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Comprehensive Study Of Stroke And Hemorrhage In Humans And Greyhounds

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Abstract
Introduction:
In today's world, as we move forward; there are a lot of issues related to blood and the circulatory system of the body. Predominately because of heart related issues. But an increasing trend now as due to undulant and sedentary life style, which causes increased consumption of fast food.
In this paper we will be understanding what and how blood related issues can be fatal. We will be learning about stroke and hemorrhage; predominantly because there are highly increasing cases of these and also due to the lack of knowledge of "what" is a stroke and how it can be prevented and "why" it should be prevented.
Objective:
India has been a free country for more than 78 years, and a society that promotes education. However, still there is lack of knowledge about our own body and the circulatory system, which tends to show us that we are lack in the field of spreading awareness.
This paper will be aimed at creating awareness about what stroke and hemorrhage is, its various types, its environmental various other predisposition, in what circumstances are they prevalent, help in understanding the epidemiology of the disease and in which age group they are more prevalent.
We will also be doing a comparative study of stroke and hemorrhage between humans and greyhound, which is a breed of dog that shows the most cases of hemorrhage and stroke in animals.
This study is done to show that it is not only limited to humans but to animals as well.
Hence it makes us a topic of complete importance and relevance which requires
an integrated study between its medical, physiological, pathological and pharmacological impact.
India, has seen a 51% increase in these cases of stroke since just the last 3 decades. Which makes it a matter of concern
Age standardised rates of ischemic stroke and subarachnoid hemorrhage have increased among young adults since 2015.
Lifestyle factors and increased obesity are some of the factors that are causing the increased cases. Hemorrhage makes up about 13%, of the complication of a stroke, which shows that they are highly related because of the stroke there is direct effect on the large arteries and causing severe trauma injury, leading to hemorrhage.
Keywords: *Stroke, hemorrhage, epidemiology, treatment, genetic predisposition, AI usage, comparative study in humans and greyhounds, treatment and prophylaxis.*

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I. Introduction:

"The Spirit of the Circulatory System The Sun guides the circulatory system. And just as the Sun is the center and warms each orbiting planet, the heart is our center, pumping blood, oxygen, and warmth to each organ. The Sun, the heart, and the circulatory system remind us to center ourselves and be present in our power, changing the focus from others to ourselves."--- Said by Karen rose, a rewound physician and also a professor of ancestral medicine.

The circulatory system [1]of the body is a huge part as all the transportation of the nutrition and the also the exchange of the gases such as the oxygen and the carbon dioxide which is very important for the human survival. Hence it is very important to study about the pathological aspects of blood and the circulatory system; in this paper predominantly the stroke.

A stroke is a medical emergency that happens when something prevents your brain from getting enough blood flow. A blocked blood vessel or bleeding in your brain can cause stroke.

Globally ,stroke remains a significant cause of both mortality and disability among the people presenting with a defect in the circulatory system, with the increasing cases set to be projecting to increase by 81% in stroke incidents and 71% in prevalent cases from 2021 to 2050, which is just less than 3 decades ahead.

Projections[2] of stroke burden up to 2050 were generated using the optimal model selected based on the Akaike information criterion, encompassing global, World Bank income levels, national levels, and sex-age groups. In 2050, we projected 21.43 million stroke cases, 159.31 million survivors, 12.05 million deaths, and 224.86 million disability-adjusted life years due to stroke globally.

Stroke is a vast topic and can be better dealt when we know of the varieties of stroke that is presented in all the major cases and also the miscellaneous cases.

Strokes can be classified into two main categories:

1) Ischemic Stroke
2) Hemorrhagic stroke

An ischemic stroke occurs when a blood vessel that supplies the brain becomes clogged or "obstructed" and impairs or reduces the blood flow to part of the brain. The brain cells and tissues begin to die within minutes from lack of oxygen and nutrients.

The later or the hemorrhagic stroke occur when a blood vessel that supplies the brain ruptures and bleeds. When an artery bleeds into the brain, brain cells and tissues do not get oxygen and nutrients. In addition, pressure builds up in surrounding tissues and irritation and swelling occur, which can lead to further brain damage.

The pathology of a stroke is based on the obstruction of blood supply or rupturing of the artery that has been upstated.

One of the major complication of stroke is the hemorrhage. Hemorrhage is the loss of blood components from the vascular system of the body and can lead to decreased and inadequate tissue oxygenation causing disruption of the perfusion of the tissues. Hemorrhagic shock occurs when this blood loss leads to inadequate tissue oxygenation.

According to studies hemorrhage secondary to traumatic injury is [3]the leading cause of death of Americans from one to 46 years of age. There are various types of hemorrhage that are caused by different causes. Many a times a trauma such as car accident, an assasination attempt by a heavy object can also lead to a hemorrhage due to leaking of the vascular components and accumulation in the head, leading to death.

Based on which layer or between which space the hemorrhage is caused it is of various types such as the:-

1) Epidural hemorrhage
2) Subdural hemorrhage
3) Subarachnoid hemorrhage

An epidural hematoma (EDH) or epidural hemorrhage is an emergency condition that occurs when blood accumulates between the skull and the dura mater,which is the brain's protective membrane.

Subdural hematoma (SDH) or The subdural hemorrhage is caused by when there is accumulation of blood under the dura mater, mostly caused after a head injury that can be fatal. Subarachnoid hematoma(SAH) or the subarachnoid hemorrhage is a condition caused when there is accumulation of blood in the subarachnoid space of the head.

In this paper we will be looking at all the various types, epidermiology, the genetic predisposition and various other components and the treatment of stroke hemorrhage along with a comparative study.

The aim is to provide a comprehensive and an integrated review between the medical, pathological, physiological and the forensic knot of the topic and give an entire overview about the topic so that there is more awareness about it.

II. Discussion:

Complications Of stroke:

There are various compications of stroke but in this paper we will be looking at what is hemorrhage which makes around 14-20% leading cases of a stroke.

Hemorrhage is caused when there is an injury or a stroke, that causes the rupture of the blood vessels of the brain leading the blood to flow out and get accumulated. This causes the oxygen and the nutrients to not reach the neurons and the tissues of the brain, causing them to die due to pressure of the blood against the brain and skull.

There are various types of hemorrhages that occur, to understand that we need To first understand the layers of the brain-

The brain has three membranes under the bony skull and the brain. These are the dura mater, arachnoid and the pia mater.

1)Epidural hemorrhage: An epidural hematoma (EDH) or epidural hemorrhage is an emergency condition that occurs when blood accumulates between the skull and the dura mater,which is the brain's protective membrane.

2)Subdural hematoma (SDH) or The subdural hemorrhage is caused by when there is accumulation of blood under the dura mater, mostly caused after a head injury that can be fatal. 3)Subarachnoid hematoma(SAH) or the subarachnoid hemorrhage is a condition caused when there is accumulation of blood in the subarachnoid space of the head.

We will be looking at all these in detail now:

Epidural hemorrhage:

An EDH is often caused by a skull fracture during childhood or adolescence. The membrane covering the brain is not as closely attached to the skull as it is in older people and children younger than 2 years. Therefore, this type of bleeding is more common in young people.

The affected vessels get often torn by skull fractures. The fractures are commonly the result of a severe head injury, such as those caused by bicycl[5]e, skateboard, snow boarding or automobile accidents. Less severe blunt trauma also result in an EDH.

Due To the bleeding the intracranial pressure increases rapidly, which causes severe brain injury.The condition typically involves artery, most commonly from a lacerated middle meningeal artery secondary or a temporal bone fracture.

Epidermiology:

Adolescents and young adults, particularly males and individuals involved in high-impact injuries, are disproportionately affected.

The reason being as the dura mater is not very well attached to the brain during the early years of the life, and in adolescence, there are more likely cases of an injury while playing outdoor games or a blunt trauma injury due to negligence.

EDH occurs in 2% of all head injuries and up to 15% of fatal head traumas. Males are more frequently affected than females, with a higher incidence among adolescents and young adults. The mean age of affected patients ranges from 20 to 30 years, and EDH is rare in those older than 50. With advancing age, the dura mater becomes increasingly adherent to the inner table of the skull, reducing the likelihood of blood accumulating. In the 65-center Collaborative European NeuroTrauma Effectiveness Research in Traumatic Brain Injury (CENTER-TBI) study, EDH was present on initial computed tomography (CT) in 11% of all TBI cases and 16% of severe TBI. Only 29% of EDHs were presented with no such history of a trauma, with most patients exhibiting concurrent subdural or intraparenchymal hemorrhages. The median patient age was 41 years. In an Australian study, nearly 50% of EDH cases occurred in individuals less than 24 years of age. Falls predominated among children younger than 10, meanwhile road-traffic accidents were the leading cause in adolescents. Skull fractures accompanied 75% of EDH and were associated with larger hematoma volumes and higher operative rates.

