high mortality and morbidity rate attributed to stroke, there is little available data on stroke in Rwanda. Most importantly, there is no available data from referral hospitals addressing the neuroimaging patterns of ischemic stroke and the drivers of dynamics in ASPECT score.

Objective: This study investigated the neuroimaging patterns of ischemic stroke and the drivers of dynamics in ASPECT score in Rwanda for the period of January 2019 to December 2021.

Methods: A retrospective cross-sectional study was conducted. Three hundred and eighty-nine (389) patients who underwent brain CT scans were recruited in the study done in the four referral hospitals in Rwanda. The data analysis was performed by SPSS version 21 and checked once more for omissions and errors before being analysed

Results: The findings show that 77.1% were at least 51 years of age with an average of 62.89±19.19years. Furthermore, results show that 55.3% of the population were females and 44.7% were males. Regarding residence of study participants 237(60.9%) of patients with ischemic stroke were coming from rural area, while 152 (39.1%) live in urban areas. Among the study population ASPECT score of less than 7 was prevalent at 58.1% and the mean ASPECT score was 6.86±1.62. The majority of ischemic stroke patients in Rwanda avail themselves to imaging facilities between 1-7days post symptoms, while only 1% of them show up within the golden window of time within 3 hours of the stroke symptoms. Hypertension (AOR=2.034, 95% CI =1.258-3.288, P=0.011), the distance to the receiving referral hospital (AOR=1.772, 95% CI =1.056-2.976, P=0.033), duration of symptoms before neuroimaging (AOR=0.514, 95% CI =0.280-0.943, P=0.031) and location of the lesion (AOR=0.289, 95% CI =0.102-0.818, P=0.032) significantly influence the occurrence of low ASPECT score in the study population. The ischemic stroke patients with low ASPECT scores (less than 7) were two times more likely to develop hemorrhagic transformation [AOR=2.661, 95%CI: 1.118-6.336, p<0.027].

Conclusion: Ischemic stroke trends more among females in the rural population. The dynamics of ASPECT score among patients with ischemic stroke are driven by hypertension, increased distance from the equipped hospital, and increased duration from symptoms onset.

Keywords: Stroke, ASPECT score, ischemia, haemorrhage, neuroimaging, luxury perfusion

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Definition of key terms

Stroke: According to WHO guidelines, it is clinically defined as the rapid onset of localised or generalised disturbances of brain function with symptoms that last for 24 hours or more or result in death and have no other known cause than vascular origin (37).

Ischemic Stroke: Is an episode of neurological dysfunction due to focal or global brain infarct attributed to arterial thrombosis, embolization, or critical perfusion ischemic stroke (38). Ischaemic stroke is account for brain, spinal cord, and retinal infarcts. This study considers cerebral infarction.

Haemorrhagic Stroke: It happens as a result of blood vessels becoming weaker to the point where they could rupture and leak into the surrounding brain tissues (39).

Neuroimaging patterns: Those are the locations of ischemic lesions in different regions of the brain as shown by brain CT scan.

Luxury perfusion: It describes blood flow to infarcted brain regions that is higher than what is required for local metabolic requirements.

ASPECT (**Alberta stroke program early CT**) **score**: Is a quantitative topographic score out of 10 points which quantifies ischemic stroke lesions in patients with middle cerebral artery (MCA)on non-contrast brain CT stroke (40).

CHAPTER I: INTRODUCTION

1.0. Introduction

The background, problem statement, goals, objectives, and research questions of the study, as well as its significance and structural organization, are covered in this chapter.

1.1 Background of the study

Globally, stroke is one of the major causes of mortality and morbidity, and the expense of caring for patients with stroke is significant (1,2).

Despite being largely preventable, as seen by declining incidence rates internationally, stroke remained the world's number two leading cause of death and the 3rd leading cause of both death and disability in 2019 (3,4).

According to data from the Global Burden of Diseases (GBD), more than 17.3 million deaths per year are due to cardiovascular disease, which is the most common cause of death worldwide. This number is anticipated to increase to more than 23.6 million by 2030 (5).

Up to 19% of patients initially diagnosed as stroke and up to 14% of patients treated for acute stroke are due to stroke mimics, which can complicate management and prognosis (7). For the evaluation of stroke patients, neuroimaging is important because it enables the rapid differentiation between haemorrhagic and more common ischemic causes of stroke (6).

The goal of the Alberta Stroke Program Early CT Score (ASPECTS) scale is to detect and quantify early infarct lesions using non-contrast CT(NCCT) (8). This tool facilitates identification of the thrombolysis criteria and stratifies the risk for haemorrhagic transformation of ischemic brain regions (9).

The ASPECTS is a standardized semi-quantitative CT grading system that evaluates early ischemia symptoms in 10 regions of the brain parenchyma for patients with acute anterior circulation ischemic stroke (Goyal et al., 2011). Final infarct size is significantly correlated with non-contrast-CT ASPECT score (10).

On a scale of 0 to 10, ASPECTS is evaluated as 10 (having no signs of ischemia) and 0 (early ischemic changes in all ten regions). Low ASPECT scores on non-contrast CT were included as an exclusion criterion in most Randomised control trials (RCTs) for endovascular therapy because they had been associated with poor outcomes following reperfusion (11).

According to reports of 2013, cardiovascular disease is disproportionately prevalent in low and middle-income countries (LMICs), where even more than 80% of cardiovascular disease-related deaths occur (12).

According to projections, stroke will be number two, leading cause of mortality all over the world and the 1st leading cause of death in LMIC by 2030 based on 2015 risk factor prevalence, incidence velocity, population-attributable risks, relative risk for risk factors and trends (13).

Stroke is the second-leading cause of death in the European Union and a major contributor to adult disability (Wilkins et al., 2017). It affects 1.1 million people in Europe each year and causes 440 000 deaths (15,16).

In 2017, it was anticipated that management of stroke would cost €45 billion, combining indirect and direct costs for providing healthcare and lost productivity (17).

Projecting stroke incidence in all European Union (EU) nations, plus Switzerland, Iceland, and Norway, they estimated that if the 2000's rates remained stable, incident stroke events would rise from 1.1 million in 2000 to over 1.5 million in 2025, and they discovered that if rates reduced by 2% in five years, incident stroke events would increase to over 1.35 million (Truelsen, Begg, et al., 2006; Piechowski-Jóźwiak, et al., 2006).

Stroke risk appears to be higher in Africans than in other ethnicities, with substantially worse outcomes and a higher burden of psycho-social post-stroke comorbidities (20).

Similar to other non-communicable diseases, the incidence of stroke, particularly haemorrhagic stroke, may have increased significantly in sub-Saharan Africa over the past 20 years. adoption of a Western style of life, dietary modifications, urbanization, and a shift in the population's demographics with an increase in life expectancy and population increase are all thought to be contributing factors to this epidemiologic change (21).

The main focus of the sub-Saharan African healthcare system is infectious diseases. As a result, there are not enough resources available to prevent or treat non-communicable diseases including stroke. Stroke management is inadequate in clinical practice in this region (22,23).

Although there has been a 42% decline in incidence in developed countries, there is a marked increase in incidence in low-income countries (24). This increase might be linked not only to the high prevalence but also the availability of diagnostic tools in low income countries.

The projected average cost of a stroke in the US is $34 billion, where almost 800,000 people experience stroke each year (5). Morbidity is significant, with chronic impairments remaining in more than half of stroke patients (25).

Significant numbers of ischemic stroke patients in Rwanda were diagnosed with severe stroke scores, which were linked to the worst outcomes. After one year of ischemic stroke patients' follow-up, 24.7% of them had no or minor disabilities, 14.3% had substantial disabilities, and 61% had died (26).

1.2 Problem statement

Globally, Stroke is the single most important cause of mortality, disability, and dementia. (27,28). It is responsible for 9-10.2% of all deaths worldwide and ranks number two after ischemic heart disease (29,30).

In African countries, management of acute stroke is substandard with lack of adherence to the protocols and stroke units. By far they end up with poor outcomes of patients presenting with ischemic stroke (31,32).

The age-standardised stroke incidence and prevalence are highest in Sub-Saharan Africa (SSA), where an unexpected increase in the burden of stroke is currently occurring (316/100,000), with a three-year death rate of 84% (33,34).

The number of stroke deaths in Rwanda reached 2,915 in 2018 (5.14% of all deaths), according to the most recent WHO data. Rwanda is ranked #105 in the world by its age-adjusted death rate of 64.24/100,000 population (35).

Despite the high mortality and morbidity rates linked to stroke, Sub-Saharan Africa has relatively limited data on this disease. Community-based research is the main type of stroke study in the area (36).

Despite the fact that that stroke is becoming a public health problem in low- and middle-income nations, little information on stroke in Rwanda is available at the moment; most importantly there is no available data from referral hospitals of Rwanda addressing the neuroimaging patterns of ischemic stroke and the drivers of dynamics in ASPECT score.

This prompted the researcher to conduct a study on neuroimaging patterns of ischemic stroke and the drivers of dynamics in ASPECT score in Rwanda.

1.3 Research questions

The following are the research questions of this study:

1. What is the proportion of patients presenting with ischemic stroke by ASPECT score category?
2. What is the average time interval spent by the patients from onset of stroke symptoms to CT scan examination?
3. What are the drivers of ASPECT score in patients with ischemic stroke?
4. What is the influence of ASPECT scores on haemorrhagic transformation at initial presentation?

1.4. Objectives of the study

1.4.1 General objective

To study the neuroimaging patterns of ischemic stroke and drivers of dynamics in ASPECT score in the Rwandan population for the period of January 2019 to December 2021.

1.4.2 Specific objectives

The following are the study's particular objectives:

1. To determine the proportions of patients presenting with ischemic stroke by ASPECT score categories.
2. To determine the average time interval from onset of stroke symptoms to the acquisition of CT scan.
3. To determine the risk factors which drive the ASPECT score in the study population.
4. To determine the influence of ASPECT scores on haemorrhagic transformation at initial presentation.

1.5 Significance of the study

The study is vital in demonstrating the burden of ischemic stroke together with the factors that drive the severity of ASPECT score among patients with stroke in Rwanda. These findings are necessary in directing the clinicians to the rightful approach to address and manage ischemic stroke proactively from the community to tertiary hospital levels.

Furthermore, from the recommendations of this study, health policy makers will be enlightened on the ways they can mobilise multi-sectoral approaches in the endeavour to mitigate and manage stroke in the Rwandan population.

Other investigators in the same field will be able to use the new information this study provides.

1.6. Structural organisation of the study

The following chapters comprise this dissertation:

1. The study's introduction.
2. Literature review
3. The study's methodology.
4. Results of the study.
5. Discussions of the results.
6. Conclusions and recommendations.

CHAPTER II: LITERATURE REVIEW

2.0 Introduction

This chapter focuses on the existing literature review related to ischemic stroke. It contains theoretical literature, critical review, empirical literature, conceptual framework of the study and conclusion.

2.1 Theoretical literature

2.1.1 Pathophysiology of ischemic stroke

Reductions in the brain's blood flow result in ischemic stroke. The distribution of blood flow in cerebral ischemic stroke is frequently localised (41). There are tissues that are at risk, where cerebral blood flow levels may temporarily exceed the threshold for cell death despite falling below functional thresholds (penumbra) and the tissue that is permanently damaged with essentially cessation of cerebral blood flow (ischemic core) (42).

Only cells can survive in the penumbra, a metastable zone, for a specific amount of time. Thus, the goal of neuroprotective therapy is to protect this potentially recoverable tissue.

Because the nervous system has such high energy requirements, the blood flow to the brain must constantly be sufficient (43).

Most of oxygen used by brain tissue proceeds toward the oxidative glucose metabolism, as this is essentially just one substrate for the energy metabolism of the brain under physiologically normal conditions.

A complex destructive cascade of biochemical and molecular events is brought on by circulatory disturbances and insufficient blood supply, and it actually results in ischemic cell death (43).

Adenosine triphosphate (ATP) is still being used by neurons, which is the theory underlying cell death, despite the fact that cellular hypoxia prevents the cell from synthesizing the energy molecule (44). As result of simultaneous loss of ionic equilibrium, there is a decline in total ATP levels, and the development of lactic acidosis (45). This then starts a set of downstream mechanisms that are multistep and multicellular then lead into rapid and lethal ischemic cascade. Neurotransmitters release and restriction of reuptake are two additional significant processes that have an impact on brain tissue. The main neurotransmitter, glutamate, which is the primary excitatory neurotransmitter, is one of the many involved.

High levels of calcium are produced when it interacts with the ionotropic N-Methyl D-Aspartate (NMDA) and Amino-3-Hydroxy-5-Methyl-4-Isoxazolepropionic Acid (AMPA) receptors (46). Cells' activation of phospholipase, lipases, nucleases, and proteases is carried on by calcium overload. Critical proteins and

membranes of the cell are degraded by these enzymes. Glutamate also facilitates water and sodium intake, resulting in edema and cell swelling which later lead to the extracellular space to shrink (47).

The overall effect of the aforementioned process is an excessive creation of oxygen radicals in the mitochondria, together with additional free radical sources including hypoxanthine catabolism and prostaglandin synthesis (48). Direct cellular damage from reactive oxygen species (ROS) will affect proteins, lipids, carbohydrates and nucleic acids. Concurrently, antioxidant enzymes provide cellular protection against ROS, e.g: Superoxide dismutase (SOD) and glutathione and scavenging mechanisms (e.g.: vitamin C and α-tocopherol anymore able to prevent the generation of ROS) (49). Other pathways that cause neuronal death are also active throughout this phase. These include the activation of the lipoxygenase cascade, the activation of poly ADP-ribose polymerase (PARP), the subsequent recruitment of calcium-permeable transient receptor potential ion (TRP) channels, the development of mitochondrial transition pores, and worsening ionic imbalance (50). When paired with reactive oxygen species, nitrogen reactive species, frequently found in neurons, can change the intrinsic protein activities as well. The majority of these have a neuroprotective role. Therefore, these cascades will ultimately result in a complicated mixture of apoptosis, autophagy and necrosis, with the neuronal death as the last stage (51).

On the other hand, other factors have an impact on the white matter, predominantly made up of axonal bundles that are encased in myelin that have been created by oligodendrocytes. The variation in blood flow between the white and grey matter is one of the primary contributors. Compared to the grey matter, it has a dramatically lower blood supply and fewer collaterals (52). As a result, there is severe ischemia in this region, which causes rapid cellular and tissue swelling. Axon structural integrity and the myelin sheath are also weakened as a result of the process' activation of many proteases (53). More importantly; recovery and function restoration rely on the repair of the white matter and its reconnection to other neural networks. Several endogenous mechanisms that restore the white matter injury can be used to induce this (41).

