An Overview on Ischemic and Hemorrhagic Strokes and Treatments

Clara Tanseul Hwang

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Strokes are the leading cause of neurological damage and disability in the world. Strokes are classified into two types: ischemic, in which an artery in the brain is blocked, and hemorrhagic strokes, in which a blood vessel in the brain ruptures. Both types of strokes can cause severe mental and physical impairments, including paralysis and speech impairments. In this paper, an overview of the diagnosis, disorders, and surgical/ non-surgical treatments for each ischemic and hemorrhagic stroke are described, as each type requires distinct courses of action. Further, an overview of the potential long-term consequences is provided such as speech and movement disorders, as well as treatments such as physical therapies to regain movement, occupational therapies to regain awareness, and speech therapy is used to regain speaking abilities.

Introduction

Strokes occur when blood supply to an artery in the brain is interrupted and are the leading cause of neurological disability and the fifth leading cause of death in the United States (Dillon et al., 2019)[1]. Strokes can cause drastic physical and cognitive impairments affecting all parts of the body. Risk of stroke increases with age and certain medical conditions such as high blood pressure, diabetes, and atrial fibrillation (Kuriakose & Xiao, 2020)[2]. Two different types of strokes will be covered in this paper: ischemic, in which an artery in the brain becomes clotted due to a buildup in the blood stream and hemorrhagic, in which a blood vessel in the brain ruptures. Ischemic and hemorrhagic strokes account for collectively $\tilde{9}7\%$ of strokes, of which the majority (85%) are ischemic, though hemorrhagic stroke has a much higher mortality rate (50%). The remaining percentage of strokes belong in other categories, such as transient ischemic attacks.(Kuriakose & Xiao, 2020)[2].

In extreme cases, strokes can lead to paralysis or hemiplegia. When strokes affect parts of the brain that control movement , like the basal ganglia or thalamus, they can lead to range of disorders like hemichorea, which causes rapid and involuntary movements of flexion of distal body parts, and dystonia, which causes muscle contractions causing repetitive movements or postures (Tater & Pandey, 2021)[3].

This is caused by any lesions on segments of the brain such as the basal ganglia or thalamus. One of the most common movement disorders caused by strokes is hemichorea. This creates rapid involuntary movements of flexion and extension from mostly distal body parts. Another common movement disorder is dystonia. Dystonia is characterized by muscle contractions causing repetitive movements or postures. Dystonia can cause significant disability if left untreated, but can be sometimes helped with use of medication, such as botulinum toxin injections which prevent muscle movements in specific areas, and therapy (Tater & Pandey, 2021)[3].

Stroke Rating Scales

There are many scales used to determine the initial impact of strokes and what treatments should follow. The modified Rankin Scale (mRS) ranks symptoms from 0 to 6 to help physicians decide what steps to take next in treating their patients (Linwood, 2022)[4]. This scale allows physicians to determine what the proper course of treatment is for their patient and predict clinic outcomes. However, it does not factor some individual concerns that could affect the patient's repair timeline. The NIH stroke scale is a similar ranking system that determines the patient's level of consciousness post-stroke, eye movements, facial palsy, and motor arm/leg function. It also evaluates sensory function along with speech and language skills. There are eleven categories of evaluation for this ranking system, and the categories range from 0 (the least symptomatic), to 2, 3 , or 4. The Alberta Stroke Program Early CT (ASPECT) Score helps judge whether patients are likely to be affected by ischemic strokes in their sleep, which helps patients who may be usually excluded from thrombolytic therapy. The ASPECT system is used in conjunction with mRS scores and NIH Stroke Scale scores to make decisions about further treatment plans (Alijanpour et al., 2021)[5]. Treatments may include further medications, or different approaches like physical therapy.

