PROPORTION OF VARIANT ANATOMY OF THE CIRCLE OF WILLIS AND ASSOCIATION WITH OTHER VASCULAR ANOMALIES ON CEREBRAL CT ANGIOGRAPHY

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DEDICATION

I dedicate this research to my parents the late George Wanyama Machasio and Jermina Namagera Ddamulira.

ACKNOWLEDGEMENT

I am extremely grateful to God almighty for giving me the courage and wisdom to undertake this study.

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ABBREVIATIONS

ACA…….Anterior cerebral artery

AChA……Anterior Choroidal artery

ACoA……..Anterior communicating artery.

AVM…….Arteriovenous malformation.

BA……..Basilar artery

CW……..Circle of Willis

CT……Computed tomography

CTA…….Computed tomography angiography

HA …….Hypoglossal artery

ICA…….Internal carotid artery

ICH…….Intracranial hemorrhage

KNH……..Kenyatta National Hospital

KNH-UoN-ERC…….Kenyatta National Hospital University of Nairobi Ethics and Research Committee

LOCM……Low osmolar contrast media.

MCA…….Middle cerebral artery

MIP……Maximum intensity projection

MRA……....Magnetic resonance angiography

MRA-TOF …….Magnetic resonance angiography time of flight

OA ……Otic artery.

PCA……...Posterior cerebral artery

PChA……..Posterior choroidal artery

PCoA……Posterior communicating artery

ProA……Pro-atlantal artery

PTA…….Persistent trigeminal artery

SAH…….Subarachnoid hemorrhage

SCA…….Superior cerebellar artery

VA……Vertebral artery

VRT…….Volume Rendered Technique

ABSTRACT

BACKGROUND AND PURPOSE

There is a wide variation in the anatomy of the CW in different individuals and population groups. Knowledge of variant anatomy of the circle of Willis is important for general radiologists, interventional radiologists and neurosurgeons.

The purpose of this study was to determine the proportion of variant anatomy of the circle of Willis and association with other vascular anomalies in patients referred for cerebral CTA.

METHODOLOGY

This was a cross-sectional descriptive study conducted on 94 patients referred for cerebral CTA at the Kenyatta National Hospital and Nairobi Hospital from August 2017 to February 2018. MIP and 3D reformatted images were analyzed by two senior radiologists to determine the final configuration of the CW and presence of vascular pathology. A vessel with a diameter of <0.8 mm was considered to be absent or hypoplastic. Chen et al classification was used to determine the final configuration of CW. Final data analysis was done using Statistical Package for Social sciences Program (SPSS) version 20.0.

RESULTS

A complete CW was seen in 37.2% with a slightly higher prevalence in males than females (37.7% vs 36.6% p=0.909). Type A anterior CW variant was the commonest accounting for 78.7% of anterior variants while type E posterior variant was the dominant posterior variant at 41.5%.Fetal PCA was demonstrated in 25.5% with unilateral fetal PCA being more common than bilateral fetal PCA. Aneurysms were seen in 24.5% of patients with ACoA aneurysms being commonest at 43.6%.AVMs were seen in 8.5% of patients.

Azygous ACA, fenestration and duplication of vessels and persistent TA were not demonstrated. No significant association between aneurysms and CW configuration.

CONCLUSION

The variant anatomy of CW in patients undergoing cerebral CTA in this study are similar to other studies done in different population groups.

This study however demonstrates slight differences in proportion of variant anatomy of the circle of Willis which could be due to genetics, sample size and technique used.

No significant association was found between aneurysms and CW configuration. No association was demonstrated between AVMs and the CW configuration.

CHAPTER 1

1.1 INTRODUCTION

The circle of Willis (CW) was first elucidated by Thomas Willis approximately 400 years ago. It is an important anastomotic arterial polygon located at the base of the brain that connects the carotid and vertebra-basilar systems. It is an essential route for collateral supply of blood to the brain in cases of occlusion in either system(1). The complete circle of Willis has 10 components: Two internal carotid arteries (ICAs), two A1 segments of anterior cerebral arteries (ACA), anterior communicating artery (ACoA), two posterior communicating arteries (PCoAs), the tip of the basilar artery (BA) and two P1 segments of the posterior cerebral artery (PCA). The middle cerebral artery (MCA) is not part of the CW. Important perforating branches arising from all parts of the CW to supply most of the basal brain structures. Anatomic and radiological studies have shown considerable variability in the CW with less than half of individuals having a complete CW. The ICA is the first to develop at about day 24 of embryological life providing the entire blood supply to the primordial brain(2).With development of the occipital region, brain stem and the cerebellum, there is inadequate supply from the ICA thus triggering formation of the posterior circulation. The posterior circulation initially comprises of primitive arterial networks originating from distal ICA and proximal carotid vertebra-basilar anastomoses(2).There is gradual regression of these anastomoses with development of the vertebro-basilar system but they can persist e.g. persistent trigeminal artery. Other prevalent variants include: fenestration, duplication, hypoplasia or agenesis(2).These variants influence the cerebral blood flow hemodynamics with influence on vascular territories, pathophysiology of cerebral arterial remodeling, aneurysm formation/rupture and stroke development(3).CT angiography is a fast, reliable and noninvasive modality for evaluation of the circle of Willis as well as other intracranial arteries with high sensitivity and specificity comparable to gold standard catheter angiography.

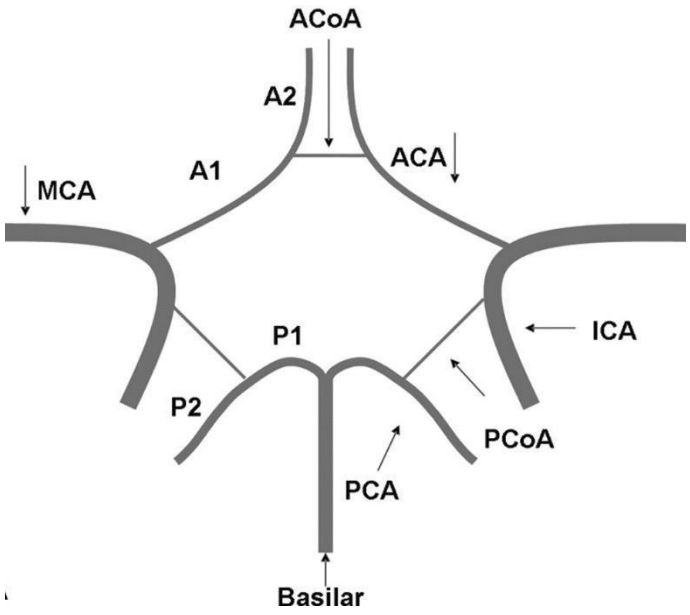

Figure 1: *Schematic diagram depicting the classical complete circle of Willis*

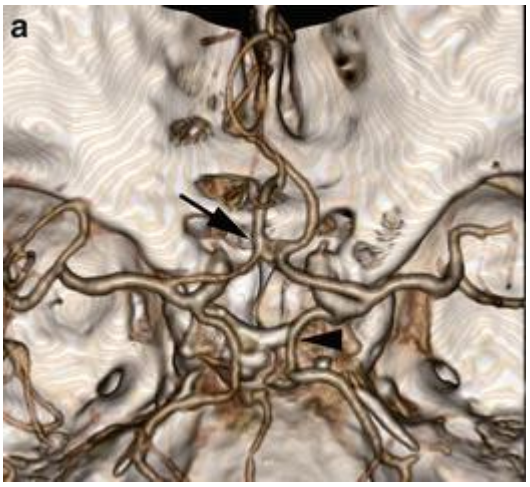

Figure 2: *3D CT angiogram of the circle of Willis. Arrow points to fenestrated anterior communicating artery. Bilateral fetal Posterior cerebral arteries are also demonstrated (arrowhead).*Image courtesy of postern.netkey.at

1.2 LITERATURE REVIEW

1.2.1 EMBRYOLOGY OF THE CIRCLE OF WILLIS

Development of the cerebral circulation commences with formation of 6 pairs of primordial branchial arch arteries at the 1.3-millimeter (mm) embryological phase.

The ICAs develop during the 3 mm stage (day 24) from coalescence of 3rd branchial arch arteries with the distal segments of the paired dorsal aorta.

At the 4 mm stage (day 28) the ICA separates into the anterior and posterior division. The anterior division supplies the olfactory and optic regions via primitive arteries.

In later embryological stages the anterior division of the ICA gives rise to ACA, MCA and Anterior choroidal artery (AChA) while the posterior division gives fetal PCA and Posterior choroidal artery (PChA). At this embryological stage, Superior cerebellar artery (SCA), a branch of the BA is the sole blood source to the primordial cerebellum.

The development of the occipital lobe and brainstem serve as a stimulus for the formation of the posterior circulation. At 4-5 millimeter embryonic stage the posterior fossa is supplied by 2 parallel neural arteries that derive their blood supply from the carotid-vertebro-basilar anastomosis. This is through trigeminal artery (TA), the otic artery (OA), hypoglossal artery (HA) and the pro-atlantal artery (ProA).BA forms at the 5-8mm stage via fusion of the neural arteries.

The TA, OA, and the HA last for a week after which they regress with formation of PCoA that connects to the BA.
The ProA persists until the vertebral arteries are fully developed.
The MCA develops as a bud proximal to the ACA on the anterior branch of the primordial ICA at the 11-12 mm embryological stage(4).

The olfactory artery develops from the ACA at the 18 mm embryological stage.

There is persistent growth of the ACA medially towards the contralateral ACA giving rise to formation of ACoA at the 21-24mm stage(5).

Posterior CW forms at an earlier stage when fetal PCA transforms into PCoA.

The adult PCA joins with the BA as branches of the fetal PCA merge medially to form the distal end of the BA. The PChA is incorporated into the adult PCA(4).

Full maturation of the ACA and the ACoA mark the ultimate recognition of the adult CW at 6-7 weeks of embryological development (4).

1.2.2 CLASSIFICATION OF ANATOMIC VARIANTS OF THE CIRCLE OF WILLIS

Various methods have been proposed for classification of the morphology of the CW due to complex anterior and posterior circulation variations. The CW has been divided into archetype, modern type, transition type and combined types by some researchers from the evolutionary point of view(6).This classification however neglects the integral conformation of the CW.

Krabbe-Hartkamp et al categorised the CW into integrity, partial integrity, and non-integrity based on magnetic resonance angiography. Integrity referring to a situation in which the entire vessels of the CW are depicted and each measures more than 0.8 mm in cross-sectional diameter. In partial integrity, only the anterior or posterior circulation is integral. Anterior CW was considered incomplete if the A1 segment of ACA was hypoplastic (<0.8 mm) or absent. The posterior CW was considered incomplete if one of the PCoA or P1 segment of PCA was hypoplastic (<0.8 mm) or absent (7).

Chen et al classified variations in both anterior and posterior CW from A-J (8). For the purposes of this study Chen et al classification was used.

1.2.3 ANTERIOR CIRCLE OF WILLIS VARIANTS

Anatomic variations of the anterior CW are classified from A-J. Types A-F are complete while G-J are incomplete.

1. Type A: A single ACoA
2. Type B: Two or more ACoAs
3. Type C: A medial artery of corpus callosum arising from the ACoA.
4. Type D: The ACAs are fused for a small distance.
5. Type E: The ACAs form a common trunk and split distally into two A2 segments.
6. Type F: The MCA arises from the ICA as two separate trunks.
7. Type G: The ACoA is absent or hypoplastic.
8. Type H: Both A2 segments arising from one A1 segment.
9. Type I: Hypoplasia or absence of an ICA with both ACAs and both MCAs arising from a single ICA.
10. Type J: Hypoplastic/absent ACoA with the MCA arising as 2 discrete trunks.