Another event that occurs after a stroke is the inflammatory response.
It is significant because it regulates the immune system and may result in a reduction of the total size of the i nfarct (54).

Microglial cells appear to be the major contributor to the inflammatory process. After an event of stroke, the number of microglia increase in the infarcted area. However, these cells can protect the tissue or be destructive to it. Interleukin-1 (IL-1), TNF-, and IL-6, as well as Nitric Oxide (NO), ROS, and prostanoids, are among these cytokines. Additionally, these cells have the ability to attract in additional inflammatory cells to the penumbras, which would result in more damage (55). As a result of the new therapeutic method, it appears to

be a decrease in overall inflammation in the infarcted area. To determine the prognosis and severity of a stroke, a variety of mediators and cells have been proposed. Other cells, such as regulatory T cells, have been demonstrated to reduce the risk of stroke, while others, like IL-6 and Toll-like receptor 4, have been associated to the severity of stroke (56). Metalloproteinase will assist in the treatment of stroke because of their capacity to reduce inflammation (57).

2.1.2 Risk factors of ischemic stroke

In order to reduce the risk in specific populations, this disease has undergone extensive research to identify the risk factors which are associated with it. These risk factors are divided into those that are modifiable (which can be controlled) and those that cannot be modified (42,58). A family history of fibromuscular dysplasia, transient ischemic attacks (TIAs), or stroke, prior headaches of migraine type, race, sex, ethnicity and advanced age are the key non-modifiable risk factors (59).

Because they may be controlled and eliminated in the majority of patients, changeable risk factors are also very prevalent and are relevant to treating doctors. The most important condition is hypertension and is the most prevalent modifiable risk factor, accounting for more than 50% of all small vessel strokes (39). Resistant hypertensive patients develop stroke up to 90% more likely than the general population (60). Cerebrovascular attacks are much more common among people who have other chronic medical conditions such as dyslipidaemia, diabetes mellitus, hyperhomocysteinemia, obesity and carotid stenosis (61). In certain research, the risk of ischemic stroke was discovered to be raised in emotional stress (62,63).

Smoking, illegal substance use, excessive consumption of alcohol and physical inactivity are among the lifestyles which have been found to increase risk. Some medications can increase risk, with postmenopausal hormones and oral contraceptives acting as the primary examples (64).

Significant number of cardiac pathologies have been linked to and known as risk factors for embolic events, which are one of the main causes of ischemic stroke and are mostly driven on by malfunctioning heart valves (65). These include fibrous nonbacterial endocarditis (known as Libman Sacks endocarditis), rheumatic mitral or aortic valve, infective endocarditis, the use of bioprosthetic (or mechanical) heart valves, and antiphospholipid syndrome (65). According to some studies, arrhythmias may accompany and be the cause of around 20% of stroke (66). These arrhythmias include sick sinus syndrome, paroxysmal atrial fibrillation, flutter, and atrial fibrillation (66). Important factors to be taken into consideration with any patient presenting with stroke including prior coronary artery bypass graft surgery, existing morphological heart pathologies including any recent myocardial infarction and dilated cardiomyopathy (67,68).

2.1.3 Clinical Features of ischemic stroke

The clinical features of a stroke differ greatly depending on the area affected. To facilitate public awareness of stroke signs in a pre-hospital setting and improve patient outcomes, the American stroke association and the American heart association (AHA/ASA) established the "FAST" algorithm (49). This acronym comprises the sudden onset of facial drooping, arm weakness (which can also encompass the leg, face, or all), slurred or slurred speech and time of onset, all of which should act as a warning to run directly to the emergency department. Other symptoms of a possible stroke are vertigo, severe headache, and balance problems (69). Other abbreviations that are in use include the BEFAST and the 6S among others, can all be used to signify the likelihood for a stroke if certain conditions are present. The 6S acronym stands for severe headache, side weakening, slurred speech and sudden onset of symptoms. Balance loss, eyes (disturbance of vision), face drop, arm weakness, speech slur, and time to contact an ambulance are all abbreviations for BEFAST (49).

2.1.4 Imaging in acute ischemic stroke

The non-contrast brain CT (NCCT) is commonly the initial imaging option for patients suspected to have acute ischemic stroke due to its accuracy in excluding bleeding, speed of acquisition, general safety for both stable and unstable patients, and widespread availability (70).

To assess the extent and location of ischemia change in the middle cerebral artery's territory (MCA), ASPECTS was developed (73). This scale is related to the functional outcome measured by the modified Rankin Scale (mRS) 3-months after the stroke. When age and the degree of neurologic impairment were combined, a subacute ASPECTS score of higher than 5 significantly predicted improved functional independence at 3-months and one year after a stroke (74). Additionally, the initial lesion volume was a potent and independent predictor of stroke outcome in a statistical regression model that also took accounts for age and NIHSS(75). In clinical trials of acute treatments and rehabilitative techniques for ischemic stroke, sample stratification might well be improved and the power for accurate detection may be increased by using lesion size in outcome prediction models (76).

When choosing patients for aggressive treatment, computed tomography CTA) offers crucial information on vascular patency in acute stroke(1) Frequently, less aggressive treatment and testing decisions are linked to awareness of CTA results

Perfusion imaging improve diagnostic accuracy in acute ischemic stroke, help in determining therapeutic targets, and provide prognostic information on functional prognosis. Additionally, perfusion imaging can identify patients whose times of symptom onset are unknown or who benefit from reperfusion outside of the typical time window(2)

The two main advantages of perfusion imaging in acute stroke are the measurement of the volume of tissue at risk and the vascular distribution of the ischemia. The amount of tissue at risk has a major impact on the morbidity and mortality related to thrombolytic therapy (78).

According to Latchaw et al., 2003's study, the following recommendations from experts for CT perfusion were:

a) Quantitative CTP may be useful in identifying tissues that are permanently and reversibly ischemic in acute stroke patients (grade C).
b) It may be beneficial to quantitatively map the CBV using the slow-infusion technique in conjunction with the acquisition of CTA for acute stroke patients (grade C).
c) It is not recommended to use this approach in patients who have chronic ischemia, head trauma, vasospasm, or as part of the balloon occlusion test (BOT) (grade D).

Magnetic Resonance Imaging is more sensitive and specific than CT scans for early diagnosis and quantification of ischemic stroke. Infarcts are visible during the first 24 hours in about 80%(3). Within a few hours of the stroke's onset, MRI can identify an ischemic stroke and timely selection of patients for thrombolytic therapy, and prognostic estimation. DWI is a very powerful method for diagnosing acute ischemia. Within minutes of artery occlusion, DWI and apparent diffusion coefficient (ADC) identify and quantify this event (3,4).

2.1.5 The ASPECTS system

The Alberta stroke program early CT scores (ASPECTS), a quantitative topographic CT scan score of 10 points, given to patients who have suffered a MCA stroke.

In furthermore, the posterior circulation has been adjusted (Fig. 3). Smaller brain regions (such as basal ganglia, caudate nucleus and the internal capsule) are assigned the same weight as larger cortical regions. ASPECTS is a weighted volumetric scale as a consequence. It should be carefully regarded as an ordered categorical scale for statistical purposes.

M1 to M3: At the level of basal ganglia.

M4 to M6: At ventricular level, this is situated directly above the basal ganglia.

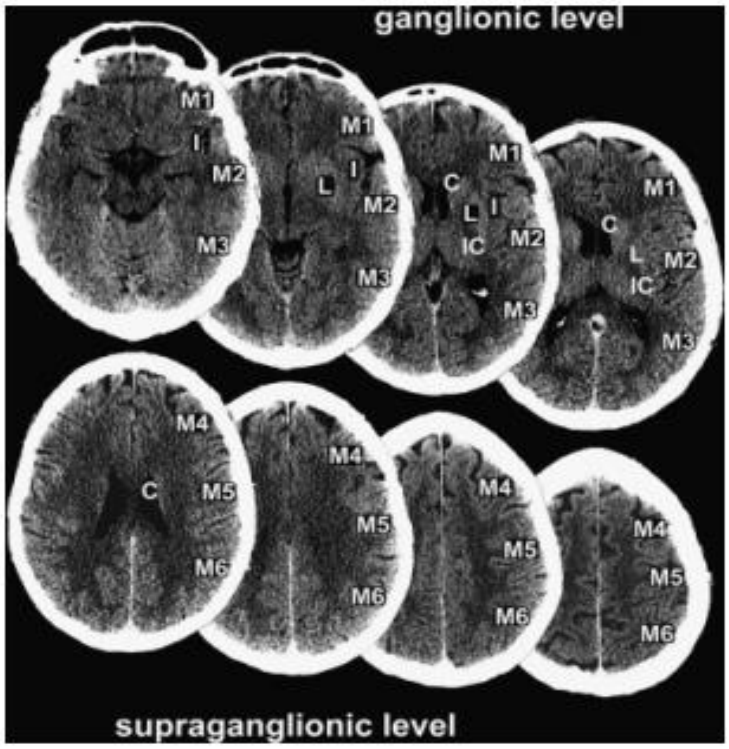

Figure 1a: Alberta Stroke Program Early CT Score (ASPECTS) scoring scheme

Figure 1 shows: Axial CT cuts of the ganglionic ASPECTS level are shown in the top row (M1-M3). They include the internal capsule, posterior limb (IC), the insula (I), the lentiform nucleus (L), and the caudate nucleus. The supraganglionic ASPECTS level is cut on the CT scan in the lower row (M4–M6). Cuts at the inferior orbitomeatal line include what we prefer to use (as opposed to superior orbitomeatal line). All axial slices are evaluated for ASPECTS score. Early ischemia changes are assessed by supraganglionic level (caudate nucleus) and the caudate head at the ganglionic level (8)

Scoring system

Anterior circulation

The segmental estimation of MCA vascular territory is performed, and the initial score of 10 is reduced by 1 point for each affected region:

1. Caudate=C
2. Lentiform nucleus=L
3. Internal capsule=IC
4. Insular cortex= I
5. M1: "anterior MCA cortex," that is the frontal operculum's equivalent
6. M2: The anterior temporal lobes "MCA cortex lateral to insular ribbon"
7. M3: "posterior MCA cortex," which is a reference to the posterior temporal lobe.
8. M4= "anterior MCA territory immediately superior to M1"
9. M5= "lateral MCA territory immediately superior to M2"
10. M6="posterior MCA territory immediately superior to M3"

The Alberta Stroke Program Early Computed Tomography Score was created using a non-contrast CT template with 10 regions distributed over the MCA territory at ganglionic and supraganglionic levels.

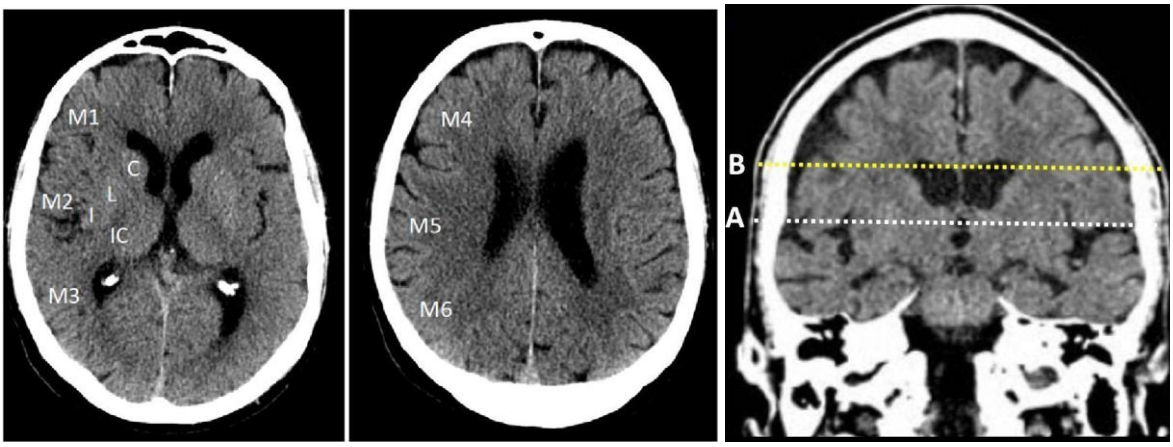

Figure 1b: Alberta Stroke Program Early CT Score (ASPECTS) scoring scheme with cut levels on coronal image

The above images are CT axial slice with 4 deep and 3 cortical areas at the level of the thalamus and basal ganglia (Left image), three (3) cortical MCA territories are next to the ganglionic structures' most superior margin (middle image) and coronal non-contrasted images showing cuts levels (Right image) (79).

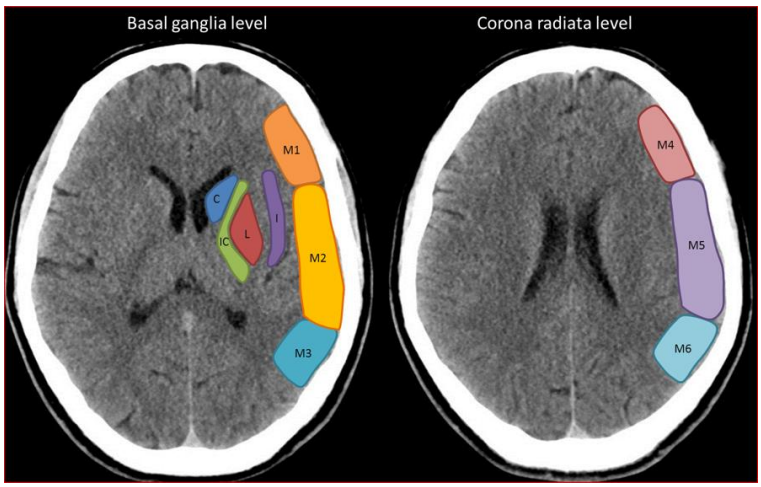

Figure 2: MCA-Alberta Stroke Program Early CT score (ASPECTS) by May 2022(80).

Labels used in this figure2: Refer to page 12

Posterior circulation

A variation of the ASPECT scoring system that has been described for use in the posterior circulation is the pc-ASPECTS scoring system.

The pc-ASPECTS is a 10-point scale, just like the anterior circulation, where points are deducted for each area that is affected. The midbrain and the pons, in opposition to ASPECTS, are each worth two points (irrespective of the presence of bilateral alterations; for instance, if the pons were involved, two points are deducted).

- Thalami (T) =1 point each.
- Occipital lobes (OL) =1 point each.
- Midbrain (M) =2 points.
- Pons (P) =2 points.
- Cerebellar hemispheres (C) =1 point each.

