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## New Data in Stroke Patient's Rehabilitation: Review

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**Abstract---***Stroke has a special place in clinical neurology as the brain is the center of the nervous system. They require immediate treatment as the time burden can dramatically worsen their development. The distinction of stroke it is done in the form of damage. 80-88% are ischemic strokes and 12-20% are hemorrhagic strokes. The clinical manifestations of cerebrovascular attacks depend on the location of the damage in the brain parenchyma and specifically in the affected vessel. The separation of cerebral ischemia and hemorrhage syndromes follows anatomical criteria because it depends on the arterial branch that is damaged. The factors that favor stroke with the main causes being hypertension, atherosclerotic plaque rupture, heart diseases as well as people's lifestyle, are a large part of nursing for their prevention in the general population. The global knowledge of the brain (anatomy and physiology) and the understanding of the functioning of strokes helps us as nurses to enrich our knowledge and have a general picture of the patient, without focusing only on the treatment. The treatment requires very good medical and nursing staff and their cooperation with physiotherapists, speech therapists, and other health scientists, who will plan the treatment.*

**Keywords---***hemorrhagic strokes, hypertension, physiotherapists, speech therapists, stroke.*

## Introduction

Stroke is a cerebrovascular disease that occurs when the blood supply to the brain is interrupted, or when bleeding occurs in brain tissue, resulting in loss of brain function (Lee et al., 2022). Stroke is a terrifying disease occurring every two seconds, with people dying every six seconds due to stroke worldwide, and 15 million new cases occurring yearly (Westlake et al., 2023). Stroke is a complex disease with a substantial genetic component, the heritability of which ranges from 16% to 40%, and remains the second leading cause of death globally and the third leading cause of death and disability (Potter et al., 2022). Over the last two decades (1990–2019), there has been an increase in the absolute number of incident strokes by 70%, prevalent strokes by 85%, deaths from stroke by 43%, and disability-adjusted life-years (DALYs) by 32% (Potter et al., 2022). Around 85–90% of all stroke cases account for ischemic stroke (IS) due to an embolus or thrombosis causing vascular occlusion in situ in certain brain parts; in the rest of cases, hemorrhagic stroke (HS) occurs (Nikolic et al., 2020). Approximately 40% of patients suffer from functional impairment after stroke onset, and 15–30% experience severe motor, sensory, cognitive, perceptual, and/or language impairments (Lee et al., 2022). In particular, more than 85% of patients with stroke experience hemiplegia, which results in impaired upper limb function and decreased motor ability (Lee et al., 2022). This impairment is a major factor that affects the ability to balance, and the levels of daily and social activities (Lee et al., 2022).

The middle-aged and the elderly are the high-incidence population of stroke. The function of tissues and organs of the elderly is declining, the autonomic nerve activity is disordered, the ability to regulate vasomotor and systolic is reduced, the degree of vascular wall sclerosis is aggravated, and the possibility of ischemic stroke is increased. After rescuing from death stroke patients nearly always have some kind of sequelae, such as coma, expression disorder, sensory disturbance, and limb hemiplegia, which create a self-care ability decline and affect their quality of life (Huang et al., 2022).

### *Historical review*

The first appearance of the term "stroke" was in 1599. Until then, the term apoplexy was used, a diagnosis that had existed since the time of the writings of Hippocrates. It was not until the 17th century and the rise of physician-anatomists that these ideas were questioned. In 1602, the Swedish physician Felix Platter performed a brain autopsy after one of his patients died from a stroke. He concluded, with the findings of the autopsy, in the following words: "A phlegmatic humor is obstructing the inner passages of the brain". This brief statement summarizes two critical insights that the study of historical disease evidence provides: First, every scientific observation is based on theories, then and now. Second, it is quite difficult to renounce traditional beliefs. Platter and practically all his associates subscribed to the antiquated idea of Galen, that apoplexy was due to the accumulation of phlegm in the ventricles of the brain. And what did the brain autopsy show: phlegm in the cerebral ventricles. Brain autopsies and the idea of brain circulation marked the end of the pre-modern era of stroke.

A true figure of this change was another Swedish physician named Johann Jakob Wepfer. Thanks to his research apoplexy became a cerebrocirculatory disorder. From the 1850s to the 1930s, vascular anatomy and clinical-anatomical correlations, including various brain lesions, were a focus of interest.

Between 1920 and 1970, the pathophysiology of vascular lesions reached its zenith, with the contribution of such important figures as the French Charles Foix, Capitoline Wolkoff of St. Petersburg, and the Canadian Charles Miller-Fisher. From 1975 onward, research into risk factors, stroke registries, randomized trials, databases, and a general mobilization toward "new treatments" can be observed. Therefore, by the end of the twentieth century, stroke medicine became a subdiscipline of neurology, in theory as well as in practice (Karenberg, 2020).