Treatments for Ischemic Strokes

The gray matter in the brain is at a higher risk than the white matter in the brain, and the cerebral artery is at most risk for ischemic attacks. Ischemic strokes can be caused by embolisms, in which a clot travels from a different part of the body, or thrombosis, in which a clot forms within a blood vessel. One of the most commonly used treatments for ischemic strokes was Aspirin, which prevents platelets from forming another clot or clots from forming in the first place. Aspirin was a widely used medication for strokes until it was discovered that it could worsen hemorrhagic strokes by leading to increased intracranial bleeding, as aspirin is a blood thinner. It is now used primarily in stroke prevention, and studies such as the International Stroke Trial (IST) have shown that taking daily Aspirins can decrease the risk for ischemic attacks (Chen et al., 2000)[6]. The trial showed a significant decrease in risk for recurrent ischemic insult in those taking daily Aspirin. Clopidogrel, a drug that binds to platelet receptors in order to inhibit platelet activation, and dipyridamole, a drug that inhibits platelet function by blocking reuptake of vascular and blood cells, may be administered as alternatives for Aspirin. Clopidogrel and Aspirin have similar risks for increased bleeding and hemorrhage, but dipyridamole has the potential to decrease bleeding. In some cases, these drugs may be used in conjunction to break down clots and prevent clots from ever forming (Chen et al., 2000)[6].

1. **Thrombolysis Medicines:** Thrombolysis medicines are used to cleave clots with minimal invasiveness. Alteplase was first approved in the 1990s and includes t-PA (tissue plasminogen activator), one of the most commonly used drugs to treat ischemic strokes, which is injected via catheter into the bloodstream. The drug acts by catalyzing the conversion of plasminogen to plasmin, the primary enzyme used in dissolving clots. Examples of this drug include alteplase and tenecteplase. The more quickly t-PA is administered after a stroke, the more efficacious it is: alteplase should be administered within 4.5 hours of stroke onset. It can also be used to treat acute myocardial infarction, or blockage of blood flow to the heart, and acute massive pulmonary embolism, or blockage of blood flow to the lung (Herpich & Rincon, 2020)[7]. Tenecteplase is a newer thrombolytic agent, which is more specifically targeted to the onset of fibrin and contains a longer half-life. It is derived from the naturally occurring t-PA. This was administered to patients with a single bolus in clinical trials, and shows promise, with its cost efficiency and its efficient dose (Herpich & Rincon, 2020)[7]. Tenecteplase is significantly less costly than alteplase, which may be an important factor in deciding treatments, as it can be up to $3000 dollars cheaper (Dillon et al., 2019)[1]. However, IV thrombolysis using Tenecteplase is not yet FDA approved for AIS (arterial ischemic stroke) patients. This treatment has only yet been approved to be used for patients with minor neurological impairments and no major intracranial occlusions (Dillon et al., 2019)[1]. Anticoagulants are used post-stroke and include warfarin and heparin, which help prevent further blood clots. However, anti-coagulation medicines have both risks and benefits. For the prevention of strokes, anticoagulants can hold great risks for patients who may experience increased risks of excessive bleeding. Anticoagulants are also not suitable for patients with liver problems, impaired renal functions, and severe hematomas. The greatest risk for using anticoagulants post ischemic stroke is the risk of conversion to hemorrhagic stroke. Furthermore, these medications can not be used in patients with a low platelet count (under 10,000) (Seiffge et al., 2019)[8]. Seizures are also mildly common after a stroke as a study found that 23% of 423 patients had a seizure early-post stroke. Although the risk for seizures is higher in hemorrhagic strokes, with a prospective 15.4% risk, the risk for seizures in ischemic patients is 8.7%. Anticonvulsant drugs include gabapentin, levetiracetam, and lamotrigine, which act by preventing abnormal electrical activity in the brain and the release of excitatory neurotransmitters (Tanaka et al., 2021)[9]. Some newer advancements have been made in treating ischemic strokes. Beta blockers can be used to stop immediate stress hormones and stop the constriction of blood vessels. However, beta blockers pose a risk of greater vascular disease, and may lead to a more severe second stroke or greater vascular complications. The proposed benefits of beta blockers include preventing post-stroke myocardial infarction and infections that are associated with excessive sympathetic activation after stroke (Balla et al., 2021)[10]. In observations and randomized clinical trials, treatment was conducted as monotherapy as well as in combination with other hypertensive drugs. However, meta-analysis from these studies did not produce great evidence for benefits of using beta blockers post-stroke (Balla et al., 2021)[10].

