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Evaluation Of Modified MRI protocol in Diagnosis of Acute Cerebral Stroke Among Sudanese

تقويم بروتوكول التصوير بالرنين المغناطيسي المعدل في تشخيص

السكتة الدماغية الحادة لدي السودانيين

A thesis submitted for awarded of Ph D

in Radiological science Technology

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قال تعالى :

(وَقُـل رَّبِّ زِدْنِـي عِـلْمـاً)

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Dedication

To the soul of my father and

My mother who support me by all means.

To all whom I love and respect.

Acknowledge

Firstly thanks to Allah for giving me strength and patience to do this work.

I would like to offer my deepest thanks to my supervisor Dr. Hussain Ahmed Hassan for his great effort and patience.

Thanks also extended to all patients who donated the samples. I would like to express my special gratitude to the staff of Alamal National Hospital diagnostic center and almoalem medical city for their help in the selection of patients and collection of samples.

ABSTRACT

Stroke is one of the major causes of disability and mortality worldwide. The aim of this study is to evaluate of modified MRI protocol in diagnosis of acute cerebral stroke among Sudanese

This is a practical study carried out during period from April 2016 to June 2019 and was conducted on 200 patients (male 94, female 106) with average age 47, rang from (17- 84 years).

This study was carried out in Alamal National Hospital diagnostic center in Khartoum.

The MRI scanner used in this study was PHILIPS (1.5tesla), with 8-channel phased array neurovascular coil.

All patients underwent MRI study with different pulse sequences (T2, DWI and FLAIR), and additional modified T2* pulse sequence.

All data were entered and analysed using Microsoft Excel including description statistic of frequency tables and graphs.

The study showed that the stroke patients with old ages more affected than younger patients , the risk of stroke rises with age after 55years.

The preliminary investigations obtained from this study revealed that the patients participated in this study, female's (53%) was being more affected than males (47%) in regards with stroke disease.

The preliminary investigations obtained from this study revealed that there was difference between the hemispheres , Left hemispheric strokes frequent was 52,(26%) whereas right hemispheric strokes frequent was 23 (11%) ,there was more high incidence of stroke in left side than right side.

The results showed that the modified T2* pulse sequence had ability in detection of cerebral micro bleeding rather than other routine sequences.

The study conclude that the modified MRI protocol T2* should be the sequence of choice in microbleeding detection for accurate diagnosis of patients with suspected acute cerebral stroke.

الملخص

السكته الدماغيه هي احد الاسباب الرئيسيه للاعاقه والوفيات في جميع انحاء العالم , الهدف من هذه الدراسه هو تقويم بروتوكول التصوير بالرنين المغناطيسي المعدل للسكته الدماغيه الحاده لدي السودانيين.

أجريت هذه الدراسة العمليه في الفتره من ابريل 2016 حتي يونيو 2019 بمستشفي الأمل في ولايه الخرطوم., شملت علي 200 مريض من كلا الجنسين (ذكور=94 , اناث = 106) تتراوح اعمارهم بين 18الي 84 سنه كان متوسط العمر 47 سنه.

تم استخدام جهاز الرنين المغناطيسي ,(PHILIPS (1.5tesla.

كل المرضى تم فحصهم باستخدام بروتوكول التصوير بالرنين المغناطيسي للدماغ بالسلسله الروتينيه (T2, DWI , FLAIR) . بالاضافه لزمن الراحه الثاني المعدل (*T2).

تم ادخال جميع البيانات وتحليلها باستخدام برنامج مايكروسوفت اكسيل بما في ذلك وصف احصائي لجداول التكرارات والرسوم البيانيه.

أوضحت الدراسة أن الأشخاص الأكثر عرضه للسكتة الدماغية الحادة الذين كانوا في أعمار متقدمه أكثر تأثرا من المرضى الأصغر سنا. , حيث تزيد خطوره السكته الدماغيه في الاعمار مابعد 55سنه .

نسبه السكته الدماغيه في الاناث كانت اكتر من الذكور (53% اناث , 47% ذكور).

من هذه الدراسة وجد أن السكته الدماغيه في النصف الشمالي من الدماغ كانت اكثر من النصف اليمين (النصف الشمالي 26%, النصف اليمين 11%).

اظهرت نتائج الدراسه ان زمن الراحه الثاني المعدل (*T2) اكثر حساسيه في كشفِ النزيف الدماغي الدقيق اكثر من السلسله الروتينيه المستخدمه لتصوير للدماغ.

اظهرت الدراسه ان سلسله البروتوكول المعدله *T2 لها فاعليه عاليه لكشفِ النزيف الدقيق ، لذلك نَوصي بها كسلسلة إختيارِ اساسيه ضمن البروتوكول الروتيني لتصوير الدماغ.

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ACA	Anterior Cerebellar Artery
AICA	Anterior Inferior Cerebellar Artery
AIS	Acute ischemic stroke
AVM	Arteriovenous Malformation
BMI	Body Mass Index
C I	Confidence Interval
CAA	Cerebral amyloid angiopathy.
CMB	Cerebral Micro Bleeding
CSF	Cerebrospinal Fluid
CT	Computed Tomography
CVA	Cerebrovascular Accident
CVI	Cerebrovascular insult
D M	Diabetes Mellitus
DWI	Diffusion Weighted Imaging
EPI	Echo planer image
FLAIR	Fluid Attenuation Inversion Recovery
GE	Gradient echo
GRE	Gradient Recalled Echo
H T	Hypertension
ICH	Intracranial Hemorrhage
Kg	kilogram
LT	Left
MCA	Middle Cerebellar Artery
MRI	Magnetic Resonance Imaging
MRI	Magnetic resonance imaging
MS	Multiple Sclerosis

PCA	Posterior Cerebellar Artery
PICA	Posterior Inferior Cerebellar Artery
PWI	Perfusion-weighted imaging
RR	Relative Risks
RT	Right
SPSS	Statistical Package for Social Sciences
SWI	Suscpility weighted image
TIA	Transient Ischemic Attack
W I	Weighted Image
WT	Weight

CHAPTER ONE

1.1 Introduction:

Since the discovery of x-rays by W C Roentgen in 1895, medical imaging has contributed significantly to progress in medicine; diagnostic imaging has grown during the last 50 years from a state of infancy to a high level of maturity. And become having an important role in patient management, and especially radiologic diagnosis (Herman, 2009).

The application of magnetic resonance imaging(MRI) has evolved rapidly since i ts clinical development in the early 1980s. Presently, examinations of the brain ar e the second most commonly requestedMR study following spine examinations (Radiology Dept Statistics, 2001) and (Slichter, 1978). MRI is becoming one of the most important diagnostic tools in clinical decision making for the treatment and management of acute and chronic stroke. Diffusion- weighted imaging (DWI) in which image contrast is based on water motion is remarkably sensitive to ischemic brain injury (i.e., within minutes) whereas other conventional imaging techniques such as computed tomography (CT) and T1 and T2 MRI fail to detail such injury for at least a few hours, the anatomical mismatch between DWI and perfusion-weighted imaging (PWI) abnormality is indicative of tissue at risk (i.e., approximating the ischemic penumbra) that is potentially salvageable and is the primary target for therapeutic intervention .In addition to DWI and PWI, there are many exciting MRI modalities (such as diffusion tensor imaging, blood brain barrier permeability imaging, pH MRI (Slichter,1978).

Magnetic resonance imaging (MRI) is a test that uses a magnetic field and pulses of radio wave energy to take pictures of the head. In many cases, MRI gives information that can't be seen on an X-ray, ultrasound, or (CT) scan. For an (MRI) of the head, lie head inside a special machine (scanner) that has a strong magnet. The MRI can show tissue damage or disease, such as infection or inflammation, or a tumor, stroke , or seizure . Information from an MRI can be

saved and stored on a computer for more study. Photographs or films of certain views can also be made. In some cases, contrast material may be used during the MRI to show pictures of structures more clearly. The contrast may help show blood flow, look for some types of tumors, and show areas of inflammation (Marks, et al 1996). (MRI) of the head is done to looking for the cause of headaches.

Help diagnose a stroke or blood vessel problems in the head, problems with blood vessels may include an aneurysm or abnormal twisted blood vessels that are present at birth (this is called an arteriovenous malformation [AVM]), check blood flow or blood clots to the brain, checking symptoms of a known or suspected head injury, check symptoms such as change in consciousness, confusion, or abnormal movements , these symptoms may be caused by brain diseases, such as Huntington's disease, multiple sclerosis (MS) ,Parkinson's disease, or Alzheimer's disease ,check for "water on the brain" (hydrocephaly) look for tumors , infections, an abscess, or conditions of the brain or brain stem, such as encephalitis or meningitis, check the eyes, the nerves from the eyes to the brain (optic nerves), the ears, and the nerves from the ears to the brain (auditory nerves), look for problems of the pituitary gland, investigate or follow a finding seen on another tests. (Nitz, 1999).

1.2 Problem of study:

Acute stroke cause temporary or permanent disabilities, depending on how long the brain lacks blood flow and which part was affected. Complications may include: Paralysis or loss of muscle movement, Difficulty talking or swallowing, Memory loss or thinking difficulties, Pain, numbness or other strange sensations may occur in the parts of the body affected by stroke.

Acute stroke is one of the leading causes of mortality and morbidity worldwide. Statistics from the American Heart Association estimate an average

of 1 stroke every 40 seconds in the United States amounting to approximately 795,000 people experiencing new or recurrent strokes per year. (Roger, et al 2013).

Worldwide Statistics:

According to the World Health Organization, 15 million people suffer from stroke worldwide each year. Of these, 5 million die and another 5 million are permanently disabled.

High blood pressure contributes to more than 12.7 million strokes worldwide.

In developed countries, the incidence of stroke is declining, largely due to efforts to lower blood pressure and reduce smoking. However, the overall rate of stroke remains high due to the aging of the population (WHO report 2015).

Stroke patients had opposed way of treatment either coagulant or anti-coagulant in case of hemorrhage and infarction consequence. CT scanner and MRI examinations are answers the question concerning type of stroke location and size, although number of disease may happen in the brain and can be diagnosed in sectional studies but some of them can't be detected early so the study of the stroke with studding the anticoagulant factor related to the clinical findings which shone in brain MRI scanning.

Approximately 20% to 40% of all stroke patients experience hemorrhagic transformation within the first week after symptom onset. Although cerebral bleeding (CB) is a common event that occurs independently of therapy, caution is required when thrombolysis or anticoagulants are administered.

1.3 Justification:

A wide variety of imaging techniques has become available to assess vascular lesions and brain tissue status in acute cerebral stroke patients. However, the practical challenge is to understand the multiple facets of these imaging techniques, including which imaging techniques to implement and how to optimally use them, with given available resources

Some pulse sequences imaging are not performed, and specific pulse sequence–magnetic resonance (MR) imaging findings may help determine the accurate diagnose of the acute cerebral stroke, for this we will use multiparametric MRI pulse sequences to generates different zones that reflect heterogeneity of tissue damage to improving the early anatomic diagnosis of acute cerebral stroke and therefore in the development and implementation of early stroke interventions and treatments.

1.4 Objectives:

1.4.1 General objective:

To evaluate the modified MRI protocol in diagnosis of acute cerebral stroke among Sudanese.

1.4.2 Specific objectives:

-To detect the ability of modified T2* sequence in diagnosis cerebral stroke.

-To describe the importance and limitations of MRI pulse sequences in detecting cerebral microbleeding stroke.

-To correlate the stroke with age and gender.

-To measure the percentage of ischemia to hemorrhage.

-To determine hemispheric differences in ischemic stroke left hemispheric v.s right hemispheric.