Pathophysiology of EDH:

EDH mostly occurs due to occlusion and bleeding of the middle meningeal artery and the temporal artery, due to a hit on the temporal lobe of the skull.

Angiographic evaluation in around 35 surgical cases identified meningeal arterial extravasation with arteriovenous shunting in 60% of patients. Individuals with shunting experienced frequent clinical deterioration, suggesting that ongoing hemorrhage contributes to hematoma expansion and herniation risk.[13] Shunting may also increase the likelihood of a lucid interval. By diverting blood flow, the arteriovenous shunt can delay hematoma formation and the rise in intracranial pressure (ICP), postponing symptom onset.

About 10% of EDH cases result from venous bleeding, typically due to laceration of a dural venous sinus or hemorrhage from diploic veins associated with skull fractures

EDH may be further classified by stage of evolution. Type I, or acute EDH, occurs on day 1 and is characterized by a swirl sign indicating uncoagulated blood. Type II, or subacute EDH, emerges between days 2 and 4 and typically appears solid. Type III, or chronic EDH, develops between days 7 and 20 and exhibits mixed or lucent characteristics with contrast enhancement While epidural hemorrhage is not directly inherited, some genetic conditions can increase the risk, primarily those that affect blood clotting, such as hemophilia and sickle cell anemia. In these cases[5], a genetic predisposition to bleeding disorders makes a person more susceptible to developing an epidural hematoma, even from minor trauma or spontaneously.

Subdural hemorrhage:-

A subdural hemorrhage is a type of bleeding that causes the accumulation of blood between the dura mater and the arachnoid mater of the [6] meninges surrounding the brain.

A subdural hematoma can have various causes, including trauma, arteriovenous malformation, and the use of anticoagulation medications. In rare cases, it can spontaneously occur in the absence of any pathology.[7] Subdural haemorrhage can present with neurological signs similar to Brown-Séquard syndrome, in which the half side of the spinal cord is effected and paralysed.

Epidemiology:

SDH is a very complex disease with an overall incidence of 1.7–20.6 per 100,000 persons per year and is more commonly encountered in the elderly population. Recurrence of SDH can occur in 10%–20% of patients and is associated with several clinical and radiographic predictors that indicate the re occuring of the disease.

According [8] to an analysis that was done, a total of 95 individuals were included in the study. Of these, 66.3 % were male and 7.4 % died. The mean age was 72 years of age. The most common symptoms and history findings were history of trauma (69.9 %), motor deficit (68.4 %) and cognitive deficit (26.3 %). The average hematoma size was similar on both sides, and showed an increasing trend with aging

There is increase in SDH cases with increasing age, because as we grow old the normal size of the brain starts to shrinks, this leads to less adherence of the emissary veins present in between the dur mater and the arachnoid mater, leading to easy rupturing even on a very light impact.

Hence the cases of SDH are much more in elderly patients as compared to young adults.

Pathophysiology of SDH:

It is due to the accelerating and decelerating forces of the brain during violent shaking of the head, which causes the brain to move in an opposite direction to the layers causing the bridging veins to rupture and leads to the blood to leak in the subdural space [9]. This space may accumulate a significant quantity of blood in various stages to exist in an acute or sub-acute form. Often, the bleeding is not detected initially, later discovered as a chronic subdural hematoma (chronic because it is discovered after several weeks to months). When there is a sufficient accumulation of blood to occupy a large intracranial space, the brain midline shifts toward the opposite side, encroaching on the brain structures against the inner surface of the calvarium after decreasing the volume of the lateral third and fourth ventricles. As the intracranial space becomes limited, the volumetric forces push the uncal portion of the temporal lobe toward the foramen magnum causing herniation of the brain.

While [10] trauma Is the major cause of SDH,a mutation Glutaric Aciduria Type 1 (GA1), which can cause cerebral atrophy and enlarged cerebrospinal fluid (CSF) spaces, and X-linked myotubular myopathy, leading to a dolichocephalic head shape and stretched bridging veins. This lead to rupture of the veins and cause subdural hemorrhage.

Sub Arachnoid Hemorrhage

A subarachnoid hemorrhage is bleeding in the space between the brain and the tissues that cover the brain. The space is known as the subarachnoid space. A subarachnoid hemorrhage is [31] a type of stroke. It is a medical emergency that needs treatment right away.

The primary symptom of a subarachnoid hemorrhage is a sudden, very bad headache. Some people describe it as the worst headache they have ever felt. A subarachnoid hemorrhage also may cause nausea, vomiting, a stiff neck and other symptoms.

Bleeding usually happens when an irregular bulge in a blood vessel, known as an aneurysm, bursts in the brain. Bleeding also can happen because of a head injury. Sometimes a tangle of blood vessels in the brain, known as an arteriovenous malformation, causes the bleeding. And other health conditions, including conditions that affect the blood vessels, can cause bleeding. If a subarachnoid hemorrhage isn't treated, it can lead to permanent brain damage or death, so it's important to get treatment right away.

Epidermiology:

The overall global incidence of aneurysmal SAH was 7.9 per 100,000 person-years.By time trends, in 2010 the incidence of SAH was 6.1 per 100,000 person-years, declining from 1980 when the reported incidence was 10.2 per 100,000 person-years. Around the world, Japan and Finland have higher cases of subarachnoid hemorrhage for reasons unknown.

Most aSAH occur between 40 and 60 years of age, and young children and older adults can be affected.The mean age of aneurysmal rupture ranges from 50-55 years. It is more prevalent in the Blacks and Hispanic populations than the white Americans.There is a slightly higher incidence of aneurysmal SAH in

females, which may be related to their hormonal status.Patients with a history of smoking and previously ruptured intracerebral aneurysm are highly associated with new subarachnoid hemorrhage.

Pathophysiology of SAH:

Hemodynamic stress is the initiating factor for intracranial aneurysm (IA) formation. The observation best illustrates that IAs occur at arterial junctions, bifurcations, or abrupt vascular[32] angles where excessive hemodynamic stresses are exerted on arterial walls.The typical locations include the bifurcation of the basilar artery at the junction of the ipsilateral posterior inferior cerebellar artery (PICA), vertebral artery, and the anterior communicating artery.Large unruptured aneurysms compress the adjacent cerebral tissue causing neurological signs.

However, the rupture of these lesions creates a state of reduced blood flow and vasospasm leading to cerebral ischemia. The pathophysiological mechanisms by which these lesions are formed and eventually rupture are not fully understood. The hemodynamic stress to the vessel wall caused by increased blood pressure and other risk factors promotes the formation and rupture of IA. Multiple studies point to inflammation as a dominant factor in the pathogenesis of IA.A hemodynamic insult initiates the inflammatory process. It leads to matrix metalloproteinases (MMPs)–mediated degradation of the extracellular matrix and apoptosis of smooth muscle cells (SMCs), which are the predominant matrix-synthesizing cells of the vascular wall. These processes significantly weaken the arterial wall, resulting in dilatation, aneurysm formation, and ultimately rupture. Notably, The two main constituents of the inflammatory response and the associated degenerative response are macrophages and SMC

Epidermiology:

Hemorrhagic stroke contributes to 10% to 20% of strokes annually. The percentage of hemorrhage in stroke is 8-15% in the United States of America, the United Kingdom, and Australia, and 18% to 24% in Japan and Korea. The incidence[11]is around 12% to 15% of cases per 1,00,000 per year. A recent study from 2014 estimated that over 103 million adults in the United have been diagnosed with hypertension and patients with hypertension are three or four times more likely to have a stroke. The incidence is high in low and middle-income countries and AsiansThe global incidence is increasing, predominantly in African and Asian countries. The case fatality rate is 25% to 30% in high-income countries, while it is 30% to 48% in low- to middle-income countries.

Risk Factors - The risk factors can typically be categorized into two separate groups: modifiable and non-modifiable risk factors.

Modifiable Risk Factors - Modifiable risk factors are susceptible to various interventions to help reduce the risk of stroke whereas non-modifiable factors cannot be controlled and serve as indicators for high risk of stroke.

A recent INTERSTROKE study from 2016 analyzed the potential effects of modifiable risk factors associated with stroke in 32 countries. Among the 13,000 stroke cases, it was shown that modifiable risk factors such as diet, physical inactivity, hypertension, psychosocial factors, cardiac causes, diabetes, smoking, abdominal obesity, hyperlipidemia, and alcohol consumption accounted for approximately 90% of all strokes. Furthermore, the Global Burden of Disease study highlighted that 90.5% of all strokes can be explained by modifiable risk factors as well.

Hypertension is the most important modifiable risk factor for stroke. Japanese data studies have shown that control of hypertension reduces the incidence of Intra Cerebral haemorrhage.

