Stroke: Diagnosis, Treatment, and Rehabilitation

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Abstract— **Stroke is an episode of acute neurological dysfunction occurs when a blood vessel which carries oxygen and nutrients to the brain is either blocked by a clot or bursts. When this happens, part of the brain cannot get the blood it needs and starts to die. Stroke is a severe global healthcare problem and the second most common cause of death. Stroke can be subdivided into two broad categories: ischemic and hemorrhagic stroke. Though ischemic stroke is the most common one (87%), hemorrhagic stroke is responsible for 40% of stroke deaths. In this report, different types of stroke, symptoms, diagnosis, previous and present treatments, stroke rehabilitation and preventions are briefly discussed. Intravenous recombinant tissue plasminogen activator (IV rtPA) remains the standard of care for patients with acute ischemic stroke who present within 3 hours (4.5 hours at best) of symptom onset. Endovascular thrombectomy in selected patients with acute ischemic stroke has shown complete or partial recanalization and improved recovery compared to IV rtPA. Regardless of reperfusion method (i.e., IV rtPA vs. thrombectomy), early reperfusion is highly important for better outcomes. Stroke rehabilitation should be an interdisciplinary approach including doctor, nurses, and therapists, where engaging family members is essential. Novel therapies, especially virtual reality and robotics therapies will play an important role in stroke rehabilitation. However, growing public awareness, rapid access to stroke care units, and leading a healthy life style must be addressed to fight against stroke.**

Keywords: Stroke, ischemic, hemorrhagic, rtPA, thrombectomy

I. INTRODUCTION

Stroke is the second highest reason for death, disability, and dementia worldwide and for the last 15 years, it remained as one of the two leading causes of death globally. It is expected that it will increase significantly in the coming years due to a significant increase in the elderly population in many developed and developing countries [1][2]. Every year, around 800,000 people in the United States experience a stroke which results in more than 140,000 deaths [3]. A stroke is a "brain attack"; it happens when the blood flow to an area of the brain is cut off or interrupted. When this interruption takes place, brain cells deprived of oxygen start to die. As a result, functionalities controlled by that part of the brain such as muscle control and memory are lost or reduced [4]. It is estimated that for each minute of blood vessel occlusion, 1.9 million neurons, 14 billion synapses, and 12 km (7.5 miles) of myelinated fibers are destroyed in the affected brain region. Compared to the normal rate of neuron loss during brain aging, an ischemic stroked brain without treatment ages 3.6 years each hour [5].

Strokes can be divided into three types [6], sometimes only ischemic and hemorrhagic strokes are counted as two subtypes of stroke:

1. Ischemic stroke
2. Hemorrhagic stroke
3. Transient ischemic attack (TIA)

It is estimated that around 84-87 percent of the strokes are ischemic whereas hemorrhagic stroke is around 13-15 percent. Though hemorrhagic strokes are less common, they are responsible for about 40 percent of all stroke related deaths. An ischemic stroke occurs when the blood flow in the brain is interrupted due to clot formation or blockages. Ischemic strokes can be subdivided into two types: Embolic and Thrombotic ischemic stroke. Embolic strokes happen when the blood clots travel from another part of the body to the brain [7]. These clots can form due to air bubbles, fat globules, plaque form an artery wall and atrial fibrillation (AFib). Embolisms from cardiac regions are responsible for 15% to 40% of ischemic strokes and transient ischemic attacks. In the case of the thrombotic ischemic strokes, it is caused by the clots form in the blood vessel within the brain [8]. A clot may form due to fatty deposits (plaque) in the artery wall and causes decreased blood flow (atherosclerosis) or other artery conditions [9]. Fig. 1 depicts ischemic and hemorrhagic stroke, happen due to blockage and bursts of the blood vessel respectively.
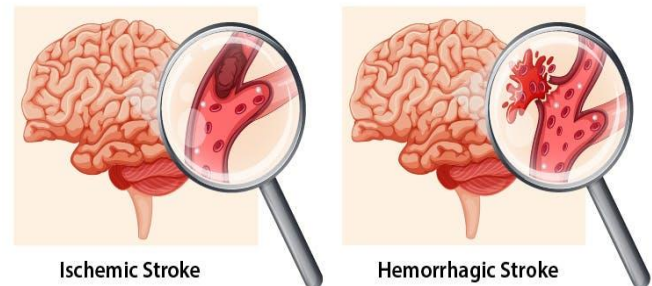