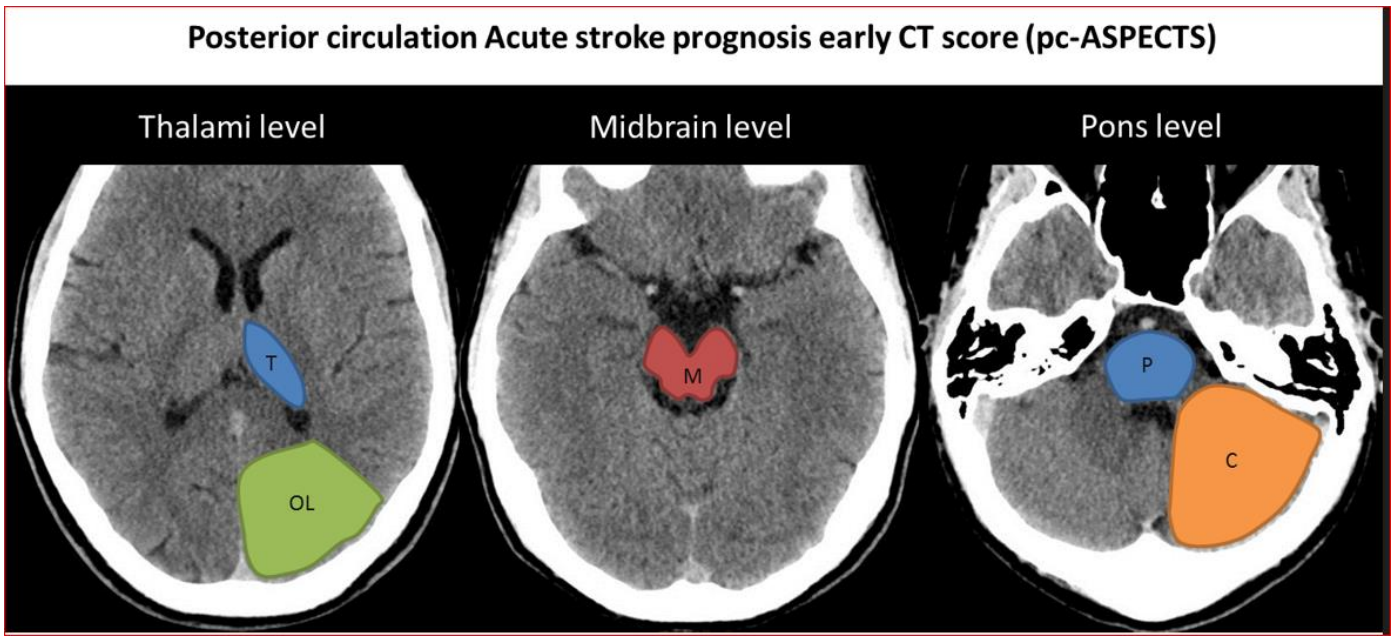

Figure 3: Posterior circulation of acute stroke (81).

T: Thalamus; OL: Occipital lobe M: Any part of midbrain; P: Any parts of pons; C: Cerebellar hemisphere.

2.1.6 The use of ASPECTS in clinical decision making

With time since the beginning of symptoms, the importance of early ischemic change (EIC) for clinical decision-making varies. Though time is likely most important in the early time windows, patient selection with a "tissue window" will become increasingly essential beyond 3h (82).

NCCT may be performed as the primary and only brain imaging for the examination of patients presenting with suspected acute ischemic stroke since it reliably diagnoses the majority of cases of intracranial haemorrhage (ICH) and may be able to identify nonvascular sources of focal neurologic deficits. (70).

Less than 3-h time window

ASPECTS are utilised to assist in patient selection for intra-arterial recanalization therapy and as a prognostic tool. Although patients with severe early ischemic change (ASPECTS 0-3) are more inclined to experience bleeding as a result of thrombolysis and are less likely to have a good clinical outcome (83).

With intravenous thrombolysis, approximately 50% of patients with mild early ischemic change (ASPECTS 8–10) will experience a good clinical outcome. Additional imaging approaches to assess cerebrovascular status are required for improved prognostic information and therapeutic decision-making. In these cases, urgent CT angiography (CTA) following non-contrast brain CT is recommended for further evaluation, unless a clear hyperdense MCA sign or MCA dot sign is present (58,84).

Patients with cerebral artery occlusion and large thrombus burden are unlikely to experience recanalization with intravenous thrombolysis alone; thus, early intravenous thrombolysis or mechanical thrombus removal should be taken into account (85). Patients with ASPECT score >7 will benefit from further intra-arterial thrombolysis based on the findings of the interventional management of stroke study-1 analysis. Benefit with ASPECTS 5 to 7 is less certain; however, it might be taken into consideration in patients who are considered exceptional (clinical deficit, cortical involvement, large thrombus burden, and young age). Due to an extremely small likelihood of benefit and a significant risk of harm, an additional intraarterial treatment is not recommended if early ischemic changes are severe (ASPECTS<5). Intraarterial treatment methods should, whenever possible, be used in randomised controlled trials, like the IMS-3 study (86).

3–6hours time window

Over three hours following the onset of symptoms, any recanalizing therapy is now considered off-label. The European Cooperative Acute Stroke Study-3 (ECASS-3) trial's results might lead to the approval of use recombinant tissue plasminogen activator (rtPA) for intravenous thrombolysis up to 4.5 hours after the onset of symptoms (87). An ischemic stroke patient could benefit from intravenous thrombolysis with rtPA up to 4.5 hours after the symptoms onset, according to a pooled analysis of randomized thrombolysis trials, which is supported by ECASS-3 (88). In another review article the Cochrane meta-analysis of thrombolysis trials has also supported the above finding and further, in the study it was found that patients with a high ASPECTS (ASPECTS>7) in the presence of an MCA blockage may be the best candidates for intervention based on the PROACT-II ASPECTS evaluation (87).

Greater than 6hours time window

Additionally, the ASPECT score in patients with so-called "wake-up" strokes and those with time windows longer than six hours may be useful especially for salvageable penumbra to prevent infarction if recanalization can be achieved (89). The patients who have both MCA occlusion and a high admission ASPECTS score are a subgroup who will likely benefit from delayed thrombolysis, and preliminary results from 20 of these patients have seemed to support this (8).

Patients with a good non-contrast CT scan (ASPECTS>7) who also have an intracranial occlusion and a disabling clinical deficit may be carefully considered for intravenous or intra-arterial thrombolytic and/or mechanical recanalization therapy (90).

2.1.7 Management of ischemic stroke

Since time is the key element in ischemic stroke management, the main idea is to react as quickly as you can. As a stroke develops, brain tissue is rapidly lost, necessitating urgent evaluation and intervention [time = brain tissue] (91).

The "wait and see" approach to manage ischemic stroke has changed dramatically in recent years (92). Thanks to medical advancements, it has been adjusted and modified into a more effective program. These discoveries have led to the implementation of new therapeutic techniques. Additionally, patient treatment with intravenous (i.v.) thrombolysis, mechanical thrombectomy, and endovascular therapy had shown very successful results (93). The main therapeutic goals are to decrease mortality and enhance quality of life after surviving, and these goals are affected by the onset-to-arrival time (94).

To advance in the therapy of these instances, the airway, breathing, and circulation must be evaluated and appropriately managed using the ABC method. Some posterior circulation strokes and/or large strokes can present with respiratory distress, in coma and bulbar dysfunction (95). After ABC approach in accordance with procedures, a non-contrast CT scan must be obtained before starting thrombolytic treatment to identify whether the stroke is hemorrhagic or not (96).

However, other tests, such as CBC, an electrocardiogram PT, aPTT, INR, Troponin, ecarin clotting time, thrombin time, and direct factor Xa activity assay, may be recommended if the patient has a history of bleeding disorders, anticoagulant use, and/or prior thrombocytopenia (94).

As soon as there is no patient limitation, CT is recommended for imaging stroke. To rule out major artery occlusion, a CT angiography of the brain and neck is recommended if the patient presents within the first 6 hours of the onset of symptoms (97). To avoid wasting time waiting for potential mechanical interventions, the completion of the CT angiography should be the goal whenever possible (98).

Intravenous thrombolysis and mechanical thrombectomy are the two main therapeutic techniques that are currently offered. The patient's condition determines the treatment to be used (91).

2.1.8 Management of acute ischemic stroke in Rwanda

Management of ischemic stroke in Rwanda consists of pharmacologic and non-pharmacological management depending on time of presentation of patients.

If there are no contraindications and the patient presents within 6 hours of the onset of symptoms and an ischemic stroke is diagnosed either by CT or MRI, antithrombolytics (where available) are indicated(5).

If thrombolytic therapy is required, lower blood pressure to 185/110 mm Hg before administering thrombolytic medications, and keep it there for the first 24 hours. The approach depends on blood pressure if thrombolytic therapy is not required and there is no immediate target organ damage other than stroke. No intervention is needed for the first 48 to 72 hours if the blood pressure is less than 220/120 mm Hg. Reduce blood pressure by 15% within 1 hour if it is below 220/120 mm Hg or if there is additional acute target-organ damage, such as heart failure or myocardial infarction(6).

2.2 Empirical literature

According to a study on the predictive value of the ASPECT score, among ischemic stroke subtypes, lacunar stroke was the most prevalent and affected about 44%, cardioembolic stroke (26%), and large artery atherosclerosis (LAA) stroke, which affected about 20% of cases in the outcome of the acute ischemic stroke and its correlation with stroke subtypes, NIHSS, and cognitive impairment (99). Compared to other ischemic stroke types, the ASPECT score for the cardioembolic stroke was statistically lower (P 0.05). Older patients had higher percentages of lower ASPECTS values (worse result) and were associated with lower initial GCS levels, according to Spearman correlation. The initial NIHSS, inpatient complications, hospital stay, death, and modified Rankin Scale all had a negative association with ASPECTS scores. The cut-off value for ASPECTS used to predict poor outcomes was set at 7. ASPECTS less or equal to 7 was found to be strongly associated with a fourfold increased chance of poor outcomes (99).

One of the ischemic stroke's complications is hemorrhagic transformation (100). The majority of risk factors have included the amount of ischemia, the severity of the neurological condition, the age, the level of hyperglycemia at presentation, the level of admission hypertension, and the cardioembolism (100). The majority of factors were also present in previously published predictive scores, but the authors reported their frequency in different ways.

Another study on the parameters that contribute to haemorrhagic transformation in ischemic stroke found that patients with hemorrhagic transformation (HT) had a considerably larger proportion of patients with CBV-ASPECTS 0-7 than patients without HT (44 versus 9%, P = 0.005). After adjustment for clinical baseline characteristics, CBV ASPECTS 0–7 continued to be independent predictive indicators for HT. Before

beginning reperfusion therapy, a rapid risk assessment method using CBV ASPECTS may be useful for predicting the likelihood of HT following an acute cardioembolic stroke (101).

Lesions in the frontal and superior parietal ASPECTS regions were substantially linked to lower functional independence measure scores at all timepoints evaluated in a study on the long-term prediction of functional outcome following stroke using the ASPECT Score in the subacute stage (102). When combination of marital status, age, and the severity of the initial neurologic impairment, at three months and a year after a stroke, a subacute ASPECTS score of >5 was significantly associated with greater functional independence (74).

2.3 Critical review and research gap identification

While some of the studies assessed patterns and ASPECT score, some included the timing after onset of stroke symptoms(7). No study done in Rwanda to assess factors associated with ASPECT score and some studies mentioned the socio-demographic factors of the participants while majority did not take this into account.

In Rwanda, a multicenter study was conducted on burden of stroke but did not put into consideration ASPECT score and the time between symptom onset and the CT scan (26).

Indeed, no work is available addressing the neuroimaging patterns of ischemic stroke and the drivers of dynamics in ASPECT scores in the country.

2.4 Conceptual framework

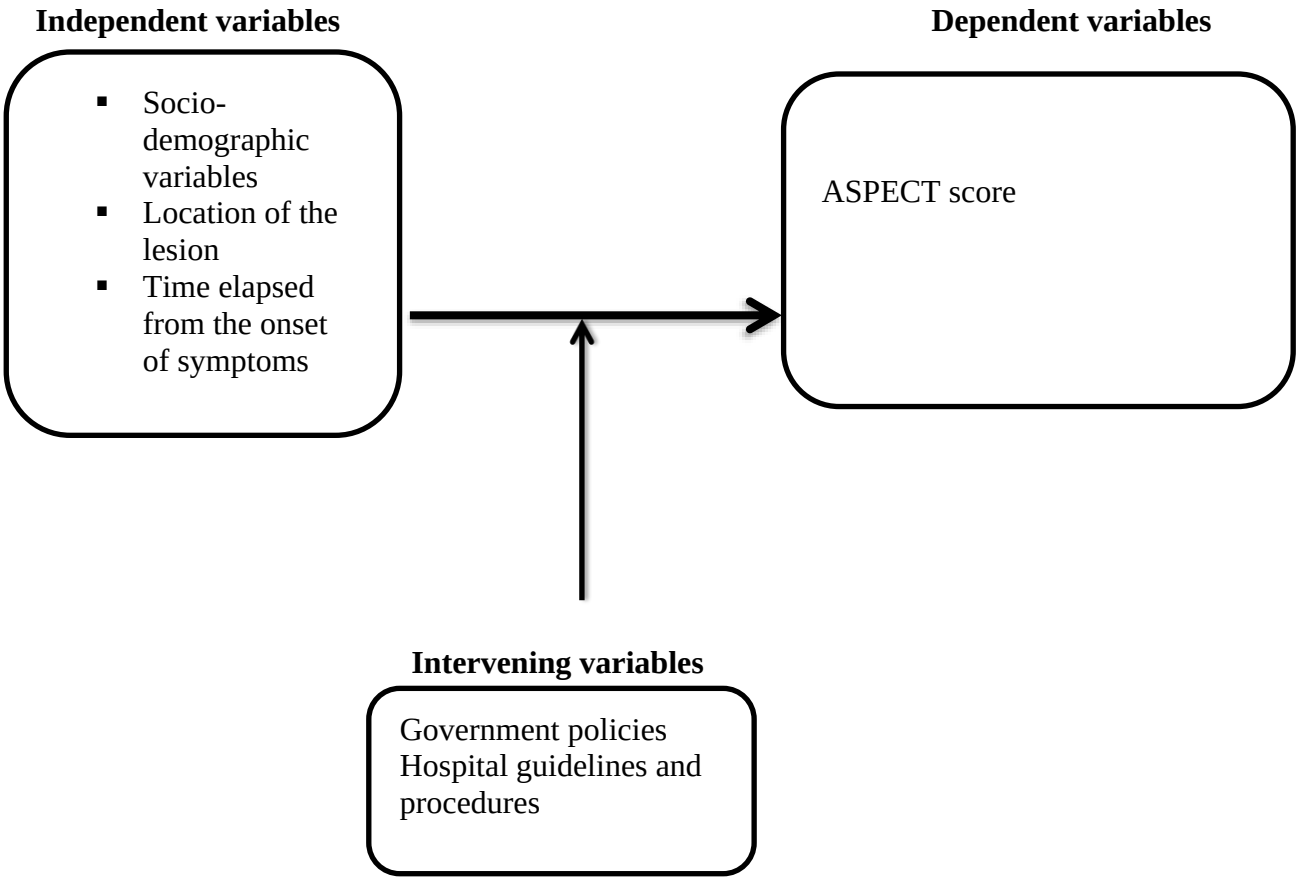

Figure 4: Conceptual framework

This figure indicates that the ASPECT score depends on socio-demographic characteristics, location of the lesion, and time elapsed from the onset of symptoms of stroke. This particular relationship is further influenced by government policies, and hospital guidelines and procedures.