Diabetes is another well-established modifiable risk factor for stroke. Approximately 537 million people have diabetes worldwide and this number is projected is to increase to 643 million by 2030 and 783 million by 2045. In the Emerging Risk Factors Collaboration study, the hazard ratios with diabetes for ischemic stroke, hemorrhagic stroke, and unclassified stroke were 2.27, 1.56, and 1.84, respectively. Furthermore, in a Greater Cincinnati/Northern Kentucky stroke study, it was found that younger individuals with diabetes had a higher risk of stroke. The incidence of stroke increased in all age groups, the risk of stroke was much more prominent before the age of 65 in Whites and before the age of 55 in African American populations.

Non-modifiable Risk Factors - There are relatively few non-modifiable risk factors, and the most significant ones are age and sex. Age is the strongest non-modifiable risk factor for stroke and elderly patients with strokes typically have higher mortality rates and reduced ability for functional recovery. Thus, as you age, there is a higher chance of developing a stroke.[12] The likelihood of having a stroke double after every 10 years after the age of 55. However, even though stroke is more prevalent in older populations, about one in seven strokes take place in people between the ages of 15 and 49 due to the presence of modifiable risk factors such as high blood pressure, diabetes, and obesity. Another study investigated stroke outcomes and its subtypes in younger populations compared to older populations and found that patients younger than the age of 45 had a higher incidence of hemorrhagic stroke compared to other age groups.

The most significant risk factor associated with this trend was hypertension in young adults.

Sex differences play an integral in stroke outcomes as well. Historically, it has been well-documented that the incidence of stroke is higher in men compared to women. However, recent studies have shown that there is a decrease in ischemic stroke among men which means that the incidence of stroke is declining more in men than women and the overall incidence of stroke is decreasing over time. Furthermore, women also tend to have increased disability post-stroke, decreased quality of life, and overall worse outcomes likely due to depression, anxiety, pain, and decreased mobility compared to men.

The Framingham Heart Study is an ongoing longitudinal epidemiologic study that has been going on since 1948 to investigate different risk factors for stroke and other cardiovascular diseases. After analyzing results from the first cohort of subjects, it was found that hypertensive patients with a blood pressure (BP) >160/95 mmHg had a five to 30 times higher likelihood of having a stroke compared to normotensive patients who had a BP <140/90 mmHg. These results led to the creation of the Framingham stroke prediction algorithm which now takes into account age, smoking, history of cardiovascular diseases, and other risk factors.

Additionally, the Prospective Study Collaboration is a combination of 61 prospective studies that explored established risk factors' effects on mortality rates from different vascular causes such as stroke. Results from this study concluded that patients between the ages of 40-89 had a strong correlation between blood pressure and total vascular and stroke mortality. Moreover, the risk of death from stroke doubles with every 20 mmHg increase in systolic blood pressure or 10 mmHg increase in diastolic blood pressure. This association remained consistent down to a blood pressure of at least 115/75 mmHg. In addition average blood pressure was a more accurate predictor of stroke-related deaths than either systolic or diastolic blood pressure measurements. Systolic blood pressure provided more information regarding stroke mortality than either diastolic blood pressure or pulse pressure. These trends were found to be similar in both male and female patients as well.

Stroke:

According to the World Health Organization (WHO) in 1970, "stroke is rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 h or longer, or leading to death, with no apparent cause other than of vascular origin" . Recently, the American Stroke Association proposed a new definition of stroke, which states that "stroke is an episode of acute neurological dysfunction presumed to be caused by ischemia or hemorrhage, persisting ≥ 24 h or until death" .[13]Globally, stroke is the second leading cause of mortality, claiming 5.5 million lives annually.The burden of stroke does not rest entirely with its high mortality but also with its high morbidity, which results in about 50% of survivors being left chronically disabled .

History of stroke:

Over 2,000 years ago, physicians described this condition in the Hippocratic Corpus and gave it the name "apoplexia" - a word that implies a sudden ,violent blow . Treatment options were extremely limited : " It is impossible to cure a severe attack of apoplexy and difficult to cure a mild one". The celebrated Greek physician Galen therefore recommended a balanced diet in combination with running and sport - preventive measures that are just as applicable to reducing risk of stroke today . Until[14,15] the seventeenth century, it was assumed that strokes were caused by an imbalance in the mixture of blood, yellow bile, black bile and phlegm - that is , the four humours described the hum oral theory that was developed in antiquity to explain the processes taking place in the human body .

It was not until 1658 that Johan Jacob Wepfer , a physician practising in Schaffhausen, Switzerland, identified the root cause of stroke. Based on post-mortem examination of people who had died of condition Wepfer identified two forms of stroke that modern medicine still distinguishes between today .

Almost 85% of strokes are triggered by " ischemic insult" ,in which a blood clot blocks a vessel in the brain, interrupting the blood supply to certain areas of the organ .

Types Of Stroke :
Strokes can be classified into 2 main categories:

Ischemic strokes:

These are strokes caused by blockage of an artery (or, in rare instances, a vein). About 87% of all strokes are ischemicThe brain cells and tissues[16] begin to die within minutes from lack of oxygen and nutrients.

Pathophysiology:

The pathophysiology of ischemic stroke begins with insufficient blood supply to a focal area of brain

tissue. Within minutes, the central core of tissue in this affected area progresses toward irreversible damage, known as the area of infarction. However, the surrounding tissue, referred to as the penumbra, does not experience immediate cell death and has the potential for recovery if early reperfusion is achieved.

In regions of reduced blood flow, there is an imbalance between the consumption and production of adenosine triphosphate (ATP), resulting in diminished energy stores. This leads to ionic imbalances, electrical disturbances, and a cascade of ischemia-related changes. These changes increase the production of reactive oxygen species (ROS) and nitric oxide (NO). Over time, the pathophysiological cascade destroys cell membranes, cell lysis, and cell death through mechanisms such as necrosis or apoptosis.

Following ischemic stroke, microglia are swiftly activated in the affected ischemic area and extend to the penumbra region. Their activation peaks 48 to 72 hours after the stroke onset and can persist for several weeks. Activated microglia cause an increase in proinflammatory cytokines such as ROS, NO, interleukin-1β, and tumor necrosis factor-α. However, they also release anti-inflammatory cytokines and neurotrophic factors, including brain-derived neurotrophic factor, glial cell-line-derived neurotrophic factor, and basic fibroblast growth factor.The intricate ischemic cascade triggered by acute stroke ultimately leads to the loss of neurons and supporting structures.

Ischemic strokes are further divided into 2 groups:
Thrombotic stroke: These are caused by a blood clot that develops in the blood vessels inside the brain.
Embolic strokes: These are caused by a blood clot or plaque debris that develops elsewhere in the body and then travels to one of the blood vessels in the brain through the bloodstream.

Thrombotic stroke

Thrombotic strokes are strokes caused by a thrombus (blood clot) that develops in the arteries supplying blood to the brain. This type of stroke is usually seen in older persons, especially those with high cholesterol and atherosclerosis (a buildup of fat and lipids inside the walls of blood vessels) or diabetes.Sometimes[17], symptoms of a thrombotic stroke can occur suddenly and often during sleep or in the early morning. At other times, it may occur gradually over a period of hours or even days.

Thrombotic strokes may be preceded by one or more "mini-strokes," called transient ischemic attacks, or TIAs. TIAs may last for a few minutes or up to 24 hours, and are often a warning sign that a stroke may occur. Although usually mild and transient, the symptoms caused by a TIA are similar to those caused by a stroke.

Another type of stroke that occurs in the small blood vessels in the brain is called a lacunar infarct. The word lacunar comes from the Latin word meaning "hole" or "cavity." Lacunar infarctions are often found in people who have diabetes or high blood pressure.

Embolic stroke

Embolic strokes are usually caused by a blood clot that forms elsewhere in the body (embolus) and travels through the bloodstream to the brain. Embolic strokes often result from heart disease or heart surgery and occur rapidly and without any warning signs. About 15% of embolic strokes occur in people with atrial fibrillation, a type of abnormal heart rhythm in which the upper chambers of the heart do not beat effectively.