2. **Surgical Procedures:** A thrombectomy is a procedure in which a catheter is inserted in the blood vessel and allows a clot to be suctioned out. An incision is made, and a temporary balloon may be placed to help open up the blood vessel. Large bore aspiration catheters are used to suction out the thrombus, along with the use of an aspiration pump that creates the necessary negative pressure to remove the thrombus. Microcatheters are also used to aid the more complex and complete occlusions in the vascular structure (Elgendy et al., 2015)[11]. Mechanical thrombectomies are used for patients with a mRS score that is less than 2 and an ASPECT score that is greater or equal to 6. This procedure is mostly used for patients with insult to the proximal middle cerebral artery (Elgendy et al., 2015)[11]. A decompressive craniotomy, in which a portion of the skull is removed to relieve pressure on the brain, is an alternative procedure that can be used to treat ischemic strokes, as brain swelling secondary to the stroke may lead to a high mortality rate. In this procedure, a portion of the

skull is removed, which allows the affected tissue to move through the affected area without damaging the unaffected regions of the brain. Decompressive craniotomies are typically used for patients with large cerebellar infarctions and patients with infarctions of the middle cerebral artery territories (Pallesen et al., 2019)[12]. This procedure helps prevent cerebral herniation which may occur due to the pressure buildup in the brain after an ischemic stroke. A fairly new endovascular stroke therapy uses "stentrievers " which deploy a stent within the clot and as the stent expands, the procedure results in partial flow restoration. This differs from other older procedures, like the mechanical thrombectomy because it also provides immediate partial blood flow restoration as the clot is captured. The main devices used for this procedure both produced good patient outcomes, around 50%. High recanalization rates were also recorded, and more clinical trials are ongoing to prove efficacy for these devices (Walcott et al., 2013)[13].

Treatments for Hemorrhagic Strokes

Hemorrhagic strokes can be further divided into two types (1) intracerebral hemorrhage within the white/gray matter of the brain, generally due to hypertension caused by the overuse of anticoagulants and (2) subarachnoid hemorrhages, which are usually caused by trauma to the head.

1. **Pharmaceutical Treatments:** When a patient is admitted and has received a CT to confirm bleeding in the brain, antihypertensive and diuretic drugs may be administered to lessen intracranial hemorrhage. These drugs help prevent enzymes from making angiotensin II, a substance that narrows and constricts blood vessels. ACE inhibitors are a drug that produce similar actions to the body, helping prevent the constriction of blood vessels (Padma, 2010)[14]. Other drugs may be administered to lessen inflammation and decrease stress such as pioglitazone, misoprostol, and celecoxib. Edaravone, flavonoid, nicotinamide mononucleotide (NMN) are administered to help reduce oxidative stress which contributes to bleeding (Badillo & Navarro, 2023)[15].