CHAPTER III: METHODOLOGY

3.0 Introduction

Along with the methodology used in this study, the research design, study area, target population, sampling technique, sample size calculation, data management, data analysis, and ethical issues are all discussed in this chapter.

3.1 Research setting

The study was carried out in four referral hospitals, namely Butare University Teaching Hospital (CHUB), Rwanda Military Hospital (RMH), Kigali University Teaching Hospital (CHUK) and King Faisal Hospital (KFH-Kigali).

CHUB is a public, national referral and teaching hospitals located in HUYE district, Southern province. It has catchment area in South and one part of Western province close to it.

RMH is military, referral and university teaching hospitals located in Kicukiro district, Kigali City. Its catchment area is: Kicukiro District and Eastern province of Rwanda.

CHUK is a public, national referral and teaching hospitals located in Nyarugenge district, Kigali City. It has catchment area composed of: Nyarugenge, Gasabo Districts of Kigali, Northern province and closer District of South.

KFH is a partial public and private referral and University teaching Hospital locate in Gasabo District.

3.2 Research design

A retrospective cross-sectional design was used to assess neuroimaging patterns of ischemic stroke and the drivers of dynamics in ASPECT score. This particular study used a quantitative approach.

3.3 Target population

In this study the population consists of patients' file/records of patients who attended Radiology department of selected hospitals with symptoms and CT finding of ischemic stroke from January 2019 to December 2021. Both paediatric and adult participants were considered. They ranged from 2 to 100years of age.

3.3.1 Inclusion Criteria

This study included patient data with ischemic stroke who consulted selected hospitals from January 2019 to December 2021.

During the study period, all ischemic stroke patients were enrolled

3.3.2 Exclusion Criteria

Participants whose information was incomplete were excluded (for example files of unknown patients).

The study excluded patients with hemorrhagic stroke.

The study excluded patients with stroke mimics (Seizures, brain tumors, infection and similar stroke-like conditions).

3.4 Sample Design

3.4.1 Sample Size

In order to make conclusions, a sample is a subset of the population that has been chosen to be representative of the population. Naing et al.,. (2016) used the Fisher's formula to determine the sample size for this study, and the results are as follows.:

In this study the prevalence is estimated at 50% as the prevalence of ischemic stroke was not assessed in Rwanda or in the region.

$$N = \frac{Z^2(p)(1-p)}{d^2}$$

Z=Standard normal variate at 5% type I error P<0.05, it is 1.96.

P= 50% as prevalence of ischemic stroke is unknown (103)

d= absolute error or precision 5%

N= sample size

$$N = \frac{1.96^2(0.5)(1-05)}{0.05^2} = 385 \text{ patients}$$

From this formula, the sample size for our population was 385 patients. Table1 indicates the estimated minimum sample size for confidence level of 95%.

Table 1: Minimum sample size for confidence level of 95%

The sample size for prevalence of 50% and absolute error of 5% is 384

(*a*) Confidence level **95%**

d \ *P*	0.05	0.10	0.15	0.20	0.25	0.30	0.35	0.40	0.45	0.50	0.55	0.60	0.65	0.70	0.75	0.80	0.85	0.90	0.95
0.01	1825	3457	4898	6147	7203	8067	8740	9220	9508	9604	9508	9220	8740	8067	7203	6147	4898	3457	1825
0.02	456	864	1225	1537	1801	2017	2185	2305	2377	2401	2377	2305	2185	2017	1801	1537	1225	864	456
0.03	203	384	544	683	800	896	971	1024	1056	1067	1056	1024	971	896	800	683	544	384	203
0.04	114	216	306	384	450	504	546	576	594	600	594	576	546	504	450	384	306	216	114
0.05	73	138	196	246	288	323	350	369	380	384	380	369	350	323	288	246	196	138	73
0.06	51	96	136	171	200	224	243	256	264	267	264	256	243	224	200	171	136	96	51
0.07	37	71	100	125	147	165	178	188	194	196	194	188	178	165	147	125	100	71	37
0.08	29	54	77	96	113	126	137	144	149	150	149	144	137	126	113	96	77	54	29
0.09	23	43	60	76	89	100	108	114	117	119	117	114	108	100	89	76	60	43	23
0.10	18	35	49	61	72	81	87	92	95	96	95	92	87	81	72	61	49	35	18
0.11	15	29	40	51	60	67	72	76	79	79	79	76	72	67	60	51	40	29	15
0.12	13	24	34	43	50	56	61	64	66	67	66	64	61	56	50	43	34	24	13
0.13	11	20	29	36	43	48	52	55	56	57	56	55	52	48	43	36	29	20	11
0.14	9	18	25	31	37	41	45	47	49	49	49	47	45	41	37	31	25	18	9
0.15	8	15	22	27	32	36	39	41	42	43	42	41	39	36	32	27	22	15	8
0.20	5	9	12	15	18	20	22	23	24	24	24	23	22	20	18	15	12	9	5
0.25	*	6	8	10	12	13	14	15	15	15	15	15	14	13	12	10	8	6	*

*Sample size less than 5.

Source: (104)

3.4.2 Sampling techniques

A simple random sampling technique was used to select a representative sample of patient files in this study.

3.5 Data collection methods

3.5.1 Data collection

To obtain data for this study, a questionnaire was used. The questionnaire which comprises close-ended questions was used to capture data on demographic characteristics, timing of patients presenting with ischemic stroke at Radiology department for brain CT from the onset of symptoms and the risk factors of ischemic stroke. It was further used to capture data on magnitude of patients presenting with ischemic stroke by ASPECT score categories, and haemorrhagic transformation.

The collected risk factors are the one recorded in patients' file regardless the diagnostic method used.

3.5.2 Administration of data collection instrument

After obtaining an ethical approval letter from the University of Rwanda and selected hospitals, the researcher introduced himself to the staff working in Radiology departments. The researcher recorded clinical data then looked at each brain CT of every enrolled ischemic stroke patient. Those who met criteria were recorded on questionnaires. The researcher went further for non-contrast brain CT images of enrolled patients to record ASPECT score and haemorrhagic transformation.

3.5.3 Imaging consideration

Our patients were scanned using multi-detector CT scanners Philips 128 slices, (Siemens 64 slices, General Electric/GE 128 slices and General Electric/GE 16 slices, available at KFH, CHUK,RMH, and CHUB, respectively.

We only considered brain CT scans with no contrast.

Images obtained from CT were reviewed by an experienced general radiologist who provided the report.

For all CT images used in the study, no ASPECT score was calculated. During the study, all images were reviewed by the researcher together with the supervisors and ASPECT score was determined and recorded.

3.5.4 Validity and reliability

Validity

Validity is the degree to which a concept in a quantitative research is exactly quantified (105). The questionnaire was carefully developed to ensure that its contents were consistent, unambiguous, relevant, and clear. A supervisor assessed the quality and made the necessary adjustments to ensure that it complies with the study's objectives.

Reliability

Pilot research with 5 patients who weren't going to be in the study sample was carried out to ensure reliability. The researcher made the necessary corrections to the issues which have been identified.

3.6 Data analysis procedure

After data gathering, the information was encoded, entered into a computer, and checked for mistakes and omissions. The data were then imported into SPSS version 21 and checked once more for omissions and errors before being analysed.

Table 2: Activities & Data analysis plan

No	OBJECTIVE	ACTIVITY	TYPE OF DATA	TYPE OF ANALYSIS
1	To Identify the demographics among the studied population with ischemic stroke.	Recording data from medical files using questionnaires of the patients with ischemic stroke in Rwanda.	Age, sex, Residence, place and examination site.	Descriptive statistics was used to generate percentage and frequency.
2.	To Identify the time interval elapsed from the onset of symptoms of ischemic stroke to brain CT scan exam.	Record from medical file: time given by patients, close relatives and referring doctor (the best possible estimation of the time elapsed in-between CT scan exam and onset of symptoms).	Time intervals (from stroke symptom to brain imaging exam)	Descriptive statistics was used to generate percentage and frequency.
3.	To analyse CT findings of patients with ischemic stroke and determine severity of those patients by ASPECT score categories.	-Size determination of the ischemic stroke. -Anatomical localization of stroke lesions. -determining ASPECT total score of stroke severity.	Brain CT evidence of -stroke presence -Ischemia location -stroke size -Numerical value of ASPECT scores.	Descriptive statistics was used to generate percentage and frequency.

Table 3: Activities & Data analysis plan

No	OBJECTIVE	ACTIVITY	TYPE OF DATA	TYPE OF ANALYSIS
4	To determine the drivers of ASPECT score in the study population	Medical history was recorded in patients' files along with scrutiny of the medical examination reports to identify occurrence of risk factors.	Identified risk factors such as: -Age -Smoking -Atrial fibrillation -Hypertension -Diabetes -Obesity/ Hypercholesterolemia -Bee bite	Logistic regression analysis involving comparative study of the Odds ratios and p-values for both univariate and multivariate analyses. The level of significance of statistics was confirmed using 95% confidence interval and P value (<0.05).
5.	To Study the determine the influence of ASPECT scores on haemorrhagic transformation at initial presentation	- CT scan images were examined to identify any hyperdense changes by Hounsfield unit to confirm presence of blood leakage within ischemic back ground lesions. -ASPECT values were scored according to the involvement of the known anatomical landmark to make a final score out of 10 total ASPECT scores.	-Presence of blood in the main lesion -Total ASPECT score of the ischemic stroke event	Logistic regression analysis was used to determine the odds of ASPECT score on hemorrhagic transformation at initial presentation. The level of significance of statistics was confirmed using 95% confidence interval and P value (<0.05).

3.7 Risk to subjects

3.7.1 Costs to patients:

No additional testing or fees were incurred for the patients, and all imaging studies were clinically indicated.

3.7.2 Benefits to hospital or patients:

The hospital or the patients in this study did not gain any immediate or particular benefits. However, we anticipate that the study's findings would considerably improve the care provided to ischemic strokes' patients in Rwanda.

3.7.3 Plan for utilisation and dissemination of results

As a requirement for the Master of Medicine in diagnostic Radiology, a research report is sent to the University of Rwanda. The hospitals also received this work as appreciation for accepting the study. A national or global journal may accept it for publication

3.8 Ethical consideration

The ethical approval for this study was obtained from both the University of Rwanda and respective hospitals this study was carried in.

Throughout this research, the investigator respected the protection of human rights. In order to maintain privacy, neither the questionnaire forms nor the participants' identification were known or disclosed. These findings of the study are exclusively designated for academic use.

CHAPTER IV: RESULTS

4.0 Introduction

This chapter presents the results of the study on patterns of ischemic stroke and drivers of ASPECT score in the studied population. Data were analysed by SPSS 21 tool, in which the p value and percentage were obtained for different variables. The findings are grouped according to specific objectives of this study.

These findings include:

- Patients' Socio-demographic (age, gender and residence).
- Proportions of patients presenting with ischemic stroke by ASPECT score categories.
- Average time interval from stroke symptoms and non-contrast brain CT scan exam.
- Risk factors associated with ASPECT score in the study population.
- The influence of ASPECT scores on haemorrhagic transformation at initial presentation.

4.1 Socio-demographic description of Rwandan participants with ischemic stroke

In this study, the total population consists of 389 patients who underwent brain CT scan exams in Radiology departments of the University referral hospitals in Rwanda. The demographic characteristics include age, Gender, residence, distance to referral hospital and the hospital where brain CT scan was performed.

Among them 8 participants were paediatrics (between 2 to 13 years) and 381 were adults (Between 21 to 100 years old).

The results showed that Kigali University teaching hospital (CHUK) had 110 (28.3%), King Faisal hospital (KFH) had 88(22.5%), Rwanda military hospital (RMH) had 99(25.5%) and Butare University teaching hospital (CHUB) had 92 (23.7%) patients.

Hospital	Numbers of participants	Percentage
CHUK	110	28.3
RMH	99	25.5
CHUB	92	23.7
KFH	88	22.5
Total	389	100.0

4.1.1 Demographics characteristics of the participants

Our results present different ages of patients in the studied population in which 50.9% are above 66, 26.2% aged between 51and 65 and 22.9% are less or equal to 50 years old. The mean age of the study population is 62.89 with standard deviation of 19.19 years and the median age for the study population is 66 years (Figure 5).

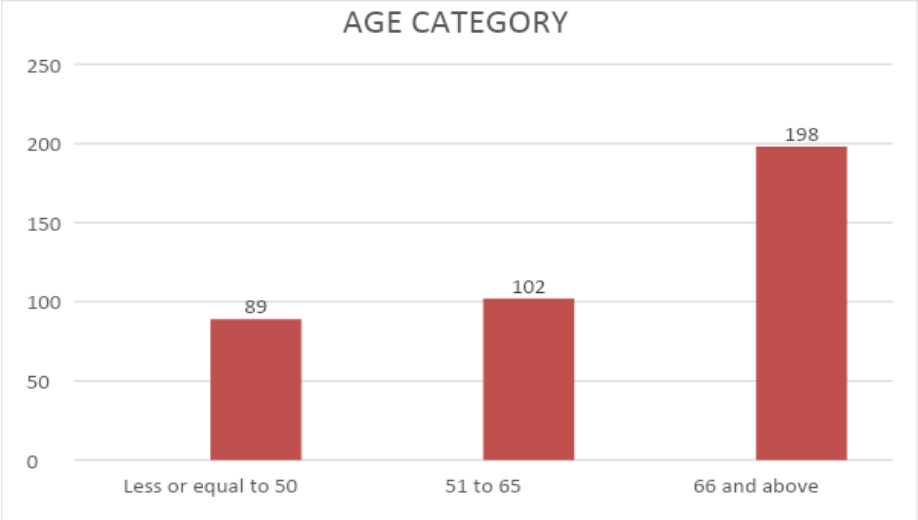

Figure 5: Age category

The majority of ischemic stroke patients involved in this study were adults with 77.1% above 50 years.