Transient ischaemic attack:
What it is: Often called a "mini-stroke," a TIA is a temporary disruption of blood flow to the brain.Symptoms are similar to a stroke but are short-lived and resolve completely without lasting effects. A TIA is a serious warning sign of a high risk for a future true stroke, requiring immediate medical attention. Hemorrhagic strokes occur when a blood vessel that supplies the brain ruptures and bleeds. When an artery bleeds into the brain, brain cells and tissues do not get oxygen and nutrients. In addition, pressure builds up in surrounding tissues and irritation and swelling occur, which can lead to further brain damage. Hemorrhagic strokes are divided into 2 main categories, including the following:
-Intracerebral hemorrhage. Bleeding is from the blood vessels within the brain.
-**Subarachnoid hemorrhage.** Bleeding is in the subarachnoid space (the space between the brain and the membranes that cover the brain).
Intercerebral haemorrhage: Intracerebral hemorrhage is usually caused by high blood pressure. Bleeding occurs suddenly and rapidly. There are usually no warning signs and bleeding can be severe enough to cause coma or death.
Subarachnoid hemorrhage: Subarachnoid hemorrhage results when bleeding occurs between the brain and the membrane that covers the brain (meninges) in the subarachnoid space. This type of hemorrhage is often due to an aneurysm or an arteriovenous malformation (AVM). It can also be caused by trauma.An aneurysm is a weakened, ballooned area on an artery wall and has a risk for rupturing. Aneurysms may be congenital (present

at birth), or may develop later in life due to such factors as high blood pressure or atherosclerosis.An AVM is a congenital disorder that consists of a disorderly tangled web of arteries and veins. The cause of AVM is unknown, but it is sometimes genetic or part of certain syndromes.

Causes of stroke.

Ischemic strokes usually happen because a blood clot blocks a blood vessel connected to your brain. Issues that [13] can cause these kinds of clots include Atherosclerosis (hardened arteries) Atrial fibrillation (especially when sleep apnea causes it), clotting disorders Heart defects (including atrial septal defect and ventricular septal defect),?microvascular ischemic disease,hemorrhagic strokes happen when a blood vessel in your brain breaks or tears (ruptures). Causes can include,brain aneurysm ,hypertension (especially if it's very high or you have it for a long time) and moyamoya disease (and any other condition that weakens blood vessels in your brain).Unlike myocardial infarction, which is almost always because of large vessel atherosclerotic disease affecting the coronary arteries.The majority (≈80%) of strokes are ischemic, Hemorrhagic strokes can be either primarily intraparenchymal or subarachnoid. Ischemic stroke can be further divided into what have been referred to as etiologic subtypes or categories thought to represent the causes of the stroke: cardioembolic, atherosclerotic, lacunar, other specific causes (dissections, vasculitis, specific genetic disorders, and others), and strokes of unknown cause.Risk factors for hemorrhagic and ischemic stroke are similar, but there are some notable differences; there are also differences in risk factors among the etiologic categories of ischemic stroke. Hypertension is a particularly important risk factor for hemorrhagic stroke, although it contributes to atherosclerotic disease that can lead to ischemic stroke as well. Hyperlipidemia, however, is a particularly important risk factor for strokes because of atherosclerosis of extracranial and intracranial blood vessels,10 just as it is a risk factor for coronary atherosclerosis. Atrial fibrillation (AF) is a risk factor for cardioembolic stroke.Sedentary Behavior, Diet/Nutrition, Obesity, and Metabolic Syndrome.Dyslipidemia an increased risk for ischemic stroke with increased total cholesterol and a decreased risk for ischemic stroke with elevated high-density lipoprotein cholesterol.

Genes Associated With Stroke and Stroke Risk Factors:

European cohorts [14], MetaStroke confirmed an association of stroke with gene variants in the blood type gene ABO (rs505922), which is associated with levels of the coagulation proteins von Willebrand factor and factor 8; the associations were present for large vessel and cardioembolic stroke subtypes but not for small vessel disease.

PITX2 and ZFHX3 genes were also associated with cardioembolic stroke, and the HDAC9 gene and 9p21 locus were associated with large vessel stroke.186 In a separate genome-wide association study by the National Institute of Neurological Disorders and Stroke-Stroke Genetics Network project, a locus near the TSPAN2 gene on chromosome 1 was also associated with large artery stroke.Fabry disease is the second most common lysosomal storage disorder. Cerebrovascular involvement typically occurs in both large and small vessels, especially affecting the posterior circulation, and can occur in young stroke patients. Fabry occurs due to missense and nonsense mutations in the GLA gene.Marfan syndrome and ACTA2-associated vasculopathy, are similarly associated with vascular fragility and can lead to arterial dissections.Type 4 EDS (Ehlers–Danlos syndrome) is because of mutations of collagen type-III (COL3A1). Mutations in the gene encoding the α-1 chain of type 4 collagen (COL4A1) can also result in impaired vessel-wall integrity. Deletion of FOXF2 in young patients was associated with extensive white matter disease, and mutations in other forkhead transcription factors (FOXC1) have been associated with white matter disease syndromes.Cerebrovascular complications are well recognized in sickle cell anemia and result from polymerized red blood cells at low oxygen tensions, leading to small vessel occlusion and sickle-related arterial disease (moyamoya syndrome). The HDAC9 gene encodes histone deacetylase, although its mechanism for causing atherosclerotic stroke remains uncertain

Why The Topic 'Hemorrhage And Stroke'

Hemorrhage is a severe form of stroke characterized by bleeding into the parenchyma. These are very devastating conditions which are often associated with high morbidity and mortality rates. Its progression can lead to worse outcomes. A better understanding of its complex pathophysiology and lifestyle modifications may lead to better prevention and management. A highly detailed and in-depth research in this area helps identify and investigate- the risk factors, efficient and improved early diagnostic tools, new & effective treatment options- to decrease the severity of the disease.Stroke is a worldwide health problem and it a major contributor to the morbidity, mortality and disability rates in both developed and developing countries. The most common form of stroke is the cerebral thrombosis followed by[19] cerebral hemorrhage and then comes subarachnoid hemorrhage and cerebral embolism.In 2021, it was estimated that stroke constituted 10.7% of all deaths worldwide. The severity of the condition is evidenced by a substantial burden increase between 1990 and 2021,

which saw an 86.0% increase in its prevalence, 70.0% rise in incidence and 44.0% increase in deaths from stroke. Majority of these deaths occurred in developing countries like India, and 33.72% of the subjects were aged less that 70 years. The case fatality rate is 25% to 30% in high income nations while in low to middle income countries, it is 30% to 48% which depends on the efficiency of critical care available at health centers.Major risk factors include hypertension, cerebral amyloid angiopathy, dual antiplatelet therapy, smoking, heavy alcohol consumption, chronic liver disease, cerebral microbleeds (as in diabetes mellitus, hypertension), old age, male sex etc. Japanese studies have shown that controlling hypertension decreases the risk of intracerebral hemorrhage. The occurrence of hemorrhagic stroke has increased worldwide over the past 40 years, with shift of major risk factor from hypertension to antiplatelet therapy because there is improved hypertension management but increased anticoagulant usage.

Longitudinal data analysis of stroke provides strong evidence of a rapidly worsening situation. Studies from 1970-2021 shows a dramatic escalation of the incidences with more than 100% increase in low- and middle-income countries (LIMCs), including India. This trend along with recent data highlights a clear gap in prevention strategies. In developing countries, there has been a concerning[20] increase in prevalence of cases and deaths among younger adults which contrasts with the declining trends in developed countries.The strokes are striking a growing productive population of the country leading to economic and societal drain. It leads to profound and serious effects on social, physical and economic life, including severe social, emotional, physical, vocational and economic connotations. Due to the high death rates, families and the country as a whole face a huge economic and financial loss. Hence, urgent targeted research in this field is the need of the hour.The high mortality rate and disability rates associated with stroke in India and not just due to the pathological disease but also due to lack of public awareness and an efficient health system organization. The critically low level of public health awareness serves as the largest pre-hospital barrier to timely care. Surveys revealed that less than 22% of Indians are aware of the stroke symptoms and risk factors. Low recognition of these stroke symptoms causes low threat perception and delayed seeking health practitioner advice. The awareness levels Regarding treatment options are as low as 10%. It was observed that around 85.7% of surveyed subjects (patients) diagnosed with stroke were unaware of the symptoms.The lack of awareness is a major cause of adverse and worse clinical outcomes.

Studies show that this awareness deficit is the direct factor contributing to over 50% of early deaths from heart attack and stroke. For hemorrhagic stroke this awareness lacks clearly mean a failure to identify the severity and medical emergency leading to delayed consultation, evaluation diagnosis of complications (such as Seizures, brain herniation hydrocephalus) And delayed neurosurgical consultation. these delays can further worsen the already high fatality rates and leading to worsened disabilities. Currently, less than1.4% of all stroke patients in India are receiving advanced therapies like mechanical thrombectomy. Hence, public awareness and better public health knowledgeThe prognosis of stroke is usually not good, especially in cases of hemorrhage. Even when patients survive, many are left with weakness of limbs, slurred speech, memory loss or difficulty in doing simple daily activities. Many require long term physiotherapy, speech therapy, and rehabilitation support. Many do not regain full independence and remain dependent on family members for routine work, which adds to the social and economic burden. Access to rehabilitation services in India is limited, which worsens long term disability outcomes. In recent years, stroke has become a very common health problem, both in India and outside. It is now among the leading causes of death, and many patients cannot go back to normal living. The World Health Organization states that stroke is the second leading cause of death worldwide, and most of these cases are from low- and middle-income countries. India alone adds around 1.8 million new cases every year, and stroke is already listed as one of the top four causes of death here. Hemorrhagic stroke is not as frequent as ischemic stroke, but it is much more dangerous, with almost half of the patients not surviving. Increasing number of cases have been observed in the hospitals, including younger patients. This shows that stroke and hemorrhage are no longer rare conditions of the elderly, and that is why there is an urgent need to give this topic more attention from doctors and the community.