2. **Surgeries:** Surgeries are used to control intracranial bleeding that leads to hemorrhagic strokes. A decompressive craniectomy or craniotomy may be used in this case, similar to craniotomies used for ischemic strokes, can be used to remove a hemorrhage. In this procedure, instead of the surgeon, the skull is opened in order for the neurosurgeon to clip the aneurysm, a weakened area kin an artery which starts ballooning, which is identified through cerebral angiography images (Badea et al., 2020)[15]. Titanium clips with spring mechanisms are placed on a ballooning blood vessel aneurysm, enabling it to deflate. A secondary angiography is used to determine the restoration of regular blood flow in the brain after the permanent clip is placed. Suboccipital craniotomies are used for cerebral hematoma, but brainstem hemorrhages are not usually removed via craniotomy. Other procedures such as an endovascular microcoil embolism, a procedure that uses small platinum coils to treat aneurysms, may be used to prevent the flow of blood to an aneurysm and help a clot form on the inside of the artery. These procedures are far less invasive, as they do not require a surgeon to actually open up the skull. A needle is placed into the femoral artery of the leg, and a microcatheter is advanced into the brain by using the path of the body's arterial system. This catheter is then used to remove excessive bleeding from the artery. Additional coils that help prevent excessive bleeding may also be used to help the clotting process inside the aneurysm (Badea et al., 2020)[16]. Balloon-assisted coiling is a relatively new technology that uses a balloon catheter surrounded by a coil such that when the balloon is filled with material, the coil expands and reduces risk of bleeding. This may be used in conjunction with a stent which then provides a durable scaffolding for the coiling to stay in place. Balloon-assisted coiling provides an advantage over traditional coils as it may be a better "fit" in aneurysms of "pear" or irregular shapes. Endovascular microcoil embolisms and balloon-assisted coiling are new less invasive technologies than craniotomies which require a part of the skull to be removed, which are used to treat hemorrhages in the brain (Vivanco-Suarez et al., 2023)[17]. One recent advancement is a simultaneous image-based guide during surgery, which helps minimize collateral damage (MISTIE, minimally invasive surgical thrombolysis with intracerebral hemorrhage evacuation). This surgery is an alternative for a more invasive craniotomy, and has only been created in the last few decades. In numerous trials, surgeons initiated hematoma aspiration and withdrew blood, then followed with thrombolysis. This procedure has yet to produce better results than standard medical care, so it is not yet recommended to surgeons to use. However, the management of time could provide different results for this procedure, and results may vary if done sooner after the stroke onset. Because minimally invasive trials are preferred, more research is being conducted on the efficacy of MISTIE, although risks of infection, bleeding, and incomplete evacuation of the clot can increase.(Lovelock et al., 2007)[18]. In the clot lysis surgery trial, low dose rt-PA was administered with the primary objective of accelerating the evacuation process of intraventricular hemorrhage. Rt-PA is rarely used in hemorrhages, as it can increase risks of hemorrhage, but in this trial it was administered to patients in low doses so the clot could be reduced. Patients in this program re-

ceived an injection of one milligram of rt-PA through an intravenous drain every 8 hours, until the clot was reduced or the endpoint was met. Preliminary analyses of this trial determined that rt-PA could be administered during the treatment of hemorrhagic strokes in low doses in order to stabilize intraventricular hemorrhagic clots, which was a different approach as rt-PA is usually used to treat ischemic strokes. Hemostatic therapy is used to reduce the progression of hematomas for patients who are most at risk, most of whom are on anticoagulants, which increases the risk for brain bleeds. Fresh plasma is inserted alongside vitamin K, helping decrease bleeding and promote clot production. First, primary hemostasis includes platelet transfusion and encourages new platelets to form clots, followed by secondary hemostasis with clotting factors that continues encouraging clot formation (Diringer & Zazulia, 2012)[19].

Therapies

Therapies to help improve patient function are done very soon after stroke onset, for both ischemic and hemorrhagic strokes. Patients develop many types of disorders after strokes, which may affect every part of the body, with both physical and mental impairments. The goals of therapies are usually to prevent complications with muscle atrophies and reduce pain. Rehabilitations are used to help patients regain the abilities they lost from the stroke.

1. **Timeline of Repair:** During the acute phase, about 72 hours after stroke onset, patients begin low-intensity rehabilitation in the ICU. Not all patients begin rehabilitation at this time, as it varies due to the patient's medical stability and vitals. Early rehabilitation can also pose some risk factors including increasing intracranial pressure or weakening cardiovascular strength. This early rehabilitation is primarily focused on positioning, focused mobility training, bed mobility, and range of motion. Acting early after a stroke can help prevent mental deterioration, stress, and improve consciousness for the patient. Patients may develop movement disorders caused by lesions on the brain, so it is best to act quickly to help develop a plan to treat the movement disorders (Green & Shuaib, 2006)[20]. After six months, patients enter the sub-acute phase in which they are referred to home or in-patient rehabilitation. Patients perform constraint-induced movement therapy and supportive walking. Some hospitals use VR training, which helps motivate patients as well as increasing upper extremity functionality (Shahid et al., 2023)[21]. Six months after the stroke, patients are also given a home exercise program that helps prevent falls and maintain exercise intensity. Studies conducted in the past have proved that performing over 90 hours of physical therapy over the course of three weeks led to a significant increase in upper limb mobility. Another study proved that 300 hours of physical therapy spread over 3 weeks produced similar results, although the degree of improvement may vary (Shahid et al., 2023)[21].