1.5 Thesis layout:

Chapter one: Introduction, statement of the problem, objectives of the study, and thesis layout.

Chapter two: The literature review (Anatomy, Pathology, previous studies).

Chapter three: Methodology and data analysis.

Chapter four: Results

Chapter five: Discussion, Conclusion and Recommendations.

Appendix and References.

CHAPTER TWO

2.1 Background of stroke:

A stroke is a medical emergency and can cause permanent neurological damage or death. An ischemic stroke is occasionally treated in a hospital with thrombolysis (also known as a "clot buster"), and some hemorrhagic strokes benefit from neurosurgery , treatment to recover any lost function is termed stroke rehabilitation, ideally in a stroke unit and involving health professions such as speech and language therapy, physical therapy and occupational therapy , prevention of recurrence may involve the administration of antiplatelet drugs such as aspirin, control of high blood pressure, and the use of statins , some people may benefit from carotid endarterectomy and the use of anticoagulants. Stroke was the second most frequent cause of death worldwide in 2011, accounting for 6.2 million deaths (~11% of the total) , approximately 17 million people had a stroke in 2010 and 33 million people have previously had a stroke and were still alive. Between 1990 and 2010 the number of strokes decrease by approximately 10% in the developed world and increased by 10% in the developing world , overall two thirds of strokes occurred in those over 65 years old (Gorelick, 2009).

Colloquially brain attack is the loss of brain function due to a disturbance in the blood supply to the brain. This disturbance is due to either ischemia (lack of blood flow) or hemorrhage. As a result, the affected area of the brain cannot function normally, which might result in an inability to move one or more limbs on one side of the body, failure to understand or formulate speech, or a vision impairment of one side of the visual field. Ischemia is caused by either blockage of a blood vessel via thrombosis or arterial embolism, or by cerebral hypo perfusion , hemorrhagic stroke is caused by bleeding of blood vessels of the brain, either directly into the brain parenchyma or into the

subarachnoid surrounding brain tissue. Risk factors for stroke include old age, high blood pressure, previous stroke or transient (TIA), diabetes, high cholesterol, tobacco smoking and atrial fibrillation. High blood pressure is the most important modifiable risk factor of stroke (Hacke, et al 2008).

A stroke is a medical emergency and can cause permanent neurological damage or death. An ischemic stroke is occasionally treated in a hospital with thrombolysis (also known as a "clot buster"), and some hemorrhagic strokes benefit from neurosurgery , treatment to recover any lost function is termed stroke rehabilitation, ideally in a stroke unit and involving health professions such as speech and language therapy, physical therapy and occupational therapy , prevention of recurrence may involve the administration of antiplatelet drugs such as aspirin, control of high blood pressure, and the use of statins , some people may benefit from carotid endarterectomy and the use of anticoagulants. Stroke was the second most frequent cause of death worldwide in 2011, accounting for 6.2 million deaths (~11% of the total) , approximately 17 million people had a stroke in 2010 and 33 million people have previously had a stroke and were still alive. Between 1990 and 2010 the number of strokes decrease by approximately 10% in the developed world and increased by 10% in the developing world , overall two thirds of strokes occurred in those over 65 years old (Gorelick, 2009).

Stroke is a condition related to reduced blood flow and perfusion caused by a thrombus/embolus or hemorrhage. There are generally three territories associated with stroke: The ischemic core (less than 12 mL/100 g/min), the penumbra (12-20 mL/100 g/min), and oligemic tissue (greater than 20 mL/100 g/min); the first two are the most severely affected by the reduced perfusion, the penumbra being less hypoxic/ ischemic. The ischemic tissue may not represent salvageable tissue unless the flow is recovered within a few hours, while the

latter is associated more with secondary damage, being at risk if the blood flow is not returned to normal. In the ischemic region, the lack of oxygen supply reduces the availability of high-energy phosphates such as adenosine triphosphate (ATP) and elevates inorganic phosphates. Subsequent dysfunction of the Na^+/K^+ channels results in an influx of Na+ to cause osmotic disruption and cytotoxic edema. On the other hand, the penumbra still has marginal blood supply from collateral sources and retains intact cellular metabolism. Thus, it has the potential to be restored under reperfusion conditions and is vital in determining treatment options. The oligemic tissue is less at risk than the penumbral tissue. Ideally, it should also be possible to detect the size and age of the stroke. (Potchen, et al 1992).

2.2 Brain anatomy:

The brain is one of the most complex and magnificent organs in the human body. Our brain gives us awareness of ourselves and of our environment, processing a constant stream of sensory data. It controls our muscle movements, the secretions of our glands, and even our breathing and internal temperature, every creative thought, feeling, and plan is developed by our brain. The brain's neurons record the memory of every event in our lives (Siesjo, 1989).

There are different ways of dividing the brain anatomically into regions. A common method and divide the brain into three main regions based on embryonic development: the forebrain, midbrain and hindbrain, under these divisions:

The forebrain (or prosencephalon) is made up of our incredible cerebrum, thalamus, hypothalamus and pineal gland among other features, neuroanatomists call the cerebral area the telencephalon and use the term diencephalon (or

interbrain) to refer to the area where our thalamus, hypothalamus and pineal gland reside (Guyton, and John, 1996).

The midbrain (or mesencephalon), located near the very center of the brain between the interbrain and the hindbrain, is composed of a portion of the brainstem. The hindbrain (or rhombencephalon) consists of the remaining brainstem as well as our cerebellum and pons, neuroanatomists have a word to describe the brainstem sub-region of our hindbrain, calling it the myelencephalon, while they use the word metencephalon in reference to our cerebellum and pons collectively (Guyton, and John, 1996).

2.2.1 Hindbrain (rhombencephalon):

Connecting the brain to the spinal cord, the brainstem is the most inferior portion of our brain. Many of the most basic survival functions of the brain are controlled by the brainstem (Afshar , et al 1978).

The brainstem is made of three regions: the medulla oblongata, the pons, and the midbrain. A net-like structure of mixed gray and white matter known as the reticular formation is found in all three regions of the brainstem. The reticular formation controls muscle tone in the body and acts as the switch between consciousness and sleep in the brain (Afshar, et al 1978).

The medulla oblongata is a roughly cylindrical mass of nervous tissue that connects to the spinal cord on its inferior border and to the pons on its superior border, the medulla contains mostly white matter that carries nerve signals ascending into the brain and descending into the spinal cord, within the medulla are several regions of gray matter that process involuntary body functions related to homeostasis, the cardiovascular center of the medulla monitors blood pressure and oxygen levels and regulates heart rate to provide sufficient oxygen supplies to the body's tissues, the medullary rhythmicity center controls the rate of breathing to provide oxygen to the body, vomiting, sneezing, coughing, and swallowing reflexes are coordinated in this region of the brain as well,

the pons is the region of the brainstem found superior to the medulla oblongata, inferior to the midbrain, and anterior to the cerebellum, together with the cerebellum, it forms what is called the metencephalon , about an inch long and somewhat larger and wider than the medulla, the pons acts as the bridge for nerve signals traveling to and from the cerebellum and carries signals between the superior regions of the brain and the medulla and spinal cord (Naidich, et al 2009).

2.2.2Cerebellum:

The cerebellum is a wrinkled, hemispherical region of the brain located posterior to the brainstem and inferior to the cerebrum , the outer layer of the cerebellum, known as the cerebellar cortex, is made of tightly folded gray matter that provides the processing power of the cerebellum , deep to the cerebellar cortex is a tree-shaped layer of white matter called the arbor vitae, which means 'tree of life' , the arbor vitae connects the processing regions of cerebellar cortex to the rest of the brain and body (Duvernoy, 1999).

The cerebellum helps to control motor functions such as balance, posture, and coordination of complex muscle activities, and receives sensory inputs from the muscles and joints of the body and uses this information to keep the body balanced and to maintain posture. also controls the timing and finesse of complex motor actions such as walking, writing, and speech (Duvernoy, 1999).

2.2.3 Midbrain (mesencephalon):

The midbrain also known as the mesencephalon, is the most superior region of the brainstem, found between the pons and the diencephalon, the midbrain can be further subdivided into 2 main regions: the tectum and the cerebral peduncles (Duvernoy, 1999).

The tectum is the posterior region of the midbrain, containing relays for reflexes that involve auditory and visual information, the pupillary reflex

(adjustment for light intensity), accommodation reflex (focus on near or far away objects), and startle reflexes are among the many reflexes relayed through this region , forming the anterior region of the midbrain, the cerebral peduncles contain many nerve tracts and the substantia nigra , nerve tracts passing through the cerebral peduncles connect regions of the cerebrum and thalamus to the spinal cord and lower regions of the brainstem , the substantia nigra is a region of dark melanin-containing neurons that is involved in the inhibition of movement , degeneration of the substantia nigra leads to a loss of motor control known as Parkinson's disease (Duvernoy,1999).

2.2.4. Forebrain (prosencephalon):

Superior and anterior to the midbrain is the region known as the interbrain, or diencephalon , the thalamus, hypothalamus, and pineal glands make up the major regions of the diencephalon. The thalamus consists of a pair of oval masses of gray matter inferior to the lateral ventricles and surrounding the third ventricle. Sensory neurons entering the brain from the peripheral nervous system form relays with neurons in the thalamus that continue on to the cerebral cortex. In this way the thalamus acts like the switchboard operator of the brain by routing sensory inputs to the correct regions of the cerebral cortex , the thalamus has an important role in learning by routing sensory information into processing and memory centers of the cerebrum (Woolsey, et al 2003).

The hypothalamus is a region of the brain located inferior to the thalamus and superior to the pituitary gland , the hypothalamus acts as the brain's control center for body temperature, hunger, thirst, blood pressure, heart rate, and the production of hormones , in response to changes in the condition of the body detected by sensory receptors, the hypothalamus sends signals to glands, smooth muscles, and the heart to counteract these changes , for example, in response to increases in body temperature, the hypothalamus stimulates the secretion of sweat by sweat glands in the skin , the hypothalamus also sends signals to the

cerebral cortex to produce the feelings of hunger and thirst when the body is lacking food or water , these signals stimulate the conscious mind to seek out food or water to correct this situation , also directly controls the pituitary gland by producing hormones , some of these hormones, such as oxytocin and antidiuretic hormone, are produced in the hypothalamus and stored in the posterior pituitary gland , other hormones, such as releasing and inhibiting hormones, are secreted into the blood to stimulate or inhibit hormone production in the anterior pituitary gland (Woolsey, et al 2003).

The pineal gland is a small gland located posterior to the thalamus in a sub-region called the epithalamus, the pineal gland produces the hormone melatonin. Light striking the retina of the eyes sends signals to inhibit the function of the pineal gland. In the dark, the pineal gland secretes melatonin, which has a sedative effect on the brain and helps to induce sleep. This function of the pineal gland helps to explain why darkness is sleep-inducing and light tends to disturb sleep. Babies produce large amounts of melatonin, allowing them to sleep as long as 16 hours per day. The pineal gland produces less melatonin as people age, resulting in difficulty sleeping during adulthood (Van Buren, et al 1972).

2.2.5Cerebrum:

The largest region of the human brain, our cerebrum controls higher brain functions such as language, logic, reasoning, and creativity , the cerebrum surrounds the diencephalon and is located superior to the cerebellum and brainstem ,a deep furrow known as the longitudinal fissure runs midsagittally down the center of the cerebrum, dividing the cerebrum into the left and right hemispheres ,each hemisphere can be further divided into 4 lobes: frontal, parietal, temporal, and occipital ,the lobes are named for the skull bones that cover them ,the surface of the cerebrum is a convoluted layer of gray matter known as the cerebral cortex. Most of the processing of the cerebrum takes place within the cerebral cortex, the bulges of cortex are

called gyri (singular: gyrus) while the indentations are called sulci (singular: sulcus). Deep to the cerebral cortex is a layer of cerebral white matter, white matter contains the connections between the regions of the cerebrum as well as between the cerebrum and the rest of the body, band of white matter called the corpus callosum connects the left and right hemispheres of the cerebrum and allows the hemispheres to communicate with each other (Schitzlein, and Murtagh, 1990).