Treatment -

The approach to treatment varies with the type of stroke that we are dealing with ,since ischemic and hemorrhagic stroke have different causes and effects on the body, both require different treatments.

Strategies for stroke management -Acute care of stroke - involves management of risk factors like blood pressure, diabetes, alcohol and drugs, hyperlipidemia.Reperfusion therapies - includes intra-arterial thrombolysis [IAT] and intravenous thrombolytics [IVT]. There Is also a rehabilitation which [21,22] includes the physical therapy. Various others methord include:

1) Occupational therapy Speech therapy Neurorehabilitations.
2) Cognitive decline -Drug development
3) Robotics
4) Cortical stimulation Stem cell therapies.

5) Neuroprotective and Repair Anti-excitability.

Current therapies for ischemic stroke –

Thrombolytic Agents

Acute ischemic stroke is primarily treated via intravenous thrombolysis and sometimes followed by endovascular thrombolysis to enhance vessel recanalization. It was originally developed to treat patients with coronary thrombolysis but was later found to be of a great significance in treating stroke patients.Factors affecting the efficacy of thrombolytics- Age of the clot, the specificity of the thrombolytics agent for fibrin, and the presence and the half life of neutralizing agent. Drug - Alteplase, a second generation thrombolytic, for the dissolution of blood clots. Other drugs include - prourokinase, tenecteplase, and staphylokinase are under clinical trials.For large vessel occlusion strokes, mechanical thrombectomy is becoming a routine. Adjunctive anti-thrombolytic therapy increases the risk for intracranial hemorrhage hence the treatment modality varies significantly and should be kept in mind, however it might improve angiographic reperfusion.

Adjuvent therapies:

Anti-thrombolytic Agents - Argatroban, and tirofiban.Then there is the dual antiplatelet therapy - It involves the combination of Clopidogrel, prasugrel, ticagrelor with aspirin. There are also the fibrinogen-depleting agents - they reduce the blood thickness and increase the blood flow ,as indicated by research findings. Ancrod (70mg/dl) is a defibrinogenating agent derived from snake venom. Various other methords such as the Gamma aminobutyric acid (GABA) agonists like Clomethiazole, and also the famous sodium channel blockers.They prevent neuronal death and reduce white matter damage as tested in various animal models of stroke. Mexiletine has been proved to be effective in grey and white matter ischemic stroke.Sipatrigine is a sodium and calcium channel blocker which failed in a Phase 2 clinical trial.

Antioxidants

In ischemic stroke, excess production of free radicals and inactivation of detoxifying agents cause redox disequilibrium. [21,22,23] This phenomenon leads to oxidative stress followed by neuronal injury. Antioxidant AEOL 10,150 effectively regulated the gene expression profiles to decrease the ischemic damage and reperfusion in stroke patients.

Hemorrhagic stroke: The hemorrhagic stroke management can be done via:-

1)Blood pressure management-Gradual reduction in BP to 150/90 mmHg should be done using different antihypertensive drugs.

2)Beta-blockers - such as thelabetalol, esmolol.

3)ACE inhibitors- enalapril, lisinopril, captopril.

4) CCBs - nicardipine. Early intensive BP lowering increases the risk for hematoma growth over 72 hours. However, for patients presenting with SBP>220 mmHg, an aggressive reduction in BP with a continuous iv infusion is needed. 5)Management of raised intracranial pressure:

Elevating the head of the bed to 30 degrees and using osmotic agents like mannitol 20%, hypertonic saline.Monitoring of ICP is done using parenchymal and ventricular catheter for all patients with a Glasgow coma scale <8 or those with evidence of transtentorial herniation or hydrocephalus.Aim is to keep ICP between 50 to 70 mmHg. 6)Antiepileptic therapy–however it is not recommended as per AHA/ASA guidelines for primary prophylaxis. 7) Surgery, 8) Craniotomy, 9) Decompressive craniectomy 10) Stereotactic aspiration 11) Endoscopic aspiration. Emergency surgical evacuation is indicated in cerebellar hemorrhage with hydrocephalus or brainstem compression. It is evacuated by suboccipital craniectomy.

Prevention:

Stroke prevention involves modifying risk factors within a population or individuals, while stroke management depends on treating its pathophysiology. The overall direction of current stroke research is to generate novel therapies that modulate factors leading to primary and secondary stroke. 1. Excitotoxicity:- Neuronal death is a key manifestation of stroke. A key reason for this phenomenon neuronal depolarization and inability to maintain membrane[21,22,23] potential within the cell. This process is neuronal depolarization and inability to maintain membrane potential within This process is mediated by glutamate receptors .Reactive oxygen species produced in the normal brain are balanced by antioxidants generated in a responsive mechanism. However, in the ischemic stroke model, excess production of free radicals and inactivation of detoxifying agents cause redox disequilibrium. 3. Reperfusion:The intravenous thrombolytics (IVT): The IVT treatment paradigm was originally developed to treat coronary thrombolysis but was found to be effective in treating stroke patients. The efficiency of thrombolytic drugs depends on factors including the age of the clot, the specificity of the thrombolytic agent for fibrin and the presence and half-life of neutralizing antibodies.

Intra-arterial thrombolysis (IAT): IAT is another approach designed to combat acute stroke. This treatment is most effective in the first six hours of onset of MCA occlusion, and requires experienced clinicians and angiographic techniques.

Others:-Antihypertensive therapy: Hypertension is a risk factor for stroke. There are many reasons for high BP in stroke, including a history of hypertension, acute neuroendocrine stimulation, increased intracranial pressure, stress linked to hospital admission and intermittent painful spells Glucose management: Hyperglycemia (elevated blood glucose) is common in stroke patients, so targeting blood glucose levels is an efficient stroke management strategy. Hyperglycemia >6.0 mmol/L (108 mg/dL) is observed in most stroke patients. Antiplatelet therapy: This therapy is used for acute ischemic stroke management and for prevention of stroke incidence. It is also vital in controlling non-cardioembolic ischemic stroke and TIA. Antiplatelet agents like aspirin, clopidogrel and ticagrelor are the most widely used drugs administered to stroke sufferers within the first few days of attack .d) Stem cell therapy: It offers promising therapeutic opportunities, safety and efficacy to stroke patients. Research on embryonic stem cells, mesenchymal cells and induced pluripotent stem cells has assessed their potential for tissue regeneration, maintenance, migration and proliferation, rewiring of neural circuitry and physical and behavioral rejuvenation.

Minimally Invaise Neurosurgical Evacuation

Introduction

Spontaneous intracerebral hemorrhage(ICH) accounts for 2 million strokes worldwide per year and is the most deadly subtype of stroke with a 1- year mortality rate up to 50%. Among survivors, 61% to 88% are dependent on others for activities of daily living 6 months after the hemorrhage. Given the high morbidity and mortality of this disease process, surgical options have been repeatedly evaluated in large multicenter randomized controlled trials (RCTs) that unfortunately have not demonstrated improved outcomes. In parallel[24], RCTs have been performed to evaluate minimally invasive surgery (MIS) in comparison to either medical therapy or conventional craniotomy withvarying degrees of success with different surgical techniques and in different patient subgroups.Ongoing RCTs include the National Institutes of Health- sponsored MISTIE trial (Minimally Invasive Surgery Plus rtPA for ICH Evacuation) evaluating stereotactic thrombolysis, the endoscopic arm of MISTIE referred to as the ICES trial (Intraoperative Stereotactic Computer Tomography-Guided Endoscopic Surgery) and 2 industry sponsored trials, including the ENRICH trial (Early Minimally-Invasive Removal of Intracerebral Hemorrhage) sponsored by NICO Corporation and the INVEST .Minimally analysis incorporates multiple recent RCTs to evaluate MIS technique subgroups, as well as important patient selection subgroups for time to evacuation.

Understanding the effect of MIS for ICH in these technique subgroups and patient- selection subgroups will contribute to planning for future clinical trials.

Principle –

Minimally invasive subcortical parafascicular access for clot evacuation (MISPACE) of ICH was initially described as a means of reducing subcortical injury, with access through a port at a sulcus with orientation at the horizontal axis of white- matter tracts.