2. **Physical, Occupational, and Speech:** Speech therapy is also widely used after strokes as patients commonly face swallowing difficulties. Stroke survivors are commonly affected by dysphagia or difficultly swallowing and buccal hemineglect, or the inability to detect the presence of substances in the buccal cavity in the left side of the mouth; speech therapy helps improve language and communication for survivors. Up to 50% of patients who face acute stroke attacks are likely to face dysphagia, which can lead to other complications such as pneumonia, undernutrition, and dehydration (Green & Shuaib, 2006)[20]. Patients face thorough screenings like the Modified Barium Swallow Study (MBSS) or the Fiberoptic Endoscopic Evaluation of Swallowing (FEES) to evaluate the extent of their dysphagia, which helps physicians determine the diet and steps of further treatment for patients. To help patients regain the ability to swallow, speech pathologists use EMG (electromagnetic) stimulation to promote activity in the base of the tongue and pharyngeal wall muscles. Electromagnetic stimulation is also used to stimulate the faucial arch in the throat and nerves in the mouth for tasting. Aphasia affects approximately 20-40% of patients post-stroke, and affects the patient's ability to understand instructions. Language therapy can help combat this condition, helping patients regain the ability to form words and sentences (Naeser et al., 2012)[22]. Some patients face a lack of awareness after their stroke, as they are unknowing of their disabilities. Daily functional activities such as pouring water and cleaning can help increase consciousness for these patients that suffer from unilateral neglect: caused by damage to the right brain hemisphere, resulting in difficulties attending to stimuli in the left hemifield. This is included in occupational therapy, which helps patients regain a sense of their lives before the stroke (Rowland et al., 2008)[23]. Through occupational therapies, patients slowly try to regain motor control and limb control, which helps them through activities such as personal care and domestic tasks. These tasks include grooming, eating, cleaning, and learning how to manage medications to take post-stroke. Specific therapies are also conducted to help patients who suffer from movement disorder post-stroke. Upper-limb robot assisted therapy is used widely in order to help patients gain increased flexibility and improved joint integrity. Studies proved that robot assisted gait training (RAGT), in which a robot tethered to the patients' legs provides physical assistance in achieving the correct gait pattern, improved flexibility and lessened the physical burden they faced (Huang et al.,

2022)[24]. Mirror therapy is used to improve motor function, and helps the brain assemble, clarify, and utilize sensory information. The therapy often involves tricking the brain into perceiving movement in affected extremities by having patients look at the movements from reflections in a mirror. This therapy is most suitable for stable patients who have increased brain function than they initially did after stroke onset. This therapy includes testing sensory functions by having patients differentiate between incoming sensory figures. Laser point drills, which give patients visual feedback for motor control, help improve these skills: improving hand eye coordination, visual neglect, and balance (Thieme et al., 2018)[25].Therapies need to be done routinely to improve patient quality of life.

Discussion

The outcomes of this research have provided insight inside the differences between ischemic and hemorrhagic strokes and the treatment options available. The results should be interpreted with caution as treatment plans can vary depending on the hospital and equipment available. The potential consequences of treatment plans are discussed, and this paper shows a broad overview of ways to treat strokes.

Conclusion

Strokes can devastate a patient's life and patient's need a great deal of support to try to improve impairments that strokes may cause. Both ischemic and hemorrhagic strokes require distinct courses of treatment, but the patient in most cases requires therapeutic rehabilitation to overcome the multimodal deficits that strokes produce. Therapies aid in improving patient function and quality of life. Patients must be closely monitored post-stroke, and often continue taking medications to prevent a secondary stroke from occurring. The course of treatment will depend greatly on the hospital and its capabilities, while also focusing on the individual needs of the patient.

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