## Classification of Stroke

### *Ischemic Stroke (IS)*

Of all strokes, ≈87% are ischemic, 10% are intracranial hemorrhage, and 3% are subarachnoid hemorrhage. Blockages in ischemic strokes are usually due to blood clots that become trapped in one of the cerebral arteries. Until now, tissue plasminogen activator (tPA), a thrombolytic drug that can break up clots, is the only treatment for ischemic stroke approved by the FDA. However, the patient experiencing the stroke should receive this treatment within a time window of 4.5 hours from the onset of the first symptoms. Treatment with tPA beyond the temporal therapeutic window can lead to hemorrhagic transformation, which can cause brain damage.

If the patient is unable to present to the hospital for tPA treatment, there are other treatment options if the clots are not self-clearing, including thrombectomy which involves physical removal of the clot. Preventive methods, such as anticoagulants and blood pressure and cholesterol-lowering drugs, could also be given, as there is an increased risk of a second stroke occurring soon after the initial stroke. Giving these drugs quickly can help reduce the disabling effects that a stroke can cause (Karenberg, 2020).

### *Hemorrhagic stroke*

Hemorrhagic strokes account for approximately 10-15% of strokes and have a high mortality rate. In this case of pathology, stress on the brain tissues and internal injury lead the blood vessels to rupture. This is a condition that produces toxic effects on the vascular system, thus leading to a heart attack (Grysiewicz et al., 2008; Krishnamurthi et al., 2014). Based on the literature, a distinction is made between intracerebral and subarachnoid hemorrhage. In intracerebral hemorrhage, blood vessels rupture and cause an abnormal pooling of blood within the brain. The main causes of intracerebral hemorrhage are hypertension, disorders in the vascular system, and excessive consumption of anticoagulant and thrombolytic drugs. In subarachnoid hemorrhage, blood collects in the subarachnoid space of the brain due to a head injury or brain aneurysm (Kuriakose & Xiao, 2020).

### *Subarachnoid hemorrhage*

A subarachnoid hemorrhage is a spontaneous and unexpected expulsion of blood into the subarachnoid space, a condition that occurs after trauma. It accounts for 5% of all strokes. It occurs mainly in the young population and has a high degree of mortality and disability, resulting in a societal impact and loss of productive life years comparable to that resulting from cerebral hemorrhage and ischemic stroke. Therefore, although it represents a small percentage of the total number of strokes, subarachnoid hemorrhage is a serious condition and medical emergency, posing a diagnostic and therapeutic challenge in emergency departments (Boccardi et al., 2017).

### *Brainstem stroke*

Lesions involving and affecting the brainstem area make up 25% of all strokes. Typically, cerebral strokes are the result of an interruption of circulation that occurs in the areas of the basilar or vertebral arteries, although a significant percentage have a hemorrhagic etiology. The stem plays an important role in balance control, coordination, hearing, speech, eye movement, and swallowing. For this reason, patients who have suffered a stroke often show ataxia and dysphagia, while a smaller percentage may show hemiparesis, diplopia, and dysarthria. Signs of cortical damage such as neglect, visual-intuitive disturbances, aphasia, and apraxia are generally absent as hemispheric cortical and subcortical areas are intact (Kruger et al., 2007).

### *Epidemiology*

Although a decline in age-standardized incidence rate has been reported, among people < 70 years both prevalence and incidence rates have increased by 22% and 15%, respectively. In 2010, the estimated number of incident ischemic strokes (IS) and HS across the globe was 11.6 million and 5.3 million, respectively; 63% of IS and 80% of HS occurred in low- and middle-income countries (Saini et al., 2021). In 2016, the number of incident new strokes increased to 13.7 million (Saini et al., 2021). In the same year, 5.5 million deaths worldwide were attributed to stroke; IS and HS accounted for 2.7 million and 2.8 million deaths, respectively (Saini et al., 2021).

A geographic distribution of the burden of stroke can be constructed with methodologic limitations including variability in research approaches for reporting the incidence of stroke in different countries as well as a lack of information for many. Worldwide stroke prevalence in 2016 was 80.1 million, 41.1 million in women, and 39.0 million in men (Saini et al., 2021). Annually,  $\approx 795,000$  people experience a new or recurrent stroke in the United States;  $\approx 610,000$  of these are first-time strokes (Saini et al., 2021). This translates to a global stroke prevalence and incidence of  $\approx 1,322$  and 156 per 100,000 persons, respectively, in 2016, and a US stroke prevalence and incidence of  $\approx 2,320$  and 184 per 100,000 persons, respectively, in 2016 (Saini et al., 2021). Stroke is the second leading cause of disability and accounted for  $\approx 116$  million global disability-adjusted life-years (DALYs) lost in 2016 (Saini et al., 2021). Recent data from 2010 to 2017 continue to show alarming increases in stroke incidence and mortality by 5.3% each, prevalence by 19.3%, and DALYs lost by 2.7% (Saini et al., 2021). Most of the burden of this absolute increase in the incidence of strokes is borne by low- and middle-income countries (Saini et al., 2021).