Fig. 1. Ischemic and hemorrhagic stroke

A hemorrhagic stroke happens when a blood vessel in the brain ruptures or breaks and leaking blood to the surrounding tissues of that vessel, which ultimately leads to brain cells death. Two types of hemorrhagic strokes are intracerebral hemorrhage and subarachnoid hemorrhage. Intracerebral hemorrhage can happen when a weakened blood vessel inside the brain bursts and leaks blood into the surrounding tissues which causes the cells to die and that part of the brain stops working correctly. The reasons behind this type of hemorrhagic stroke can be high blood pressure and aging of the blood vessel [10]. The other type of hemorrhagic stroke, i.e., subarachnoid hemorrhage happens when there is a bleeding in the area between the brain and the tissue covering the brain. The subarachnoid space is the area between the brain and the skull. The space is filled with cerebrospinal fluid (CSF), which acts as a floating cushion and protects the brain from extra pressure and outside injury. However, during subarachnoid hemorrhage, this balance is interrupted due to the released blood from the affected artery

which then increases the pressure on the brain and damages brain cells. Subarachnoid hemorrhage can happen due to a burst of an aneurysm, arteriovenous malformations (AVM), bleeding disorders, blood thinners, and head injury [11]. Ruptured brain aneurysms (inflated and weak wall of blood vessels) are fatal in about 40% of cases. The deaths are mainly due to rapid and immense brain injury from the initial bleeding. Those who survive, about two-thirds of them suffer from permanent neurological deficit [12].

Transient ischemic attacks (TIA), also known as a mini-stroke, causes a temporary blockage of blood flow in the brain. Usually, the blood clots and the effects of TIA last for a short period of time (<24 hours), but if necessary steps or immediate treatments are not taken, there is a huge chance of having a major stroke after TIA.

II. STROKE DIAGNOSIS

A. Stroke symptoms and prehospital evaluation

Growing public awareness is vital for stroke-related death reduction. Educating people to quickly recognize the signs of an acute stroke, use of urgent triage and treatments are essential to improve outcomes. These efforts include public campaigning, emergency medical services (EMS) and increasing rapid access of patients to nearby stroke centers [13]. Different prehospital assessment scales have been introduced to identify stroke, and it's severity. Usually 7 stroke recognition instruments or scales are used in hospital and prehospital settings, which are: Los Angeles Prehospital Stroke Screen (LAPSS) [14], Face Arm Speech Test (FAST), Recognition of Stroke in the Emergency Room (ROSIER), Melbourne Ambulance Stroke Scale (MASS), Ontario Prehospital Stroke Screening tool (OPSS), Medic Prehospital Assessment for Code Stroke (MedPACS) and Cincinnati Prehospital Stroke Scale (CPSS) [15]. FAST and CPSS are found to report a higher level of sensitivity, while more complex instruments like LAPSS reports higher specificity at the cost of lower detection rate. It is hard to conclude which recognition method is superior and the

selection of a stroke recognition method depends on the consequence of the false negative and vary place to place [15]. The FAST acronym (F: Face drooping, A: Arm weakness, S: Speech difficulties and T: Time to call for emergency help, 911 for the United States) has been used by multiple professional organizations and mostly used as the centerpiece of educational campaigns to grow stroke awareness [16].