In the studied population 8 out of 389 participants were less or equal to 13 years old, while 381 were above 18 years.

Ischemic stroke is common in senile age with its mean age standing at 62.89-year-old with standard deviation (SD) of 19.19 years in the studied population in Rwanda.

4.1.2 Gender demographic characteristics of the participants

In regard to the Gender, ischemic stroke in our population is 215 females and 174 males, representing 55.3% and 44.7% respectively (Figure 6).

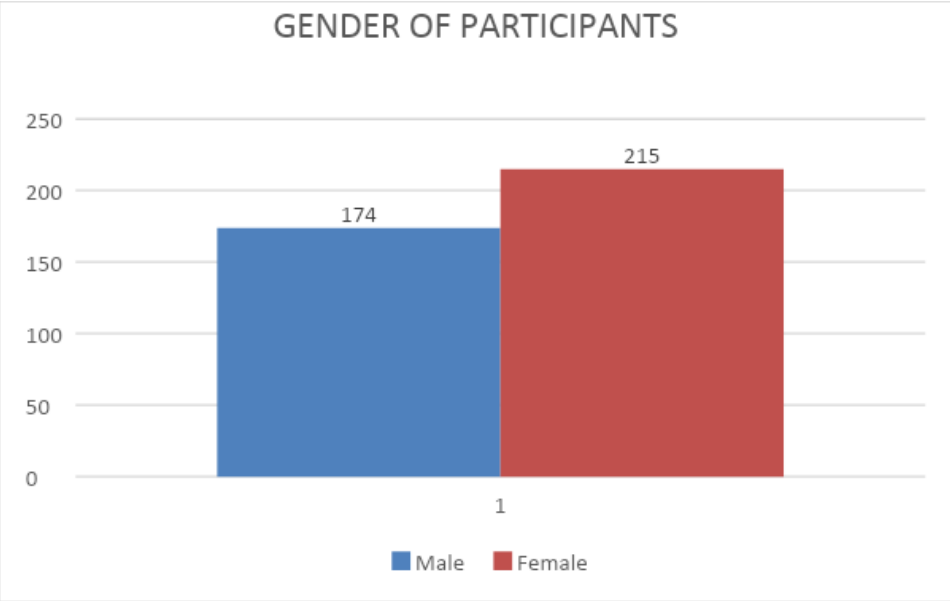

Figure 6: Gender of participants

Ischemic stroke is more prevalent in females than it is in males in the study population standing at 55.3% and 44.7% respectively.

4.1.3 Residence of the participants

The study participants were divided into groups according to their residence or the location of the transferring District Hospital. The results are presented into two groups: either urban or rural.

Regarding residence of study participants 237 (60.9%) of patients with ischemic stroke were coming from rural areas, while 152 (39.1%) live in Urban (Figure 7).

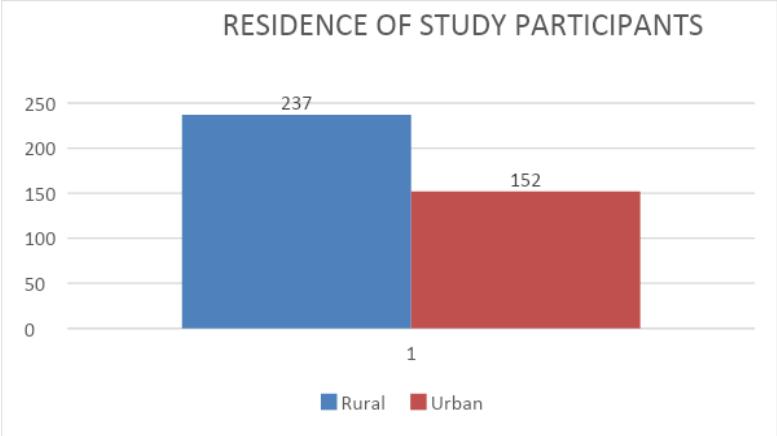

Figure 7: Residence of study participants

There are more cases of ischemic stroke in rural areas more predominantly than urban in the study population in Rwanda.

4.1.4 Travel distance to referral hospital of study population

For instance, a patient at Gisenyi District Hospital who is considered a candidate for transfer to a nearby referral hospital with a CT scan machine (CHUK) would travel 155 km with an earth ambulance.

The population was divided into 3 groups based on the distance from the referral hospital and where they live: Less than 5km, 5-10 km and more than 10km. The predominant population involved were a distance group of more than 10 km: 252 (64.5%), at 5-10 km: 94 (24%) while the group of patients at less than 5 km constituted a relatively lower population: 45 (11.5%), (Figure 8).

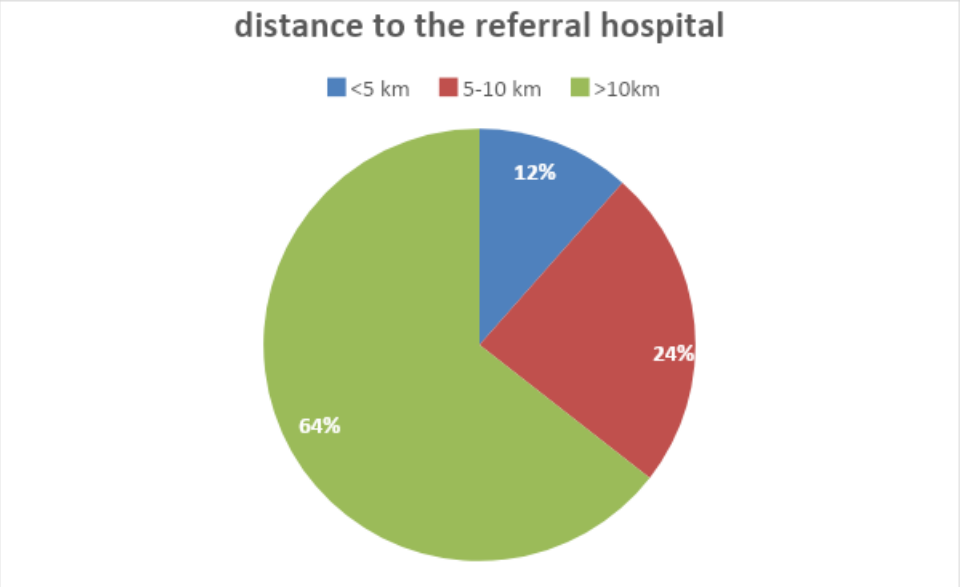

Figure 8: Participants' estimated distance to referral hospital.

Most patients received for stroke imaging were found to have traversed through a long distance of at least 10km to reach referral hospitals where stroke care could be initiated. Only the minority about 12% could be served within 5 km distance and hence meet the brain salvaging timing.

4.2 Proportions of patients presenting with ischemic stroke by ASPECT score categories

The descriptive statistics were used to classify patients according to ASPECT score which is a significant indicator of functional outcome. The score less than 7 was termed ‘low’ and known to be associated with poor prognosis while score of 7 and above was termed high and associated with relatively good prognosis (10,106).

Our results show that among 389 participants with ischemic stroke, 226 (58.1%) had low (Pc)ASPECT and 163 (41.9%) had high (Pc)ASPECT score (Table 3). The mean ASPECT score in studied population is 6.86 with standard deviation of 1.62

Table 4: ASPECT score categories of patients with ischemic stroke

The neuroimaging shows significantly higher proportion of patients who present with low or worse ASPECT scores than it is for the patients with higher or better score

Score		**ASPECT**	**Pc ASPECT**	**Frequency**	**Percentage**
ASPECT Score	Low (Less than 7)	221	5	226	58.1
	High (7 and above)	148	15	163	41.9
	Total	369	20	389	100.0

4.3 The average time interval from stroke symptoms and stroke CT scan exam

This part entails the time elapsed between symptoms onset and the arrival to the Radiology department. The time is classified into categories, but after 24 hours, it's a typical delay which predisposes patients with ischemic stroke to poor outcome.

The patients with ischemic stroke underwent non-contrast brain CT at selected hospitals. The findings revealed that 152(39%) arrived between 24 hours and one week, 136 (35%) arrived after one week of stroke symptoms, 78 (20%) within 6 to 24 hours while a small number of 19 (5%,) presented at 3 to 6 hours and 4 (1%) did brain CT scan in less than 3 hours of onset of symptoms (Figure 9).

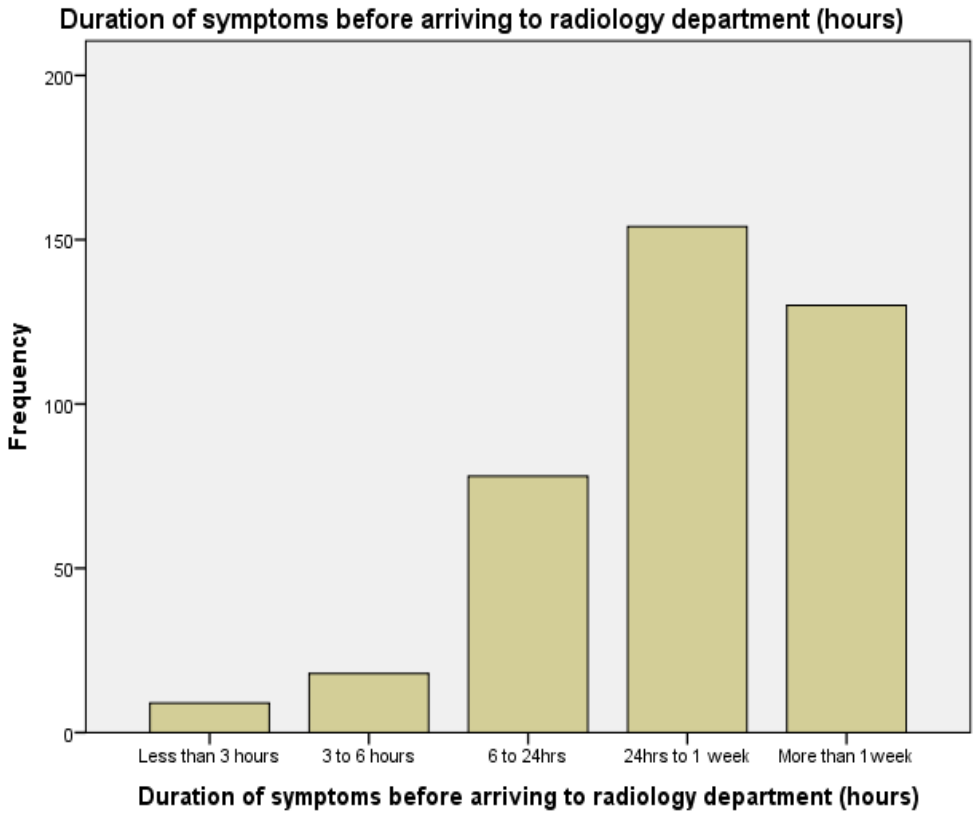

Figure 9: The time interval from stroke symptoms and stroke CT scan.

The majority of ischemic stroke patients in Rwanda avail themselves to the imaging facilities between 1-7days post symptoms, while only 1% of them show up within the golden window of time within 3 hours of the stroke symptoms.

4.4 The risk factors influencing the ASPECT score in the study population.

A bivariate analysis was done through cross tabulation to reveal statistically significance of different variables. The statistically significant variables are those with p value less than 0.05 (were bolded) in the table 5. The latter were subjected to multiple logistic regressions with 95% confidence interval to reveal independent risk factors associated with ASPECT score in the study population.

The Chi-square analysis was performed to measure the independence of the drivers of dynamics in ASPECT score including demographic data, smoking, family history of ischemic stroke, hypertension, hypercholesterolemia/obesity, and location of the lesion, diabetes mellitus, bee bite and arrhythmia. Among them, distance to receiving referral hospital, location of the lesion, duration of symptoms before arriving to Radiology department, hypertension and arrhythmia showed a significant impact on ASPECT score in ischemic stroke patients at p-value <0.005.

The results show that 65.4% of patients who spent 24hrs to 1 week, 55.6% spent 3 to 6 hours, 50.4% spent more than 1week and 22.2% spent less than 3 hours before arriving at the Radiology department had low ASPECT Score. With a p value less than 0.05, the correlation between the duration of the symptoms and the ASPECT Score is statistically significant.

Furthermore, results show that 57.9% of participants with lesions in the right hemisphere, 60.6% in the left hemisphere, and 30.0% with lesions in posterior circulation had low ASPECT Score. The relationship between the location of the lesions and ASPECT Score is statistically significant($p<0.05$). Between hypertension and ASPECT Score, there is a statistically significant relationship (Chi-Square=6.478; P=0.011). There is a statistically significant relationship between Arrhythmia and ASPECT Score (Chi-Square=4.395; P=0.036), (Table 5).

Table 5: Bivariate analysis of the risk factors influencing the ASPECT scores in the study population

Binary logistic regression analysis showing factors responsible for low ASPECT score. Most factors including hypertension, duration of symptoms before imaging, arrhythmia, location of the lesion and distance to the receiving referral hospital have significant impact in lowering ASPECT score which is known to be a major determinant of the prognosis in patients with acute ischemic stroke.