Incidence of stroke is higher in older women (>50% higher incidence compared to men aged 75 years or older), the less educated population, and some racial or ethnic groups (for example, 1.91 per 1,000 in the Black population vs 0.88 per 1,000 in the White population) (Saini et al., 2021). Conventional projections show that by 2030, an additional 3.4 million US adults, representing 3.9% of the adult population, would have had a stroke and absolute stroke mortality would increase by  $\approx 50\%$ , which is  $\approx 64,000$  additional stroke deaths per year compared to 2012 (Saini et al., 2021). These values are higher in middle- or lower-income countries.

### *Risk factors*

A variety of risk factors contribute to the process of having a stroke. In the effort to manage and reduce the latter, the first step is to identify and categorize them. Thus, starting from the base, we see how strokes are divided into hemorrhagic and ischemic, with ischemic representing the majority. Hemorrhagic occurs in the form of subarachnoid and intraparenchymal. Ischemic are subdivided according to the etiology of their appearance into cardioembolic and atherosclerotic, lacunar, or other specific etiologies (sections, vasculitis, specific genetic disorders), and of unknown cause. Although the risk factors between hemorrhagic and ischemic strokes are similar, there are some differentiating factors both between the two major categories and between the subcategories of ischemic strokes. To cite one case, hypertension is a significant risk factor associated with the occurrence of hemorrhagic stroke. However, looking for the cause of hypertension, we end up with atherosclerotic disease, which can pave the way for the occurrence of ischemic stroke (Kumar, 2013; Gradman et al., 2010). One encounters a multitude of risk factors, which of course have undergone a separation for better understanding and treatment. The first and simplest division is into non-modifiable and modifiable. Non-modifiable include age, sex, race-ethnicity, and genes. Non-Modifiable Factors In general, stroke is a condition that is closely related to the process of transitioning to an older age. The incidence of stroke increases with age, with cases doubling for each decade after age 55. The average age of stroke onset is 69.2 years.

### *Sex*

The analysis of the impact of gender on the probability of stroke shows that here too age has assumed a decisive role. At young ages, women have a high or higher risk of stroke compared to men, a condition that owes its existence to the risks of pregnancy and the post-partum state, as well as other hormonal factors, such as hormonal contraceptives. Due to the longer life expectancy found in women, the latter accumulate a greater number of stroke cases.

### *Race*

Racial differences in the odds of having a stroke are also observed. Blacks are twice as likely to have a stroke compared to similar groups of whites and have a higher mortality rate. This difference is pronounced in the field comparing young black adults with white peers, where the risk of subarachnoid and intracranial hemorrhage is greater in the former. One reason for the racial differences could be the higher presence of risk factors, such as hypertension, obesity, and diabetes among blacks, it follows that these factors are not sufficient to justify the prevailing situation. So, one concludes that the basis may be the problems faced by this racial group in trying to access health benefits. Hispanic/Latino Americans, as well as American Indians compared to non-Hispanic whites, also have an increased risk of stroke.

### *Hereditary factors*

Although hereditary factors increase the occurrence of stroke, it is often difficult to separate the causes of whether a pathological condition is due purely to heredity or to shared family habits and lifestyle. Until now, heredity has been recognized as a non-modifiable risk factor, a condition that gene therapies could in the future change.

Some genetic factors, however, may be modifiable, if not curable. Genetic factors can also become modifiable when environmental factors interact with genetic mutations (gene-environment interaction).

Also, people with a predisposition to diabetes or hypertension should change their diet and lifestyle, aimed at reducing the likelihood of developing the disease. In an attempt to explain the way of operation and interaction of genetic information and hereditary elements with the probability of occurrence of a stroke, a distribution of the cases and forms of appearance of this relationship will be made. The first is the case in which specific rare single-gene disorders may pave the way for the emergence of individual familial syndromes for which stroke is the primary or

sole expression, as is, for example, cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy). Second, comes the case in which single-gene disorders may cause a multisystem disorder, through which stroke will appear as an expression of it, as in the case of sickle cell anemia. Third, some common parameters of genetic polymorphisms (common variants of genetic polymorphisms) have been linked to the possibility of stroke, although the specific and individual contribution of such polymorphisms is considered moderate. Fourth, the genetic causes of common and conventional risk factors such as atrial fibrillation (AF), diabetes mellitus, and hypertension are associated with the likelihood of stroke.

Emerging research suggests that genetic investigations could help distinguish subtypes and even contribute to patient management. For example, there is an association between gene mutations that increase the risk of atrial fibrillation (AF) and ischemic stroke. This raises the possibility that genetic testing could help diagnose strokes that may be due to atrial fibrillation (Boehme et al., 2017).