Procedure

First, the collection of blood within the brain causes mass effects leading to mechanical distortion and increased intracranial pressure (ICP). Elevated ICP leads to mitochondrial injury and aberrant neurotransmitter release.Second, the release of thrombin leads to infiltration of mesenchymal cells, microglia, and inflammatory cells resulting in significant perihematomal edema (PHE) . PHE can cause additional neurological insult and some research asserts that PHE expansion accurately predicts ICH morbidity and mortality, butthe true implications of PHE on outcomes remains controversial .Nevertheless, improving ICH outcomeslikely requires rapid removal of blood from the parenchyma and restraining edema formation while also limiting further neuronal damage due to the surgical intervention. Minimally invasive surgery (MIS) approaches promise to provide these benefits and, for this reason, have become alluring options for management of ICH. However, the results of rigorous clinical trials of MIS ICH methods over the past decade have been mixed. In addition to describing current methods of ICH diagnosis and prognosis, this article reviews theminimally invasive ICH evacuation methods and the literature describing each of their efficacies.

Key Techniques

● Stereotactic Aspiration: A catheter is placed into the hematoma using stereotactic guidance to aspirate the blood.

● Neuroendoscopic Surgery: An endoscope, a thin tube with a camera, is inserted through a small burr hole to visualize and remove the clot, sometimes with the help of aspiration wands or other tools.

● Two- in- One Technique:This combines stereotactic aspiration with neuroendoscopy to leverage the benefits of both methods for more efficient and effective evacuation Minimally invasive neurosurgical evacuation is used primarily for intracerebral hemorrhage (ICH), aiming to remove blood clots to relieve pressure, prevent brain herniation, control symptoms, and accelerate recovery.
Uses :-Intracerebral Hemorrhage (ICH): This is the primary use, focusing on removing blood from within the brain caused by a ruptured vessel. Traumatic Brain Injury (TBI): Endoscopic- assisted minimally invasive surgery can also be used for decompression and neurological recovery in patients with TBI. Deep ICHs: For deep hematomas, minimally invasive techniques are preferred to limit operative damage to healthy brain tissue.

MACHINES – Minimally [26] invasive neurosurgical evacuation involves specialized instruments like the Apollo/Artemis system, MindsEye port, and NICO BrainPath/Myriad system to remove brain hematomas through small incisions or naturally occurring brain corridors, often using robotic guidance, stereotactic navigation, and neuroendoscopy for visualization and control. These techniques allow for precise targeting and aspiration of blood clots, aiming to improve patient outcomes compared to traditional open craniotomy. There are various types.
Types of Devices and Techniques: Neuroendoscopy with Aspiration / Irrigation Systems, Tubular Retractor Systems, Robot- Assisted Systems,Catheter- Based Approaches. But how do they work? 1. Image Guidance: High- resolution CT or MRI scans are used with stereotactic navigation systems to plan the surgical approach. 2. Access: A small incision is made, and a small opening is created in the skull.
3. Insertion: A tubular retractor, a metal trocar, or a robot- guided instrument is inserted through the opening to create a channel to the hematoma.
4. Evacuation: A neuroendoscope provides visualization while the surgeon uses an instrument, like an Apollo/Artemis wand or other aspirator, to remove the blood clot.
5. Monitoring: The instruments allow for simultaneous suction, irrigation, and coagulation to control bleeding.

TRIAL OVERVIEW – MISTIE 3 The key procedural goal was to reduce residual clot volume to <15ml , which was considered a threshold for likely functional benefits.This trial was - Type : Randomized, open label,blinded endpoint i.e.(outcome assessors masked) Phase 3 trial . Sites: conducted at 78 hospitals across USA,Canada,Europe,Australia and Asia.Inclusion Criteria >18 yrs old. Spontaneous,non traumatic,supranteriorial ICH of at least 30ml.Exclusion of others with planned eary care withdraw, need for urgent craniotomy,or secondary cause.(e.g.. aneurysm).

INTERVENTION
Image guided catheter placement(stereotactic) into hematoma.Alteplase 1.0mg every 8h(upto 9 doses0via the catheter to liquify clot and assist drainage.Periodic CT to monitor removal evacuation stopped when residual <15ml or max dosing reached.

ENROLLMENT/EXECUTION/POPULATION: Between December 30,2013 and August 15,2017 506 patients were randomized. Key results-Primary outcome: 45%in MISTIE vs 41%in medical care. Safety and mortality -At 7 days : 1% mortality in MISTIE vs 4% in control. At 30 days : 9% in MISTIE vs 15% in control

CLOT REMOVAL PERFORMANCE
Mean Hematoma reduction in the MISTIE arm was 69% compared to standard therapy, but >40% of MISTIE patients did not reach the <15ml threshold. In patients who did achieve residual volume <15 ml better functional outcomes were observed relative to those who did not, and relative to controls.

ADVANTAGES AND LIMITATIONS.
Acute stroke due to supratentorial intracerebral haemorrhage is associated with high morbidity and mortality. Open craniotomy haematoma evacuation has not been found to have any benefit in large randomised trials. So assessment was done on minimally invasive catheter evacuation followed by thrombolysis (MISTIE), with the aim that decreasing clot size to improve functional outcome in patients with intracerebral haemorrhage.

Following are the advantages and limitations of MISTIE-III.
Advantages:
Substantial clot volume reduction — MISTIE reliably reduces hematoma volume compared with conservative care. 2. If the target residual volume is achieved (≤15 mL), the data suggest improved survival and better functional outcomes.(After surgical clot evacuation, both ICH and intraventricular hemorrhage volumes have a strong association with good neurological outcome). 3.Less invasive than open craniotomy -There is potential for lower procedural trauma, lower blood loss and suitability for patients not candidates for open surgery.(

Bayesian reanalysis of the minimally invasive surgery with thrombolysis for intracerebral hemorrhage (ICH) evacuation (MISTIE-III) trial derived probabilities of potential intervention effect on functional and survival outcomes).

III. Limitations / Challenges:

1. The effect depends on achieving an adequate clot removal . The benefit appears contingent on reaching a low residual volume; however many treated patients did not reach the ≤15 mL threshold, thus reducing the observed average effect.
2.Operator/surgeon experience and technique variability : outcomes correlated with how effectively surgeons evacuated the clot; variability across centers influenced the results. This limits generalizability unless training or quality metrics are standardized. 3.Timing and patient selection are unresolved , including the optimal timing (how early to intervene) and which subgroups benefit most are still being refined by subsequent analyses and trials.
4. Risk of

procedure-related complications : while overall safety was acceptable in the trial, there remain concerns about rebleeding, infection, catheter-related issues, and the need for repeat procedures. These risks must be balanced against potential benefit.

IV. Future Directions And Conclusion

Future directions include standardizing surgical training, improving technical tools to reliably achieve low residual clot volumes, expanding trials to broader patient populations, and employing alternative statistical frameworks and outcome measures.

Ultimately, while MISTIE III underscores the feasibility and safety of minimally invasive clot evacuation, its mixed results highlight that further refined, technically optimized, and more inclusive trials are needed to establish its role in routine stroke and hemorrhage care.

Methods Of Detection And Screening Of Stroke:

Detection- Stroke remains a leading cause of death and disability worldwide, necessitating improved diagnostic tools for early detection and classification.

Machine learning (ML) techniques have shown promise in addressing this critical healthcare challenge by enabling efficient analysis of stroke-related data.However, the lack of standardised datasets, limited real-time clinical applicability, and the complexity of model interpretability hinder broader adoption.[26] This review critically examines 34 research articles published between 2014 and 2025, focusing on traditional ML, deep learning, transfer learning, and hybrid approaches for stroke detection and classification. Key findings highlight that Traditional ML models such as Support Vector Machines (SVM) and Random Forests (RF) have been widely used but show limitations in high-dimensional medical imaging tasks. Conversely, advanced deep learning models, such as EEG-DenseNet and ResNet50, excel in stroke segmentation and classification tasks, while hybrid methods demonstrate potential for improving accuracy through ensemble strategies. The review also under scores the challenges of dataset scarcity, ethical concerns, and integration barriers in clinical settings.Recommendations for future research include developing more representative datasets, advancing explainable AI methods, and exploring real-time implementation frameworks to bridge the gap between research and clinical practice.Detecting a stroke quickly and accurately is critical for effective treatment. Here are the main methods of stroke detection, categorised into clinical assessment, imaging techniques, and laboratory tests:

1. Clinical Assessment

FAST Test A quick bedside assessment used to identify stroke symptoms such asa drooping of face on one side, they raise both arms,Slurred or strange speech is presented as well.

Other Symptoms include sudden numbness or weakness (especially on one side),Vision changes, loss of coordination or balance,severe headache with no known cause.