Deep within the cerebral white matter are several regions of gray matter that make up the basal nuclei and the limbic system , the basal nuclei, including the globus pallidus, striatum, and subthalamic nucleus, work together with the substantia nigra of the midbrain to regulate and control muscle movements , specifically, these regions help to control muscle tone, posture, and subconscious skeletal muscle , the limbic system is another group of deep gray matter regions, including the hippocampus and amygdala, which are involved in memory, survival, and emotions , the limbic system helps the body to react to emergency and highly emotional situations with fast, almost involuntary actions (Schitzlein, ,and Murtagh, 1990).

2.2.6Meninges:

Three layers of tissue, collectively known as the meninges, surround and protect the brain and spinal cord , the dura mater forms the leathery, outermost layer of the meninges , dense irregular connective tissue made of tough collagen fibers gives the dura mater its strength , the dura mater forms a pocket around the brain and spinal cord to hold the cerebrospinal fluid and prevent mechanical damage to the soft nervous tissue , the arachnoid mater is found lining the inside of the dura mater , much thinner and more delicate than the dura mater, it contains many thin fibers that connect the dura mater and pia mater, as its fibers resemble a spider web , beneath the arachnoid mater is a fluid-filled region known as the subarachnoid space , as the innermost of the meningeal layers,

the pia mater rests directly on the surface of the brain and spinal cord. The pia mater's many blood vessels provide nutrients and oxygen to the nervous tissue of the brain , the pia mater also helps to regulate the flow of materials from the bloodstream and cerebrospinal fluid into nervous tissue (Morel, et al 1997).

2.2.7Cerebrospinal fluid:

Cerebrospinal fluid (CSF) a clear fluid that surrounds the brain and spinal cord – provides many important functions to the central nervous system, rather than being firmly anchored to their surrounding bones, the brain and spinal cord float within the CSF. CSF fills the subarachnoid space and exerts pressure on the outside of the brain and spinal cord , the pressure of the CSF acts as a stabilizer and shock absorber for the brain and spinal cord as they float within the hollow spaces of the skull and vertebrae , inside of the brain, small CSF-filled cavities called ventricles expand under the pressure of CSF to lift and inflate the soft brain tissue , cerebrospinal fluid is produced in the brain by capillaries lined with ependymal cells known as choroid plexuses , blood plasma passing through the capillaries is filtered by the ependymal cells and released into the subarachnoid space as CSF , the CSF contains glucose, oxygen, and ions, which it helps to distribute throughout the nervous tissue. CSF also transports waste products away from nervous tissues , after circulating around the brain and spinal cord, CSF enters small structures known as arachnoid villi where it is reabsorbed into the bloodstream , arachnoid villi are finger-like extensions of the arachnoid mater that pass through the dura mater and into the superior sagittal sinus , the superior sagittal sinus is a vein that runs through the longitudinal fissure of the brain and carries blood and cerebrospinal fluid from the brain back to the heart , the brain is the most metabolically active organ in the body , while representing only 2% of the body's mass, it requires 15-20% of the total resting cardiac output to provide the necessary glucose and oxygen for its metabolism (Orrison, 2008).

2.2.8Arterial distributions:

Knowledge of cerebrovascular arterial anatomy and the territories supplied by the cerebral arteries is useful in determining which vessels are involved in acute stroke. Atypical patterns of brain ischemia that do not conform to specific vascular distributions may indicate a diagnosis other than ischemic stroke, such as venous infarction (Nowinski, et al 2006).

In a simplified model, the cerebral hemispheres are supplied by 3 paired major arteries, specifically, the anterior, middle, and posterior cerebral arteries , the anterior and middle cerebral arteries carry the anterior circulation and arise from the supraclinoid internal carotid arteries , the anterior cerebral artery (ACA) supplies the medial portion of the frontal and parietal lobes and anterior portions of basal ganglia and anterior internal capsule, the middle cerebral artery (MCA) supplies the lateral portions of the frontal and parietal lobes, as well as the anterior and lateral portions of the temporal lobes, and gives rise to perforating branches to the globus pallidus, putamen, and internal capsule, the (MCA) is the dominant source of vascular supply to the hemispheres, the posterior cerebral arteries arise from the basilar artery and carry the posterior circulation the posterior cerebral artery (PCA) gives rise to perforating branches that supply the thalami and brainstem and the cortical branches to the posterior and medial temporal lobes and occipital lobes (Nowinski, et al 2006).

The cerebellar hemispheres are supplied as follows: Inferiorly by the posterior inferior cerebellar artery (PICA), arising from the vertebral artery Superiorly by the superior cerebellar artery, anterolaterally by the anterior inferior cerebellar artery (AICA), from the basilar artery (Nowinski, et al 2006).

2.3 Pathophysiology:

Stroke is defined as an "acute neurologic dysfunction of vascular origin with sudden (within seconds) or at least rapid (within hours) occurrence of symptoms and signs corresponding to the involvement of focal areas in the brain" (Goldstein, et al 1989).

The two main types of stroke are ischemic and hemorrhagic, accounting for approximately 85% and 15%, respectively (Wise, et al 1999).

When an ischemic stroke occurs, the blood supply to the brain is interrupted, and brain cells are deprived of the glucose and oxygen they need to function, ischemic stroke is a complex entity with multiple etiologies and variable clinical manifestations, approximately 45% of ischemic strokes are caused by small or large artery thrombus, 20% are embolic in origin, and others have an unknown cause (Wise, et al 1999).

Acute ischemic stroke (AIS) is characterized by the sudden loss of blood circulation to an area of the brain, typically in a vascular territory, resulting in a corresponding loss of neurologic function , also previously called cerebrovascular accident (CVA) or stroke syndrome, stroke is a nonspecific state of brain injury with neuronal dysfunction that has several pathophysiologic causes. Strokes can be divided into 2 types: hemorrhagic or ischemic , acute ischemic stroke is caused by thrombotic or embolic occlusion of a cerebral artery , thrombosis can form in the extra cranial and intracranial arteries when the intima is roughened and plaque forms along the injured vessel , the endothelial injury (roughing) permits platelets to adhere and aggregate, then coagulation is activated and thrombus develops at site of plaque , blood flow through the extra cranial and intracranial systems decreases, and the collateral circulation maintains function. When the compensatory mechanism of collateral circulation fails, perfusion is compromised, leading to decreased perfusion and cell death ,

during an embolic stroke, a clot travels from a distant source and lodges in cerebral vessels , micro emboli can break away from a sclerosed plaque in the carotid artery or from cardiac sources such as atrial fibrillation, patent foramen ovale, or a hypokinetic left ventricle , emboli in the form of blood, fat, or air can occur during surgical procedures, most commonly during cardiac surgery, but also after long bone surgeries, less common causes of ischemic stroke include carotid dissection (Heros ,R. et al 1994). And the presence of coagulopathies, such as those resulting from antiphospholipid antibodies, other causes include arteritis, infection, and drug abuse, such as the use of cocaine (Siesjo, 1989), while still not completely understood, the presence of periodontal disease and tooth loss is also an associated risk for ischemic stroke (Siesjo, 1981).

As a thrombosis or emboli cause a decrease in blood supply to the brain tissue, events occur at the cellular level, referred to as the ischemic cascade , neurons and support cells require a careful balance of variables such as temperature, pH, nutrition, and waste removal in their environment to function optimally, intensive basic scientific research during the last two decades has given healthcare professionals an increased understanding of the ischemic cascade in the format of the precise environmental alterations involved in the pathophysiology of ischemic injury at the cellular level , understanding the ischemic cascade has led to the concept of a therapeutic time window for treatment possibilities , often, there is a core region of dead cells surrounded by an area of hypoperfused tissue , the hypoperfused area may be rescued; this area is referred to as the penumbra region (Fuster , et al 1990).

Neuroprotection is a broad term that refers to pharmacological and no pharmacological treatments used to halt the cellular events in the ischemic cascade, forming the theoretical basis for many of the acute stroke therapies

under study, as well as the rationale for intervening within a therapeutic time window following ischemic stroke (Zivin, 1991).

2.4 Neuroimaging:

Neuroimaging in cerebral stroke is essential for establishment of an accurate diagnosis, characterization of disease progression, and monitoring of the response to interventions. MRI has demonstrably higher accuracy, carries fewer safety risks and provides a greater range of information's in brain tissue.

Neuroimaging plays a central role in the evaluation of patients with acute cerebral stroke with improved technology over the last decade, imaging now provides information beyond the mere presence or absence of intra cranial hemorrhage including tissue viability, site of occlusion, and collateral status. While computed tomography (CT) is the most widely available and faster imaging modality, some comprehensive stroke centers favor streamlined MR protocols over CT in the acute cerebral stroke setting due to the higher specificity and superior tissue characterization afforded by MRI.

Neuroimaging plays a critical role in early diagnosis and yields essential information regarding tissue integrity, a factor that remains a key therapeutic determinant. Given the widespread public health implications of stroke and central role of neuroimaging in overall management, acute cerebral stroke imaging remains a heavily debated, extensively researched, and rapidly evolving subject. There has been recent debate in the scientific community.

2.4.1Mri principles:

Magnetic resonance (MR) is based upon the interaction between an applied magnetic field and a nucleus that possesses spin. Nuclear spin or, more precisely, nuclear spin angular momentum, is one of several intrinsic properties of an atom and its value depends on the precise atomic composition. Every

element in the Periodic Table except argon and cerium has at least one naturally occurring isotope that possesses spin. Thus, in principle, nearly every element can be examined using MR, and the basic ideas of resonance absorption and relaxation are common to all of these elements. The precise details will vary from nucleus to nucleus and from system to system. Atoms consist of three fundamental particles: protons, which possess a positive charge; neutrons, which have no charge; and electrons, which have a negative charge. The protons and neutrons are located in the nucleus or core of an atom, whereas the electrons are located in shells orbital surrounding the nucleus (Robert, et al 1991).

The characteristic chemical reactions of elements depend upon the particular number of each of these particles. The properties most commonly used to categorize elements are the atomic number and the atomic weight. The atomic number is the number of protons in the nucleus, and is the primary index used to differentiate between atoms. All atoms of an element have the same atomic number. The atomic weight is the sum of the number of protons and the number of neutrons. Atoms with the same atomic number but different atomic weights are called isotopes (Debatin, et al 1998).

A third property of the nucleus is spin or intrinsic spin angular momentum, the nucleus can be considered to be constantly rotating about an axis at a constant rate or velocity (Nitz, 1999), this self-rotation axis is perpendicular to the direction of rotation, a limited number of values for the spin are found in nature; that is, the spin, I, is quantized to certain discrete values. These values depend on the atomic number and atomic weight of the particular nucleus There are three groups of values for I: zero, half-integral values, and integral values. A nucleus has no spin (I = 0) if it has an even number atomic weight and an even atomic number. Such a nucleus does not interact with an external magnetic field and cannot be studied using MR. A nucleus has an integral value for I (e.g., 1, 2,

3) if it has an even atomic weight and an odd atomic number. A nucleus has a half-integral value for I (e.g., 1/2, 3/2, 5/2) if it has an odd atomic weight, the 1H nucleus, consisting of a single proton, is a natural choice for probing the body using MR techniques for several reasons, it has a spin of ½ and is the most abundant isotope for hydrogen, its response to an applied magnetic field is one of the largest found in nature. Finally, the human body is composed of tissues that contain primarily water and fat, both of which contain hydrogen (Nitz, 2002).