### *Modifiable factors*

The modifiable factors are of great value, since with the help of strategic interventions aimed at reducing these factors, a reduction in the probability of stroke is created as a product of this effort. The sooner these factors are identified and modified, the better. Modifiable factors can be divided into medical and behavioral.

### *Hypertension*

Hypertension is the most important modifiable risk factor that exhibits a strong, direct, linear, and continuous relationship between blood pressure and the likelihood of stroke. With hypertension defined by a definition that includes both a history of hypertension and a quantitative blood pressure reading of 160/90 mmHg, the portion of the stroke population whose condition is attributed to hypertension reaches 54%. The effect of pressure appears to be greater in hemorrhagic than in ischemic stroke. Even in people who have not been diagnosed with hypertension, the higher the pressure, the greater the risk of stroke. As we age, blood pressure increases, with more than two-thirds of people over 65 having high blood pressure. Hypertension control is something that has improved due to increased attention and treatment options, with 50% under control in 2008, and the prevalence of hypertension in the US reaching 29%. Research shows that fluctuations in pressure values in the same person may also pose a risk, a situation that implies a disturbance in the mechanism and function of cardiovascular homeostasis.

As a way of managing and dealing with hypertension, in addition to medication, it is of utmost importance to implement changes in diet and physical activity, with the latter needing to be increased. Blood pressure is a strong factor in the occurrence of ischemic stroke and intracranial hemorrhage, and there are data to support that controlling blood pressure below values of 150/90 mmHg reduces the risk of stroke. However, a lower blood pressure value that would result from an intensive blood pressure regulation intervention does not seem to be supported by the data, especially when the intervention refers to people of advanced age (Wajngarten & Silva, 2019)

### *Diabetes mellitus*

Diabetes mellitus is an independent risk factor for stroke, with a 2-fold increased risk for diabetic patients. Stroke accounts for about 20% of deaths in diabetics. Prediabetics are also at increased risk for stroke. About 8% of Americans have diabetes, with nearly half of the American population age 65 and older having prediabetes. The length of time someone has had diabetes also influences the outcome of the events. Diabetic patients who have suffered a stroke are more likely to be young, black, and more likely to have other risk factors in their lives. There are marked differences in the potential course of stroke between patients who have diabetes and those who do not. Diabetic patients have more frequent ischemic strokes than hemorrhagic strokes, and lacunar infarctions are the most common type of stroke. This may be due to the higher prevalence of microvascular disease and coexisting hypertension seen in this group of patients. Prognostic characteristics also differ from the general stroke population, as diabetes is associated with an increased risk of subsequent strokes, greater functional disability, longer hospital stays, and increased mortality. A higher risk of stroke-related dementia has also been reported (Tun et al., 2017).

The combined use of a change in the person's behavior and medication has been shown to reduce the risk of having a stroke. Of interest, glycemic control alone in diabetics does not provide the risk reduction afforded by intensive behavior modification interventions combined with medical intervention (Tun et al., 2017).

### *Dyslipidemia*

Atherosclerosis is a major cause of vascular disease worldwide, including heart disease, peripheral vascular disease, and stroke. The development of atherosclerosis is multifactorial and is associated with the traditional risk factors of hypertension, diabetes, smoking, and hyperlipidemia. Specific lipid abnormalities associated with atherosclerosis include elevated triglycerides, low-density lipoprotein (HDL), and high-low-density lipoprotein (LDL). (<https://link.springer.com/content/pdf/10.1007/s11910-020-01052-4.pdf>) However, it seems that dyslipidemia is a risk factor for the occurrence of a stroke. Nevertheless, the way of connecting dyslipidemia with the two forms of stroke, ischemic and hemorrhagic, is special. There appears to be an increased risk of ischemic stroke with elevated total cholesterol, and a decreased risk when high-density lipoprotein cholesterol is elevated. The effect of triglycerides on stroke is controversial (Smyth et al., 2023).

The risk appears to depend on the type of stroke, with cholesterol levels having the greatest association with large-artery ischemic stroke compared to other types of ischemic stroke. Total cholesterol is inversely related to hemorrhagic stroke, with the latter being more likely to occur as total cholesterol levels decrease (Boehme et al., 2017).

An abundance of results has supported the importance of lipid-lowering therapy in reducing the risk of cardiovascular complications. However, there are still outstanding questions regarding the optimal management of dyslipidemia in stroke patients. Until now, statin therapy has been the gold standard for secondary stroke prevention in all stroke patients, and an intensive statin therapy aimed at lower and lower low-density lipoprotein cholesterol (LDL-C) values. Lipid-lowering therapy should be started as soon as possible after a sudden and immediate stroke event with statins being the first choice of treatment. If a statin therapy reaching the maximal intake values of the particular formulation fails to approach the desired goals, a combination therapy, or switching to another lipid-lowering intervention is suggested (Rahayu et al., 2020).