		ASPECT Score			
		Low n (%)	High n (%)		
Variables	Indicators	<7	≥ 7	Chi-square	P-Value
Age category	Less or equal to 50	52(60.5)	34(39.5)	1.138	0.566
	51 to 65	61(60.4)	40(39.6)		
	66 and above	109(55.1)	89(44.9)		
Sex	Male	100(58.5)	71(41.5)	0.084	0.722
	Female	122(57.1)	92(42.9)		
Residence	Rural	140(59.6)	95(40.4)	0.903	0.342
	Urban	82(54.7)	68(45.3)		
Distance to the receiving referral hospital	Less than 5 km	26(49.1)	27(50.9)	6.810	**0.033**
	5 to 10 km	42(48.8)	44(51.2)		
	More than 10km	154(62.6)	92(37.4)		
Duration of symptoms before arriving to Radiology department (hours)	Less than 3 hours	2(22.2)	7(77.8)	10.668	**0.031**
	3 to 6 hours	10(55.6)	8(44.4)		
	6 to 24hrs	51(65.4)	27(34.6)		
	24hrs to 1 week	94(62.3)	57(37.7)		
	More than 1 week	65(50.4)	64(49.6)		

Location of the lesion	Right hemisphere	110(57.9)	80(42.1)	6.880	**0.032**
	Left hemisphere	106(60.6)	69(39.4)		
	posterior circulation	6(30.0)	14(70.0)		
Smoking	Yes	9(47.4)	10(52.6)	0.868	0.352
	No	213(58.2)	153(41.8)		
Family history of ischemic stroke	Yes	1(50.0)	1(50.0)	0.048	0.826
	No	221(57.7)	162(42.3)		
Hypertension	Yes	77(67.5)	37(32.5)	6.478	**0.011**
	No	145(53.5)	126(46.5)		
Hypercholesterolemia /obesity	Yes	10(50.0)	10(50.0)	0.507	0.476
	No	212(58.1)	153(41.9)		
Diabetes mellitus	Yes	38(67.9)	18(32.1)	2.559	0.110
	No	184(55.9)	145(44.1)		
Bee bite	yes	3(100.0)	0(0.0)	2.181	0.140
	No	219(57.3)	163(42,7)		
Arrhythmia	yes	6(100.0)	0(0.0)	4.395	**0.036**
	No	220(57.4)	163(42.6)		

4.4.1 Test of independence among the drivers of dynamics in ASPECT score in Rwanda.

In fact, being far, for instance at more than 10km of receiving hospital and low ASPECT score among studied population was statistically significant, as indicated by adjusted odd ratio of 1.772 [AOR=1.772, 95%CI: 1.056-2.976, p=0.030]. This suggested that patients with acute ischemic stroke at more than 10km are 1.772 times more likely to have low ASPECT score (<7) than those living in close proximity with the hospital.

The relationship between patients with hypertension and low ASPECT score was statistically significant, as indicated by an AOR of 2.034 (1.258-3.288). This finding implied that the patients with ischemic stroke on background of hypertension are 2.034 times more likely to have low ASPECT score than those with no history of hypertension. The relationship between lesion location in anterior circulation and low ASPECT score among patients with ischemic stroke in Rwandan population was statistically significant, as indicated by adjusted odd ratio of AOR=0.289, 95%CI: 0.102-0.818, p=0.019 and 0.256(0.090-0.728) p=0.011 for right and left hemisphere respectively (Table 6).

Table 6: Multivariate analysis of the drivers of the dynamics in ASPECT score in the study population

Multiple logistic regression analysis shows that hypertension, increased duration of symptoms before arriving at the Radiology department, location of the lesion and distance to the receiving referral hospital remained factors responsible for the low ASPECT score.

	ASPECT Score	
	AOR (95%CI)	P-value
Distance to the receiving referral hospital		
Less than 5 km	1.757 (0.904-3.414)	0.096
5 to 10 km	1.772(1.056-2.976)	**0.030**
More than 10km	Ref	
Duration of symptoms before arriving to Radiology department		
Less than 3 hours	0.138(0.494-14.379)	0.255

3 to 6 hours	0.795(0.275-2.295)	0.671
6 to 24hrs	0.514(0.280-0.943)	**0.031**
24hrs to 1 week	0.694(0.425-1.135)	0.146
More than 1 week	Ref	
Location of the lesions		
Right hemisphere	0.289(0.102-0.818)	**0.019**
Left hemisphere	0.256(0.090-0.728)	**0.011**
Posterior circulation	Ref	
Hypertension		
Yes	2.034(1.258-3.288)	**0.004**
No	Ref	
Arrhythmia		
Yes	34.707(0.000-3.984)	0.999
No	Ref	

AOR: odd ratio, 95%CI: 95% confidence interval

4.5 The influence of ASPECT scores in haemorrhagic transformation at initial presentation

Using a logistic regression to measure the influence of low ASPECT score (less than 7) in patients with haemorrhagic transformation on ischemic stroke, we found that low ASPECT score increases 2.66 times the risk of haemorrhagic transformation with comparison to high ASPECT score [AOR=2.661, 95%CI: 1.118-6.336, p<0.027] (table 7).

Table 7: The odds of ASPECT score on haemorrhagic transformation of ischemic stroke

Low ASPECT score is a strong predictor of haemorrhagic transformation in patients with ischemic stroke.

	AOR (95%CI)	P-value
ASPECT Score		
Low (less than 7)	2.661(1.118-6.336)	**0.027**
High (7 and above)	Ref	

4.6 Selected radiological images from the studied population

Some few cases of patients presented with ischemic stroke were selected and their images are hereby presented to demonstrate common ischemic lesions found in Rwanda and the corresponding ASPECT score values in this study population (Figure 10-15).

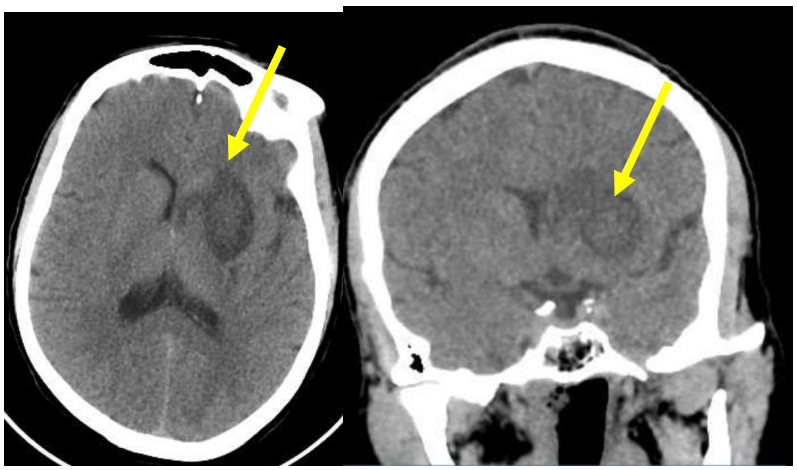

Figure 10: Left lentiform and internal capsule infarct.

Images of 55 years old female presented with right hemiplegia after 2days of symptoms onset.

Axial (Left) and coronal (Right) unenhanced CT show a hypoattenuating lesion in the left lentiform nucleus and internal capsule (yellow arrows) causing mass effect on left lateral ventricle. The A**SPECT score is 8**

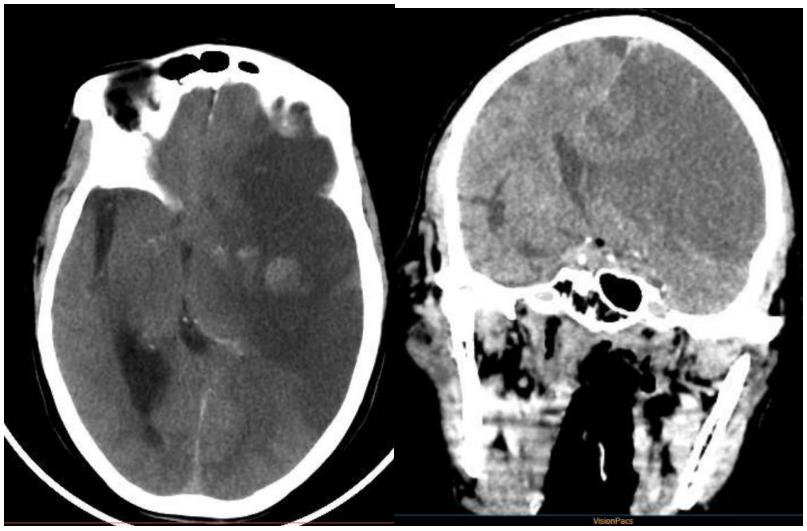

Figure 11: Left MCA infarct.

Images of an 86 years old brought into a coma for 2 days with right hemiplegia.

Axial (Left) and coronal (Right) unenhanced CT show extensive left fronto-temporal and parietal hypoattenuating lesion with intra lesion haemorrhagic transformation and midline shift to the right. left MCA subacute ischemic stroke with haemorrhagic transformation, compatible with **ASPECT score of 4**

Fig 10-11: In courtesy of the radiology Head of department at RMH

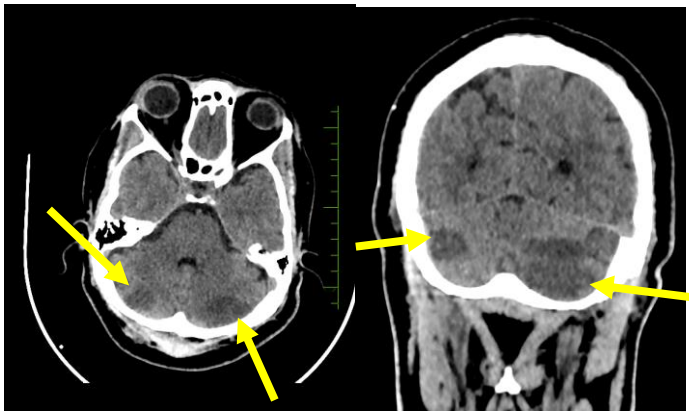

Figure 12: Cerebellar infarct

59 years old presented with upper and lower limbs weakness.

Axial (Left) and coronal (Right) unenhanced CT show wedge shaped hypoattenuating lesions in both cerebellar hemispheres (Left > Right). The **Pc-ASPECT is 8**

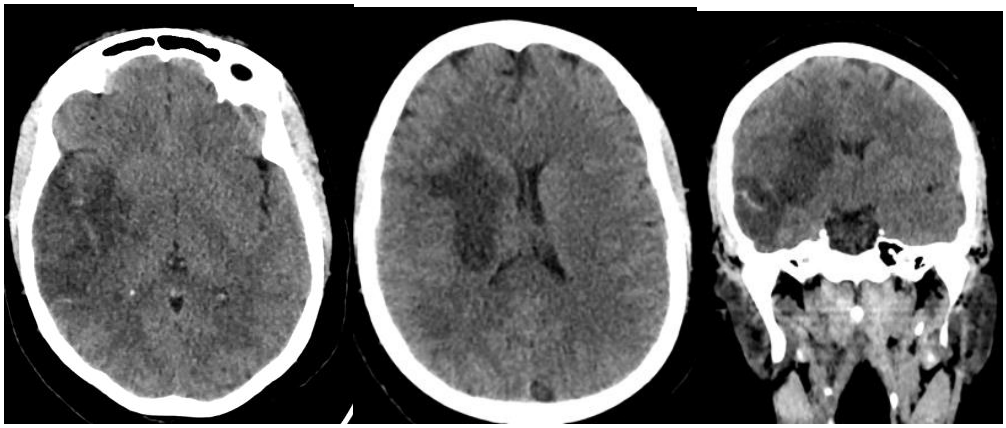

Figure 13: Right MCA infarct.

40 years old, female presented with severe headache and left hemiplegia for 1 week

Axial (Left and middle) and coronal (Right) unenhanced CT show loss of the grey–white matter differentiation in the MCA and hypodense lesions involving M2, M3, M5 and M6 territories. Grey–white differentiation is preserved on the normal left side. The **ASPECT score is 6**

Fig 12-13: In courtesy of the radiology Head of department at CHUK

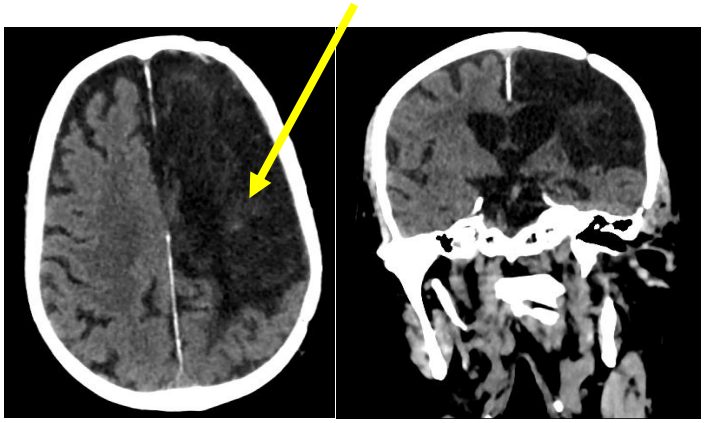

Figure 14: Left MCA ischemic infarct with petechial haemorrhagic transformation.

83 years old, male Presented with behaviour changes, vomiting and was on anticoagulant medication for 1 week.

Axial (Left) and coronal (Right) unenhanced CT show extensive left fronto-temporal and parietal hypoattenuating lesion with intralesional dot hyperdensity (yellow arrow) in keeping with petechial haemorrhagic transformation. The **ASPECT score is 4**

Fig 14: In courtesy of the radiology Head of department at KFH

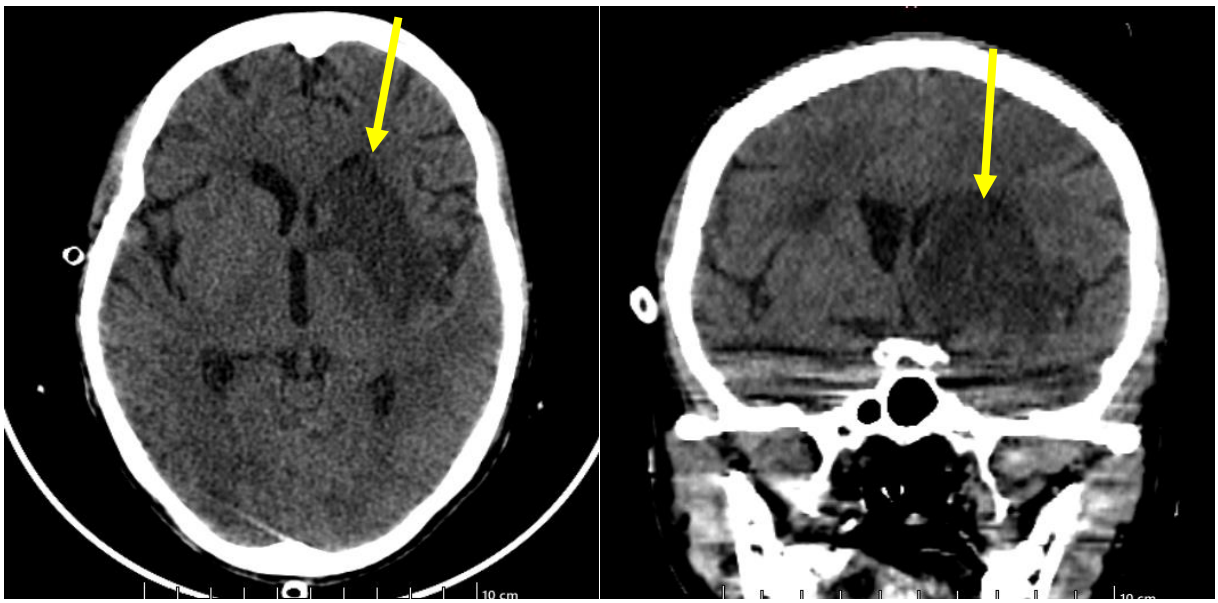

Figure 15: Left basal ganglia & internal capsule infarct.