However, common stroke warning signs and symptoms can be noted as [17]

- Sudden numbness or weakness of the face, arm, or leg, especially on one side of the body (left side or right side)
- Confusion, difficulties in speaking and understanding
- Sudden troubles in sight in one or both eyes (double vision, blurry vision, losing eyesight)
- Sudden trouble in walking, dizziness, and balance
- Sudden severe headache with no known reason

Quick treatment is vital for stroke patients, to emphasize this importance; the phrase "time is brain" is widely used in stroke research and treatments. Hence whenever these signs are observed, the patient or the family members should immediately contact the emergency services, nearest stroke care unit or hospital. Unfortunately, many of the stroke patients are not lucky enough to get their first treatment as soon as they should. Hence, Mobile Stroke Units (MSU) are introduced in some of the developed countries. MSUs are ambulances equipped with an imaging system (mainly Computed Tomography (CT) scanner), point of care laboratory, a telemedicine connection to the hospital and necessary medications. Studies found that these stroke units are safe and able to reduce the time to get first medication i.e., helpful for early thrombolysis [18]. Though these units are beneficial, they are costly, hard to maintain and operate, and available only in a few developed country, especially in large cities.
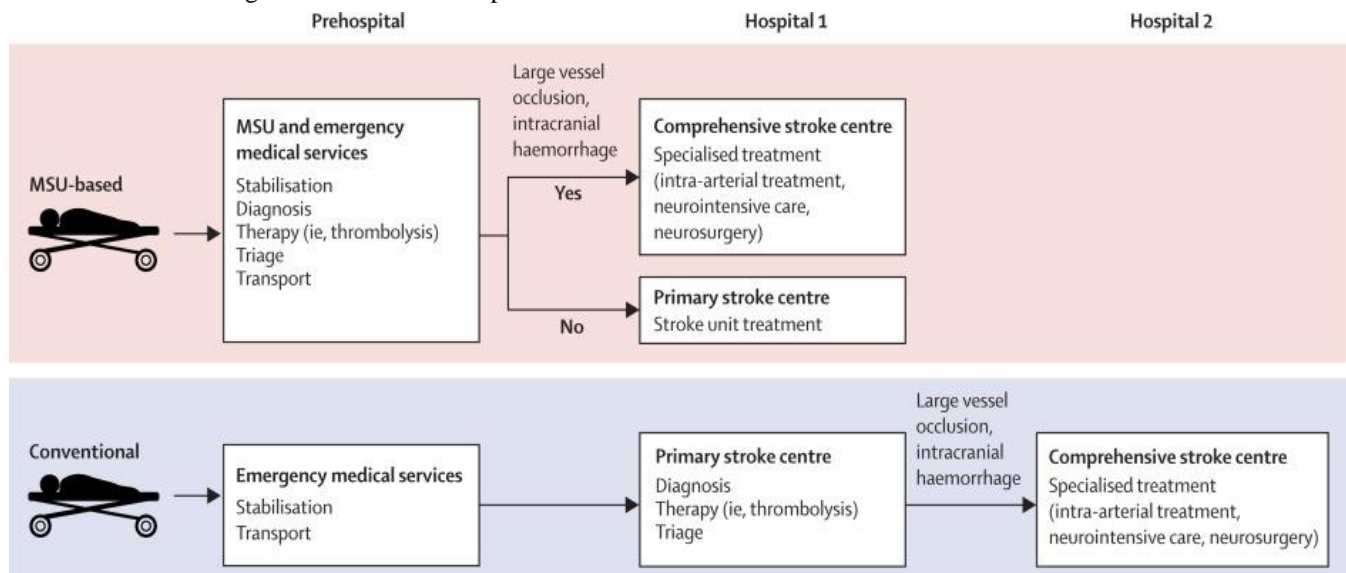

Fig. 2. Steps need to be followed after a stoke and the effect of the Mobile Stroke Unit for increasing access to treatment [15].

B. Evaluation in hospital settings

History and physical examinations remain as the pillars of stroke diagnosis. The most common feature of the ischemic stroke is its acute onset, and among the physical findings, focal weakness and speech difficulties are evident [19]. However, the first step should be followed by the doctors in the emergency department is to verify that the patient is medically stable with a general examination focused on the vital signs and cardiovascular system. Comorbidities are common in stroke patients, where most of them have a history of hypertension and about one-third suffer from diabetes mellitus [13]. The presence of a transient ischemic attack and other medical conditions should be ruled out to ensure that the patient receives appropriate medications. A large number of conditions or abnormalities can mimic stroke such as migraine, hypoglycemia, seizure, hyponatremia, eclampsia, trauma, and brain tumors [20][21]. Hence, to detect the type of stroke and exact location of the stroke, different tests are performed, named Computed Tomography (CT), Electrocardiography (to check the cardiovascular status and to evaluate for cardioembolic source), Magnetic Resonance Imaging (MRI), Computed Tomography or Magnetic Resonance Angiogram (most of the time CT guided Angiography or CTA) to find the exact location of the clot or hemorrhage, and hemoglobin A_{1c} to evaluate the diabetes mellitus [22].