In general, MR measurements are made on collections of similar spins rather than on an individual spin. It is useful to consider such a collection both as individual spins acting independently (a "microscopic" picture) and as a single entity (a "macroscopic" picture). For many concepts, the two pictures provide equivalent results, even though the microscopic picture is more complete. Conversion between the two pictures requires the principles of statistical mechanics, the macroscopic picture is sufficient for an adequate description. When necessary, the microscopic picture will be used (Mezrich, 1995).

Measurement techniques can be divided into 2D and 3D categories based on the volume of excited tissue that is used to generate the signal. The most common technique is 2D-multislice imaging, in which a narrow volume of tissue (typically < 10 mm) is excited by a slice-selective RF pulse and generates the echo signal (Shaw and Derek. 1984).

2.4.2MRI limitations and contraindications:

MRI has some limitations, such as high cost, long scanning duration, and relative contraindications for MRI include the following: Metallic implants, Claustrophobia, Pacemakers ,MR-incompatible prosthetic heart valves, Contrast allergy ,Patients with metallic implants may have a variety of potential complications, such as heating and pacemaker malfunction and its consequences

, for patients with a metallic implant, checking with the manufacturer regarding its MR compatibility is advisable if such information is not available elsewhere. Claustrophobic patients may be unable to complete the sequence of MRI, in selected patients, mild sedation or imaging in an open MR system may be attempted, however, most open MR scanners provide lesser-quality images. Rarely, patients may be allergic to the contrast agent (e.g., gadolinium) used in MRI, in the presence of any of these contraindications, a regular radiograph may be indicated (Young, 2000).

2.4.3 MRI in stroke diagnosis:

Brain imaging provides an objective basis for the clinical inferences that direct individual patient management in the acute stroke setting. A brain MRI scan is required for all patients with suspected stroke or transient ischemic attack. Thrombolytic therapy is arguably the most important aspect of acute stroke management; however, most decisions in acute stroke do not relate to this treatment. Stroke imaging must, therefore, provide information beyond the presence or absence of intracranial hemorrhage (ICH) and early evidence of a large infarct, gradient-recalled echo MRI show comparable accuracy in the diagnosis of acute ICH. Diffusion-weighted MRI is more sensitive than noncontrast CT for differentiation of acute ischemic stroke from nonstroke conditions. Combined multimodal parenchymal, perfusion and vascular imaging with CT or MRI have the potential to identify patients with an ischemic penumbra that might be appropriate for acute reperfusion therapies (Leys, et al 1992).

Today, CT remains the mainstay in evaluating acute stroke, although more and more sites are following CT with an MRI scan within the first day. CT can rapidly assess the presence of major intracranial hemorrhage and rule out giving tPA. However, CT fails to register smaller cerebral microbleeds (CMBs), an area

that MRI is able to investigate very well, especially with susceptibility-weighted imaging (SWI), (Ota, et al 2010), This could have important consequences for follow-up treatment with antiplatelet therapy. (Arenillas, et al 2011). There is much more to studying stroke than just seeing the embolus. One wants to know the changes in function and the hemodynamics of the tissue. This is where the ability to study magnetic resonance angiography (MRA), and perfusion and diffusion with MRI plays a key role. CT can also perform perfusion-weighted imaging (PWI), but still remains unable to compete with MRI when it comes to studying CMBs and diffusion (Elnekeidy, et al 2014). In fact, one of the critical elements in determining what tissue may still be viable lies in the concept of the diffusion/perfusion mismatch. There is evidence here that a larger perfusion abnormality relative to a diffusion-weighted imaging (DWI) abnormality is a marker of viable or penumbral tissue. This can affect the decision for treatment, with the mismatch indicating a higher chance of tissue recovery and perhaps extending the window of treatment for the patient (Neumann, et al 1999).

Magnetic resonance imaging (MRI) is increasingly being used in the diagnosis and management of cerebral stroke and is sensitive and relatively specific in detecting changes that occur after such strokes, advances in MRI include higher strength of magnetic field (1.5-3.0 T field strength) yielding better resolution of images, newer sequences of images, and the advent of the open MRI for patients who are claustrophobic or overweight., inpatients may often continue to be monitored and receive treatment while undergoing MRI, because MRI-compatible electrocardiographic monitors, intravenous infusion pumps, and ventilators are available (Patel, et al 2001).

MRI has been increasingly used to characterize stroke injury in infarct age, volume and territory, clotted vascular structure, degree of hypoperfusion, cerebral metabolite, penumbra evolution, and viability of tissue at risk after stroke onset (Jacobs, et al 2001). As each MRI parameter can be associated with

one or multiple specific tissue structural or physiological properties, the combined usage and analysis of these complementary MRI parameters, or multiparameter MRI approach, can provide integrated and systematic information about the ischemic cascade after stroke insult. However, due to the intrinsic limitation of MRI techniques [each k-space line is usually acquired after every repetition time (TR)] and physiological limitations [rapidly switched gradients result in neuromuscular stimulation and excessive radio frequency (RF) pulses cause RF power over-exposure and tissue heating], one MRI measurement can take from minutes to hours to obtain optimal images. As speed is a critical consideration in acute stroke imaging, multiparameter MRI in clinic is usually conducted with only 2-3 MRI modalities [mostly diffusion- weighted imaging (DWI), perfusion MRI, and T2-weighted imaging (T2W)], limiting its effectiveness and application in acute stroke examination. The advent of parallel imaging with multichannel RF coils lead to a dramatic acceleration of imaging speed in conventional MRI scans, resulting in revolutionary advances in MRI techniques and increasing applications in the clinic and preclinical studies. Therefore, parallel imaging technique can provide an effective approach to facilitate multiparameter MRI studies in stroke disease (Sodickson, et al 2002)

The interest in MRI as a tool for acute cerebral stroke management lies not only in the capability of this technique to detect early ischemic and hemorrhagic with high sensitivity, but also in the breadth of the cerebrovascular pathology revealed by such imaging .MRI can delineate the presence, size, location, extent and effects of acute brain ischemia, identify the hypo perfused tissue that is at risk of infarction, and show additional features of the cerebrovascular pathology. MRI can also detect or exclude ICH with an accuracy comparable to CT. A full clinical stroke MRI study for acute stroke takes 15–20 min and is feasible even within a 3 hr thrombolysis time window. The additional diagnostic information obtained with MRI could result in improvements in patient outcomes and cost-

effectiveness. Several large stroke centers rely on MRI to screen patients for thrombolytic and other interventional treatments ((Patel, et al 2001).

When evaluating a patient with symptoms suggestive of stroke, the clinician must address several issues, notably whether the case represents an instance of acute cerebrovascular disease and, if so, whether the primary lesion is ischemic or hemorrhagic. The cause of the stroke must be ascertained, along with the nature of the vessel pathology, the pattern and extent of the damage, and the acute intervention that is indicated. In addition, the clinician must decide which secondary prevention therapy is appropriate, and evaluate the patient's prognosis. Brain imaging provides an objective basis for the clinical inferences that direct individual patient management. An accurate diagnosis will determine whether a patient is treated with thrombolytic or other acute interventions, is admitted to a stroke unit, and/or is started on secondary prevention therapies, an error in diagnosis could deprive the patient of effective interventions or unnecessarily expose the individual to potentially harmful treatments (Kucinski, et al 2003).

MRI identifies a broader range of acute and chronic cerebrovascular pathologies than does CT and, hence, could aid decisions about acute intervention, in-hospital management, and secondary prevention. Here, we present an overview of the diagnostic information that clinicians might gain from MRI in the setting of acute stroke (Wintermark, et al 2009).

2.4.4. Differential diagnosis:

- Both calcium and iron deposits may appear as small foci of low signal intensity on T2*-weighted MRI. These abnormalities are usually found bilaterally in the basal ganglia, although calcification can also occur in the choroid plexus, pineal gland, and lobar locations. CT can help identify suspected calcification, though its routine use is infrequent.(Cordonnier, et al 2007).

- Flow voids in pial blood vessels caught in cross-section in cortical sulci can be distinguished from CMB by their sulcal location, their equal visibility on T2- weighted SE and GRE sequences (as arterial flow voids do not generate a blooming effect), and their linear structure when examined over contiguous slices, particularly evident at smaller slice thickness. The presence of paramagnetic deoxyhemoglobin in cerebral venules produces its own blooming effect, however, requiring the reader to rely on their tubular structure for differentiating them from CMB .The distinction from flow voids can also be difficult when a CMB appears immediately adjacent to a small vessel, but is suggested by the lesion's termination as a blind end rather than continuing linearly as a vessel branch. (Cordonnier, et al 2007).

Partial volume artifact from bone (with associated susceptibility artifact from air in the sinuses) may obscure CMB or confuse their interpretation, especially in the temporal and frontal lobes because of the orbit and mastoid bones. (Cordonnier, et al 2007).

Cavernous malformations can be considered as a secondary cause of CMB (particularly the small “type IV” cavernous malformations), but are distinguishable from typical primary CMB by the appearance on both T1- and T2- weighted sequences of stagnant blood in the sinusoidal lumen, extravasated blood at varying stages of degradation and the characteristic hemosiderin rim. This CMB mimic can itself be mimicked by the “ringing artifact” seen on T2*-weighted MRI, representing increased signal within flow void. Ringing artifact is typically absent on T2-weighted SE MRI, highlighting the importance of incorporating SE in conjunction with T2*-weighted MRI. Metastatic melanoma in the brain can appear hypointense on T2*-weighted MRI, a result of both the presence of melanin and the tendency of these tumors to bleed. These lesions can often be distinguished from primary CMB by the concomitant presence of T1

hyperintensity (caused by the melanin) or of surrounding edema (particularly following recent intra-tumor hemorrhage), but small non-edematous lesions may mimic primary CMB. (Cordonnier, et al 2007).

- Diffuse axonal injury following head trauma is another potential secondary cause of CMB, distinguishable from primary CMB by the clinical history and concomitant imaging abnormalities. (Cordonnier, et al 2007).

MRI protocols are a combination of various MRI sequences, designed to optimally assess a particular region of the body and pathological process.

There are some general principles of protocol designed for each area. However, the specifics of a protocol are dependent on MRI hardware and software, radiologists and referrer's preference, patient factors (e.g. allergy) and time constraints.

The following MRI techniques are commonly used in brain imaging:

T1-weighted imaging (T1-WI) in which (CSF) has a low signal intensity in relation to brain tissue.

T2-weighted imaging (T2-WI) in which (CSF) has a high signal intensity in relation to brain tissue.

Spin density–weighted imaging in which CSF has a density similar to brain tissue.

Fluid Attenuation Inversion Recovery (FLAIR).

(DWI) in which the images reflect the microscopic random motion of water molecules.

(PWI) in which thermodynamically weighted MR sequences are based on passage of MR contrast through brain tissue.