### **Sedentary Behavior, Diet/Nutrition, Obesity and Metabolic Syndrome Physical activity**

Physical inactivity is linked to many negative health effects, including stroke. Physically active people have a lower risk of stroke and stroke mortality compared to those who are inactive. The relationship between physical activity and stroke may be due to the relative reduction in blood pressure, reduction in diabetes, and reduction in excess body weight.

#### *Diet*

Diet affects stroke risk and other stroke risk factors such as diabetes, hypertension, and dyslipidemia. There are several limitations in diet studies, such as recall bias and measurement error, but some specific diet and diet components are well-established risk factors for stroke. For example, salt intake is associated with an increased risk of hypertension and stroke, while increased potassium intake is associated with a decreased risk of stroke. A Mediterranean diet, or a diet rich in fruits and vegetables, reduces the risk of stroke (Boehme et al., 2017).

#### *Obesity*

Obesity is the second preventable cause of death worldwide (after tobacco use) and is considered a public health problem, with prevalence doubling since 1990 due to the global spread of its risk factors and the exponential increase in its consequences. Factors that have helped to establish a large number of obesity cases are dietary changes, sugar intake, chemicals added to food, larger food portions, low/insufficient physical activity, poor eating habits, more processed foods, and foods with high calorific value. All of the above contribute to the increase in body weight of the population, a situation that presents obesity as a pandemic. The diagnosis of obesity is associated with BMI (Body Mass Index) values above 30kg/m<sup>2</sup>.

However, different regions and countries must be considered, as measurements may vary. BMI assessments are not used in ages 2-18 years. Reference is made in the literature to a conjecture called the Obesity paradox theory, which states that patients with a high BMI could have a better prognosis than leaner patients. This means that even if obesity leads to higher complications and risk of numerous diseases and complications, high fat concentration may play a protective role against infections and, always about stroke, and better survival outcomes (Boehme et al., 2017). Body weight and obesity are risk factors for stroke, although the specific ways in which they increase stroke risk are under debate.

Obesity is associated with stroke risk factors such as hypertension and diabetes (Boehme et al., 2017). BMI is associated with stroke risk. Nevertheless, it seems that after adjusting for the risk factors of hypertension and diabetes, BMI itself loses its statistical value (Boehme et al., 2017).

### *Metabolic syndrome*

Metabolic syndrome (MetS) is an accumulation of vascular risk factors and metabolic abnormalities, such as (1) the central distribution of obesity, (2) atherogenic dyslipidemia, which is mainly characterized by elevated triglycerides and low high-density lipoprotein, (3) high blood pressure, and (4) hyperglycemia. This cluster of closely related factors appears to increase the risk of vascular disease, promoting the development of atherosclerotic vascular disease and type II diabetes mellitus (Boehme et al., 2017). Metabolic syndrome is prevalent in the US with 34% of the population meeting the criteria, and although it is associated with an increased risk of cardiovascular disease, the relationship between metabolic syndrome and stroke is on the rise, although this relationship has not been discussed enough. The risk of ischemic stroke due to metabolic syndrome, with the risk of stroke increasing as the components of the syndrome increase. Given that the components of the metabolic syndrome are individually associated with stroke, the combination of these risk factors appears to be associated with an increased risk of stroke (Boehme et al., 2017). Specific therapies targeting insulin resistance (insulin sensitizers) may provide additional benefits in stroke prevention beyond the risk reduction achieved by treating the individual components of the metabolic syndrome (Boehme et al., 2017).

### *Alcohol consumption*

A person's current daily alcohol consumption appears to be associated with all strokes, with a greater bias toward intracranial hemorrhage after multivariate adjustment. Heavy episodic drinking, and heavy drinking in general, has been linked to a higher risk of all strokes, ischemic and hemorrhagic, and no reduction in stroke was observed with low alcohol consumption, compared to non-drinkers. Differences in association by predominant type of alcohol consumed with increased risk were seen with spirits, beer, or other alcoholic beverages, but not wine. Additional adjustments and changes in the incidence of binge drinking and the overall amount of alcohol consumption led to a significant reduction in the odds of all types of strokes (Tun et al., 2017).

### *Substance abuse and smoking*

Abuse of illicit substances, such as cocaine, heroin, amphetamines, and ecstasy, is associated with an increased risk of ischemic and hemorrhagic types of strokes. Smoking remains a significant risk factor for stroke, nearly doubling the risk, with a dose-response relationship between years of smoking and stroke risk. It is estimated that smoking contributes to approximately 15% of all stroke deaths annually. Quitting smoking rapidly reduces the risk of stroke, with the additional risk nearly disappearing 2 to 4 years after quitting. Secondhand smoke has been identified as an independent risk factor for stroke, with the risk of stroke increasing by 30% after adjusting for other stroke risk factors, for those exposed to secondhand smoke compared to those not exposed (Boehme et al., 2017).