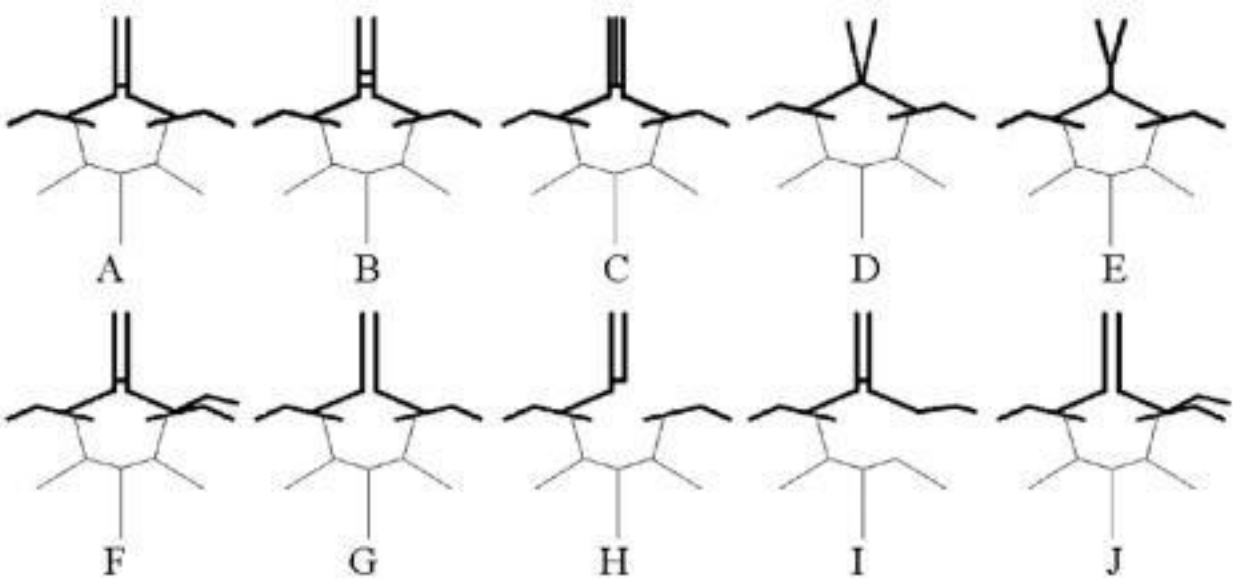

Figure 3: *Schematic diagram for variations in the anterior CW according to Chen et al*

1.2.4 POSTERIOR CIRCLE OF WILLIS VARIANTS

Anatomic variations of the posterior CW are classified from A-J. Types A-C are complete while the remainders are considered incomplete.

Type A: Both PCoA are present.
Type B: Unilateral fPCA.
Type C: Bilateral fetal PCA with bilateral patent P1 segments.
Type D: Presence of unilateral PCoA.
Type E: Bilateral hypoplasia/absence of PCoAs
Type F: Unilateral Fetal PCA with hypoplasia/absence of the P1 segment of the PCA.
Type G: Unilateral fPCA with hypoplasia/absence of the contralateral PCoA.
Type H: Unilateral fPCA with hypoplasia/absence of P1segment of PCA and PCoA.
Type I: Bilateral fPCA with hypoplasia/absence of both P1 segments
Type J: Bilateral fPCA with hypoplasia/absence of one P1 segment.

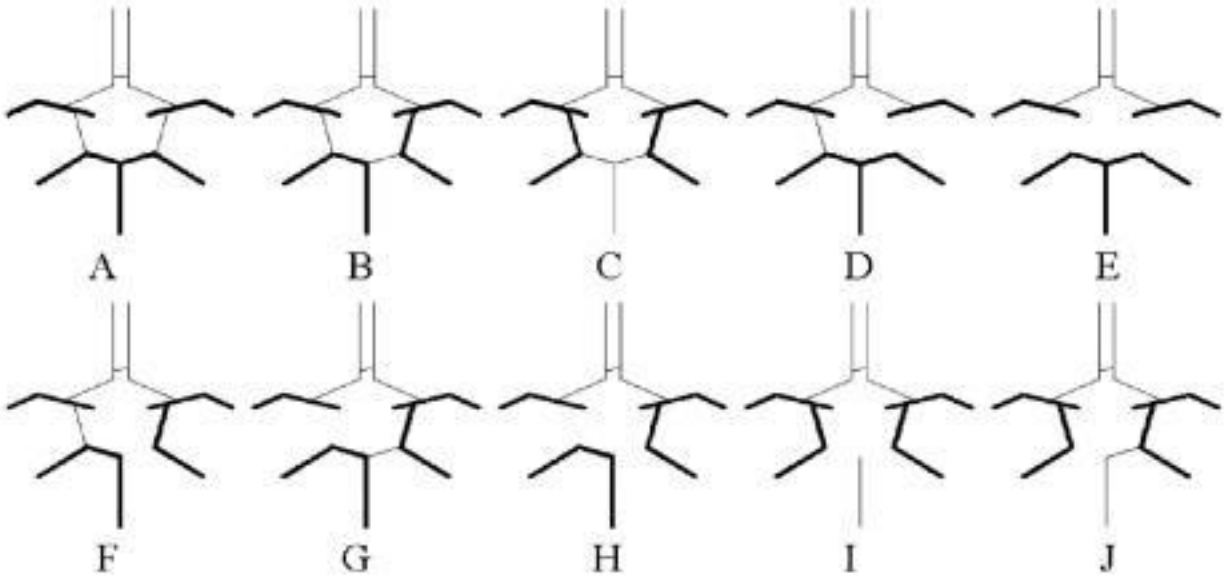

Figure 4: Schematic diagram showing anatomic variations of the posterior CW according to Chen et al

1.2.5 FETAL TYPE PCA

Fetal PCA (fPCA) is a frequent variant of the posterior circulation. There is an embryonic origin of the PCA from the ICA. There are 2 types: complete and partial fetal PCA. In complete fPCA there is no contact with the basilar artery and the PCA originates completely from the ICA. Partial fPCA is defined as PCA arising from ICA with a small/atretic connection with the basilar artery. In partial fPCA, PCoA is greater than the P1 segment of the PCA and supplies most of the blood to the PCA territory. This results in a greater area being dependent on the ICA. The leptomeningeal collateral vessels between anterior and posterior circulation do not develop. Fetal PCA may predispose to stroke mechanism (9)

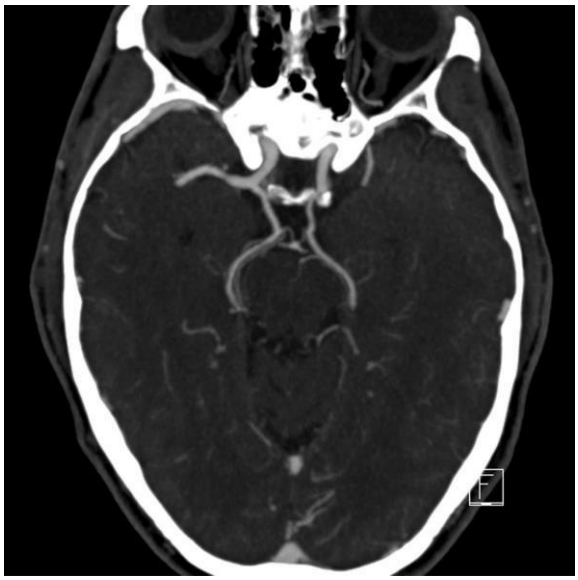

Figure 5: *Axial MIP cerebral CT angiogram depicting bilateral fetal posterior cerebral arteries (Type I posterior circle of Willis variant).* (Image courtesy of radiopedia.org)

1.2.6 DUPLICATION AND FENESTRATION OF INTRACRANIAL

ARTERIES

Duplication refers to a situation where two arteries arise separately with no distal convergence.

Fenestration on the other hand refers to separation of the arterial lumen into distinct channels with convergence distally.

Association between fenestration and development of aneurysms has been reported in literature. It is postulated that this is due to turbulent flow in the proximal and distal portions of the fenestrated segment (10).

Fenestration is more prevalent in the vertebro-basilar system than in the anterior circulation though mainly seen at autopsy as compared to angiographic studies(10)(11).

Fenestration of the ACoA is present in 12-21% while duplication is seen in 18% of the population (12)

The prevalence of fenestration A1 segment of the ACA is between 0-4% in cadaveric studies and 0.058% in imaging angiographic studies (13).

Fenestration of the posterior cerebral artery is rare. This has however been documented in both P1 and P2 segments of the PCA.

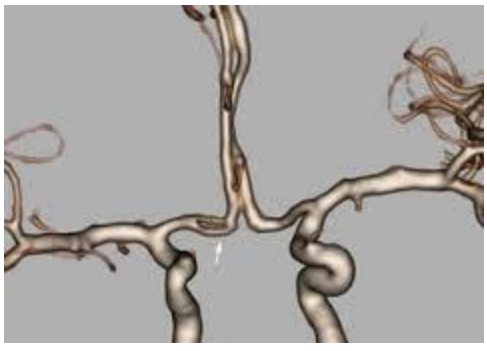

Figure 6: 3D CT angiogram showing fenestration of A1 segment of the right ACA. (Image courtesy of research gate)

1.2.7 OTHER VARIATIONS OF THE CIRCLE OF WILLIS

AZYGOUS ACA

It refers to a situation in which the two A1 segments are fused thus resulting in a single A2 segment of the ACA with absent ACoA. This represents the persistent embryonic median artery of the corpus callosum. It is rare with a prevalence of 0.2-4.0% (14)

Azygous anterior cerebral artery has been associated with other conditions e.g. holoprosencephaly, dysgenesis of the corpus callosum, septo-optic dysplasia, porencephalic cysts arteriovenous malformations and berry aneurysms at its eventual bifurcation (15).

In addition, azygous ACA has been linked to bi-hemispheric infarcts secondary to thromboembolic disease or surgical error.

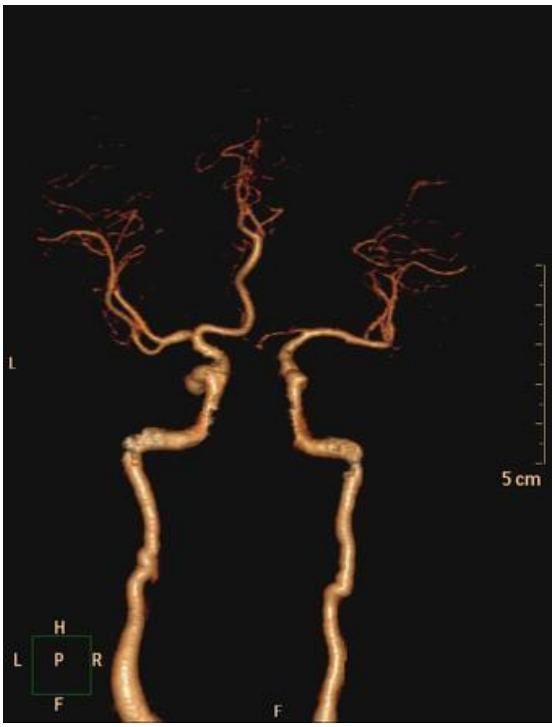

Figure 7: *3D CT angiogram depicting an azygous ACA with hypoplastic A1 segment of the left ACA (Image courtesy of radiopedia.org)*

PERSISTENT TRIGEMINAL ARTERY

It is one of the persistent embryological carotid vertebro-basilar anastomoses with a prevalence of 0.1-0.6 %. The artery usually originates from the junction between the petrous and cavernous portions of the ICA running posterolaterally crossing over or through the dorsum sella.