Images of 42 years old female presented with right hemiplegia lasting 3days

Axial (Left) and coronal (Right) unenhanced CT show a hypoattenuating lesion in the left basal ganglia and internal capsule (yellow arrows) causing mass effect on left lateral ventricle. The A**SPECT score is 7**

Fig 15: In courtesy of the radiology Head of department at CHUB

CHAPTER V: DISCUSSION

5.0. Socio-demographics of patients with ischemic stroke

In this study, a total of 389 patients who underwent brain CT scan in the Radiology departments of the University referral hospitals in Rwanda were provided with extended scope of image reporting that involved the study of the patterns of ischemic stroke and the drivers of dynamics in ASPECT score in Rwanda through review of patients' clinical backgrounds.

5.0.1 Age and sex of participants

The results of our study show that ischemic stroke is more prevalent in females than in males' population. However, with correlation to the age both males and females have increased risk of developing ischemic stroke. Ages of our patients ranged from 2 up to 100years with mean age of 62.89 ±19.19 years. There is predominance of ischemic stroke in senile age within a study population.

The observed age spectrum in Rwanda, can be attributed to significant improvement in the life expectancy of the Rwandan population in the 21st-century (69years of life expectancy).

Our findings are not different, but slightly higher to what the study done in Tanzania where the mean age was 59.7years (107). Another study done in one rural area of Kenya,2013 on ischemic stroke showed the mean age of 68.8years; female (68%) more affected than male (38%) (108). Likewise, additional study done in Rwanda, 2017 showed that 60% of the population were having equal or above 55 years in both forms (ischemic and hemorrhagic) of stroke (26). Our results are not far different from the ones found in study done in Uganda 2021 and Tanzania 2013, where the mean age of patients with stroke was 62.5 and 61.7years respectively. Females were more affected than male in both Countries (109,110).

The study done in Congo 2020, showed the mean age of 61.8 ± 2.4 years, not significantly different to our findings. However, difference on sex ratio was noted (men were 1.78 times females), this can be explained by combination of both ischemic and haemorrhagic stroke (111). From the light of literature search, study done in Italy 2020 showed the mean age of 75.0 years with female predominance (53%) among patients with ischemic stroke (112). The difference of mean age between our findings and the study done in Italy can be explained by the ageing population with life expectancy higher than in Rwanda. With the current knowledge, ischemic stroke as part of non-communicable disease is more prevalent in advanced age and female population (53%), than other groups of population which might be linked to high life expectancy among females compared to males.

5.0.2 Residence of participants and distance to receiving hospital.

According to the publication done by the Ministry of Health of Rwanda in the year 2020, it was revealed that, about 22% of patients with stroke were not aware of their previous health status and likewise 53.5% of patients with hypertension were not on treatment surprisingly (113). The unawareness of health status is construed to be due to the likelihood of low education, poor health services and behavioural issues in Rwanda rural population which is the majority according to the fourth Rwandan Population and Housing Census (RPHC4) that demonstrated that 83% of the total population resides in rural areas (114)

With regard to the residence, the current results of patients with ischemic stroke shows that 60.9% are from rural areas. Moreover, a study done in rural areas of China in 2020 showed a high prevalence of stroke in the rural population (115). Therefore, the rural predominance of ischemic stroke is likely to be related to limited access to health services and poor education and monitoring of risk factors of ischemic stroke.

5.0.3 Distance to the receiving referral hospital

Out of 389 study participants, 246 travelled more than 5km or 10 kilometres to the equipped referral hospital; of these, 154 (64.6%) had low ASPECT scores, 92 (37.4%) had high ASPECT scores, and fewer than half of the people in the neighbourhood have low ASPECT scores. This indicates that a significant proportion of patients who have low ASPECT scores travel a long distance to a hospital that is equipped.

Similar results were found in a study by Pallesen et al., which demonstrated that inter-hospital transfers at distances of more than 150 km required an average transfer time of 92 minutes by equipped ambulance or recopter and that a median ASPECT score of 6 was associated with the worst outcome. (1).

For instance, a patient at Kibogora District Hospital who is considered a candidate for transfer to a nearby referral hospital with a CT scan machine (CHUK) would travel 195 km with an earth ambulance.
As some District hospital in Rwanda, located at more than 150km of the referral Hospital and means of patients' transfer is car ambulance. There are high risks of arriving at a referral Hospital with a low ASPECT score.
The low ASPECT score associated with far distance reported in the current study can be linked to traffic jams and car ambulances that contribute to increased duration before availing patients to equipped hospitals. In addition to that Rwanda is known to be a country of thousand hills and only a few highway roads making transportation difficult and take longer than expected.

5.1 Proportions of patients presenting with ischemic stroke by ASPECT score categories

Our study showed that more than half of the studied population (58.1%) had a low ASPECT Score. On the other hand, 41.9% of participants showed high ASPECT Score. The average ASPECT Score in Rwanda for the patients with ischemic stroke is low (6.86 ±1.62).

From the light of literature search, low average ASPECT score was noted in study done in 2021 at Centre Hamburg-Eppendorf, Hamburg, Germany where median ASPECT score was 4 (116). The low ASPECT score relative to our results might be associated to the diabetes mellitus which is predominant in said study.

To the best of the light from literature, ASPECT score is a strong predictor of outcome that we measure by evaluating independency function and fatality (106,117).

Different studies have shown a low average ASPECT score. This might result in different factors.

5.2 The average time interval from stroke symptoms to neuroimaging examinations

In this study, time elapsed from the onset of ischemic stroke symptoms to the presentation at Radiology department was analysed where 74.0% of patients arrived late (after 24 hours and more). Furthermore, results showed that 33.4% of patients arrived after one week, 39.6% arrived between 24 hours and one week, 4.6% of participants arrived between 3 to 6 hours, and as few as 2.3% of the participants arrived in less than 3 hours. The delay in obtaining a CT scan service may consequently affect the management plan. This delay would lead to untimely use of IV tPA in the possibly available facilities in Rwanda during the study period. Poor use of antithrombotic was noted in the USA as well at 3.4% to 5.2% (118). Each hour delay in the time to presentation decreased chances for a good outcome by approximately 2% (119). Time is brain and the average duration of non-lacunar stroke evolution is 10 hours (6 to 18 hours) according to the literature (91). The delay of patients with ischemic stroke to CT scan examination was noted also in a study done in Tanzania by Shali et al., with mean time of 1.74 days (107). There is a significant difference with the study done in China, 2017, that found the average of 4h24min (264 minutes) (120) for baseline CT imaging. The delay of presentation to the tertiary hospital was noted in the study done in Kenya 2021. Only 25.2% arrived at the hospital within 3.5 h of stroke onset symptoms, the main causes were infrastructures related problems (121). Furthermore, another study showed that every minute count in ischemic stroke diagnosis and management, the delay of 1 min of intervention of MCA occlusion will result in 14 billion synapses, 1.9million neurons and long myelinated fibres loss (122). Further research showed that in comparison to normal rate of brain ageing, the ischemic brain ages 3.6 years each hour if no medical intervention is done (123).

To the best of our understanding, the significant delay in the Rwandan population may be associated with infrastructure, multidisciplinary approach and time of consultation in primary health facilities.

5.3 Drivers of dynamics in ASPECT score in the study population

In the current study, it was noted that hypertension, distance to the equipped referral hospital, duration of symptoms before arriving at the Radiology department and location of the lesion remained significant factors associated with worsening of the ASPECT score in the study population.

The risk factors found in this study are currently reported in most literature findings in predisposition to ischemic stroke. This is further attributed to demographic risk which results in low ASPECT score, and consequently poor outcome (39,124–127).

There is a link between ASPECT score and some known non-modifiable risk factors for ischemic stroke, such as age, race, gender, heredity, ethnicity, and several well-established modifiable risk factors for ischemic stroke particularly, hypertension, hyperlipidaemia, cardiac diseases, diabetes, physical inactivity, cigarette smoking, carotid stenosis, and atrial fibrillation (128,129). These risks can further be examined as follows.

5.3.1 Hypertension

In the current study, hypertension has shown a greater significant association with ischemic stroke and later with low ASPECT score. The study done in 2005 which showed that long standing hypertension has associated 3 to 5 risks of both ischemic and hemorrhagic stroke, as it contributes to atherosclerotic disease (130). Interventions which target hypertension help indirectly in stroke control, either medical or lifestyle change. Reduction in systolic blood pressure of 2, 3, or 4-mm Hg contributes to the risk reduction in stroke of 6%, 8% and 14%, respectively (130).

Hypertension contributes to initial tissue damage and has both a direct link to stroke and exacerbation of tissue damage which are mainly linked to atheromatous deposits (131). Injury to cerebral microvasculature results from pulsatile pressure which causes tear of endothelium and smooth muscles (132). Our current study investigated various risk factors and found that hypertension has the most influential factor of low ASPECT score among others.

5.3.2 Location of the lesion

Motor impairment scores are significantly correlated with the volume of the lesion (93). The previous study by Yassi et al., has shown that infarct size and location demonstrate importance in predilection of patient's outcome (133). The involvement of sensitive areas of deep nuclei can have an equal point in ASPECT score with a large territorial hemisphere of M branches. Ischemic stroke has its own detrimental effects on

brain functions. In a study done by Macciocchi et al.,1998, it was reported that the function outcome of ischemic stroke was closely associated with the cortical brain and the involvement of the dominant (left) hemisphere. Similarly, it was noted that the tendency of stroke recurrence was high with the involvement of the right cerebral hemisphere (134). Moreover, the current study shows that location of the lesion is associated with low ASPECT score which also determines the outcome as to the fact that low ASPECT has poor prognosis. Furthermore, lesions located in the basal ganglia are associated with low ASPECT scores in contrast to the lesions in the hemispheric regions. Again, ganglionic lesions are more associated with motor dysfunction such as dysphagia (40). Therefore, stroke location and volume have vital importance in prediction of patients' outcome.

5.3.3 The influence of distance on ASPECT score

Our results show that travelling distance more than 5km to arrive to receiving referral hospital and low ASPECT score among studied population was statistically significant, as indicated by adjusted odd ratio of 1.772. This suggested that patients with acute ischemic stroke at more than 5km and 10km are 1.772 times more likely to have low ASPECT score (<7) than those living in close proximity with the hospital by virtual of the time spent to access the stroke imaging and care resulting in further delay and progression of ischemic lesion.

A study of the infrastructures and barriers to access acute stroke care at a regional tertiary facility in Kenya was conducted in 2021and showed that significant delay to the hospital was linked to intra-hospital distance and traffic that bring significant barrier of stroke management, implies worse outcome(8). In our study population having majority of patients at more than 10km of equipped hospitals significantly correlate with low average ASPECT score. As some District hospital in Rwanda, are located in more than 150km from the referral Hospital rendering the car ambulance services becoming the only reliable mode of patients' transportation to catch up with time, such patients may have delayed interventions for stroke. Citing an example of, a patient at Kibogora District Hospital who is considered a candidate for transfer to a nearby referral hospital with a CT scan machine (CHUK) would travel 187 km with a road ambulance (2).

Therefore, lately arrival to a referral Hospital, is a risk of a low ASPECT score dynamics.

5.3.4 The influence of time from symptoms onset

Although patients from Rwanda population presents to the equipped hospitals at diverse time intervals, the patients who were imaged at the time interval between 6-24 hours had significant odds for influencing occurrence of the low ASPECT score 0.514(0.280-0.943)

The phrase "time is brain" highlights how quickly and irreversibly human nerve tissue is lost as a stroke progresses and how urgently therapeutic therapies should be undertaken (3), the study done on ASPECT score and CT perfusion show a mismatch based on time of presentation. A discrepancy between the NCCT 24 h and the mean transient time (MTT) ASPECTS scores can be used to calculate the amount of tissue salvaged because MTT estimates the amount of tissue at risk and NCCT 24 h describes the size of the actual infarct (4)

In a larger Canadian study of 936 patients receiving iv-thrombolysis during a 3-hour period between 1999 and 2001, it was found that there was a nearly linear negative connection between ASPECTS on the baseline NCCT and functional result (5).

The average time between symptoms onset and brain CT scan was 1 day in the study done in 2002 at Sriramya Lapa University Hospital Frankfurt, to study association of neurogenic dysphagia and brain lesion location in ischemic stroke (40). Therefore, the time has a significant impact on ASPECT score which later dictates treatment plan and prognosis.

5.3.5 The influence of arrhythmias on ASPECT score.

There is a statistically significant relationship between arrhythmia and ASPECT Score (Chi-Square=4.395 P=0.036). The total of six patients identified with ischemic stroke have a low ASPECT score.

The current study depicted atrial fibrillation among other types of arrhythmias, however; from the light of literature, is the most frequent cardiac arrhythmia and 23.7% of acute ischemic strokes are associated with atrial fibrillation. Therefore, atrial fibrillation is a strong predictor of low ASPECT score in other studies (6)

Our results, after multivariate analysis show arrhythmia was not proven to be an independent factor determining low ASPECT score [p value >5% (0.999)]. This might be the result of a poor diagnostic tool and/or clinical documentation system. However further research has to prove the position of our population regarding those risks after re-evaluation of this factor in more clinically improved settings.

5.4 The influence of ASPECT scores in haemorrhagic transformation at initial presentation

The results of the current study revealed that ischemic stroke patients with low ASPECT score (less than 7) were two times likely to develop haemorrhagic transformation. Having a low ASPECT score increases 2.66 times the risk of haemorrhagic transformation than having a high ASPECT score (greater than 7) [AOR=2.661, 95%CI: 1.118-6.336, p<0.027].

Barber et al,. identified ASPECTS as a significant determinant of symptomatic cerebral haemorrhage following medical therapy within 3- hours of symptoms onset (79).

In the MR CLEAN research and the American Heart Association study on imaging markers associated to hemorrhagic transformation in patients with acute ischemic stroke, There is similarity study results in imaging stroke severity parameters that were associated with hemorrhagic transformation (a multicenter randomised clinical trial in the Netherlands of endovascular therapy for acute ischemic stroke) (135,136). In these studies, risk factors such as large extensive early ischemic change (ASPECTS 0-3) are more prone to develop hemorrhagic transformation and are less likely to have a favourable clinical course, especially after thrombolysis (83). Another study done for risk of haemorrhagic transformation showed 14 times increased spontaneous intracranial haemorrhage for ASPECTS scores less than 7(106). The association between low ASPECT score and haemorrhagic transformation was reinforced by a study done in Italy 2019 which showed that cerebral lesion is the major determinant of haemorrhagic transformation with 1.12 factor (112).