2.4.5. T2* (GRE) Gradient Recalled Echo imaging principles:

T2* relaxation refers to decay of transverse magnetization caused by a combination of spin-spin relaxation and magnetic field inhomogeneity. T2* relaxation is seen only with gradient-echo (GRE) imaging because transverse relaxation caused by magnetic field inhomogeneities is eliminated by the 180° pulse at spin-echo imaging. T2* relaxation is one of the main determinants of image contrast with GRE sequences and forms the basis for many magnetic resonance (MR) applications, such as susceptibility-weighted (SW) imaging, perfusion MR imaging, and functional MR imaging. GRE sequences can be made predominantly T2* weighted by using a low flip angle, long echo time, and long repetition time. GRE sequences with T2*-based contrast are used to depict hemorrhage, calcification, and iron deposition in various tissues and lesions. SW imaging uses phase information in addition to T2*-based contrast to exploit the magnetic susceptibility differences of the blood and of iron and calcification in various tissues. Perfusion MR imaging exploits the signal intensity decrease that occurs with the passage of a high concentration of gadopentetate dimeglumine through the microvasculature. Change in oxygen saturation during specific tasks changes the local T2*, which leads to the blood oxygen level-dependent effect seen at functional MR imaging. The basics of T2* relaxation, T2*-weighted sequences, and their clinical applications are presented, followed by the principles, techniques, and clinical uses of four T2*-based applications, including SW imaging, perfusion MR imaging, functional MR imaging, and iron overload imaging. (Mugler, et al 2006).

Transverse magnetization is formed by tilting the longitudinal magnetization into the transverse plane by using a radiofrequency pulse. The transverse magnetization rotates in the transverse plane at the Larmor frequency and induces an MR signal in the radiofrequency coil. Immediately after its formation,

the transverse magnetization has a maximum magnitude, and all of the protons are in phase. The transverse magnetization starts decreasing in magnitude immediately as protons start going out of phase. This process of dephasing and reduction in the amount of transverse magnetization is called transverse relaxation. A characteristic time representing the decay of the signal by 1/e, or 37%, is called the T2 relaxation time 1/T2 is referred to as the transverse relaxation rate. (Mugler, et al 2006).

Transverse relaxation is the result of random interactions at the atomic and molecular levels Transverse relaxation is primarily related to the intrinsic field caused by adjacent protons (spins) and hence is called spin-spin relaxation. Transverse relaxation causes irreversible dephasing of the transverse magnetization .In GRE sequences, there is no 180° refocusing pulse, and these dephasing effects are not eliminated. Hence, transverse relaxation in GRE sequences (i.e., T2* relaxation) is a combination of "true" T2 relaxation and relaxation caused by magnetic field inhomogeneities. (Nitz, et al 1999).

2.4.6 MRI findings in acute stroke:

2.4.6.1 Acute phase (1-7 d):

In this phase, edema increases, maximizing at 48-72 hours, and MRI signals become more prominent and well demarcated. The ischemic area continues to appear as an area of hypo intensity on T1-WI and as a hyper intense area on T2-WI. In addition, the mass effect can be appreciated in this phase, in contrast-enhanced images, the arterial enhancement usually persists throughout the acute phase, while the parenchymal enhancement is usually appreciated at the end of this phase in complete infarction, in incomplete infarction, the parenchymal enhancement is usually earlier, during this period, reperfusion occurs and hemorrhages can be observed, typically 24-48 hours after the onset of the stroke, usually, hemorrhages cause the "fogging" phenomenon, due to hemoglobin

degradation products, that masks the infarction on T1-WI and T2-WI (Latchaw, et al 2009).

2.4.6.2 Sub-acute phase (7-21 d):

In this phase, the edema resolves and the mass effect becomes less appreciated; however, the infarcted areas still appear as a hypo intensity on T1-WI and as a hyper intensity on T2-WI, in contrast-enhanced images, the arterial enhancement is usually resolved by this time, and the parenchymal enhancement typically persists throughout this phase, the cortical parenchymal enhancement is usually in a gyri form pattern, while the sub cortical enhancement is usually a homogenous central pattern (Latchaw, et al 2009).

2.4.6.3 Chronic phase (>21 d):

In this phase, the edema completely resolves, and the infarcted area still appears as a hypo intensity on T1-WI and as a hyper intensity on T2-WI. Because of tissue loss in the infarcted area by this time, exvacuo ventricular enlargement and widening of the cortical gyri and fissures take place, in contrast-enhanced images, parenchymal enhancement typically also persists throughout this phase; it usually disappears by 3-4 months (Latchaw, et al 2009).

2.7 Previous studies:

In the study of (Viswanathan, et al 2006), Spontaneous ICH usually results in a focal neurologic deficit and is easily diagnosed by computed tomography (CT) scan. It is caused by arterial rupture, leads to hematoma formation in the lobar hemispheres or deep gray structures, and is associated with high mortality· (Woo, et al 2002), Cerebral microhemorrhages best visualized by MRI, result from rupture of small blood vessels in basal ganglia or subcortical white matter and are most often clinically asymptomatic,(Roob, et al 2000). Microhemorrhages were first described after the clinical use of GE MRI, and are usually defined as rounded foci of <5 mm in size that appear hypointense and distinct from vascular flow voids, leptomeningeal hemasiderosis, or non-hemorrhagic subcortical mineralization,(Greenberg, et al 2004). The reduction of the GE magnetic resonance (MR) signal is caused by hemosiderin, a blood breakdown product that causes magnetic susceptibility-induced relaxation leading to T2* signal loss. GE MR has a greater sensitivity for detection of hemosiderin deposits compared with conventional spin-echo MR sequences. (Atlas, et al 1988) Microhemorrhages appear larger on GE sequences compared with the actual tissue lesions because of the so-called "blooming effect" of the MR signal at the border of these lesions. (Alemany, et al 2004), (Ripoll, et al 2003) Because hemosidern remains in macro-phages for many years after hemorrhage,(Greenberg, and Roob, et al 2000) GE sequences allow for reliable assessment of an individual's recent and past hemorrhages. Although only a few studies relating these MR findings to tissue pathology have been published,(Ripoll, M.A et al 2003); all have demon¬strated that these areas of GE hypointensity correlate well with brain parenchymal areas of hemosiderin-laden macrophages. demonstrated that hypointense lesions seen on GE MRI were associated with rupture of vessels <200)mm in diameter and perivascular hemosiderin deposition in 3 cases.13 In 7 patients who died of ICH, histo

pathological examination revealed focal hemosiderin deposits in 21 of 34 hypointense areas seen on GE MRI. In all brains, cerebral vessels showed evidence of moderate to severe fibrohyalinosis. Two patients showed evidence of cerebral amyloid angiopathy (CAA). These pathologic data suggest that cerebral microhemorrhage results from underlying small vessel pathologies such as hypertensive vasculopathy(Fisher, 1971).

In the study of (Idicula, et al 2008). Showed the Effect of Physiologic Derangement in Patients with Stroke Treated with Thrombolysis, from 1998 to 2006, prospectively studied 127 patients who received intravenous thrombolysis for acute stroke. Following parameters were measured both before and after thrombolysis: body temperature, blood glucose and blood pressure. Stroke outcome was measured with mRS 3 months after the index stroke. The mean body temperature before and after thrombolysis were 36.5±0.660 C and 36.6± 0.790 C respectively. Body temperature before thrombolysis was not associated with outcome whereas high body temperature after thromlysis was associated with poor outcome (OR 0.79, p= 0.5; OR 2.84, p= 0.01). Diastolic blood pressure both before and after thrombolysis was not associated with outcome .In ischemic stroke patients, frequent monitoring of body temperature and blood glucose and the appropriate treatment of it, if elevated, are important during the phase following thrombolysis. However in the hyper acute phase, before thrombolysis, reduction of high systolic BP is important.

Another study of (Chelsea, et al 2014) had Prior study demonstrated that clinically silent microbleeds occur in up to 6% of healthy elderly subjects and 26% of patients with prior ischemic stroke. These microbleeds are most commonly caused by hypertension, cerebral amyloid angiopathy, or other causes of small vessel vasculopathy.

New MRI sequences, particularly T2*-weighted GRE and EPI-SWI, are highly accurate in the detection of prior microbleeds or petechial hemorrhages .These

sequences detect the paramagnetic effects of blood-breakdown products (deoxyhemoglobin, ferritin, and hemosiderin), which lead to a loss of signal on T2*-weighted sequences. We present a case of HT at the site of an old microbleed that was remote from the acute ischemic field in a patient receiving thrombolytic therapy, and analyze the prevalence of microbleeds in our series of patients undergoing pretreatment MR imaging and receiving intra-arterial thrombolysis, A total of 41 patients were studied with GRE (7 patients) or EPI-SWI MRI (all 41 patients) sequences before receiving intra-arterial thrombolytics. Pretreatment MRIs revealed evidence of old silent microbleeds in 5 cases (12%). Of the 5microbleed, 1 patient had evidence of 2 microbleeds, and 1patient had evidence of 12 microbleeds .There was no difference in microbleed detection rate between GRE and SWI sequences in the 7 patients who underwent both types of scans. There was no difference in baseline characteristics between patients with old microbleeds versus those without, including age, history of hypertension, diabetes, hypercholesterolemia, tobacco use, and severity of pretreatment neurologic deficit. One patient with a prior microbleed evident on the pretreatment MRI sequences but not on the pretreatment head CT scan experienced a symptomatic hemorrhage at the site of the microbleed and remote from the acute ischemic field, GRE MRI sequences detect the paramagnetic effect of blood-breakdown products, allowing visualization of clinically silent microbleeds that, often, cannot be detected with head CT. (Fazek, et al 2000) performed a histopathologic analysis of small regions of signal loss visualized on GRE MRI sequences and confirmed that these regions indicate previous extravasation of blood and are related to bleeding-prone microangiopathy. This study demonstrated that cerebral microbleeds represent collections of hemosiderin-laden macrophages that occur adjacent to small vessels. These microbleeds are most commonly associated with microangiopathy due to hypertension, cerebral amyloid angiopathy, or prior ischemic injury, and are

presumably due to weakening of the vessel walls. In hypertension, progressive lipohyalinosis and fibrinoid degeneration occur, often associated with microaneurysm formation. In cerebral amyloid angiopathy, progressive deposition of amyloid within the vessel wall leads to fibrinoid necrosis. The development of MRI sequences that are highly sensitive to the detection of blood-breakdown products has led to a growing number of studies characterizing the occurrence of microbleeds in various populations. These studies have demonstrated that MRI evidence of microbleeds is seen in 38% to 66% of patients with primary intracerebral hemorrhages, in 21% to 26% of patients with ischemic stroke, and in 5% to 6% of asymptomatic or healthy elderly individuals. In their study of patients with a history of atherosclerosis.

CHAPTER THREE

Materials and Methods

3.1 Materials:

3.1.1 Patients (study sample):

This is a practical study carried out during period from April 2016 to June 2019 and was conducted on 200 patients (male 94, female 106) with average age 47, rang from (17- 84) whom referred to the radiology department in modern medical centers in Khartoum with a known and suspected case of cerebral stroke, undergone MRI examination, to evaluate each type of stroke and their locations, and to provide additional information's to support cerebral stroke diagnosis within the narrow time window for thrombolytic therapy, by modified T2* Gradient-Echo .echo planar imaging, child's and patients with brain tumor excluded from the study, the data collected and interpreted by radiologist reports.

3.1.2 MRI scanner used:

The MRI scanner used in this study was PHILIPS (1.5tesla), Toshiba (1.5tesla) with 8-channel phased array neurovascular coil.

3.1.3 Technique used:

All patients were scanned in the supine position in the MRI scanner and their heads were placed within an 8-channel phased array neurovascular coil Whole brain was scanned

The following MRI technique was used:

Whole brain was scanned with a slice thickness of 5 mm and a 1.5 mm interslice gap, producing 19 axial images. The imaging protocol consisted of T1-weighted spin echo (TR/ TE_530/15 ms), T2-weighted fast-spin echo (TR/TE_5000/120). Fluid-attenuated inversion recovery (FLAIR) (TR/TE_9000/105 ms, inversion time 2500 ms) and diffusion-weighted imaging (TR/TE_5000/135 ms).