The vertebral, caudal basilar artery and the PCA are often hypoplastic (16).

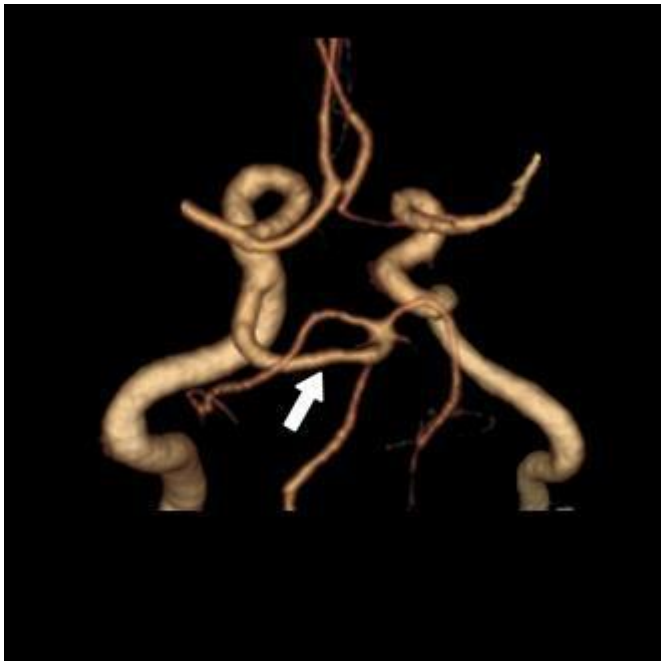

Figure 8: *3D CT angiogram showing PTA (arrow) arising from the right ICA. (Image courtesy of babymhospital.org).*

1.2.8 INTRACRANIAL ANEURYSMS

An aneurysm refers to an abnormal dilatation of blood vessels. There are two main morphological types of aneurysms: Fusiform and saccular.

Saccular aneurysms are eccentric involving only a portion of the vascular circumference while fusiform aneurysms involve the entire circumference of the vessel wall.

Intracranial aneurysms are relatively common with approximate prevalence of about 4 %(17).

Symptoms from unruptured aneurysms are due to local mass effect and secondary effects are seen following rupture with resultant subarachnoid hemorrhage.

85% of intracranial aneurysms involve the circle of Willis with as much as 30% of those with the aneurysms having multiple locations (17).

Several conditions have been linked to the development of aneurysms both congenital and acquired. They include: Autosomal dominant polycystic kidney disease, Ehler's Danlos, Neurofibromatosis, Alpha 1 antitrypsin deficiency, smoking, advanced age, alcohol abuse and hypertension.

Females are more prone to aneurysmal rupture with a prevalence of 1.6 times as compared to male patients (17).

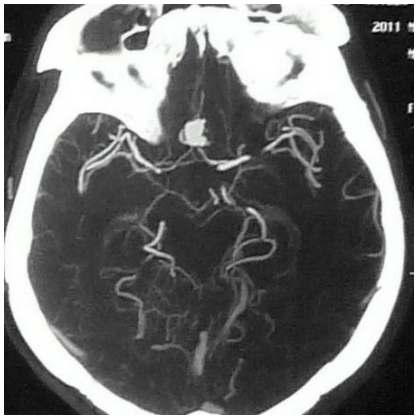

Figure 9: *MIP cerebral CT angiogram showing aneurysm involving the anterior communicating artery. (*Image courtesy of radiologyteacher.com*)*

1.2.9 ARTERIOVENOUS MALFORMATION

Cerebral arteriovenous malformations are composed of abnormal tortuous vessels forming a nidus lacking capillary bed with a feeding artery and a draining vein(18).

The presence of a discrete nidus with an abnormal intervening brain tissue differentiates AVM from other arteriovenous shunts such as pial arteriovenous fistula, dural arteriovenous fistula and cerebral proliferative angiopathy(19).Clinical presentation can occur at any age but mostly 3rd or 4th decade of life. Patients may present with seizures, headaches, ischemic events due to vascular steal syndrome, intracranial hemorrhage and occasional may be an incidental finding.

Smaller AVMs (<3cm) are usually associated with intracranial hemorrhage at the time of presentation while larger lesions (>3cm) are linked to an increased risk of future hemorrhage(20).Recent ARUBA study has an estimated annual risk of AVM rupture at 4%(21). However there is a wide spectrum of relative risk of AVM rupture from 0.9%/year to 34%/year(22).DSA is the gold standard for identification of cerebral AVMs.

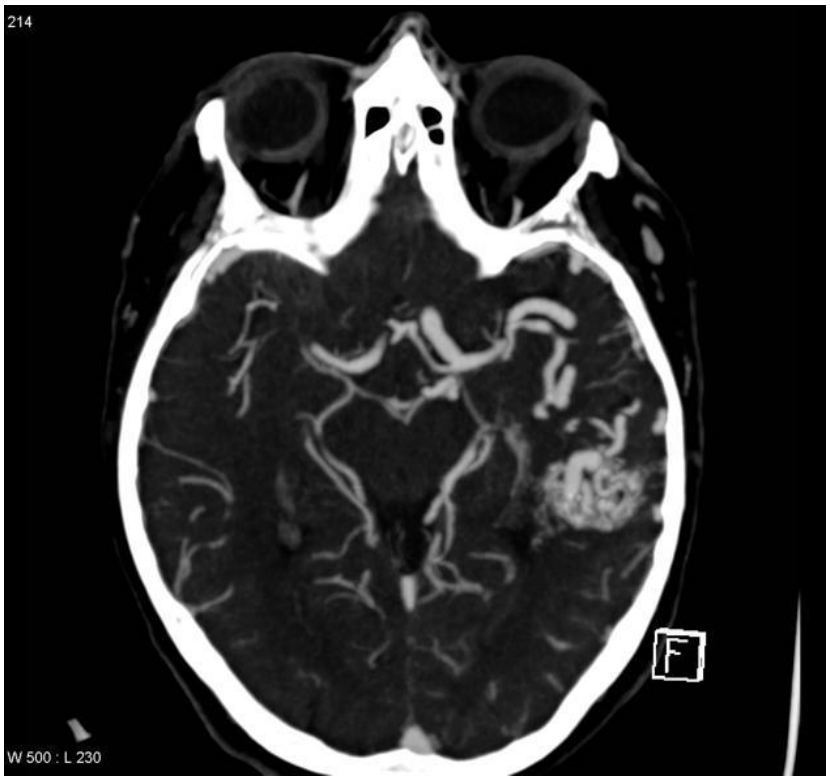

Figure 10: *Axial cerebral CTA MIP image showing a left temporal AVM.*

1.2.10 CEREBRAL CT ANGIOGRAPHY

CT angiography (CTA) plays a crucial role in evaluation of the CW and other intracerebral vessels in patients with subarachnoid hemorrhage secondary to ruptured intracranial aneurysms. Current multidetector scanners have a high spatial resolution that can reliably detect aneurysms greater than 4 millimeters with almost 100% sensitivity comparable to catheter digital subtraction angiography (DSA)(23)(24)(25)(26).

DSA is the gold standard in detection and characterization of aneurysms. It is costly and invasive technique requiring highly skilled specialist. It carries a low but significant complication risk of about 1% with 0.7-1% chance of persistent neurological deficit. On the other hand DSA can be used for vascular intervention unlike CT angiography.

Magnetic resonance angiography has also been used in the study of circle of Willis and other intracranial vessels with a high sensitivity and specificity. However due to flow artefacts it is less reliable for detection of hypoplastic vessels and aneurysms as compared to both CTA and catheter angiography (27).

Cerebral CTA is a non-invasive imaging technique that can be performed immediately after non-enhanced CT following bolus intravenous contrast thus convenient for fast diagnosis and treatment planning in the acute setting.

Cerebral CTA has also shown a high sensitivity in detection of cerebral AVMs. In a retrospective study done by Bradley .A.Gross et al comparing the sensitivity of DSA,CTA and MRA-TOF in AVM detection ,the sensitivity of CTA was 90% while MRA-TOF was 74%(28).CTA was superior to 1.5T MRA-TOF for detection of feeding artery aneurysm and intranidal aneurysms 90% vs 31% and 83% vs 0% respectively(28).

1.2.11 VARIATIONS IN CW AND ASSOCIATED VASCULAR ANOMALIES.

No local studies have been done to evaluate the integrity of the CW in the Kenyan population.

Available local data shows only studies done on individual cerebral arteries.

Hassan Said et al of The University of Nairobi, department of Human anatomy carried out a cadaveric study on variant anatomy of the anterior cerebral artery in 36 adult brains. Fenestration and duplication of ACoA was seen in 26% and 13% respectively (29).

In 2006 David Chepsiror et al did a study on pattern of cerebrovascular diseases as seen in patients undergoing four vessel catheter angiography in KNH and Nairobi Hospital. Aneurysms were seen in 40.3%, vascular stenosis/spasm (14.8%), AVM (8%) and angiographic normal (22. 7%).Anterior circulation aneurysms arising within the CW accounted for 95.2% of all aneurysms. Multiple aneurysms were seen in 16.7% of all cases with male: female of 1:5(30)

In a Magnetic resonance angiography time of flight (MRA TOF) study done on 180 participants from the general Egyptian population in 2011 by Mohamed Abdelatif et al the prevalence of an entirely complete CW was 46.7%. There was slightly higher percentage of complete CW in females (52.8%) and young males (50%). Complete anterior and posterior circulation were seen in 68.3% and 38.3% respectively (31)

Chen et al 2004 did a morphological study on variations of CW in 507 participants from the general population in Taiwan based on 3 dimensional (3D)-TOF MRA. Complete CW was seen in 21.3%, partially complete configuration at 61.14% while incomplete configuration was seen in 17.55%. Type A variant was the commonest anterior circulation variant at 64.1% while type E posterior circulation variant was commonest at 42.8% (8)

In a 3D-TOF-MRA cross sectional study in 300 healthy participants by Dr. Arjun Bahaddur et al in 2013 at Narayana Hrudayalaya Institute of Medical services on the anatomical variants of the CW in South Indian population, a complete CW was seen in 16.6% with a higher female predominance. A complete anterior CW was demonstrated in 77.3%. Type A anterior variant was the commonest with a prevalence of 66%. Type E posterior variant was the predominant type accounting for 32.6%(32)

In a 3D-TOF MRA morphological study at an Indian tertiary hospital on 300 patients undergoing neuroimaging over a period of 2 years by Naveen SR et al, a complete CW was seen in 16.6%. Partially complete CW was present in 61.3% while incomplete anterior and posterior CW was seen in 22%. Complete anterior CW was present in 77.3%. Type A anterior variant was the commonest at a prevalence of 66% while type E was the commonest posterior variant with a prevalence of 32.6% (33).