MRI is more sensitive to ischemic stroke compared to CT, but MRI procedure is lengthy and some prerequisites are required to follow. Therefore, clinicians often prefer CT to MRI. Hemorrhagic strokes can be easily detected using CT and gradient echo MR-sequences can be used as well. Once the infarction is diagnosed the next goal is to identify the exact location or to know which vessel is involved, a CTA can be performed for this [23].
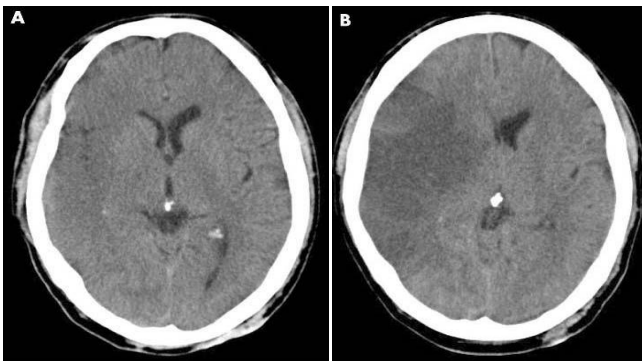
Fig. 3. Evolution of hypodensity on computed tomography (CT) scan. (A) after 4 hours of stroke onset, right MCA ischemia and (B) 24 hours after stroke onset. First CT scan shows early ischaemic changes: loss of grey-white matter definition, lentiform nucleus hypodensity, loss of insular ribbon, compression of lateral ventricle, and hemispheric sulcal effacement [24].

III. STROKE TREATMENT

After a primary assessment or stroke diagnosis, it is highly important to start the treatment as soon as possible.

The treatment for ischemic stroke and hemorrhagic stroke is quite different. For ischemic stroke, treatment mainly focuses on medications to restore the normal blood flow in the occluded arteries. A clot blasting drug is highly effective at dissolving blood clots and minimizing long term damage. In 1990s the National Institute of Neurological Disorders and Stroke (NINDS) sponsored 2 randomized clinical trials of intravenous recombinant tissue plasminogen activator (IV rtPA) vs placebo, these trials evaluated 624 patients with ischemic stroke symptoms within 3 hours of stroke onset [25]. Patients who received IV rtPA compared to patients who received placebo showed an absolute increase (16%) in favorable outcomes. Although there was a risk of brain hemorrhage due to IV rtPA, the benefits of this medication outweighed the risk. Consequently, the US Food and Drug Administration (FDA) approved rtPA to be used for acute stroke treatment within 3 hours of stroke onset [22][26]. Though there is a debate about the time frame to apply the rtPA, it should be used as soon as possible and within highest 4.5 hours for some people after the onset of stroke. Unfortunately, study shows that only a small percentage (7.2%) of stroke patients are able to get the IV rtPA within 3 hours of symptom onset [27][28]. Effect of IV rtPA treatment is shown below in Fig. 4.
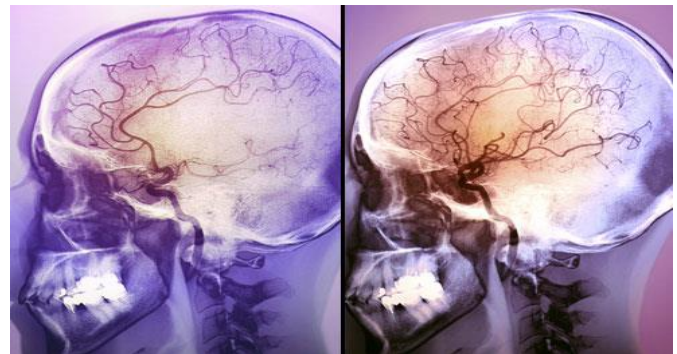
Fig. 4. Angiogram of a stroke patient before rtPA treatment and after rtPA treatment [29].