Imaging Techniques (Essential for confirming stroke type) which include the CT Scan (Computed Tomography), MRI (Magnetic Resonance Imaging),Diffusion-weighted MRI (DWI) is especially sensitive. CT Angiography (CTA) / MR Angiography (MRA) is also done which visualize blood vessels to detect clots or narrowing and can help identify large vessel occlusion needing thrombectomy, then there is Transcranial Doppler Ultrasound which measures blood flow in the brain's major arteries. 3. Laboratory Tests (Supportive, not diagnostic alone) which include Blood glucose (to rule out hypoglycemia),Complete blood count (CBC),Coagulation profile (PT/INR, aPTT – important before giving clot-busting drugs),Lipid profile,Toxicology screen (if substance use is suspected),Cardiac enzymes & ECG (stroke and heart issues are often linked).

Cardiac Evaluation methods which help to detect the source of emboli (clots from the heart) and they include

ECG (Electrocardiogram) – looks for atrial fibrillation, echocardiogram (TTE or TEE) – detects clots, PFO, or other heart abnormalities and such technologies.
Advanced Methods and Tools. Stroke scales: NIH Stroke Scale (NIHSS) for stroke severity,Artificial intelligence (AI) tools – used in some hospitals for faster imaging interpretation,Portable stroke detection devices (in development or limited use)

Screening Methods :
Introduction:- Stroke is a leading cause of death and disability worldwide, accounting for nearly 12% of all deaths globally. Early [27]identification of individuals at risk or those presenting with early symptoms can significantly reduce morbidity and mortality. Screening for stroke includes two main approaches, one is the population-level screening – identifying high-risk individuals before stroke occurs (primary prevention) and other is the symptom-based screening – rapid recognition of acute stroke to ensure timely treatment (secondary prevention).Despite major advances in diagnostic and therapeutic strategies, there is no universally recommended population-based screening program for stroke due to insufficient evidence of benefit versus cost and potential harm. However, targeted screening for risk factors and use of clinical tools for early stroke recognition are crucial research and public health areas. Its objective is to identify individuals at high risk for primary prevention, enable rapid detection of acute stroke symptoms for early treatment, reduce stroke-related mortality and long-term disability and To provide data for epidemiological surveillance and research.

Types of screening methods:- A. Primary Prevention Screening (Risk Factor Screening). Focuses on early detection of modifiable risk factors like hypertension screening – Regular blood pressure measurement in adults.Atrial fibrillation (AF) screening – Pulse palpation or ECG in elderly patients.Diabetes mellitus – Fasting glucose or HbA1c testing.Dyslipidemia – Serum lipid profile in high-risk groups.Carotid artery stenosis – Carotid Doppler ultrasound in selected populations (e.g., history of TIA or carotid bruit).
B. Secondary Prevention / Early Detection Screening which is used for rapid identification of acute stroke in prehospital and hospital settings.
Clinical Screening Tools:-FAST (Face, Arm, Speech, Time) ,BE-FAST (adds Balance, Eyes) ,CPSS (Cincinnati Prehospital Stroke Scale), ROSIER (Recognition of Stroke in the Emergency Room), LAPSS (Los Angeles Prehospital Stroke Screen)
Imaging Screening include the CT / MRI Brain: For confirmation, not for population screening, the Carotid Duplex Ultrasonography: Detects carotid stenosis.Transcranial Doppler: Used for screening intracranial stenosis or microemboli.
Biomarker-Based Screening (Emerging Research).Research is exploring the use of blood biomarkers to differentiate stroke types and identify at-risk individuals:GFAP (Glial Fibrillary Acidic Protein): Rises in hemorrhagic stroke.D-dimer: Elevated in cardioembolic stroke.S100B, NSE, MMP-9: Indicate neuronal damage.NT-proBNP: Marker for atrial fibrillation–related stroke risk.These markers are not yet validated for routine screening but show promise in triaging patients in prehospital settings.
C. Screening in Special Populations Elderly (>65 years): Opportunistic screening for atrial fibrillation, hypertension, and carotid bruit.Diabetics and hypertensives: Annual lipid and vascular screening.High-risk occupational groups (e.g., pilots, drivers): May undergo cognitive and vascular risk evaluation.

V. Current Guidelines & Recommendations

WHO (2023): Emphasises risk-factor control (hypertension, diabetes, smoking cessation).AHA/ASA Guidelines (2021): Recommend opportunistic AF screening in adults ≥65 years; discourage population imaging screening.USPSTF (2021): Recommends against carotid artery stenosis screening in asymptomatic adults.European Stroke Organisation: Supports targeted screening in high-risk groups and public awareness programs.

Data from some studies:An updated review and meta-analysis of screening tools for stroke in the emergency room and prehospital setting: Elsevier journal of the neurological sciences.Stroke screening tools should have good diagnostic performance for early diagnosis and a proper therapeutic plan. Early and comprehensive risk identification would be critical to identify people at high risk for stroke.

Therefore, a comprehensive stroke risk screening tool is needed to assess all possible stroke risks and potential at-risk populations. In the future, such an instrument would benefit early detection and stroke prevention planning.Various methods were used for it.The meta-analysis was conducted according to the Preferred Reporting Items for a Systematic Review and

Meta-analysis of Diagnostic Test Accuracy Studies (PRISMA-DTA) guidelines. The PubMed and Scopus databases were searched until December 31, 2021, for studies published on stroke screening tools. These tools' diagnostic performance (sensitivity and specificity) was pooled using a bivariate random-effects

model whenever appropriate.The result was helpful to add to the research.Eleven screening tools for stroke were identified in 29 different studies. The various tools had a wide range of sensitivity and specificity in different studies. In the meta-analysis, the Cincinnati Pre-hospital Stroke Scale, Face Arm Speech Test, and Recognition of Stroke in the Emergency Room (ROSIER) had sensitivity (between 83 and 91%) but poor specificity (all below 64%). When comparing all the tools, ROSIER had the highest sensitivity 90.5%. Los Angeles Pre-hospital Stroke Screen performed best in terms of specificity 88.7% but had low sensitivity (73.9%). Melbourne Ambulance Stroke Screen had a balanced performance in terms of sensitivity (86%) and specificity (76%). Sensitivity analysis consisting of only prospective studies showed a similar range of sensitivity and specificity.Blood-based protein biomarkers during the acute ischemic stroke treatment window: Frontiers in Neurology.Rapid and accurate acute ischemic stroke (AIS) diagnosis is needed to expedite emergent thrombolytic and mechanical thrombectomy treatment. Changes in blood-based protein biomarkers during the first 24 h of AIS, the time window for treatment, could complement imaging techniques and facilitate rapid diagnosis and treatment.

They performed a systematic review according to PRISMA guidelines. MEDLINE, EMBASE, Cochrane Library, and Web of Science databases were searched for eligible studies comparing levels of blood-based protein biomarkers in AIS patients with levels in healthy controls and stroke mimics. Protein biomarkers from the following pathophysiological categories were included: neurovascular inflammation (MMP-9, TNF-alpha), endothelial integrity (VCAM-1, ICAM-1), cell migration (E-Selectin, P-Selectin, L-Selectin), markers of glial and neuronal origin (GFAP, S100, S100B, NSE), and cardiac dysfunction (BNP, NT-proBNP). The literature search was limited to English-language publications before November 7th, 2023. A total of 61 studies from 20 different countries were identified, which included in total, 4,644 AIS patients, 2,242 stroke mimics, and 2,777 controls. Studies investigating TNF-alpha, MMP-9, VCAM-1, ICAM-1, E-Selectin, L-Selectin, GFAP, NSE, and S100B showed pronounced methodological heterogeneity, making between-study comparisons difficult. However, in 80% of NT-proBNP and BNP studies, and all P-selectin studies, higher biomarker levels were observed in AIS patients compared to healthy controls and/or patients with stroke mimics.

None of the biomarkers included showed sufficient evidence for additional diagnostic benefit for AIS. Comprehensive standardised global multicenter studies are needed to (1) permit comparability, (2) enable valid statements about protein-based biomarkers, and (3) reflect real-world scenarios. While universal stroke screening is not currently recommended, targeted screening of high-risk individuals and rapid prehospital identification of acute stroke are essential to reduce global stroke burden.Future research must focus on integrating biomarkers, AI tools, and telemedicine to enable cost-effective and scalable stroke screening programs.