In a 2015 MRA study by Chuanya Qui et al on 2246 healthy Chinese males at the Civil Aviation General Hospital Beijing China, CW integrity was reported in 12.24%. Partial integrity and non-integrity were seen in 70.17% and 17.59% respectively. Complete anterior CW was seen in 78.58%.The prevalence of incomplete posterior CW was 83.93% (34).

Another CTA based study was conducted by Zhang Ning Jin et al in 2016 on a Chinese sample with family history of stroke. They studied 281 rural residents from Jixian, Tianjin with family history of stroke. Only 15.3% demonstrated a complete CW and was slightly higher in men than women 17% versus 13.3%.The prevalence of incomplete variants was higher in the posterior than anterior circulation(75.8% versus 43.1%).Hypoplasia or absence of both PCoA was the most prevalent 52.3%.The prevalence of bilateral fPCA was 4.3%(35)

In a Polish study by Klimek-Piotrowska W et al published in 2013 involving 250 patients undergoing cerebral CTA, the typical variant CW was seen in 16.80%. The anterior and posterior segments of the CW were normal in 47.20% and 26.80%

respectively. Lack of the ACoA was the most common anterior circulation variant type accounting for 22.80%. Bilateral absence of the PCoAs was the most common posterior circulation variant accounting for 29.20%.This was the most common variant of the entire CW (36).

C.Macchi et al did an MRA study on 100 healthy subjects in the department of Human anatomy and histology at Florence University Italy in 1996.Complete CW was seen in 41% while 13% showed PCA arising from the ICA. Three ACAs were present in 9%.ACoA was not identified in 3%.In 2%,the absence of PCoAs was associated with origin of the PCA from the ICA. Hypoplasia of both ACA and PCA was seen in 2% of cases (37).

In an MRA and CTA based retrospective study on 536 patients with acute ischemic stroke by Amir Shaban et al in the USA, complete fetal PCA was seen in 9.5% while 15.1% had partial fetal PCA. Complete fetal PCA was more common in females and older patients(9).

On cadaveric studies done on 150 formalin preserved human brains by S.A Gunnal et al in 2014 at the rural medical college Loni India, normal and complete CW was seen in 60%. Gross morphological variation in the CW was seen in 40%. Maximum variation was seen in the PCoA and ACoA at 50% and 40% respectively. Morphological variations of A1 (aplasia, hypoplasia and duplication) were present in 14%.Adult type PCoA was seen in 77.3% while fetal type PCoA was seen in 18% of the cases (38).

In a 2 years retrospective study done by Lazzaro et al on 113 patients admitted with cerebral aneurysms in the USA medical college of Wisconsin and Froedtert Hospital, more anomalies of the CW were demonstrated in patients with ruptured aneurysms than those with unruptured aneurysms. CW anomalies were demonstrated in 46.9% of ruptured aneurysms and 29.6% of unruptured aneurysms. Multivariate analysis

demonstrated an increased risk of aneurysmal rupture in the presence of a CW variant (P-value of 0.0245 and an odd ratio of 3.72) (3).

A prospective study done by Yu-Ming Chuang et al on association of integrity of the CW and resultant intracerebral bleeding following intravenous thrombolysis in patients with ischemic stroke showed a higher risk of symptomatic intracerebral bleeding in those with incomplete CW almost 3 times higher than those with a complete CW. Patients with complete CW were more likely to show early improvement according to the National Institute of Health Stroke Scale(NIHSS) score (median improvement 2 vs 0 at 2 hours and 4 vs 1 at 24 hours. Complete CW was the strongest predictor of favorable functional sequelae at 3 months (odd ratio 2.32: P value=0.01) (39)

In a study by Stojanovic et al in 2009 on variations of CW in patients receiving surgical intervention for ruptured aneurysms, a higher incidence of multiple aneurysms was found in those with asymmetric configuration of the CW (75.7%).The prevalence of asymmetric CW in the whole group was 64%.Highest incidence of asymmetric CW was demonstrated in those with ACoA aneurysmal rupture (72.7%vs 100% in those with solitary aneurysms and multiple aneurysms respectively) (40)

A prospective study done by Tom Van Seeters et al on 976 patients with atherosclerosis without previous history of TIA/stroke showed that an incomplete anterior and posterior CW is related to future anterior circulation stroke. An incomplete anterior CW was associated with future anterior circulation stroke (HR 2.8 (95% CI P value =0.01)while one or two sided incomplete posterior CW were not (HR 2.2(95% CI P value=0.19) and 1.9(95% CI P value= 0.29) respectively (41).

Jean Marc Bugnicort et al conducted a 3D TOF-MRA case control study on 47 patients with proven migraine and 77 control subjects with other neurological disorders to ascertain whether an incomplete posterior CW was a risk factor for migraine. Patients with migraine demonstrated a higher prevalence of incomplete posterior CW than in

the control group (49% vs 18%:p value =<0.001. Incomplete posterior CW was the sole independent variable associated with migraine (O.R 6.5 95% CI 2.6:16.2 P<0.001) (42)

An MRA-TOF study done by Chuang YM et al on 310 acute ischemic stroke patients showed a strong association between ischemic stroke and presence of hypoplastic PCoA (p=0.036)(43).

CHAPTER 2

2.1 STUDY JUSTIFICATION

The CW is an important collateral pathway of circulation to the brain. There are no local studies done to ascertain the various configurations of the CW in the Kenyan population. Various studies done elsewhere have linked anatomic variations in the CW to causation of stroke, migraine, cerebral aneurysms, and mental illness (41)(44)(45).

Other studies have shown a correlation between the configuration of the CW and the probability of aneurysmal bleed as well as intracerebral hemorrhage following intravenous thrombolysis. My study therefore aims at creating a local data base on proportion of variations in the CW as depicted on cerebral CTA.

The study findings are important to neurologists, radiologists, neurosurgeons and interventional radiologists for endovascular and pre-surgical planning purposes.

The findings in this study can also be used to help develop guidelines in structured reporting for cerebral CTA, within the local setting.

2.2 HYPOTHESIS

1. The proportion of variant anatomy of the CW is not significantly different in the Kenyan population as compared to other studies.
2. There is no association between the CW configuration and other vascular anomalies.

2.3 STUDY QUESTION

1. What is the proportion of patients with complete Circle of Willis?
2. Is the incidence of aneurysms and other vascular pathologies influenced by the variant anatomy of CW?

2.4 OBJECTIVES

2.4.1 BROAD OBJECTIVE

To establish a local database on the CW configuration as seen on cerebral CTA and to determine whether variant anatomy of the CW is linked to other vascular anomalies.

2.4.2 SPECIFIC OBJECTIVES

- To determine the proportion of anatomic variations of the CW.
- To determine whether there is an association between the configuration of the CW and other vascular anomalies.

CHAPTER 3

3.1 STUDY DESIGN AND METHODOLOGY

3.1.1 STUDY DESIGN

This was a cross-sectional descriptive study carried out in KNH and Nairobi hospital radiology departments.

3.1.2 STUDY AREA DESCRIPTION

Department of radiology, Kenyatta National Hospital and Nairobi Hospital both situated at the Nairobi County in Kenya.

3.1.3 STUDY POPULATION

Patients referred for cerebral CTA at KNH and Nairobi Hospital.

3.1.4 STUDY SAMPLE

Same as study population.

3.1.5 SAMPLING METHOD

Consecutive sampling method was used

3.1.6 SAMPLE SIZE DETERMINATION

The sample size was calculated using Cochran formula for sample size in studies estimating proportions:

$$n = \frac{N\,Z^2 P\,(1-P)}{d^2(N-1) + Z^2 P(1-P)}$$

Sample size calculation assumptions:

Where:

Z = statistic representing 95% level of confidence (1.96)

N = Population of patient undergoing cerebral CT angiogram during the projected six month study duration estimated at 100

P = proportion of patients with variant anatomy of circle of Willis in CTA. Range in literature is between 12.2% and 60%. A prevalence of 50% was used because of the wide variation and absence of specific studies in African population.

d = the precision around the prevalence of variant anatomy of circle of Willis in CTA. (Set at 0.05)

Therefore, substituting the above assumption in the formula yield the minimum sample size shown below:

$$n = \frac{100 \times\ 1.96^2 \times 0.5\,(1-0.5)}{0.05^2(100-1) + 1.96^2 \times 0.5(1-0.5)}$$

n = 80

3.1.7 INCLUSION CRITERIA

All consecutive patients referred for cerebral CTA at KNH and Nairobi hospital.

3.1.8 EXCLUSION CRITERIA

- Patients who declined to give consent.
- Patients who only had unenhanced head CT examination.
- Pediatric and minor patients whose guardians/relatives declined to give consent.
- Patients whose vascular details were not assessed due to poor technique or motion artefacts.

3.1.9 STUDY PROCEDURES

All patients who met the inclusion criteria were incorporated in the study.
Cerebral CTA images were acquired by Siemens SOMATOM Definition AS+ 128 at KNH and Philips Brilliance 64 slice CT scanner at Nairobi Hospital. The acquired images were thereafter processed, reformatted, analyzed and reviewed by the principal investigator and two consultant radiologists to determine the final CW configuration. All processed and reformatted images were recorded on DVD and stored on an external hard drive. Reformatted images included, MPR, VRT and MIP images. Photographs depicting the configuration of the CW were attached onto the data collection form shown in the appendix.

3.1.10 MATERIALS

Cerebral CTA images were acquired by the Siemens SOMATOM Definition AS+ 128 slices at KNH and Philips Brilliance 64 slice CT scanner at Nairobi Hospital.
CT protocol used first included a non-enhanced head CT to map out any pathology e.g. hemorrhage and vascular calcification.

The following protocols were used for enhanced cerebral CTA:

SIEMENS SOMATOM DEFINITION AS+128 at KNH

100 kV, up to 175 effective (mAS), 128 x0.6mm collimation, pitch 0.9, 4mm slice thickness, tube rotation 0.5 seconds, reconstruction interval of 0.6mm with 0.4 mm increment.
80 mls of LOCM (300mg/ml) via pump injector at injection rate of 5mls/second through an antecubital vein cannula (at least gauge 20) with a delay time of 7 seconds was used for acquisition of images in adult patients.

PHILIPS BRILLIANCE 64 SLICE at Nairobi Hospital

120kV, up to 300 effective mAS, window setting 60-360 HU, slice thickness 0.67mm, pitch 0.671.

20mls saline push before contrast administration, followed by 60 mls of LOCM at an injection rate of 4-5 mls/s via pump injector and 30 mls of saline chase with a scan delay time of 4.2 seconds.
In patients weighing less than 50 kg a dose of 2ml/kg of LOCM was used.

In young children and infants a 22 or 24 gauge intravenous catheter was used and LOCM used at an injection rate of 2mls/second.

Right arm injection was preferred for all patients to prevent artifacts due to undiluted contrast within the left brachiocephalic vein.

Axial scans were acquired from the level of carotid bifurcation to the vertex.

3.1.11 PERSONNEL

- The principal investigator
- Trained data clerks (radiographers) at KNH and Nairobi Hospital.
- 2 consultant radiologists to confirm final configuration of the CW as depicted on cerebral CTA.
- Biostatistician.

3.1.12 MEASURABLE VARIABLES

- Complete/incomplete CW.
- Type of variant anatomy of the anterior/posterior CW.
- Presence or absence of aneurysms and other vascular pathologies
- Age.
- Gender.