Besides mostly used rtPA (regared as the gold standard), there is a newly developed technique used to treat ischemic stroke patients named endovascular thromboectomy or mechanical thromboectomy. Compared to rtPA, endovascular thrombectomy using catheter-based mechanical devices is found to decrease severity of global disability and improve rates of functional independence [30][31][32]. Moreover, thrombectomy is not extremely time sensitive like the rtPA but earlier thrombectomy is better due to nature of stroke. The FDA has approved different mechanical thromboectomy devices to treat ishecmic stroke based on technical efficacy and safety. These devices are able to successfully recanalize the vascular occlusion with an acceptable 7% to 19% patients experience device and procedure related complications including vessel perforation, nontarget artery embolization and hemorrhage[31][33][34].

Mechanical thrombectomy devices are inserted into the femoral artery via guided catheters and then slowly

advanced to the occluded artery using angiographic procedure. A microcatheter and guidewire are then introduced into the intracranial vessels beyond the guided catheter and thrombectomy is performed with proximal balloon occlusion which prevents further embolization during the procedure. Approved thrombectomy devices follow different techniques [22]:

    a. Coil retriever devices engage and wrap around the clot and then pull back to the catheter to remove the thrombus

    b. Aspiration devices use proximal suction to remove the blood clots

    c. Stent retrievers allow immediate blood circulation at the site of occlusion followed by entrapment of the thrombus between the stent and the vessel wall, and then the blood clot is removed when the stent is removed

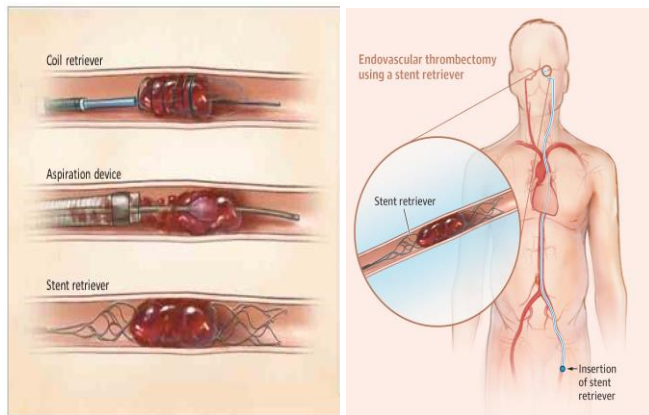Different thrombectomy devices and the thrombectomy procedure is depicted in Fig. 5.

Fig. 5. Types of thrombectomy devices and thrombectomy procedure after stroke (ischemic) [22][35].

As mentioned earlier, hemorrhagic strokes are less common (13-15%) but they are fatal compared to ischemic strokes. Hemorrhagic strokes are difficult to manage. Treatments usually involve trying to control high blood pressure, stopping hemorrhage, and reducing brain swelling [29]. Recently there are some techniques used to treat the hemorrhagic strokes, especially by using clamps/clips to close the base of the aneurysm, one of the main reasons for hemorrhagic strokes. Fig. 6 depicts the treatment procedures used for hemorrhagic stroke treatment.

A clamp can be used in this way to prevent bleeding before a stroke or to prevent re-bleeding after a stroke. This surgery requires removal of a part of the skull and identifying the location of the aneurysm (can be done using angiogram imaging). This procedure is done after the patient is given local anesthesia and often requires several hours to finish. After the procedure/surgery, the removed skull is then replaced [36].