Stroke and its effect in dogs(greyhounds)

Stroke is a sudden neurological event caused due to[28] hampered blood flow to the brain tissues which damages the brain cells. The main cause for this compromised blood flow is ischemia which can be either due to blockage or rupture of blood vessel. Dogs rarely show such cerebrovascular events but in breeds such as greyhounds these events are more common due to high predisposition to factors causing it. From year 2007 to 2013 a study was conducted that showed 21 greyhounds with stroke (ischemic), yielding a prevalence of about 0.66% among 3,161 greyhounds.Stroke is mainly of two types - ischemic (blood clot obstruction causing hampered blood supply) and hemorrhagic (blood vessel rupture)Greyhounds are a valuable model to study stroke, the reason being their anatomical and physiological pecularities, predisposing them to certain conditions. The features such as high cardiac output, high heart efficiency, unique hematological features such as high blood pressure, thin blood vessels, make them suffer similar human conditions such as hypertension, hypercoagulability and vascular stress. This breed exhibit "spontaneous stroke" making them a natural model for the studies.

We look at the anatomy of humans and greyhounds to have a comparison between the two so we can draw a line for our study.Brain anatomy - Human brain weight around 1300 to 1400 grams which is much heavier than greyhounds brain weighing around 70 to 90 grams. Human brain constitutes 2% of its body weight with highly developed sulci and gyri leading to their advanced development, the neural density is higher in cortex whereas greyhounds' brain is only 0.4% of their body weight with smoother cortex and high neural density in cerebellum. This comparison suggests that human have larger cortical region which supports their cognitive functions whereas greyhounds' brain is specialized in sensory and motor integration and rapid response.

Cerebral vascular system - in humans, circle of willis is present along with collateral circulation whereas, in greyhounds circle of willis is comparatively smaller with less collateral circulation. In humans, arteries are more profusely branched and autoregulation is seen along with well developed blood brain barrier whereas, in humans, arteries are less branched along with narrow lumen, autoregulation is seen but do not work well in stress and the blood brain barrier is more susceptible to damage due to high blood viscosity. This

comparison suggests that greyhounds are at a much higher risk of stroke due to their narrow blood vessels and low collateral blood flow whereas human cerebrovascular system, provides more protection against stroke. Cerebral Susceptibility - In humans, stroke is more often associated with risk factors such as atherosclerosis, hypertension and embolism whereas in greyhounds, the risk factors are morassociated with higher hematocrit, narrow vessels and this vessel wall.

Baseline cerebral blood flow - In humans, global CBF is around 50ml/100g brain tissue/ min with high regulations whereas, in greyhounds, global CBF is around 40 to 60 ml/100g/min.They have higher metabolic rate so adequate perfusion is crucial. Therefore, in humans, blood flow is dependant on metabolic needs. When there is high neuronal activity local vasodilation occurs causing increase in CBF whereas in greyhounds, blood flow is majorly dependant on cardiac output (higher cardiac output at rest which increase furthur on exertion, therefore, increasing CBF. Autoregulation Mechanism - Autoregulation is the ability of body to maintain a relative constant flow of blood despite of the changes in systemic blood pressure. In humans, this autoregulation aims at maintaining a mean arterial pressure through myogenic (blood vessel dilation and constriction), metabolic (hypoxic conditions cause vasodilation that increase blood flow) and neurogenic mechanisms (maintain tone of walls of blood vessels). Whereas, in Greyhounds, cerebral autoregulation aims at maintaining a mean arterial pressure that is within a limited range. They also have myogenic and metabolic responses. As we know that they have high performing cardiovascular system, they show faster adjustments in CBF. All this suggests that, humans have a stable baseline perfusion and high pressure tolerance whereas greyhounds have rapid cardiovascular dynamics with narrow autoregulation.

Cardiovascular System -Humans have a smaller heart weighing around 250 to 300 grams [29](0.4 to 0.5% of body weight) compared to greyhounds with heart weighting 500 to 700 grams (1 to 1.5% of body weight).Heart of human have thicker left ventricular chamber which is elongated and muscular in case of greyhound breed. Humans have higher mean arterial pressure, resting heart rate than greyhounds which have very high exertional heart rate (around 250 to 280 mmHg). Large arteries are more complaint, stiffs gradually in humans but in greyhounds, they are more elastic, even the smaller peripheral vessels can dilate and constrict really quickly.

Therefore, greyhound's cerebrovascular system is highly specialized for rapid oxygen delivery whereas humans have stable endurance focused cardiovascular dynamics.Greyhounds have higher hematocrit than humans with hypercoagulability, they also have higher fibrinogen than humans. The platelets shows faster aggregation than in humans. The main risk for Thrombophilia in greyhounds is increased thrombotic tendencies whereas in humans it is mainly due to genetic mutations.

Metabolic rate -Humans have a basal metabolic rate of around 22 to 24 kcal/kg/day where the brain accounts for about 20% of the total resting metabolic energy. Aerobic glucose metabolism mainly define the metabolic of the brain. Greyhounds have higher BMR than average dogs, also showing higher oxygen consumption. Racing greyhounds shows high mitochondrial density and aerobic capacity.Oxygen Consumption Humans - VO2 (rest) - 3.5 mL/O2/kg/min VO2 max - 70 to 80 mL/kg/min Brain oxygen consumption - 3.5 mL/100g/min. Greyhounds - VO2 - 4 to 5 mL/kg/min. VO2 max - 70 to 80 mL/kg/min oxygen extraction tendencies higher in sprinters. This shows that greyhounds have high oxygen delivery and utilization system whereas, human brain consumes more oxygen compared to their body size.

Susceptibilty to hypoxia -Due to constant cerebral metabolic needs, human brain is very intolerant to hypoxia but greyhounds shows tolerance to transient hypoxia due to high hematocrit and splenic contraction on exercise. There are various risk factors associated as well. Ischemic stroke is the most common type of stroke in both humans and greyhounds. The risk of stroke is higher in younger dogs and elderly humans. The major risk factor for stroke in humans is hypertension, atherosclerosis, diabetes and atrial fibrillation but in greyhounds the contribution is from high hematocrit, hypercoagulability, extreme Blood pressure swings during exercise. Not only this many blood factor such as dyslipidemia and smoking in case of humans and higher blood viscosity in greyhounds contribute to the risk factors causing stroke. Therefore, in humans, stroke is mainly caused due to chronic lifestyle and vessel conditions whereas in greyhounds, it is mainly a result of acute breed specific physiological issues Mechanism of ischemic and hemorrhagic stroke- Ischemic stroke

HUMAN - Mechanism - cerebral blood flow reduction or complete blockage due to thrombosis or embolism.Pathophysiology - blood flow obstruction due to vascular occlusion, this hampers the blood supply and the oxygen and glucose lacks into neurons causing ischemia. The sodium potassium ATPase pump fails causing cytotoxic edema leading to glutamate excitotoxicity and neuronal death. Reperfusion injury may cause oxidative stress and inflammation.

GREYHOUNDS -Mechanism - Thromboembolism or hypoperfusion Other factors effect such as - higher hematocrit and viscosity cause microcirculatory flow reduction,hyperactive platelets cause thrombus formation, splenic contraction during racing cause more increase in viscosity, sudden changes in perfusion pressure and

during intense exertion,hyperthermia and hypoxia cause increase in metabolic needs which futhur worsen the damage.

b. Hemorrhagic stroke :-HUMAN - Mechanism - Subarachnoid space bleeding due to weakness of cerebral blood vessels. Pathophysiology - mechanical compression of brain sue to rupture of blood vessels forming hematoma, due to this inflammation, oxidative stress and vasospasm occurs and secondary ischemic injury occurs in surrounding tissues. GREYHOUNDS- Mechanism - intense exertions and trauma causing rupture of vessels, severe transient hypertension cause increase in shear stress, microvessel rupture due to high cardiac output and thin vessel walls and secondary vessel wall stress cause coagulopathy or hyperviscosity.

Pathophysiology - perivascular edema maye be associated with localized intracerebral hemorrhage. They show mechanical rupture due to stress rather than any atherosclerotic changes.

Genetic and Molecular Basis:-In humans, genetic factors significantly influence stroke risk. Mutations in genes such as NOTCH3 (CADASIL), COL4A1/COL4A2 (small-vessel disease), and GLA (Fabry disease) are strongly associated with specific stroke subtypes (Lindgren et al., 2015).Genome-wide studies have also linked common variants affecting lipid metabolism, coagulation, and vascular function (Malik et al., 2018). In greyhounds, while defined stroke-related genes are not yet reported, physiological traits such as high hematocrit, unique thromboelastography profiles, and elevated plasma eicosanoids(Martinez et al., 2016) may contribute to hypertension and vascular stress — potential predisposing factors for cerebrovascular accidents(Kent et al., 2014). This suggests a conserved molecular basis involving endothelial dysfunction and oxidative stress across species.

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Conclusion:

We finally come to a conclusion that stroke and hemorrhage is a vast topic with various factors affecting life, and various pre disposing factors as well which should be looked out to. The end result is to spread awareness and knowledge about the concerned topic for the future.

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