3.1.13 DATA COLLECTION AND ANALYSIS

Cerebral CTA images were reviewed by the principle researcher and 2 senior radiologists to determine the configuration of the CW. Arteries with cross-sectional diameters of less than 0.8 mm were considered to be hypoplastic or absent. Final configuration upon reaching consensus was recorded in the data collection form.

Data depicting the configuration of the CW was entered in a table on the data collection form shown in the appendix.
Multivariate data analysis was done with the assistance of a biostatistician.

SPSS (statistical package for social sciences) version 20.0 was used.
Data analysis included calculation of percentages of complete and incomplete CW and different anatomic variants of the anterior and posterior circulation.
Comparison was made between the male and female participants.

3.1.14 ETHICAL CONSIDERATION

- Patients included in the study were referred by clinicians and only those with justifiable requests underwent cerebral CT angiography.

- Written informed consent was sought from the participants included in the study. The consent form incorporated the rights of the participants.

- Ethical approval to conduct the study was obtained from KNH-UoN-ERC.

- Institutional approval was obtained from The University of Nairobi, KNH and Nairobi Hospital.

- Confidentiality of participants was upheld throughout the study.

3.1.15 CONFIDENTIALITY OF PARTICIPANTS

There were no identifiers linking research data to patients.
Each study patient was assigned a unique numerical code used in data abstraction tool and database.

3.1.16 CONFIDENTIALITY OF DATA OBTAINED

Restricted access to patient data.
Only authorized persons were allowed access to participant records.
All electronic database was password protected.
All the records were stored in a locked cabinet.

3.1.17 BENEFICENCE/MALEFICENCE

The findings of this study will be published to improve management of patients through enhancing knowledge of general radiologists, interventional radiologists and neurosurgeons.

3.1.18 RADIATION PROTECTION

All the patients undergoing cerebral CT angiograms were referred by clinicians. The request forms were scrutinized to ensure only those that are justifiable were done. The ALARA principle was applied.

Strict study protocols were used to ensure good quality images and to avoid repeat examinations.

3.1.19 STUDY DURATION

The study was carried out over a duration of 6 months following approval by KNH-UoN-ERC from August 2017 to February 2018.

3.1.20 DISSEMINATION OF RESULTS

The findings of the study will be disseminated through the Department of Diagnostic Imaging and Radiation Medicine, University of Nairobi Library, University of Nairobi board of post graduate studies and published in peer reviewed journals.

CHAPTER 4: RESULTS

This study was conducted on 94 participants both adults and pediatric patients sent for CT angiography at KNH and The Nairobi Hospital.

53 (56.4%) were male patients while 41(43.6%) were female patients with an approximate male: female ratio of 1:1

The mean age was 46.6 years (SD +/- 17.0) age range 9 to 93 years.

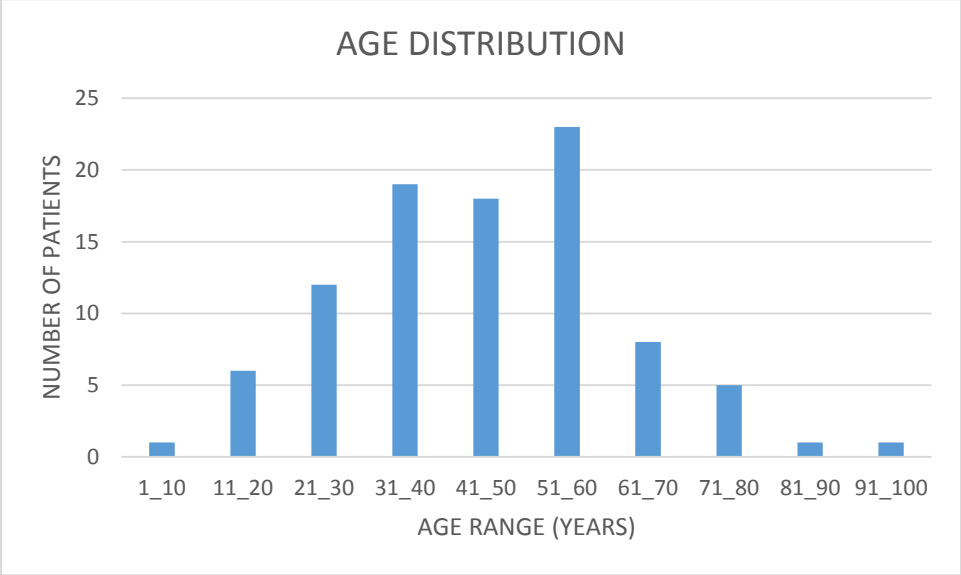

Figure 11: *Age distribution of patients referred for cerebral CTA.*

Majority of patients were referred for cerebral CTA due to intracranial hemorrhage accounting for 30.85%.

Table 1: *Indication for cerebral CTA.*

INDICATION	NO.OF PATIENTS
HEADACHE	19
?AVM	5
?ANEURYSM	16
ICH	29
SINUS THROMBOSIS	5
STROKE	15
TRAUMA	3
TUMOR	2
TOTAL NUMBER	94

4.1 PROPORTION OF COMPLETE AND INCOMPLETE CIRCLE OF WILLIS

The proportion of patients with complete CW was 37.2 %(35/94).

The prevalence of complete CW was 37.7% and 36.6% in male and female patients respectively. No significant statistical difference was found between males and females (p=0.9).

62.8 %(59/94) of patients had incomplete CW. The incomplete CW configuration was seen in 62.3% of males and 63.4% of females respectively.

Out of the 59 patients with incomplete configuration of the CW, 33(55.9%) were males and 26(44.1%) were females respectively.

Isolated incomplete posterior CW was seen in 45(76.3%).

Both anterior and posterior incomplete CW in 12(20.3%) while isolated anterior incomplete CW was seen in 2(3.4%) of patients.

Table 2: *Percentage distribution of complete and incomplete CW in male vs female patients.*

CONFIGURATION	COMPLETE	INCOMPLETE
TOTAL	37.2%(35)	62.8%(59)
MALE	37.7%(20)	62.3%(33)
FEMALE	36.6%(15)	63.4%(26)

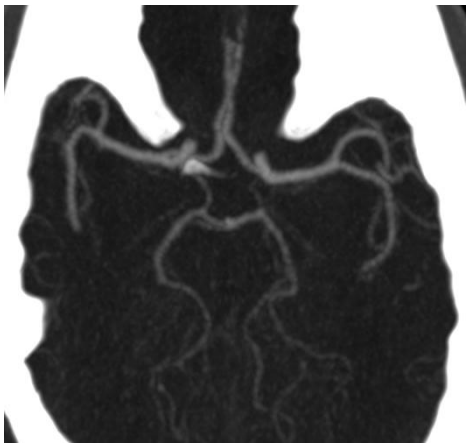

Figure 12: *Axial cerebral CTA MIP image showing a complete CW configuration*

4.2 ANTERIOR AND POSTERIOR CIRCULATION VARIANTS

Type A anterior circulation variant was the most common seen in 74 patients accounting for 78.7% of the anterior circulation variants.

Table 3: *Percentage distribution of type A anterior circulation variant*

		Variant A		
Gender	**Total**	**No**	**Yes**	**P value**
Male	53(56.4%)	16(30.2%)	37(69.8%)	0.016
Female	41(43.6%)	4(9.8%)	37(90.2%)	

Type E posterior circulation variant was the commonest seen in 39 patients accounting for 41.5% of the posterior circulation variants.

Anterior circulation variants types A 74(78.7%), C 1(1.1%),D 4(4.3%),G 4(4.3%)and H 11(11.7%) were demonstrated. Types B, E, F, I, and J anterior circulation variants were not seen.

Table 4: *Anterior circulation variant percentage distribution*

ANTERIOR CW	FREQUENCY
TYPEA	78.7%(n=74)
TYPE B	0%(n = 0)
TYPE C	1.1%(n = 1)
TYPE D	4.3%(n = 4)
TYPE E	0%(n = 0)
TYPE F	0%(n = 0)
TYPE G	4.3%(n = 4)
TYPE H	11.7%(n = 11)
TYPE I	0%(n = 0)
TYPE J	0%(n = 0)

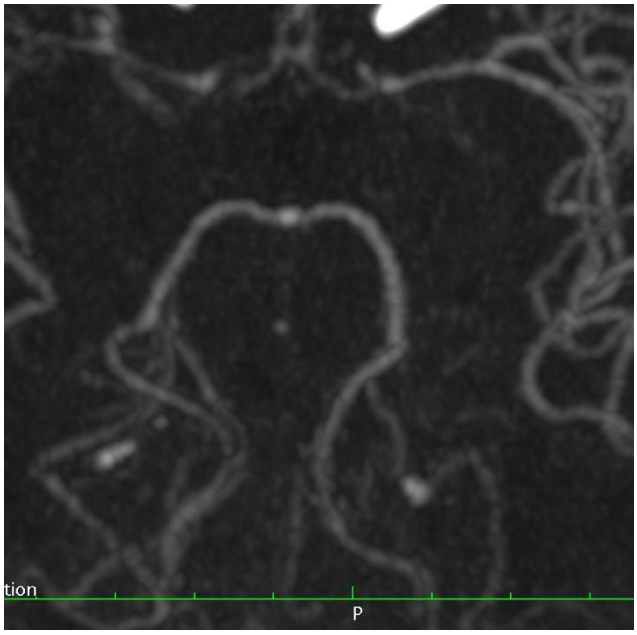

Figure 13: *Axial MIP image showing type A anterior circulation variant and type E posterior circulation variant.*

Posterior circulation variants types A 26(27.7%), B 4(4.3%), C 7(7.4%), D 4(4.3%), E 39(41.5%), F 2(2.1%), G 7(7.4%) and J 5(5.3%) were demonstrated. Types H and I posterior circulation variants were not seen.

Table 5: *Proportion of posterior circulation variants.*

POSTERIOR CW	FREQUENCY
TYPE A	27.7%(26)
TYPE B	4.3%(4)
TYPE C	7.4%(7)
TYPE D	4.3%(4)
TYPE E	41.5%(39)
TYPE F	2.1%(2)
TYPE G	7.4%(7)
TYPE H	0%(0)
TYPE I	0%(0)
TYPE J	5.3%(5)

4.3 ANTERIOR VARIANT TYPE A

Anterior variant type A accounted for 78.7% of the anterior circulation variants.

Type A variant was seen in 37(69.8%) of males and in 37(90.2%) of females.

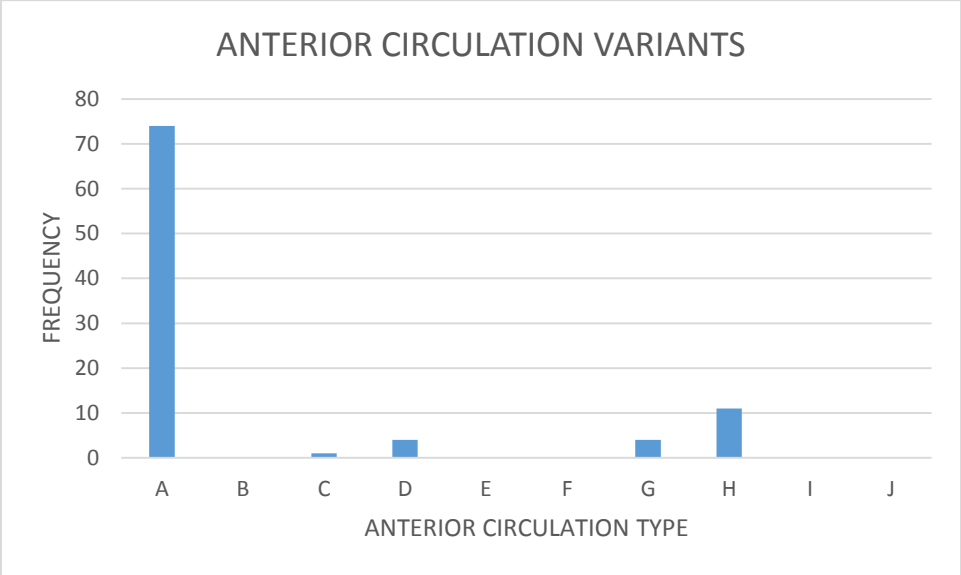

Figure 14: *Frequency of anterior circulation variants.*

4.4 POSTERIOR VARIANT TYPE E

Posterior variant type E accounted for 41.5% of the posterior circulation variants.