Coil embolism is another interventional procedure and less invasive compared to clipping technique. It can be done when the patient is sedated or put to sleep using medications. In this way, a flexible tube (catheter) is inserted into an artery in the groin. The catheter is guided through the blood vessels of the body and then the vessels in the brain. X-ray or CT guided angiograms are used to guide the movement of the catheter into the arteries. When the catheter reaches to the desired aneurysm, a tiny coil usually made of soft platinum metal and shaped like a spring is advanced to the aneurysm and fills the area with the coil. A blood clot is then formed in that weakened region or aneurysm, hence, stops the blood flow to the aneurysm and prevents the aneurysm from rupturing again. This coiling technique can be used to treat arteriovenous malformations (AVM) as well [36][37].
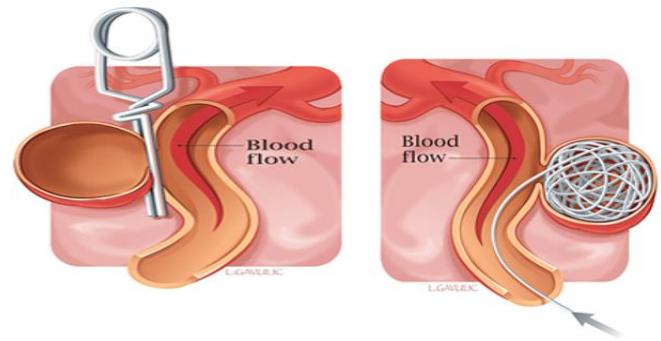

Fig. 6. Hemorrhagic stroke treatment using clipping and coiling embolism [38].

IV. REHABILITATION

Apart from longtime suffering for patients and their families, stroke also responsible for a huge cost of the society, including loss of employment and long term care expenses. Therefore, early recovery of patients is beneficial for the patient, his/her family, and the society as well.

Stroke recovery is heterogeneous by nature. The long term effect of stroke is determined by the site of the stroke, initial stroke lesion, and the extent of subsequent recovery. Stroke rehabilitation usually uses a cyclic process including:

a. Assessment, identifying and quantifying the patient's needs

b. Goal setting, defining realistic and achievable goals

c. Intervention, helping the patient to achieve the identified goals

d. Reassessment, assessing the progress of the patient to achieve the goals [39][40].

The goals of stroke rehabilitation are to support recovery, prevent any recurrent stroke, reduce complications, and ensure that the patient is able to regain the highest possible functional outcome. Consequently, rehabilitation of a stroke patient should be an interdisciplinary approach, consists of a doctor, rehabilitation nurse, speech therapist, occupational therapist and most importantly the family members of the stroke patient [20]. Admitting a patient to a stroke care unit is advisable since it helps all the disciplines to attain the desired goals. However, good and fast recovery outcomes are strongly correlated with the high motivation of the patient; encouraging and engaging family members.

Muscle weakness and balance problems are common after a stroke, which interferes in walking and performing daily activities. Physical therapy is an effective way to reclaim the

strength, balance, and coordination. Hence, physical therapist and clinicians should encourage stroke patients to build greater strength, speed, and precision of multijoint movements (such as using a knife and fork, writing, buttoning a shirt) which increase independence and helpful for performing daily activities. Imaging and other diagnostic tools can be helpful to track the progress of the patient [41]. Therapists should also look for the signs of depression, which frequently attacks a patient who is recovering from a stroke.
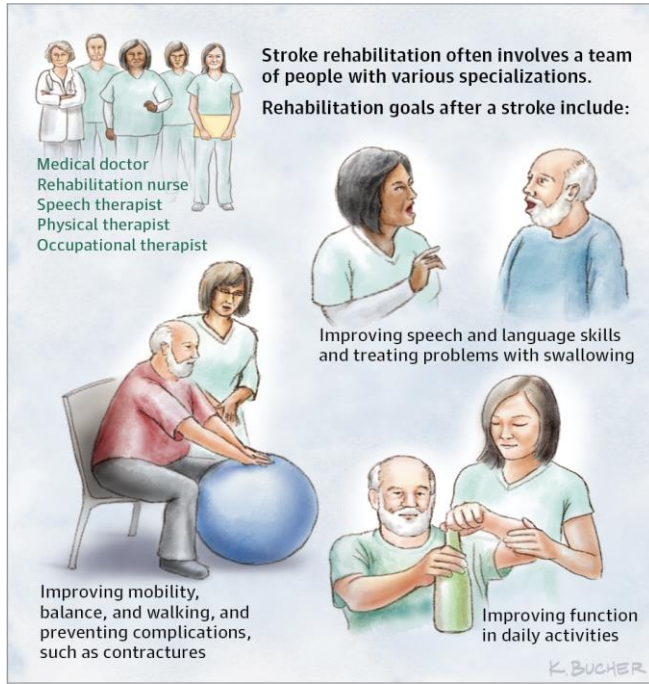

Fig. 7. Storke rehabilitation therapies [42].