### *Inflammation and infection*

Research results show that inflammation is an important factor leading to atherosclerosis, thrombosis, and diseases of the small cerebral vessels, with all important mechanisms leading to a risk of large-artery ischemic stroke, cardioembolic, foveal, and cryptogenic stroke. Randomized controlled trials in patients with coronary artery disease have shown that an anti-inflammatory treatment prevents the recurrence of vascular events (Boehme et al., 2017).

Inflammatory biomarkers include cytokines, chemokines, and acute-phase reactants that modulate the inflammatory response. Increases in the inflammatory mediator's IL (interleukin)-6, C-reactive protein (CRP), and Lp-PLA2 (lipoprotein-linked phospholipase A) have been associated with an increased risk of stroke.

An additional biomarker of high interest circulating with the English terminology soluble lectinlike oxidized LDL receptor-1 is a lipid receptor that appears with inflammation and is associated with a risk of stroke. Elevated CRP values have also been associated with stroke recurrence combined with vascular event recurrence, vascular death, and nonvascular death. IL-6 and Lp-PLA2 have similarly been linked to stroke recurrence, poststroke myocardial infarction, and death. The preponderance of evidence supports a relationship between elevated biomarkers with a concomitant increase in the risk of stroke, recurrent stroke, and post-stroke vascular events and

mortality. Elevations in biomarker values can also serve as predictors of a patient's clinical picture and functional outcomes after a stroke (Boehme et al., 2017).

### *Signs of stroke*

The stroke occurs suddenly, endangering either our own life and health or that of another familiar or foreign person. An important part of recognizing the signs that suggest the occurrence of a stroke is the knowledge of the assumption that the symptoms make their appearance suddenly. The warning signs of a stroke are signals sent by the body that the brain is not receiving the necessary oxygen. The longer stroke treatment is delayed, the more damage is allowed to occur. Most of the time the person who has been affected by the stroke does not understand that he is in a difficult situation for his health, while he may not give any basis to the signs. The stroke itself may still render the person incapable of understanding their condition and the risks it entails. If the incident also occurs in a space with the presence of other people, passers-by may believe that the person showing the signs is simply in a state of confusion. But even when those around them recognize the existence of a problem, they often don't know how to call for help or help themselves. A person who suffers a stroke has a better chance of recovery if someone around them recognizes the signs and acts immediately. In the case of a transient ischemic attack (transient ischemic attack, also known as a mini-stroke) the symptoms of the stroke may disappear after a few minutes. Although brief, TIA is a sign of a serious condition that needs medical attention. However, because the symptoms subside, many people ignore them, thus putting their lives at risk.

The best stroke treatments can be used within the first 4.5 hours of the onset of symptoms. Getting the person to the hospital as quickly as possible is a top priority. To better remember the signs that suggest the occurrence of a stroke, the acronym F.A.S.T. has been created, where:

- F – Face: Subject is asked to smile and any imbalance or drooping of one side is noted
- A – Arms: The stroke candidate is asked to raise both arms. It is noted if one hand moves in a different direction than the other, tending to be led down
- S – Speech: We put the person in the process of repeating a simple phrase and observe signs of inability to speak clearly and smoothly
- T – Time (time): In case any of the above signs are verified, the telephone number corresponding to the emergency is called immediately

Additional points that may help understand the occurrence of a stroke include:

- Sudden numbness: numbness or weakness in the face, arm, or leg, especially on one side of the body
- Sudden agitation and confusion: Difficulty speaking or understanding
- Sudden difficulty in seeing: Decreased ability to see in one or both eyes
- Sudden difficulty walking: Dizziness, lack of balance and coordination
- Sudden severe headache: Severe headache with no apparent cause

An important element that should be noted is, as far as possible, the exact time of onset of symptoms, information that will help the medical staff make the best treatment decisions. Although the recommended time window for the best course of recovery is 4.5 hours, it is still important to bring people to the hospital who either woke up with symptoms or for any other reason exceeded the recommended time window. The transport of the affected to the hospital should be undertaken by an ambulance since it is manned by medical personnel (Lee et al., 2018).

### *Symptoms*

Brain tissue is drained of blood and receives nourishment through two vascular systems, the anterior and posterior circulations. Based on the location of the infarct, an ischemic stroke can be classified as (1) anterior circulation ischemic stroke (ACIS) and (2) posterior circulation ischemic stroke (PCIS). Patients with both anterior and posterior circulation ischemic stroke often present with their own site-specific, site-dependent neurologic deficits. The anterior cerebral circulation is drained by the internal carotid arteries and their branches, including the large intracranial vessels, (1) the middle cerebral arteries (MCAs), (2) the anterior cerebral arteries (ACAs), and (3) small vessels (bitrating arteries of the aforementioned vessels). The perfusion area occupies most of the hemisphere except the occipital and medial temporal lobes. Clinical features can present as middle cerebral artery syndrome (MCA syndrome), anterior cerebral artery syndrome (ACA syndrome), or lacunar syndrome (LS).