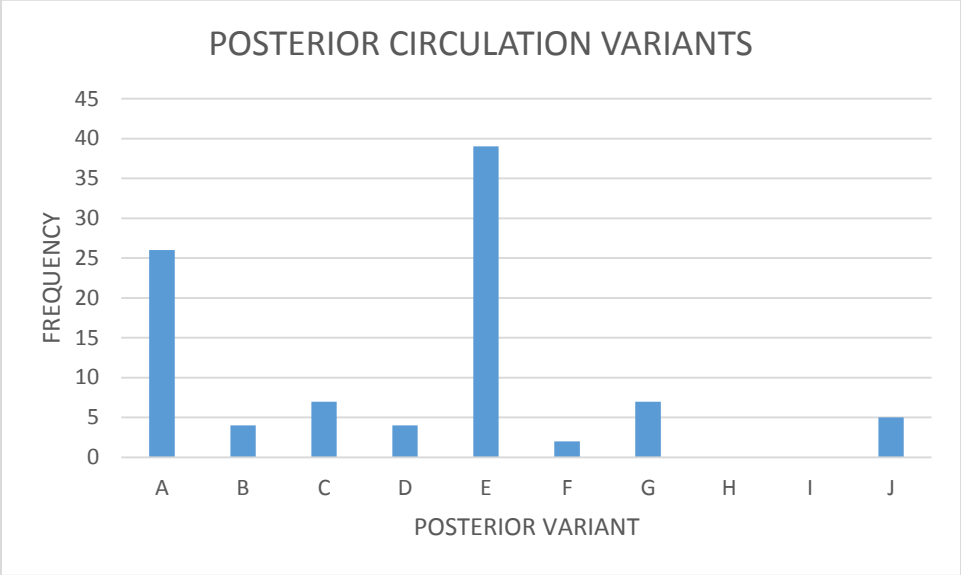

Figure 15: *Frequency of posterior circulation variants.*

4.5 COMPLETE ANTERIOR CIRCULATION VARIANTS (TYPES A-F)

79/94(84%) had complete anterior COW configuration.

The prevalence of complete anterior COW was 77.4% and 92.7% in males and females respectively.

41(51.9%) were males while 38(48.1%) were females.

4.6 COMPLETE POSTERIOR CIRCULATION VARIANTS (TYPES A-C)

37/94(39.4%) of the patients had a complete posterior COW configuration.

The prevalence of complete posterior circulation variants was 39.6% and 39% in males and females respectively.

21(56.8%) were males while 16(43.2%) were females.

4.7 ADULT CONFIGURATION OF THE PCAs.

Adult configuration of the PCAs was seen in 82 patients.

The proportion of adult PCA configuration was significantly higher in females than males (95%vs 81%) (p=0.044).

Bilateral adult type configuration seen in 69(84.1%), right sided in 5(6.1%), and left sided in 8(9.8%).

4.8 FETAL PCA

Proportion of patients with fetal PCA (complete and partial) was 25.5 %(24/94).

Partial fetal PCA was seen in 23 patients.

Bilateral fetal PCA seen in 7(30.4%), right sided fPCA in 11(47.8%) and left sided fPCA in 5(21.7%).

Complete PCA seen in 6 patients. Right sided complete fetal PCA in 1(16.7%) while left sided complete fetal PCA was seen in 5(83.3%).

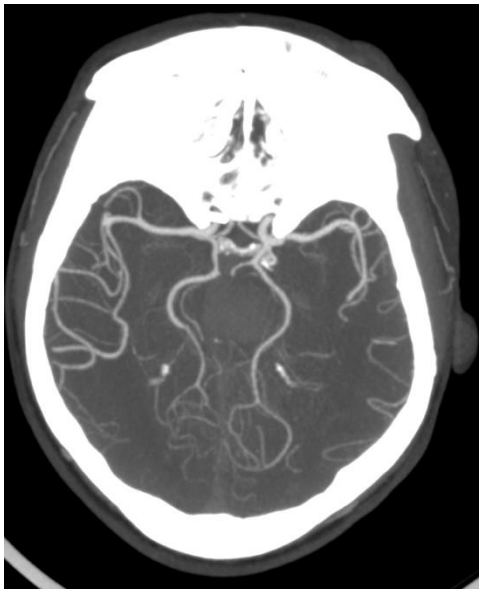

Figure 16: *Axial cerebral CTA image showing bilateral fetal PCA with right P1 segment aplasia.*

4.9 PRESENCE OF ANEURYSMS

Aneurysms were seen in 23 (24.5%) of patients referred for cerebral CTA.

Most aneurysms were located in the anterior circulation 69.6 %(n=16). 1 (4.3%) located in posterior circulation and in 6(26.1%) had aneurysms in other vessels other than the CW.

18(78.3%) had 1 aneurysm, 3(13%) had 2 aneurysms while 2(8.7%) had 3 aneurysms.

4.10 VASCULAR DISTRIBUTION OF ANEURYSMS

ACoA aneurysms were seen in 10(43.6%), MCA aneurysms 5(21.7%) ICA aneurysms 5(21.7%) while 3(13%) had aneurysms in other vessels.

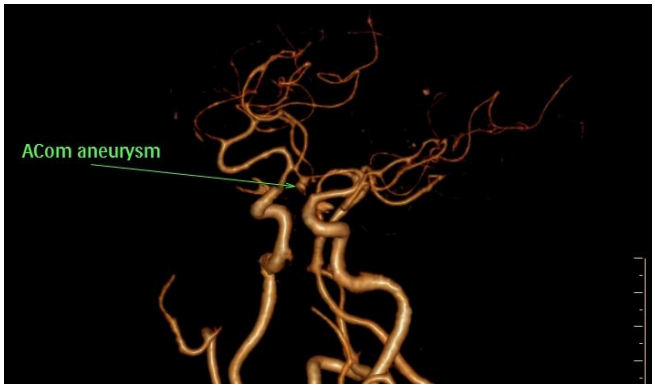

Figure 17: *3D cerebral CTA showing a saccular aneurysm at the ACoA.*

4.11 PRESENCE OF ANEURYSMS AND ASSOCIATION WITH CW CONFIGURATION

16 out of 23 (69.6%) of patients with aneurysms were found to have incomplete CW while the remaining 7 (30.4%) had complete CW configuration.

18/23 (78.3%) of patients had one aneurysm while 5/23(21.7%) had more than 1 aneurysm.

4/5 (80%) of patients with multiple aneurysms had incomplete configuration of CW while 1/5(20%) had complete CW configuration.

No association between CW configuration and presence of aneurysms (p=0.438).

No significant association was demonstrated between incomplete CW and the occurrence of multiple aneurysms (p=0.567).

4.12 PRESENCE OF CEREBRAL ARTERIOVENOUS MALFORMATIONS.

AVM were seen in 8 (8.5%) of patients undergoing cerebral CTA. 5 (62.5%) and 3(37.5%) were seen in patients with incomplete and complete CW configuration respectively.
No association was found between CW configuration and presence of AVM (P=0.987)

4.13 PRESENCE OF FENESTRATIONS DUPLICATIONS, AZYGOUS ACA AND PERSISTENT TA

Fenestrations, duplications, azygous ACA and persistent TA were not observed in this study.

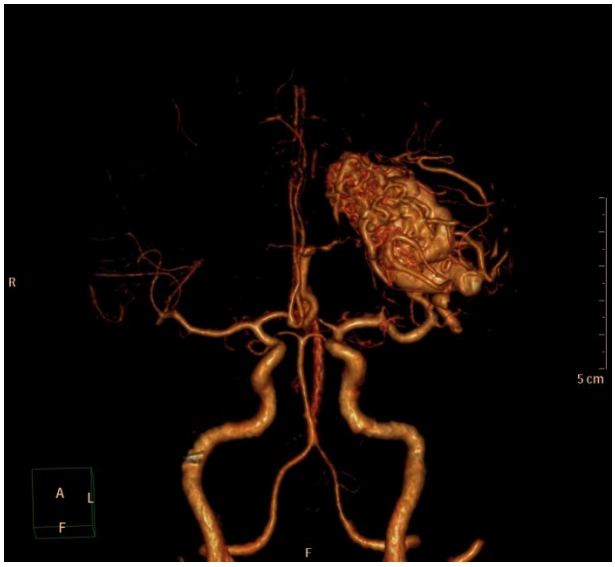

Figure 18: *3D cerebral CTA image showing an AVM with feeding artery arising from the left MCA.*

CHAPTER 5

5.1 DISCUSSION

Previous anatomic, CTA and MRA studies have demonstrated significant variations in the CW configuration in various population groups.

The current study is based on cerebral CTA to establish the configuration of the CW and association with other vascular anomalies in Kenyan patients referred for cerebral CTA.
The proportion of patients with complete CW configuration was 37.2%(n=35).This was slightly higher in males than females 37.7% vs 36.6%.Previous studies have demonstrated a prevalence of between 12.24%-60%(36)(38). These findings are in keeping with previous studies. The prevalence of this configuration is however higher than an MRA-TOF study by Chuanya Qiu et al on 2246 healthy Chinese male population which showed a prevalence of 12.24%(1). The proportion of complete CW is however lower than an MRA-TOF study done on 180 patients in an Egyptian hospital by Mohammed Abdelatif et al which showed a prevalence of 46.7%(31). This could be explained by the difference in sample size, study population, racial differences and technique used in assessment of the CW.

An incomplete CW configuration was seen in 62.8% of patients, 62.3% in males versus 63.4% in females.

A complete anterior CW was seen in 84 %(n=79).Statistically significant difference was demonstrated between males and females (77.4% vs 92.7% p=0.04). The findings in this study are comparable to MRA-TOF study by Naveen SR et al which showed prevalence of complete anterior CW at 78.58%(33)

The commonest anterior circulation variant was type A variant accounting for 78.7 %(n=74).This configuration was seen in 69.8 %(n=37) and 90.2 %(n=37) of males and females respectively. This finding is similar to studies done by Naveen SR et al and Dr. Arjun Bhaddur et al which showed type A variant being the most common anterior circulation variant(33) (32).

Complete posterior circulation configuration was seen in 39.4% of patients accounting for 39.6% and 39.0% in males and females respectively.

Type E posterior circulation variant was the commonest posterior circulation variant accounting for 41.5%.This study finding is similar to those done by Naveen SR et al and Dr. Arjun Bhaddur et al which showed type E variant to be the dominant posterior circulation variant(33) (32).