Table (3-1) the modified sequence parameters for T2*

T2* (GRE) GRADIENT ECHO IMAGING (MODIFIED):

Gradient-Echo .echo planar imaging T2* at 1.5T	
Image acquisition parameters	
TR	800 ms
TE	26 ms
Flip angle	18° to 20°
Image acquisition time	46 seconds
Coverage area	Whole brain coverage using 22 slices
Slice thickness	4 mm
Slice Gap	1.2 mm
FOV	220 ×220 mm ≈ 24 cm
In-plane voxel size	1.1×0.9
Number of scan average	2
Slice orientation	axial

With the advent of modern MRI imaging techniques, cerebral microhemorrhages have been increasingly recognized on gradient-echo (GE) or T2*-weighted MRI sequences in different populations. However, in clinical practice, their diagnostic value, associated risk, and prognostic significance are often unclear.

The hemosiderin deposits that comprise CMB are superparamagnetic and thus have considerable internal magnetization when brought into the magnetic field of MRI, a property defined as magnetic susceptibility. Internal magnetization generates local inhomogeneity in the magnetic field surrounding the CMB, leading to faster decay of the local MRI signal, designated the susceptibility effect. On MRI sequences that are particularly sensitive to susceptibility effects, CMB will appear as black or hypointense lesions (signal voids).The MRI parameters of greatest influence on CMB detection are pulse sequence, sequence parameters, spatial resolution, magnetic field strength, and post-processing. The potential effect of these factors on microbleed conspicuity and detection is

discussed below. Among available pulse sequences, T2*-weighted gradient-recalled echo (GRE) MRI lacking the 180° refocusing pulse characteristic of spin-echo (SE) or fast-spin echo techniques is highly sensitive to the susceptibility effect. T2*-weighted GRE sequences tailored to image susceptibility effects are thus substantially more sensitive to CMB than T2-weighted SE and DWI sequences. The areas of low intensity that appear on T2*-weighted MRI are larger than the corresponding hemosiderin deposits, representing the so-called "blooming" effect). It is important to note that because extent of blooming varies with MRI parameters, the size of the measured signal void will depend on factors beyond the size of the corresponding histopathological CMB. Echo-planar GRE imaging, in which an entire image is obtained from a single radiofrequency pulse excitation, can potentially lead to ultrafast acquisition with comparable CMB conspicuity, but possibly at the cost of increased artifact and distortion.

The sequence parameter that particularly affects sensitivity to magnetic susceptibility in T2*-weighted MRI is echo time (TE). TEs of 26 ms have generally been applied, with longer TEs allowing more time for dephasing and consequently enlarging the susceptibility effect. Use of longer TE can lead to a trade-off in image quality, however, because of decay of transverse magnetization. Higher spatial resolution (in particular the use of thinner scanning sections) offers the possibility of minimizing the partial-volume averaging that might interfere with CMB detection. Using a two-dimensional (2D) Fourier transform technique in T2*-weighted MRI allows acquisition of thin image slices at high signal to noise ratio, (voxel size of 1.1 x 0.9 mm) and thinner slices (4 mm) was shown to detect more CMB. The longer scan times associated with scanning at small voxel sizes in 2D T2*-weighted MRI can be reduced to acceptable limits through acceleration by parallel imaging and number of scan

average (2) ,so the whole brain can be scanned with modified T2* in approximately (46 seconds).

3.1.4 Images interpretation:

All MRI images were studied for signal intensities in different weighted images and to differentiate between types of stroke (ischemic and hemorrhagic), size and locations and radiologist reports was considered.

3.1.5 Study area:

Alamal National Hospital, Diagnostic Center, Khartoum, Sudan.

3.1.6 Type of study:

Prospective and Practical study.

3.1.7 Data collection:

Data collected from findings which appear in different MRI cuts and the data represented in tables and graphs.

The data included the general patients data (Age and genders) and accompanied by the related to Symptoms and clinical information such as clinical signs (A numb or weak feeling in the face, arm or leg, trouble speaking or understanding ,unexplained dizziness, blurred or poor vision in one or both eyes, loss of balance or an unexplained fall, , headache (usually severe or of abrupt onset) or unexplained change in the pattern of headaches, confusion), the risk factors and patients history (hypertension, D.M , heart disease).

3.1.8 Data analysis:

All data wered entered and analysed using Microsoft Excel and statistical analysis soft wered statistical package for social sciences(SPSS) version 22 statistical analysis included description statistic of frequency tables, graphs, cross tabulation to compare the variables, the difference was considered significant when p-value is less or equal 0.05**.**

CHAPTER FOUR

Results

In the present study, a total number of 200 patients with stroke were studied to evaluate the modified MRI protocol in Diagnosis of Acute Cerebral Stroke.

Variables	Min	Max	Mean	Std. D
age	17	84	47.82	18.108

Table (4.1) The appearance of cerebral micro bleeding on conventional MRI brain protocol and modified T2* Sequences (as gold standard)

Pulse Sequences	Patients number	appearance of micro bleeding Hemorrhage
T1	200	no
T2	200	no
T2 FLAIR	200	no
DWI	200	no
T2*	200	yes

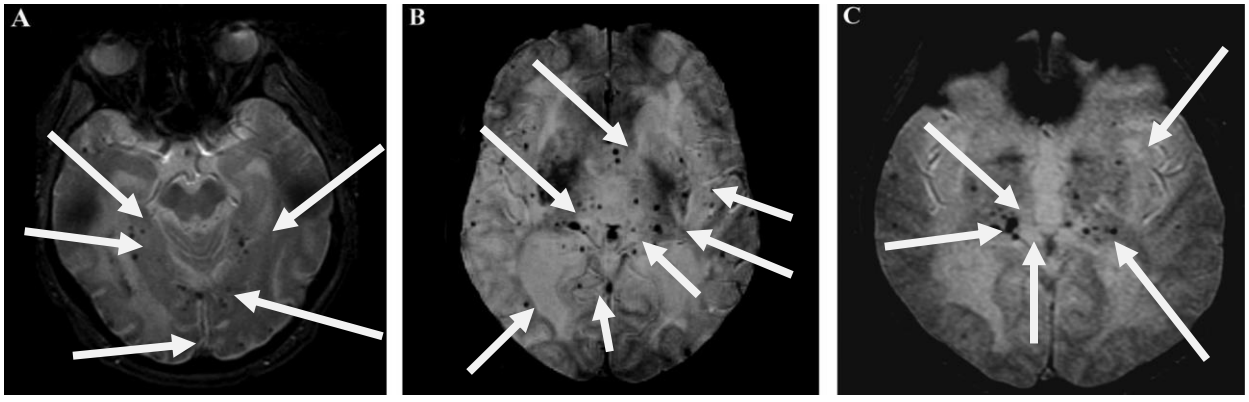

Figure (4.1): A female of 52 years old with long-standing history of hypertension, axial T2* demonstrating cerebral microhemorrhages(small black dots) seen in the temporal, occipital lobes and thalamus.

Table (4.2) The frequency and percentage of Stroke patient's according to the age.

age	Frequency	Percent
17-25.3	28	14.0%
25.4-33.7	30	15.0%
33.8-42.1	29	14.5%
42.2-50.5	24	12.0%
50.6-58.9	21	10.5%
59-67.3	31	15.5%
67.4-75.7	28	14.0%
75.8-84.1	9	4.5%
Total	200	100%

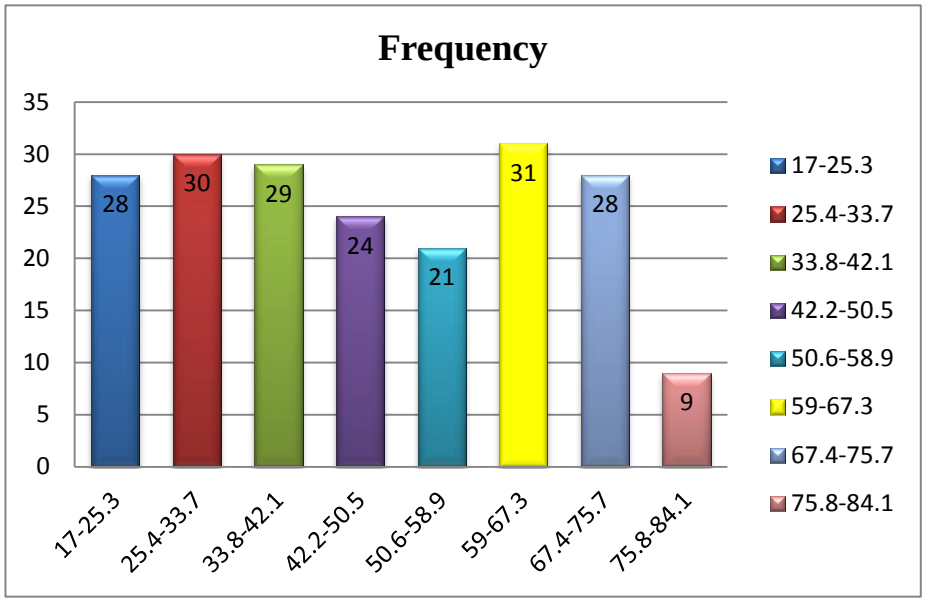

Figure (4.2.1) Represents the frequency of Stroke patient's according to the age.

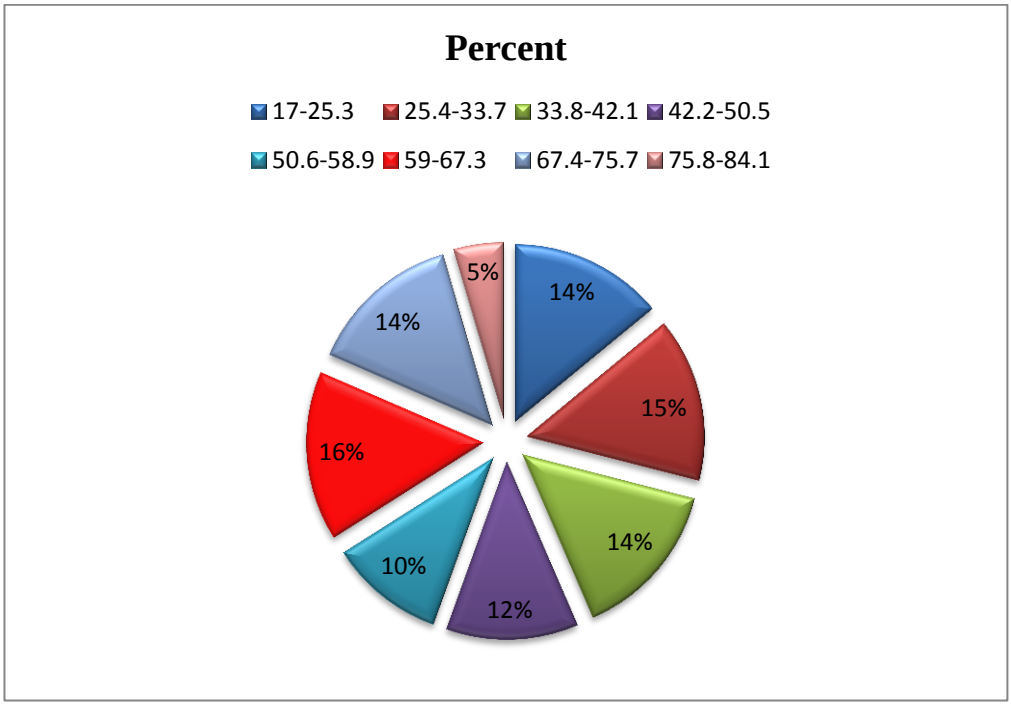

Figure (4.2.2) Represents the percentage of Stroke patient's according to the age.

Table (4.3) The frequency of Stroke patient's according to the gender.