The usual clinical features are:

- dysarthria,
- central personal paralysis
- and motor and/or sensory involvement of the opposite extremities. The typical expression of infarction in the region of the middle cerebral artery, the most common case in ischemic anterior circulation:
- is dysarthria
- opposite central personal paralysis ipsilateral deviation of eyes
- opposite hemianopsia
- opposite limb weakness and sensory deficits
- and cortical signs including aphasia (left middle cerebral artery) or neglect syndrome (hemineglect, right middle cerebral artery). Anterior cerebral artery infarction may be asymptomatic or weakness may occur mainly in the lower extremity (Peláez-Vélez et al., 2023).

## Intervention

Neuroplasticity is the ability of the brain to redevelop its neuron network at the healthy part of the brain, to take over the role of the damaged part. The success of neuroplasticity relies on the neuron growth factor proteins known as brain-derived neurotrophic factor (BDNF). BDNF plays an important role and is involved in neuron growth, synaptic transmission, and synthesis of neurotransmitters by binding to tropomyosin-receptor kinase B (TrkB). However, to activate the growth of the neuroplasticity needs for stimulation on the cells. Motor impairment is a common consequence of stroke causing difficulty in independent movement.

The first month of post-stroke rehabilitation is the most effective period for recovery. Exposure to frequent activities in an individual's daily life stimulates the brain. Rehabilitation intervention such as physiotherapy is one of the techniques to help the patient (Chemerinski & Robinson, 2000).

Physiotherapists in clinical settings usually conventionally perform interventions. Conventional physiotherapy for stroke commonly involves changing positions, breathing exercises, and exercise therapy in passive and active mobilization. It varies among settings, is non-standard, and depends on the therapist's preference. The conventional intervention however shows effectiveness but it is not optimal. Standard protocol interventions such as Brunnstorm, Bobath, Proprioceptive Neuromuscular Facilitation (PNF), and Constraint Induced Movement Therapy (CIMT) were found to be effective. It is encouraged to use the standard protocol to ensure that optimal benefits can be derived. Physiotherapy interventions were found to significantly improve balance and functional ability in daily living activities. Although it is known that rehabilitation such as physiotherapy helps to improve patients' performance and ability, it is only theorized and the impact of the physiotherapy intervention on brain plasticity is unknown (Kersten et al., 2007; Santos et al., 2010).

Balance ability is important for posture control and stabilization to allow the person to independently perform an activity and it may become an indicator to predict independence and good prognosis. Rehabilitation is vital for minimizing sequelae after stroke, and patients who undergo continuous professional and systematic rehabilitation following the acute phase tend to recover rapidly.

Drug and rehabilitation therapy are currently practiced rehabilitation treatments for stroke. Various interventions can be applied for recovery, such as bilateral training, repetitive task training, constraint-induced movement therapy, electrical stimulation, robotic therapy, and exercise (Karenberg, 2020). Among these, exercise is crucial because it helps patients return to activities of daily life by restoring the function of impaired muscles and improving physical function. Exercise is also essential for preventing secondary complications, as was reported in a study determining that continued exercise and physical activity after a stroke reduce the risk of recurrence of cardiovascular disease and mortality (Kuriakose & Xiao, 2020). Therefore, guidelines for each type of exercise (passive/isometric/isokinetic/isotonic) are necessary, as well as programs tailored to the individual functional levels of patients, such as the time since the injury occurrence.

The combination of conventional rehabilitation techniques alongside the introduction of new technologies supported by the most updated scientific evidence becomes, therefore, a cornerstone in the treatment of strokes. There are variable methods that are used for the intervention during physiotherapy such as Virtual Reality, Mirror therapy, and Motor imagery (Murphy & Werring, 2020).

### *Virtual Reality (VR)*

Virtual reality (VR) is the creation of an artificial scenario adapted to the real world, in which it is possible to interact, navigate, and immerse in a three-dimensional space by applying different sensory stimuli. Thus, it implies a

full immersion process of the person or the patient in a virtual scenario as close as possible to the real world. VR can be used in the clinical field as a non-invasive technological therapy that allows the patient to interact with a computer-created environment. The VR-based physiotherapy interventions could be classified into four categories: robot-assisted gait training, treadmill walking, stationary walking, and other interventions. The use of VR and video games in the health sector increasingly requires more evidence of their efficacy in combination with conventional treatments.

This efficacy is explained by their numerous applications and beneficial effects in patients affected by neurological, psychiatric, or musculoskeletal pathologies. The implementation of this technology in the field of neurology is of paramount importance since there is a large number of studies supporting and endorsing the beneficial effects on the patient, specifically in stroke rehabilitation, providing improvements in gait, postural balance, trunk balance, strength, spasticity, upper limb motor function and improvements in cognitive level and attention, among others (Lee et al., 2018).