A cerebral CTA study done by Zhang Ning Jin et al on Chinese population with family history of stroke showed dominance of type E posterior variant with a prevalence of 52.3%(35) which is higher than the current study.

Type E posterior variant has been linked to an increased risk of ischaemic stroke(43).A high proportion of this variant as depicted in the current study is of importance to surgeons and neurologists in the assessment of patients with intracranial tumors, trauma and cardiovascular complications.

Fetal PCA was seen in 30.9% (n=29). Complete PCA was demonstrated in 6.4% while partial PCA was seen in 24.5%. Unilateral fetal PCA was more common than bilateral fetal PCA.12.8% were right sided , 10.6% left sided and 5.6% bilateral fetal PCA.

These findings are similar to a publication by Dimmick SJ Faulder et al which showed a prevalence of 15%-32% for fetal PCA with bilateral fPCA at 8%,right sided at 10% and left sided fPCA at 10%(2).

In the current study aneurysms were seen in 24.5% (n=23) of patients referred for cerebral CTA. 69.6% of the aneurysms were located in the anterior CW while 4.3% were located in the posterior CW.

78.3% of patients had one aneurysm while 21.7% had more than 1 aneurysm.
26.1 %(n=6) were located in other vessels other than the CW.

The prevalence of aneurysms in this study is lower than an earlier Kenyan study by Chepsiror et al based on conventional angiography which showed a higher prevalence of aneurysms at 40.9% and anterior circulation aneurysms at 95.2%(30).
The difference in general prevalence of aneurysms in the two studies could be due to the higher sensitivity of conventional angiography for aneurysm detection.

In the current study ACoA aneurysms were the commonest at 43.6 %(n=10).
21.7% were located in the MCA, 21.7% in the ICA and 13% seen in other vessels other than the CW. These study findings are in contrast to the study done by Chepsiror et al which showed 30.6% at ICA-PCoA, ACoA 22.2% and MCA bifurcation 13%(30).
In the current study no association was found between the CW configuration and presence of aneurysms (p=0.567).

AVM were seen in 8.5% (n=8) in the current study.
These study findings are similar to an earlier Kenyan study by Chepsiror et al which showed a prevalence of 8%(30).
62.5% (n=5) had incomplete CW while 37.5% (n=3) had a complete CW configuration.
No significant association was demonstrated between the presence of AVMs and CW configuration.

Azygous ACA, fenestration,duplication of vessels and PTA were not observed in this study. These findings were in contrast to a previous Kenyan cadaveric study by Hassan Said et al in 36 adult brains in which fenestration and duplication of ACoA was seen in 26% and 13% respectively(29). The findings in this study could be due to the difference in the technique used and the study population.
Previous publication by Dimmick SJ Faulder et al has shown a low prevalence for duplications and fenestrations in angiographic studies of 0.058%(2).The current study findings could be due to their lower prevalence in the general population and the low sample size used in this study.

5.2 CONCLUSION

The variant anatomy of CW in patients undergoing cerebral CTA in this study are similar to other studies done in different population groups.

This study however demonstrates slight differences in proportion of variant anatomy of the circle of Willis which could be due to genetics, sample size and technique used.

No significant association was found between aneurysms and CW configuration. No association was demonstrated between AVMs and the CW configuration.

5.3 STUDY LIMITATIONS

- Lack of Picture archiving and communication system at the KNH department of radiology limited retrospective study which would have yielded a larger sample size.

- Limited numbers of patients undergoing cerebral CT angiography in KNH and Nairobi Hospital as some patients go straight for magnetic resonance angiography.

- These study findings are based on patients with neurological symptoms that were referred for cerebral CTA and not the general healthy population.

5.4 RECOMMENDATIONS

- Installation of picture archiving system at KNH to facilitate patient follow up and research.
- Create awareness among clinicians on the availability and accuracy of cerebral CTA for evaluation of intracranial vessels.
- Larger follow up study to establish association between CW variant anatomy and presence of aneurysms.
- Follow up study on larger sample size to determine the incidence of duplications, fenestrations and azygous ACA.
- Follow up study on evaluation of the CW in patients with no neurological symptoms referred for other angiographic studies in the same setting.

TIME PLAN

	SEPTEMBER-NOVEMBER 2016	NOVEMBER 2016- JANUARY 2017	JANUARY-MARCH 2017	MARCH – APRIL 2017	APRIL – MAY 2017	JUNE-JULY 2017	AUGUST-SEPT. 2017	OCTOBER 2017-JANUARY 2018
PROPOSAL WRITE UP	X	X						
CORRECTION OF SUPERVISORS INPUT		X						
1ST SUBMISSION TOKNH-UON – ERC				X				
2ND SUBMISSION & CORRECTIONS						X		
FINAL SUBMISSION & EXPECTED APPROVAL								
DATA COLLECTION						X		
DATA ENTRY							X	
DATA ANALYSIS								X
REPORT WRITING								X
DISSERTATION SUBMISSION								X

BUDGET

ITEM	UNIT COST	NUMBER	TOTAL COST
RESEARCH ASSISTANTS/DATA COLLECTION CLERKS	5000.00	8	40000.00
BIOSTATISTICIAN FEES	30000.00		30000.00
SUPPLIES AND EQUIPMENT			
PRINTING RESEARCH PROPOSAL	5.00	6(EACH WITH 40 PAGES)	1200.00
PRINTING CONSENT AND DATA COLLECTION FORMS	5.00	200(EACH WITH 8 PAGES)	8000.00
PENS	20.00	20	400.00
AIRTIME	1000.00		1000.00
INTERNET COST	5000.00		5000.00
PRINTING REPORT	5.00	10 COPIES(EACH WITH 80 PAGES)	4000.00
MISCELLANEOUS			4000.00
CONTINGENCY(10% OF THE BUDGET)			9360.00
GRAND TOTAL			105660.00

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APPENDICES

APPENDIX 1: DATA COLLECTION FORM

BIODATA

DATE OF BIRTH……..

AGE…….

GENDER……..

XRAY NUMBER……

DATE OF EXAMINATION……

PHONE NUMBER ……..

PATIENT'S UNIQUE NUMBER ……..

INDICATION ……

1. CIRCLE OF WILLIS ANATOMY

COMPLETE	INCOMPLETE

2. INCOMPLETE CIRCLE OF WILLIS

ANTERIOR	POSTERIOR	BOTH

3. ANTERIOR CIRCULATION VARIANTS

COMPLETE ANTERIOR CIRCULATION						INCOMPLETE ANTERIOR CIRCULATION			
A	B	C	D	E	F	G	H	I	J

4. POSTERIOR CIRCULATION VARIANTS

INTEGRAL POSTERIOR CIRCULATION			NON-INTEGRAL POSTERIOR CIRCULATION						
A	B	C	D	E	F	G	H	I	J

5. TYPE OF PCA (Tick where appropriate)

Type of PCA	Bilateral	Right	Left
Adult configuration			
Partial fetal PCA			
Complete fetal PCA			

6. Aneurysm

Presence of aneurysm (tick where appropriate)

YES: _____ NO: _____ (If no skip to number 7)

If YES state the location;

I. Anterior circulation and vessel involved …….

II. Posterior circulation and vessel involved …….

III. Other vessels other than the CW

……..

IV. Number of aneurysms……

7. Presence of other vascular pathologies other than aneurysms

   …….

8. Presence of duplication and vessel involved……

9. Presence of fenestration and vessel involved

   …….

10. Presence of persistent trigeminal artery (tick where appropriate)

    Yes…….. No…….

11. Presence of Azygous ACA(tick where appropriate)

    Yes…… No ……..

APPENDIX 2: CONSENT FORM FOR PARTICIPATION IN THE STUDY

This consent has three parts:

Participant information sheet; sharing information about the research
Consent form for signing
Statement by the researcher.

PARTICIPANT INFORMATION SHEET

Investigator's statement.

My name is Dr.Roy Munialo Machasio, a postgraduate student at the University of Nairobi department of diagnostic imaging and radiation medicine. I am conducting a study on the variations of the blood vessels supplying blood to the brain) using X-rays. A special dye will be injected through your veins to enable us to see the blood vessels. I am requesting you to take part in the study. The purpose of this consent form is to help you decide whether you want to be included in the study or not. Please read through the form carefully. You are free to ask any questions about the study. The investigator will be available to answer any questions during the study or thereafter.

Brief description of the study

The configuration of blood vessels supplying blood to the brain form an important route of collateral supply to the brain. Various other studies done elsewhere have shown variations from the normal configuration. These anatomic variations have been linked to development of stroke, aneurysms, migraines, and mental illness. My study therefore aims to show the proportion of the various configurations of the blood vessels supplying blood to the brain in the Kenyan population.

Benefits

This study will provide a database that will help diagnostic radiologists, interventional radiologists and neurosurgeons in treatment planning for patients.

Duration of study

6 months.

Compensation

You will not receive any compensation for participating in the study.

Right to refuse or withdraw

You are free to choose whether or not to participate in the study. You will suffer neither penalties nor loss of any benefits for declining to participate in the study.

Confidentiality

If you agree to participate in the study, information from your examination will be kept strictly confidential and will only be used for the purpose of this study. Information obtained will be kept under lock and key and soft copy information will be password protected. No specific information of any participant will be revealed to any person without their permission in writing. Your names will not appear on any of the records used for this study.

Risks

This study involves use of X-rays which is a form of ionizing radiation which may have some adverse effects. Proper protocols will be used to limit the radiation dose to the patient.

Special dye that will be injected through the veins to outline the blood vessels may cause minor side effects. Measures will be taken to minimize adverse effects from its administration.

Minor adverse reactions include: nausea, sneezing, cough, flushing. This occurs in a small proportion of patients and if any reactions occur they will be addressed immediately.

PARTICIPANT CONSENT FORM AND PARTICIPANTS STATEMENT

I hereby confirm that the doctor has explained to me about the above study and I understand fully. I have been given opportunity to ask questions regarding the study which have been adequately answered.

I understand that my participation is voluntary and that I have not been forced to participate. I understand that I can decline without giving any reason and medical care and legal rights will not be affected.

I understand that I will not receive any compensation either financial or otherwise and will not receive any preferential treatment, gift or reward for participating in the above study.

I understand that my personal information will be kept confidential but any relevant medical information will be accessible to the researcher and the supervisors where relevant to the study. I give them permission to have access to this information.

I hereby consent to take part in the above study

Respondent's signature: _____

Date: _____

STATEMENT BY RESEARCHER/RESEARCH ASSISTANT

I hereby confirm that I have accurately read out the contents of the information sheet to the participant.

To the best of my ability, I have made sure the participant understands the following; Participation in this study is on voluntary basis and no compensation will be given.

Refusal to participate or withdraw from the study at any point will not in any way compromise the quality of care accorded to the patient.

All the information that shall be given will be treated with confidentiality.

Name: _____

Signature: _____

Date: _____

CONTACTS

RESEARCHER

Dr. Roy Munialo Machasio,

Department of diagnostic radiology and radiation medicine,

University of Nairobi,

P.O box 15167-00100

NAIROBI.

Telephone number: 0719193485 Email address: rmachasio@gmail.com

If you have any questions on your rights as a research participant you can contact Kenyatta National Hospital Ethics and Research Committee whose task is to ensure research participants are protected from harm.