Gender	Frequency	Percent
Male	94	47.0%
female	106	53.0%
Total	200	100%

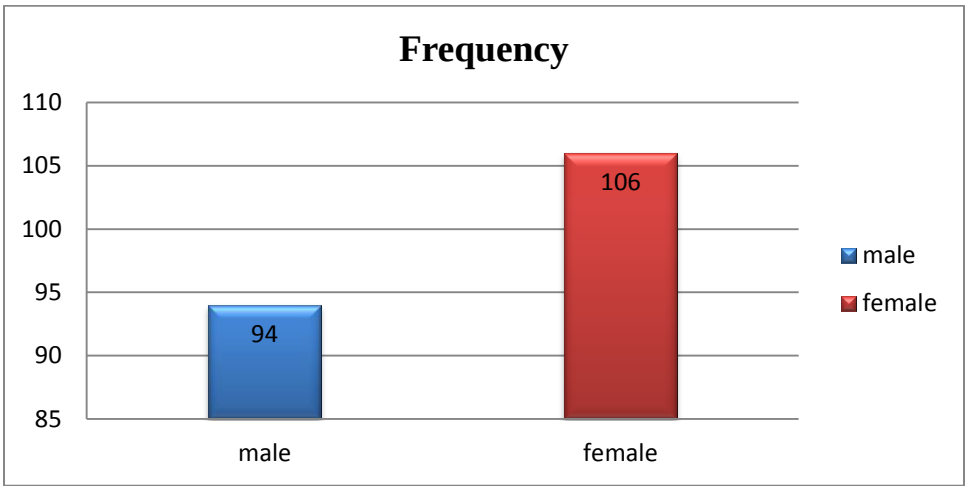

Figure (4.3.1) Represents the frequency of Stroke patient's according to the gender.

Table (4.4) The Frequency and percentage of Stroke patient's according to the final diagnosis.

Final diagnosis	Frequency	Percent
Ischemic	94	47.0%
Hemorrhagic	64	32.0%
ischemic and hemorrhagic	42	21.0%
Total	200	100%

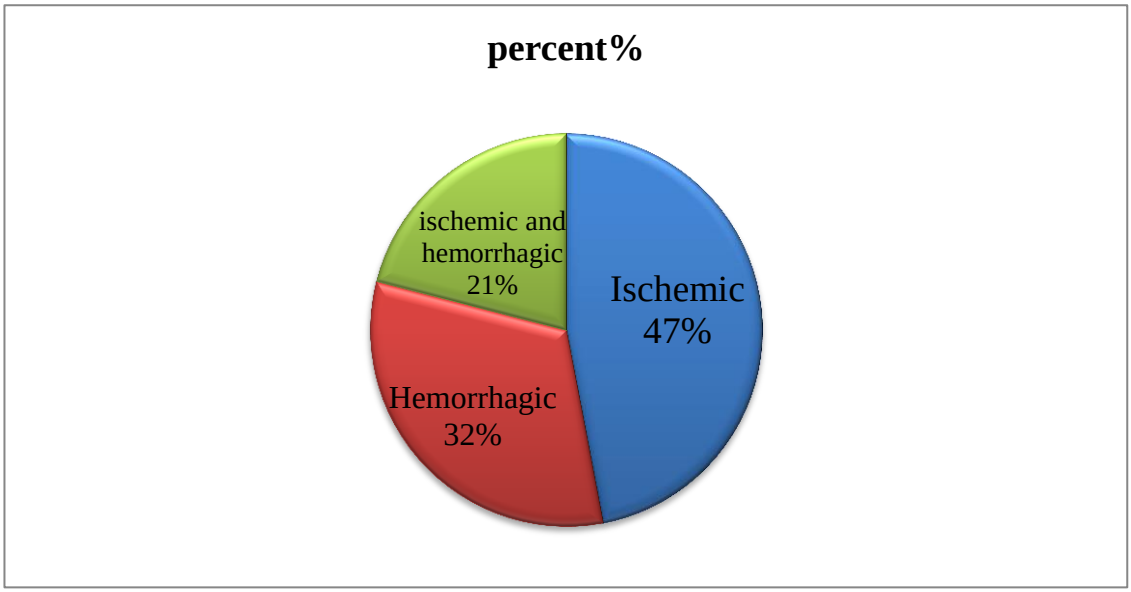

Figure (4.4.1) Represents the percentage of Stroke patient's according to the final diagnosis

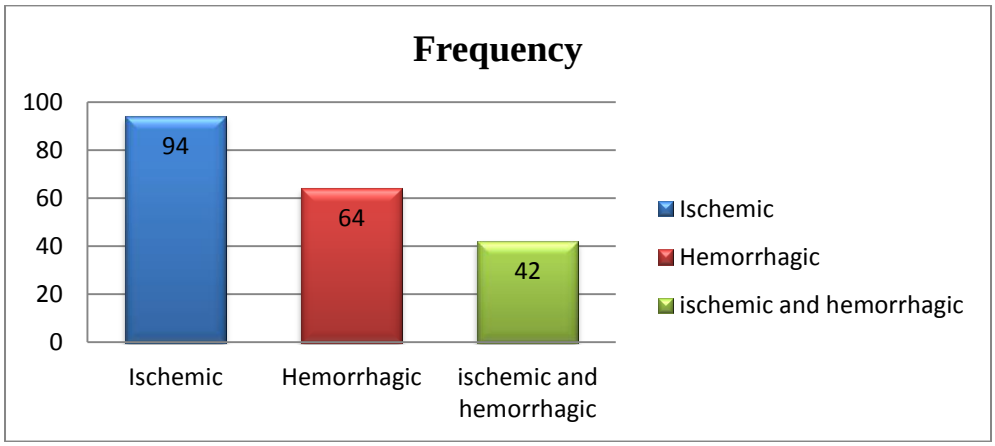

Figure (4.4.2) Represents the frequncy of Stroke patient's according to the final diagnosis

Table (4.5) The frequency and percentage of stroke in left and right side.

Side of stroke	Frequency	Percent%
RT side	23	11.5%
LT side	52	26%
Distributed	125	62.5%
Total	200	100.0%

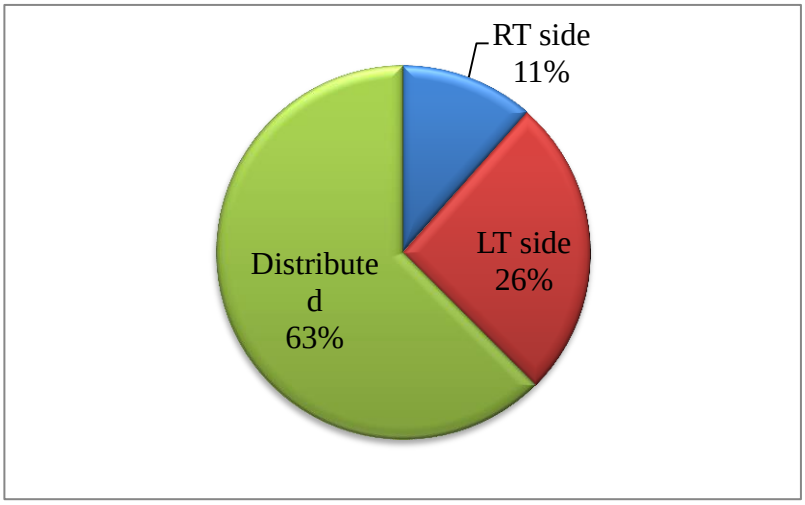

Figure (4.5.1) Represents the percentage of stroke in left and right side.

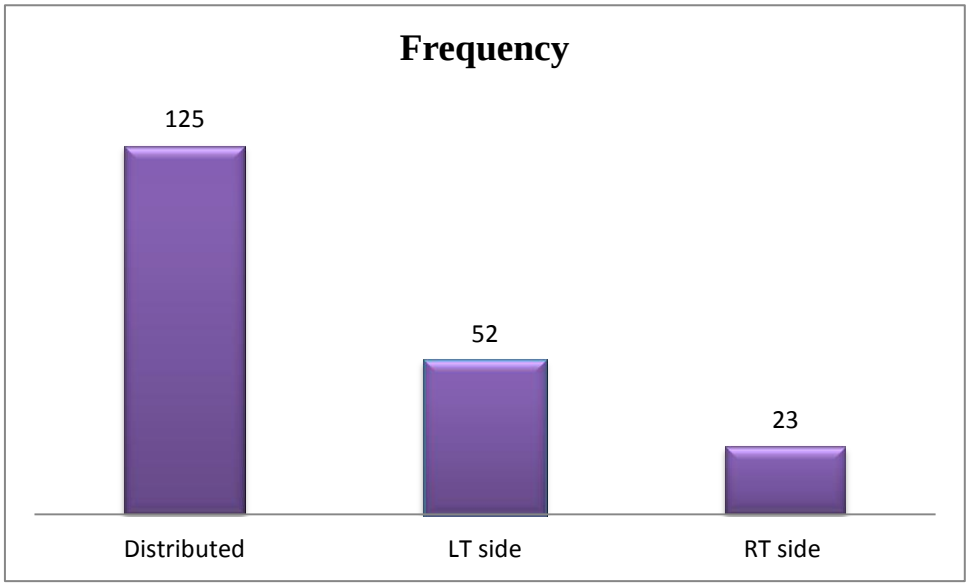

Figure (4.5.2) Represents the frequency of stroke in left and right side.

CHAPTER FIVE

5.1 Discussion:

With the development of brain imaging techniques, the diagnosis of acute cerebral stroke is no longer difficult in recent years; it is possible to diagnose an imaging positive ischemic stroke even if no symptoms are observed. However, some patients do not have any DWI abnormalities despite their acute symptoms. CMBs, generally considered asymptomatic, have been found to be a diagnostic cause of stroke symptoms. However, these CMBs may be observed in suspected stroke patients, it is difficult to establish a direct association between CMBs and acute stroke symptoms without the brain images immediately before the symptom onset.

In this study we described our modified MRI protocol (GRE T2*) sequence for acute cerebral stroke that obtained in approximately 46 sec rivaling that of any comprehensive acute cerebral stroke and cerebral micro bleeding. This study shows a high frequency and multiplicity of homogenous rounded foci of prominent signal loss by this modified GRE T2*-weighted image on brain MRI protocol.

Cerebral stroke bleeding can be a devastating complication of ischemic stroke and the main adverse effect of thrombolytic treatment. Conventional MRI often fails to detect Cerebral Bleeding at the early stage of stroke. New MRI techniques provide critical information in detecting cerebral bleeding. as blood extravasates in the tissue, the hemoglobin molecule becomes deoxygenated. Deoxyhemoglobin thereby produces a nonuniform magnetic field that results in rapid dephasing of proton spins in T2- and more so in GRE T2*-weighted images. To the best of our knowledge, this study is the earliest evaluation of Cerebral Bleeding with GRE T2*-weighted imaging in stroke patients. Our results confirm the usefulness of modified GRE T2*-weighted gradient-echo sequence in detecting early hemorrhage transformation as part of a multimodal stroke MRI protocol.

The preliminary investigations obtained from this study revealed that the stroke patient's participated in this study, patients with old ages more affected than younger patient's, and this because Brain microvasculature is potentially weakened by such factors as increasing age, sustained exposure to elevated blood pressure, hyperglycemia, and amyloid or fibrohyalinosis degeneration of brain blood vessels ,this remarks are reported by (Adams, et al 2007), who postulated that the risk of stroke rises significantly with age. After 55years, it more than doubles with each passing decade. Each year, about 1 percent of people between ages 65 and 74 have a stroke and 5 to 8 percent of people in that age group who have had a TIA go on to stroke. Although risk associated with advancing age cannot be changed, it is an important factor in assessing stroke risk and planning preventive therapies.