From studies, it's found statistically significant differences in dynamic balance and gait, except for static balance, and a statistically significant improvement after the intervention in dynamic balance and gait, with no significant correlation between postural sway and other dependent variables. Different articles use VR glasses with significant differences in balance and gait between the intervention and control groups. In the study by Lee et al. (2018), in which a game based on canoe movement is used, significant results were found in postural balance and upper extremity motor function.

The systematic review by Rutkowski et al. (2020), analyzed twenty articles based on the use of VR in different neurological and orthopedic pathologies, highlighting that the use of specialized VR approaches can improve balance in neurological patients.

### *Mirror Therapy (MT)*

Mirror therapy (MT) is a kind of rehabilitation strategy wherein patients can experience the illusion of the affected hand's movement by observing the unaffected hand's reflection in a mirror placed on a sagittal plane between the hands. For the heavy involvement of the visuomotor imagery process, MT leads to improved physical impairment through yielding activations in the motor-associated network of the brain.

Different from high-intensity motor practice, MT is a priming technique for brain activation used to re-establish the motor function of the affected limb by enriching the visual and proprioceptive inputs. The beneficial effects of mirror visual feedback from MT on motor recovery could contribute to the reduction of imbalance in the motor cortex activity between the ipsilesional and contralesional hemispheres after stroke. Recently, MT has been recommended to restore the sensorimotor function of chronic stroke patients as evidenced by a systematic review (Sayfullaevich, 2021).

The latest Cochrane review of interventions for improving upper limb function following stroke recommended using mirror therapy as a routine practice. However, asymmetry in the sitting posture during the conducting of MT using a traditional mirror box will cause problems with movement learning and control. VR technology provides beneficial effects on the management of motor symptoms for delivering highly immersive environments for motor learning. The rationale for using VR-based mirror therapy for facilitating upper limb recovery following stroke includes multisensory neuroplasticity, increasing the range and difficulty of the involved training programs, and eliciting a stronger sense of ownership of the affected limb. Arm-hand movement training in virtual reality (VR) is an effective strategy for promoting the functional motor recovery of stroke patients as VR provides a training environment involving intensive visual, auditory, and haptic feedback from computerized technology. The mirror visual illusion that emerges through VR systems strengthens multisensory integration, or the effect of visual signals interacting with bilateral proprioceptive signals. Recent research revealed that the add-on effects of VR to MT empowered rehabilitation outcomes for the engagement of a contralesional action observation network. Through the visualization of the mirrored movements of the non-paretic limb with a computer-generated scenario, VR-based MT (VR-MT) demonstrated its feasibility in interventions for patients with functional neurological disorders and stroke (Hsu et al., 2022).

The rationale for improving sensory function following VR-MT receives support from a recent research study related to brain activation patterns for mirror therapy. Stronger activation occurred in the primary sensorimotor cortex for VR-based mirror therapy than in the traditional mirror box condition. The synchronous multisensory perception, looking at the mirror hand presented in a VR scenario, increases activation in somatosensory areas more than seeing the hand in a mirror. However, the touch-pressure sensibility of the affected hand did not reveal a significant change in the VR-MT group. It is worth noting that the effects of mirror therapy on sensation have rarely

been discussed. Only 1 randomized control trial found that mirror therapy improved temperature sense. The results of previous research demonstrated that mirror therapy using advanced technology, such as a camera, augmented reflection, and VR, is a feasible strategy for improving upper extremity function safely (Metcalf et al., 2001; Schulz & Grant, 2000).

### *Movement Imagery (MI)*

Movement imagination, known as motor imagery, in combination with virtual reality, may provide a way for stroke patients with severe motor disabilities to begin rehabilitation. Motor imagery (MI) is the mental representation of a body movement. In MI, a patient is required to mentally rehearse a movement without its physical execution. It was suggested that MI could promote recovery of the lesioned brain areas using functional and other neuronal networks; hence, MI appears to be an effective alternative therapy for early post-stroke motor rehabilitation. However, MI requires training and may be challenging, particularly for stroke patients. It was shown that observing an action may activate the motor cortex and promote motor learning; thus, facilitating neural recovery. This is due to the mirror neurons being activated during both action execution and observation.

The mirror neuron system assists the observer in imitating an observed action; hence, there may be an overlap between action observation (AO) and the process of performing a physical movement. It was also reported that AO via virtual reality (VR) technology could assist stroke patients to focus on MI tasks by visually stimulating real movements within an immersive environment, minimizing distractions from the surroundings, thus, potentially reducing the difficulty of conventional MI. VR technology has also been shown to assist stroke patients in a minimally conscious state to perform MI. As a result, combining MI and AO for performing the same movement may enhance activation of the motor cortex and facilitate motor recovery of stroke patients, especially in stage 1 of the BMRS. Despite there being positive evidence of VR-assisted MI in post-stroke rehabilitation, the experimental protocol of different studies is not standardized and involves various VR machinery. The findings of different VR-MI studies are not conclusive though promising (Choy et al., 2023).

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