KENYATTA NATIONAL HOSPITAL/UNIVERSITY OF NAIROBI
ETHICS AND RESEARCH REVIEW COMMITTEE KNH/UON/ERC

University of Nairobi

College of Health Sciences

P.O Box 19676-00202

Tel. (254)0202726300 Ext 44355

Kenyatta National Hospital

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Tel. (254)020 726300 Ext 44102, 44355

Fax: 725272

Contact person

Esther Wanjiru Mbuba

E-mail: uonknh erc@uonbi.ac.ke

APPENDIX 3: KIBALI CHA KUSHIRIKI KATIKA UTAFITI

KAULI YA MTAFITI

Jina langu ni Dr. Roy Munialo Machasio, mwanafunzi wa uzamili katika Chuo Kikuu cha Nairobi idara ya radiologia na dawa mionzi.Utafiti huu unahusu kiwango cha tofauti za ugavi wa mishipa ya damu ambazo husambaza damu kwenye ubongo katika jamii ya wakenya kwa kutumia miale ya X-ray.Ningependa kukuomba ushiriki katika utafiti huu. Madhumuni ya fomu hii ya idhini ni kukusaidia kuamua kama unataka kushiriki katika utafiti huu au la. Tafadhali soma fomu hii kwa makini. Unao uhuru wa kuuliza maswali yoyote kuhusu utafiti.Mtafiti au wasaidizi wake wataweza kujibu maswali yoyote wakati wa utafiti au baada ya hapo.

MAELEZO MAFUPI KUHUSU UTAFITI

Ugavi wa mishipa yenye husambaza damu kwenye ubongo una umuhimu mkubwa sana.

Tafiti zilizofanywa kwingineko zimeonyesha tofauti kadhaa katika ugavi huu kwa kulinganisha watu wenye asili tofauti. Utafiti huu unalenga kuonyesha tofauti hizi miongoni mwa wakenya wanaofanyiwa picha ya mishipa ya damu kwa kutumia miale ya X-ray.

FAIDA

Utafiti huu utatoa msingi utakaosaidia wanaradiologia na madaktari wa upasuaji wa ubongo katika mipango ya matibabu ya wagonjwa.

MUDA WA UTAFITI

Miezi sita.

FIDIA

Hakuna fidia yoyote utakayopewa kwa kushiriki katika utafiti huu.

HAKI YA KUKATAA AU KUJIONDOA KATIKA UTAFITI

Uko na uhuru wa kuchagua kushiriki katika utafiti. Hautateseka au kunyimwa huduma unayohitaji kwa kutoshiriki katika utafiti huu.

SIRI YA UTAFITI

Taarifa zote namatokeo ya utafiti huu zitalindwa vilivyo na kuwekwa katika hali ya siri. Hakuna taarifa maalum ya mshiriki yeyote zitafafanuliwa kwa mtu yeyote bila ya idhini yako kwa maandishi.Majina yako hayataonekana kwenye kumbukumbu za utafiti huu.

MADHARA

Katika harakati ya kuchukua picha itabidi tutumie dawa itakayo onyesha mishipa ya damu.Dawa hizi zitapeanwa kupitia sindano kwenye mshipa wa damu mkononi.Utaweza kupata madhara kidogo kutokana na dawa kama vile kuhisi kutapika, kujihisi joto kichwani au maumivu ya kichwa.Madhara mengine kama vile mabadiliko katika kiwango cha ufanyaji kazi wa figo huenda ukatokea.

FOMU YA KUIDHINISHA KUSHIRIKI KATIKA UTAFITI

Mimi natoa dhibitisho kwamba daktari amenieleza vikamilifu kuhusu utafiti ambao kichwa chake kimetajwa hapo juu.Ninakiri kuwa pia nimepewa fursa ya kuuliza maswali kuhusu utafiti huu na nimeridhika na majibu niliyopewa na daktari/mtafiti msaidizi.
Ninaelewa kwamba kushiriki katika utafiti huu nikwa hiari yangu mwenyewe na sijalazimishwa.

Natambua kwamba sitapokea fidia yoyoteiwe fedha au vinginevyo, wala sitapokea matibabuyoyote ya upendeleo, takrima au tuzo kwa ajili yakushiriki kwangu katika utafiti huu.
Naelewa kuwa taarifa zangu za kibinafsi zitakuwa siri. Ingawa hivyo taarifa kuhusu matokeo ya uchunguzi zitakazokusanywa wakatiwa utafiti huu zitaangaliwa na kuchambuliwa na mtafiti mkuu pamoja na wasimamizi wake pindi itakavyohitajika.

Ninatoa idhini yangu kushiriki katika utafiti huu.

Sahihi ya mshiriki: _____

Tarehe: _____

DHIBITISHO LA MTAFITI/MTAFITI MSAIDIZI

Ninadhibitisha ya kuwa nimemwelezea mshiriki mambo yafuatayo kuhusu utafiti huu;

Kwamba kushiriki ni kwa hiari yake.

Hakuna fidia yoyote itakayopeanwa kwa kushiriki katika utafiti.

Mshiriki anaweza kubadili uamuzi wa kuendelea kushiriki katika utafiti huu bila ya kuadhiri huduma ya matibabu yake.

Haki za mshiriki zitalindwa na habari zitakazotolewa na mshiriki zitawekwa siri wakati wote na zitatumika kwa ajili ya utafiti huu pekee yake

Jina: _____

Sahihi: _____

Tarehe: _____

Kwa maelezo zaidi unaweza kuwasiliana na mtafiti mkuu kupitia anwani ifuatayo:

Dr. Roy Munialo Machasio

Idara ya radiologia na dawa mionzi

Chuo Kikuu cha Nairobi

Sanduku la Posta 37441-00100

Nairobi.

Nambari ya simu -0719193485

Au

KNH-UoN-ERC secretariat

Katibu wa utafiti

Chuo Kikuu cha Nairobi-Hospitali kuu ya Kenyatta

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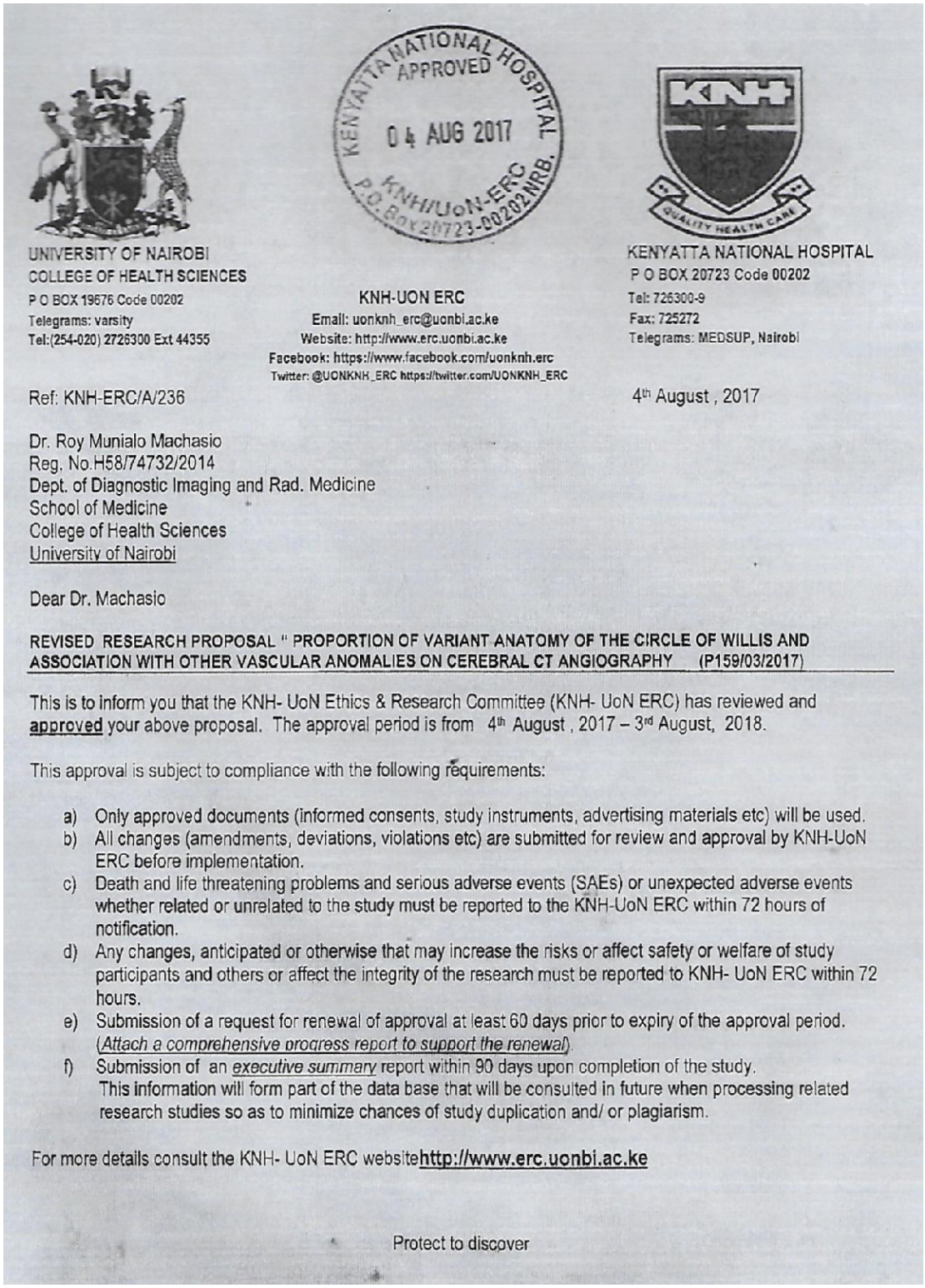
Nairobi.

Nambari ya simu: 72600-9

Fax: 725272

Barua pepe: UoNknherc@uonbi.ac.ke

APPENDIX 4: KNH ETHICAL APPROVAL LETTER



KENYATTA NATIONAL HOSPITAL APPROVED 04 AUG 2017 KNH/UoN-ERC P.O. Box 20723-00202 NRB.

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4th August , 2017

Dr. Roy Munialo Machasio
Reg. No.H58/74732/2014
Dept. of Diagnostic Imaging and Rad. Medicine
School of Medicine
College of Health Sciences
University of Nairobi

Dear Dr. Machasio

REVISED RESEARCH PROPOSAL " PROPORTION OF VARIANT ANATOMY OF THE CIRCLE OF WILLIS AND ASSOCIATION WITH OTHER VASCULAR ANOMALIES ON CEREBRAL CT ANGIOGRAPHY (P159/03/2017)

This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and **approved** your above proposal. The approval period is from 4th August , 2017 – 3rd August, 2018.

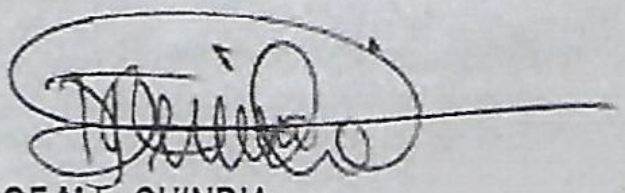
This approval is subject to compliance with the following requirements:

a) Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b) All changes (amendments, deviations, violations etc) are submitted for review and approval by KNH-UoN ERC before implementation.
c) Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
d) Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
e) Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*)
f) Submission of an *executive summary* report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

For more details consult the KNH- UoN ERC website**http://www.erc.uonbi.ac.ke**

Protect to discover

Yours sincerely,



PROF M.L. CHINDIA
SECRETARY, KNH-UoN ERC

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The Director, CS, KNH
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