Several systematic reviews have explored the benefits of high intensity trainings regarding stroke rehabilitation [43][44]. Though there is no clear guidelines for best level of training, it is widely accepted that intensive training helps in better recovery. Also, the rehabilitation should initiate as soon as possible after the stroke or when the patient's medical condition is stable [45]. Recovery can continue from months to years, there are no specific time limits and varies patient to patient.

Besides traditional therapies, several novel therapies are being introduced and tested, like stem-cell therapy [46], repetitive transcranial magnetic stimulation and transcranial direct current stimulation [47], virtual reality [48], motor imagery [49], and robotic therapies [50]. These therapies are usually combined with traditional approaches (like speech therapies, training for mobility improvement, swallowing practice) for better and faster recovery. Robotics based therapies help with some of the labor-intensive and repetitive therapies which are traditionally performed by the therapists. This way the automated devices provide the patient with greater access to therapy [51].

V. STROKE PREVENTION

"Prevention is better than cure"- like other diseases it is applicable for stroke as well. Though it is not possible to stay risk-free of stroke since the chances of stoke increase with aging and has a strong relationship with a family history of stroke, it is possible to reduce the risk by following some healthy habits. Certain chronic conditions increase the risk of stroke, including high blood pressure, high cholesterol, diabetes, and obesity. As well as certain behaviors increase the risk of stroke, including smoking, too little exercise, and heavy drinking. Table I summarizes stroke risk factors and the interventions required or recommendations should be followed to prevent stroke or recurrence of a stroke (patient who already experienced a stroke or TIA).

TABLE I. STROKE RISK FACTORS AND INTERVENTIONS FOR STROKE PREVENTION [20]

Risk factor	Intervention
Hypertension	Blood pressure should be below 120/80 mmHg
Cholesterol	High cholesterol levels should be treated with lifestyle changes, medications, and dietary guidelines
Smoking	Patients who smoked previously should be strongly advised to quit
Diabetes	Glucose level needs to be controlled
Alcohol	Consumption of no more than two drinks per day for men, and one drink for nonpregnant women
Obesity	Maintain a body mass index (BMI) between 18.5 and 24.9 kg/m^2
Physical activity	At least 30 minutes of moderate-intensity physical exercise most days

A diet with high in fruits, whole grains, vegetables, and fish may help to lower stroke risk. Patients with atrial fibrillation (AFib), the most common serious heart rhythm disorder, should take oral anticoagulation (OAC) medications/therapy to reduce the risk of stroke, and it should be balanced against an increased risk of bleeding due to OAC [52].

VI. CONCLUSION

Stroke is a medical emergency, quick and appropriate treatment help to avoid death as well as reduce brain damage and good for faster recovery. Intravenous rtPA remains as the standard treatment for patients with acute ischemic stroke but the time frame of first use within 3 hours of stroke onset should be strictly followed. Besides rtPA, endovascular thrombectomy is appeared as a promising technology to treat ischemic strokes; it improves the recanalization of proximal artery occlusions and clinical outcomes. For hemorrhagic stroke treatment, the drugs and

interventional therapies are limited. Main focuses of hemorrhagic strokes treatment involve reducing high blood pressure and stopping the hemorrhage. Clipping and coiling embolism techniques can be used to reduce or stop the hemorrhage. However, complications due to the interventional therapies are needed to be addressed. Efforts should be made to hasten the reperfusion therapy in stroke care units. Besides the traditional therapies, virtual reality and robotics-assisted therapies will play a significant role in stroke rehabilitation.

Though there is a significant improvement in the stroke diagnosis, treatment, and rehabilitation, with an increase in aging population, growing prevalence of obesity, less physical activity, and diabetes, it is expected that the prevalence of stroke will increase in the coming decades. The future directions of stroke management should focus on increasing public awareness about stroke symptoms, use of emergency medical services, promoting healthy lifestyles, controlling hypertension and diabetes, increased access to health care units, and better rehabilitation measures.

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