The preliminary investigations obtained from this study revealed that the patients participated in this study, female's was being more affected than male's in regards with stroke disease, as study including 94 males(47%) and 106 females (53%) ,and this may due to many Biological Differences between males and females ,like pregnancy, hormone levels change and blood pressure can rise. As a result, stroke risk is higher in pregnant women than in non-pregnant women, although the risk is relatively low in both cohorts. Specifically, about 3 in 10,000 pregnant women have a stroke during pregnancy compared to 2 in 10,000 who are not pregnant. The risk of stroke is elevated during the last three months of pregnancy and in the six weeks following labour (American Heart Association. 2014). Women have a higher risk of stroke; also agree with (David, 2011). Who reported that in his pooled analysis of acute ischemic stroke, Stroke has a greater effect on women than men because women have more events and are less likely to recover, this retrospective results was Agree with hypothesis of study ,but disagree with study reported by (Kajstra, et al 1996), who postulated that the risk of stroke rises in males than females, among 1,110 patients, including 615 men and 505 women, a normal or near normal outcome at 90 days was found in 37.1% of men's vs. 36.0% of women's.

In this study the result of final diagnosis in stroke patients, revealed that the percentage of ischemia was more frequently than hemorrhage in the sample of study, where the ischemic was 47% and hemorrhage was 32% ischemic and hemorrhagic was 21%.

The results from this study was revealed that the stroke distribution in Preiventricular region was more frequent (27% and frequency 55) than other brain regions.

The preliminary investigations obtained from this study revealed that there was difference between the hemispheres , Left hemispheric strokes frequent was 52,(26%) whereas right hemispheric strokes frequent was 23 (11%) ,there was more high incidence of stroke in left side than right side. This is mainly due to the higher incidence of LH large vessel strokes in the middle cerebral artery (MCA) the incidence of large vessel ischemic strokes is higher in the left middle cerebral artery distribution, contributing to these hemispheric differences. Based on anatomical cerebral blood circulation, the middle cerebral artery (MCA) is the most common artery involved in stroke. It supplies a large area of the lateral surface of the brain and part of the basal ganglia and the internal capsule via four segments (M1, M2, M3, and M4). The M1 (horizontal) segment supplies the basal ganglia, which is involved in motor control, motor learning, executive function, and emotions, the M2 (Sylvian) segment supplies the insula, superior temporal lobe, the M3 parietal lobe, and the M4 inferolateral frontal lobe (Cereda, 2012).

5.2 Conclusion:

Cerebral stroke triggers an extremely complex set of pathophysiologic events. MRI provides information on almost all the elements taking part in this setting, from cerebral tissue itself to blood vessels and blood flow dynamics, and helps us to get a grasp of this dynamic process. The development of tissue and clinical-based prediction models relying on MRI not only provide the clinician with prognostic data, but also helps in optimizing patient selection of stroke therapies. The automated lesion- outlining and volume calculation software currently present in some clinical workstations is a major step forward in individualization of stroke care. However, despite its advantages, MRI by itself cannot supply all the information needed to make accurate predictions, and ideal prognostic models should consist of a combination of clinical and imaging data.

MRI allows accurate diagnosis of the infarct lesion, detection of cerebral arterial occlusion or significant stenosis with evaluation of actual collateral flow and may also display certain reversible ischemic changes. However, the main objective for MRI still remains: improvement of non-invasive rapid and accurate identification of brain tissue at risk for infarction, which may be salvaged by safe and effective reperfusion therapy.

MRI is better for detection of acute ischemia, and can detect acute and chronic hemorrhage; therefore it should be the preferred test for accurate diagnosis of patients with suspected acute stroke.

Conventional MRI can diagnose cerebral stroke at all stages of temporal evolution but are not most sensitive after the hyper acute stage. During the hyper acute stage, the predominant findings are loss of flow voids on T2-weighted images, FLAIR hyper intensity in affected vessels, DWI, and vascular enhancement.

Gradient-echo T2*-weighted MRI is uniquely sensitive to detect silent, old hemosiderin deposits, Therefore, we investigated the incidence and the number of

micro bleeds among different stroke subtypes and the correlation with stroke recurrence.

The detection of hyper acute stroke, and micro bleeding requires the use of a T2* GRE sequence since other conventional MRI sequences are not sensitive enough for acute cerebral bleeding.

5.3 Recommendations:

Acute cerebral stroke is a heterogeneous disease, the primary role of imaging is to identify these patients rapidly and accurately. MRI is particularly powerful in depicting the most important relevant physiology in acute cerebral stroke, the occlusion site and the size of the infarct core. Patient outcomes are related to the severity of the symptoms, the site of occlusion, and size of the core of the infarct at the time of presentation, and the success of the treatment.

1- MRI Brain imaging should be performed immediately for people with acute cerebral stroke if any of the following apply: indications for thrombolysis or early anticoagulation treatment on anticoagulant treatment a known bleeding tendency, unexplained progressive or fluctuating symptoms, neck stiffness or fever, severe headache at onset of stroke symptoms.

2- For all people with acute cerebral stroke without indications for immediate MRI brain imaging, scanning should be performed as soon as possible (at most within 6 hours of admission).

Patients with suspected stroke should be assessed for thrombolysis, receiving it if clinically indicated and be admitted directly to a specialist acute stroke unit.

3- Any patient, regardless of age or stroke severity, where treatment can be started within 3 hours of known symptom onset and who has been shown not to have an intracerebral hemorrhage or other contraindications should be considered for treatment using alteplase. Between 3 and 4.5 hours of known stroke symptom onset.

4- Due to the increased detection of microbleeds, we recommend T2* GRE as the sequence of choice in microbleed detection. Microbleeds and their association with clinical parameters are robust to the effects of varying MR imaging sequences, suggesting that comparison of results across studies is possible.

5- Cerebral microbleeds appear to be a well-defined pathological lesion detectable by T2*-weighted MRI techniques with high sensitivity (particularly using newer MRI methods), high reliability (with careful image interpretation and consideration of

CMB mimics), and high specificity (demonstrated for conventional T2*-weighted MRI, still to be established for the newer methods). The full brain coverage afforded by MRI likely renders neuroimaging a more sensitive method for CMB detection than practical histopathologic techniques.

6- Choice of T2*-weighted MRI methods (including sequence parameters, spatial resolution, field strength, and post-processing) has large effects on the prevalence and number of detected CMB and thus on overall study sensitivity. Although it is premature to specify a standard sequence for all future studies, such a standard will evolve over the coming years and will likely include thin imaging slices. The process of reaching a common standard will be accelerated by further side-by-side comparisons of individual subjects with CMB imaged using varying MRI methods.

7- All studies of CMB should specify the above imaging parameters and should follow systematic rules or standardized rating instruments for excluding CMB mimics. These factors should presumably be held constant in longitudinal studies aiming for repeated measurements. Choice of precise size parameters for CMB does not appear to have major effects on their detection.

8- CMB is infrequent but not rare in the patients with acute stroke symptoms. Perihematomal edema around an acute CMB can cause a hyperintense rim on DWI. Our results suggest that a combination of DWI and GRE imaging can help diagnose acute symptomatic CMBs.

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APPENDIXS (A)

Sudan University of Science and Technology
College of Graduate Studies

Evaluation Of Modified MRI protocol in Diagnosis of Acute Cerebral Stroke Among Sudanese

تقويم بروتوكول التصوير بالرنين المغناطيسي المعدل في تشخيص
السكتة الدماغية الحادة لدي السودانيين

APPENDIXS (**B**)

IMAGES

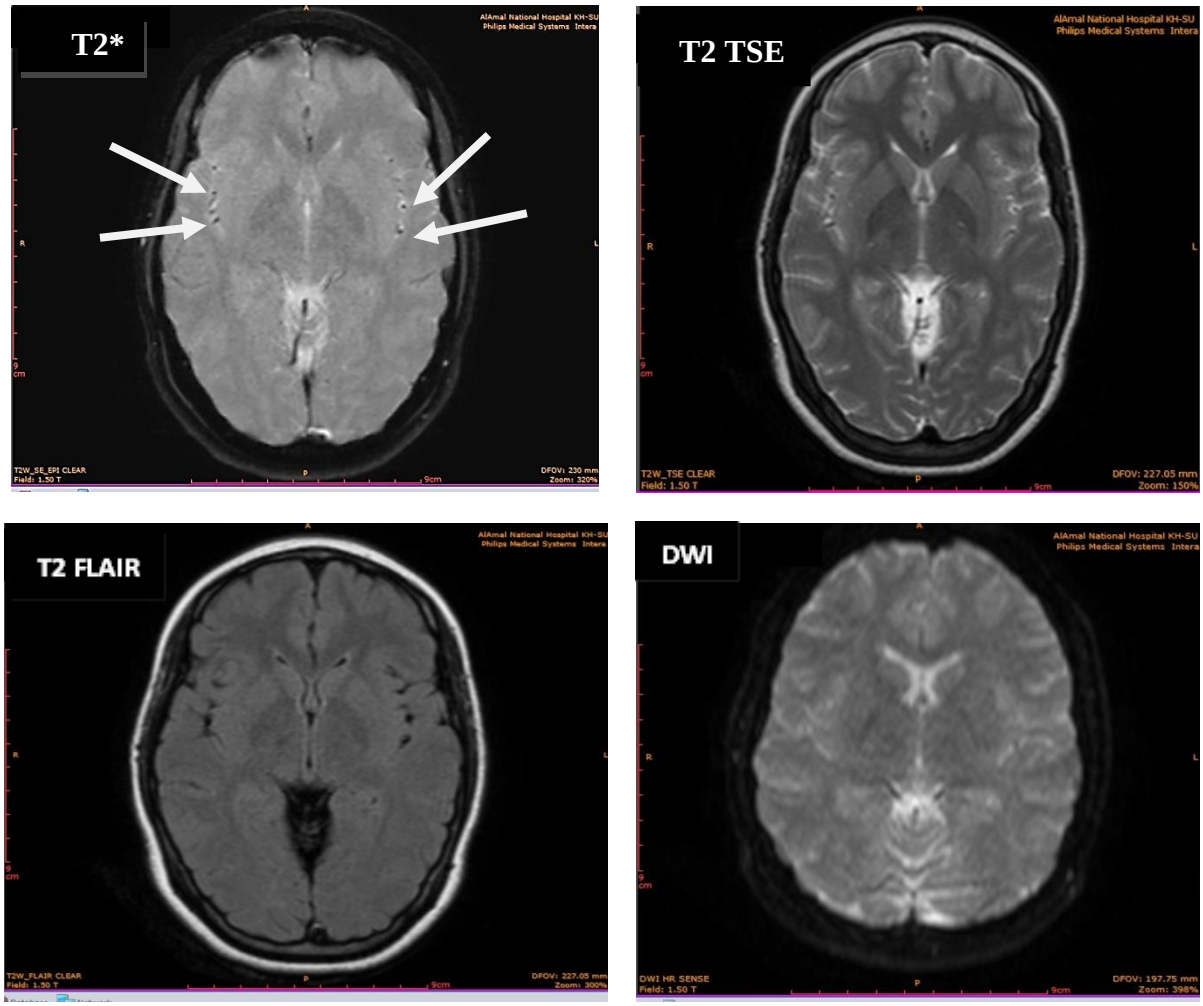

Figure 1: axial images, T2-weighted fast-spin echo MRI and, FLAIR ,DWI and T2*- Weighted gradient echo MRI of a female of 42 years Old intracerebral hemorrhages were seen bilaterally, multiple small areas of signal loss (microbleeds) were observed on T2*- Weighted MRI The microbleeds were hardly visible on other sequences.