Moreover, additional studies suggest that the most significant risk factor for hemorrhagic transformation is the size of infarcted core, which directly correlates with ASPECT score and once 1cm is decreased to infarcted size, overall probability of haemorrhagic transformation reduced by 10% (137). Therefore, this study shows that the bigger the infarct the patients have, the higher the risk of haemorrhagic transformation.

CHAPTER VI: CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusion

This study concludes the following cardinal findings:

Ischemic stroke trends more in females than it is among male subjects in 55.3% and 44.7% distribution respectively in the study population in Rwanda. The condition has its proportions standing at 60.9% from rural and 39.1% from urban population, respectively. Although imaging has a central role in ischemic stroke patients, a significant time delay between onset of symptoms and stroke imaging predisposes patients to delayed interventions and hence poor treatment outcome.

The majority of ischemic stroke patients presents with low ASPECT score by more than 58% with trivial predilection to females

The occurrence of haemorrhagic transformation increases with the presence of a low ASPECT score in ischemic stroke.

The dynamics of ASPECT score among patients with ischemic stroke in Rwanda are mainly driven by the hypertensive state, increased distance to the equipped hospital together with increased duration between symptoms onset and neuro-imaging.

6.2 Recommendations

At the end of this study, some recommendations are addressed to:

The ministry of health

1. Increase basic health infrastructure, specialised health care providers and different treatment options, especially in rural areas.
2. Education/stroke awareness and early transfer of patients with stroke symptoms to comprehensive health care centres should be the priorities among others to save the brain.
3. Develop stroke algorithms and/or stroke centres Countrywide.
4. Awareness of the population about unhealthy lifestyles, stroke risk factors, stroke symptoms and signs that need urgent attention.
5. To avail at least CT scan machine in all District hospitals and development of artificial intelligence.

The treating medical personnel (Physicians, neurosurgeons, general practitioners and nurses)

Multidisciplinary approach and good communication will save more patients. To consider patients who present with stroke symptoms as an extreme emergency in order to speed up imaging to rule out early ischemic stroke 'brain is time'. Adjust hospital-based protocols as recommended.

Hypertension as a modifiable risk factor, management and screening should be standardised.

Radiology departments (CHUK, CHUB, RMH and KFH):

To review their protocols for non-contrast CT scan especially in stroke symptoms to provide timely reports. Train and improve knowledge of radiologists, residents, nurses and imaging technicians. In case of doubt do brain MRI for patients with high risk.

Radiologists in communication with clinicians are encouraged to standardise reports of non-contrast brain CT using ASPECT score that will help in prognostic estimation and management decision.

Further studies

1. Another study needs to be done prospectively to look for association between radiological findings, interventions and outcome.
2. Given that some patients developed ischemic stroke after bees' bite. Research and public health value should clarify how it is linked with ischemic stroke.
3. Further studies to find out the time it takes from stroke symptoms to the treatment and availability of treatment options.
4. Further studies to establish the correlation between ASPECT score and clinical outcome.

6.3 Strength and limitations

Strength

Our study is the first conducted in Rwanda and in the region on neuroimaging patterns of ischemic stroke and the drivers of dynamics in ASPECT score. The information from this study: Identification of common risk factors as documented in medical file (Hypertension), delay in time of presentation at imaging department which predicts management and prognosis (Time is brain). Those findings may serve as evidence to advocate for awareness, screening risk factors and mobilise resources for management of patients presented out of time of thrombolysis.

The awareness will help not only in risk factors prevention but also early consultation, implies high ASPECT score and possibility of recanalization.

The study was carried out in four teaching/referral hospitals which receive patients with neurological symptoms for both investigations (brain CT examination) and management. Therefore, information from our study can be generalised to the whole country.

Limitations

Due to the study design, whereby no interaction was made with the patients, any error in patient recording in different materials used (Register books, medical file, Napier, open clinics, PACS and external hard discs) may have had repercussions on our findings. However, they were well checked for each and every patient for consistency of information.

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APPENDICES

Appendix 1: Questionnaire

S/N	Questions	Response
Section 1: Demographic Characteristics		
1.	Age in years	……years
2.	Sex	1=Male 2=Female
3.	Residence	1=Rural 2=Urban
4.	Distance to the receiving referral hospital	1=Less than 5 km 2=5 to 10 km 3=More than 10km
5.	Is there Haemorrhagic transformation as per CT scan findings	1=Yes 2=No
6.	Smoking	1=Yes 2=No
Section 2: Magnitude of patients presenting with ischemic stroke by ASPECT score categories		
7.	ASPECT score on NCCT scan	……..
8.	Location of the lesion	1=Right hemisphere 2=Left hemisphere 3=posterior circulation 4=Other
Section 3: Timing of patients presenting with ischemic stroke		
9.	Duration of symptoms before arriving to Radiology department (hours)	1=Less than 3 hours 2=3 to 6 hours 3=6 to 24hrs

		4=24hrs to 1 week 5=More than 1week
Section 4: Risk factors		
10.	Family history of ischemic stroke	1=Yes 2=No
11.	hypertension	1=Yes 2=No
12.	Hypercholesterolemia/obesity	1=Yes 2=No
13.	Diabetes mellitus.	1=Yes 2=No
14.	Unknown	1=Yes 2=No
	Other (specify…..)	

Appendix 2: UR and Study sites approval letters

UNIVERSITY of RWANDA

COLLEGE OF MEDICINE AND HEALTH SCIENCES

DIRECTORATE OF RESEARCH & INNOVATION

CMHS INSTITUTIONAL REVIEW BOARD (IRB)

Kigali, 31st January /2022

Dr MUSABYIMANA Joseph, MD
School of Medicine and Pharmacy, UR

Approval Notice: No 050/CMHS IRB/2022

Your Project Title "*Neuroimaging Patterns of Cerebral Vascular Accident and the Drivers of Dynamics in Aspect Score: A Study of Rwanda*" has been evaluated by CMHS Institutional Review Board.

Name of Members	Institute	Involved in the decision		
		Yes	No (Reason)	
			Absent	Withdrawn from the proceeding
Prof Kato J. Njunwa	UR-CMHS	X		
Prof Stefan Jansen	UR-CMHS	X		
Dr Brenda Asiimwe-Kateera	UR-CMHS	X		
Prof Ntaganira Joseph	UR-CMHS	X		
Dr Tumusiime K. David	UR-CMHS	X		
Dr Kayonga N. Egide	UR-CMHS	X		
Mr Kanyoni Maurice	UR-CMHS		X	
Prof Munyanshongore Cyprien	UR-CMHS	X		
Mrs Ruzindana Laudrine	Kazaki district		X	
Prof Gishoma Diclis	UR-CMHS	X		
Prof Donatilla Mukamana	UR-CMHS	X		
Prof Kyamanywa Patrick	UR-CMHS		X	
Prof Condo Umuteti Jeanine	UR-CMHS		X	
Dr Nyirazinyoye Laetitia	UR-CMHS	X		
Dr Nkeramihigo Emmanuel	UR-CMHS		X	
Sr Maliboli Marie Josee	CHUK	X		
Dr Mudenge Charles	Centre Psycho-Social	X		

After reviewing your protocol during the IRB meeting of where quorum was met and revisions made on the advice of the CMHS IRB submitted on 31st January 2022, **Approval has been** granted to your study.

Please note that approval of the protocol and consent form is valid for **12 months**.

Email: researchcenter@ur.ac.rw P.O Box 3286 Kigali, Rwanda www.ur.ac.rw

KING FAISAL HOSPITAL, RWANDA
ETHICS RESEARCH COMMITTEE

Patient Centered Care

6th, MAY 2022

ETHICAL APPROVAL

Dear MUSABYIMANA Joseph,

We acknowledge receipt of your study protocol:

"NEUROIMAGING PATTERNS OF CEREBRAL VASCULAR ACCIDENT AND THE DRIVERS OF DYNAMICS IN ASPECT SCORE IN RWANDA."

After a thorough review, the reviewers of KFH Ethics Research Committee consider this study relevant. The investigator is allowed to start data collection.

N.B.

- The investigator is ***requested to submit one hard copy of his final research results*** in the office of the Directorate of Education, Training and Research at King Faisal Hospital, Kigali

Best Regards

Dr. Dushimiyimana Jean Marie Vianney
Consultant ENT surgeon
Chair, Ethics Research Committee
King Faisal Hospital, Rwanda.

CC:

1. Chief Executive Officer_ KFH-Rwanda
2. Director of Education, Training & Research_KFH- Rwanda
3. Members of the Ethics Research Committee, KFH- Rwanda

• TEL: +250 252 588888 • FAX: +250 252 583203 • EMAIL: info@kfh.rw • Website: www.kfh.rw
GASABO DISTRICT, P.O. Box 2534 KIGALI, RWANDA

CENTRE HOSPITALIER UNIVERSITAIRE
UNIVERSITY TEACHING HOSPITAL

Quality Health Care
Training & Research

Ethics Committee / Comité d'éthique

11th Mar,2022 Ref.:EC/CHUK/031/2022

Review Approval Notice

Dear Joseph MUSABYIMANA,

Your research project: "NEUROIMAGING PATTERNS OF CEREBRAL VASCULAR ACCIDENT AND THE DRIVERS OF DYNAMICS IN ASPECT SCORE IN RWANDA "

During the meeting of the Ethics Committee of University Teaching Hospital of Kigali (CHUK) that was held on 11th Mar,2022 to evaluate your request for ethical approval of the above mentioned research project, we are pleased to inform you that the Ethics Committee/CHUK has approved your research project.

You are required to present the results of your study to CHUK Ethics Committee before publication by using this link:www.chuk.rw/research/fullreport/?appid=543&&chuk.

PS: Please note that the present approval is valid for 12 months.

Yours sincerely,

Prof. Florence MASAISA
The Vce Chair, Ethics Committee,
University Teaching Hospital of Kigali

ETHICS COMMITTEE
CHUK

Scan code to verify.

" University teaching hospital of Kigali Ethics committee operates according to standard operating procedures (Sops) which are updated on an annual basis and in compliance with GCP and Ethics guidelines and regulations "

REPUBLIC OF RWANDA
RWANDA MILITARY HOSPITAL
Website: www.rwandamilitaryhospital.rw
P.O. Box: 3377 Kigali, Tel: (+250)252586420, Hotline: 4060
Email: info@rmh.rw

REF.36.. /RMH/COMDT/2022 **March 14, 2022**

Dr. MUSABYIMANA Joseph
PGY4, MMED Radiology Program
CMHS-UR
Phone: +250 788777425
Email: josephacademic@gmail.com

RE: APPROVAL NOTICE

1. In reference to your letter dated 02 March 2022, requesting permission to conduct an academic research at Rwanda Military Hospital, I am pleased to confirm that your research project entitled **"Neuroimaging Patterns of Cerebral Vascular Accident and the Drivers of Dynamics in ASPECT Score in Rwanda"** have been approved by the Rwanda Military Hospital Institutional Review Board (RMH/IRB).

2. Please note that approval of this protocol is valid for 12 **months.**

3. Attached is the review notice from RMH/IRB for your reference.

Sincerely,

RWANDA MILITARY HOSPITAL

Dr E RURANGWA
Brig Gen
Commandant

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P.O. Box: 3377 Kigali, Tel: (+250)252586420, Hotline: 4060
Email: info@rmh.rw

March 14, 2022 **Ref.: RMH IRB/025/2022**

REVIEW NOTICE

Dr. Musabyimana Joseph
University of Rwanda

Your research project: **"Neuroimaging Patterns of Cerebral Vascular Accident and the Drivers of Dynamics in ASPECT Score in Rwanda"** has been evaluated by the Rwanda Military Hospital Institutional Review Board (RMH IRB).

Name	Institute	Involved in the decision		
		Yes	Absent	Withdrawn from the proceeding
Lt Col Dr Eric SERUYANGE	RMH	X		
Maj Dr Florent RUTAGARAMA	RMH	X		
WO II KAYITARE Pacifique	RMH		X	
Maj (Rtd) Jean Damascène GASHEREBUKA	RAHPC		X	
Dr Leila MUKARUZIMA	RMH		X	
Dr Fidèle BYIRINGIRO	RMH		X	
Janvière MUTAMULIZA	RMH	X		
Boniface NSENGIYUMVA	RMH	X		
Jean NSABIMANA	RMH	X		
Jazira Munyana	RMH	X		

After review of the protocol and other related documents during the IRB meeting of March 11, 2022, we hereby provide approval for the above-mentioned protocol.

Please note that the approval of the protocol lasts for a period of **12 months** from the date of this notice.

You are responsible for fulfilling the following requirements:

1. Changes, amendments, and addenda to the protocol must be submitted to the RMH/IRB for review and approval, prior to activation of the changes.
2. A continuing review application must be submitted to the RMH/IRB in a timely fashion and before expiry of this approval.
3. Failure to submit a continuing review application will result in termination of the study.
4. Notify the Rwanda Military Hospital IRB once the study is finished and submit the final report.
5. Present the results of your study to the RMH/IRB before publication.

Sincerely,

Date of Approval : March 14, 2022
Expiration Date : March 13, 2023

Dr. Eric SERUYANGE
Lt Col
Chairperson, RMH/IRB

CENTRE HOSPITALIER UNIVERSITAIRE

UNIVERSITY TEACHING HOSPITAL

CENTRE HOSPITALIER UNIVERSITAIRE DE BUTARE (CHUB)
CABINET DU DIRECTEUR GENERAL
OFFICE OF DIRECTOR GENERAL

Huye, 29/04/2022
Ref.: CHUB/DG/NS/04/0716/2022

Dr. MUSABYIMANA Joseph
Email: josephacademic@gmail.com
Tel. +250 7887774125

Dear Dr. Musabyimana Joseph

Re: Your request for data collection

Reference made to your letter requesting for permission to collect the data within University Teaching Hospital of Butare for your research project entitled "*Neuroimaging Patterns of Cerebral Vascular Accident (Ischemic Stroke) and The Drivers of Dynamics in Aspect Score in Rwanda*", based to the approval **N° EC/UTHB/106/2022** from our Research-Ethics Committee, we are pleased to inform you that you are accepted to collect data within University Teaching Hospital of Butare.

Please note that your final document will be submitted in our research office.

Your will not allowed to start data collection without presenting COVID 19 vaccination card.

Sincerely,

Dr. Sabin NSANZIMANA
Director General of CHUB

Cc:

- Head of Clinical Education and Research Division
- Director of Research
- Chairperson of Ethics Committee
- Research officer
- Head of Surgery Department