Acute Ischemic Stroke: Current Status and Future Directions

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Stroke is defined as a sudden onset of the neurological deficit caused by an acute focal injury to the central nervous system due to a vascular cause.

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Abstract

The evolving knowledge on stroke in conjunction with advances in the field of imaging, treatment approaches using recombinant tissue plasminogen activator (rtPA) or thrombectomy devices in recanalization, and efficient emergency stroke workflow processes have opened new frontiers in managing patients with an acute ischemic stroke. These frontiers have been reformed and overcome in overcoming the decades-long watch and wait approach towards patients with ischemic stroke. In this article, we focus on the current strategies for managing ischemic stroke and conclude by providing a brief overview of anticipating developments that can transform future stroke treatments.

Introduction

Stroke is defined as a sudden onset of a neurological deficit caused by an acute focal injury to the central nervous system due to a vascular cause.[1] The incidence of strokes occurring every year worldwide is about 17 million and it is the second leading cause of death after coronary artery disease.[2] It is the fifth leading cause of death in the United States, i.e., killing more than 130,000 Americans each year[3] and affecting 795,000 people annually.[4] It is the third most common cause of disability and reduces mobility in more than half of stroke survivors in ages 65 and over.[4,5] Furthermore, the economic burden of stroke on the nation through health care services, medications, rehabilitation and loss of productivity is around $33 billion annually.[4] By 2020 in developed countries, it is predicted that stroke will be accountable for 6.2% of the total burden of illness.[6] These data put forward the need for controlling risk factors, knowledge of identifying the signs of stroke, timely reperfusion therapies and measures to improve delivery of the aforementioned resources for the best possible outcome.

Ischemic strokes are the most common (≈85%), the rest being hemorrhagic that include cerebral and subarachnoid (≈15%).[7] The Trial of Org10172 (TOAST) is the most commonly used classification that identifies five subtypes in acute ischemic stroke: 1) large artery atherosclerosis 2) cardio-embolism 3) small vessel occlusion 4) stroke of other determined etiology 5) stroke of undetermined etiology.[8]

The events resulting from any subtype of ischemic stroke result in the loss of blood supply, oxygen, nutrients and elimination of metabolic wastes. These resulting changes obstruct normal neuronal functioning.[9] This ultimately results in neuronal death/necrosis from occlusion of the vessel. The brain tissue is exquisitely sensitive to these changes, and the therapeutic window that is needed to prevent reversible ischemia from becoming irreversible infarction[10] is narrow and stresses the phrase "time is brain". This concept is especially important to minimizing evolving insult and controlling the propagation of ischemic penumbra.[11,12,13] Furthermore

from a therapeutic point of view, this crucial time provides a "window of opportunity" in reversing the neurological symptoms either partly or completely through acute interventional approaches, either invasively or non-invasive.[14]

Over the last two decades, a lot of stroke specific structured education, intervention trials, and diagnostic approaches have targeted this time period, resulting in better clinical outcomes with decreased associated mortality and morbidity. The modern stroke field is a fast advancing with an emphasis on endovascular stroke therapy/ interventional mechanical devices, and their combined use with thrombolytic agents for better clinical benefits.[15]

In the next few sections, we will discuss management updates in acute ischemic stroke ranging from stroke education to therapeutic strategies, and conclude by providing a brief overview of the advances that are on the horizon.

Table 1
Imaging Studies in Management of Acute Ischemic Stroke

Modality	Level of Evidence[32]	Use
NIHSS[33,34,35].	Level1 /Class1.	1) For easy communication between health care personnel. 2) Initial NIHSS predicts an eventual functional outcome. (NIHSS≥16 higher probability for severe disability or death and ≤ 6 good recovery. 3) Monitors on progression or worsening of the patient during a hospital stay. 4) NIHSS ≥12 likely for a presence of larger vessel occlusion.
NCCT[36,37].	Level1/Class1. Level2/ Class2.	1) Ruling out ICH and Mass Lesions. 2) To detect infarct core volume during first few hours of stroke onset.
CT Angiogram[38,39]	Level1/Class 1	1) To detect large vessel occlusion.
DW MRI[40,41,42].	Level1 /Class1	1) Early detection of Infarct core and 100 % sensitive in diagnosing acute stroke.

∗ ICH=Intra Cerebral hemorrhage; ∗NCCT=Non-contrast CT; ∗DW=Diffusion weighted.

Table 2
Initial Evaluation and Management of Acute Ischemic Stroke

Initial Evaluation and Management
1) Establishing for **C**irculation, **A**irway and **B**reathing. (**C-A-B**).
2) I.V Fluids=0.9% Normal Saline
3) If needed rapid sequence intubation
4) Blood pressure Management:(See Below)
5) Screening for Dysphagia
6) DVT prophylaxis with Mechanical devices
7) G.I prophylaxis with either H2 blockers or proton pump inhibitors
8) Maintenance of core body temperature to <32.7° C either with a use of acetaminophen or ibuprofen or external cooling devices in refractory cases.
9) Target of blood Glucose between 140-180 mg/dl

Stroke Education - Literacy, Behavior, and Proficiency

The frequency in administration of tPA to patients with an acute ischemic stroke within three hours of symptom onset has nearly doubled (4% to 7%) from 2003 to 2011.[15] Still the percent of ischemic stroke patients reaching the hospital within three hours of symptom onset is between 15% to 32%.[15,16,17] The percent of ischemic stroke patient receiving intravenous tPA therapy is in between 2% to 3%,[18] and patients who arrive at the hospital in time for stroke revascularization therapies is between 1% to 7%.[19] The central key for an effective treatment delivery and management of an ischemic stroke patient rely upon 1)Stroke Literacy, 2) Stroke Behavior, and 3) Stroke Proficiency.

1) Stroke Literacy

- Recognition of modifiable (Hypertension, Hyperlipidemia, Diabetes Mellitus) and non-modifiable stroke risk factors (age, gender and ethnicity).[20,21,22]
- Demonstrated stroke symptom awareness. [23,24,25,26]
- Correctly identifying the brain as where a stroke occurs.

2) Stroke Behavior

It is a response to use EMS/911 service[27,28,29] when stroke symptoms occur. EMS services, by contacting nearby stroke centers, bypass non-stroke centers and prepare the emergency staff and neurologist at the receiving hospital. This approach facilitates the rapid transportation for receiving reperfusion therapies within the window period.

3) Stroke Proficiency

Stroke proficiency is described as for having both stroke literacy and stroke behavior.[26]

The public initiatives (media, support groups, and annual stroke awareness day) have promoted stroke literacy, stroke behavior, and stroke proficiency among the communities. Likewise, tele-health stroke education has proven effective in educating remote and rural areas.[30]

The development of validated stroke assessments tools, neuroimaging and stroke teams have helped in early detection and increasing the eligibility for treatment. On arrival to the ED, an initial clinic assessment (history, medications, and comorbidities), time of symptom onset, NIHSS (National Institutes of Health Stroke Scale), "code stroke" order set (complete blood count, coagulation studies, EKG, emergent head CT) will help in determining eligibility for thrombolytic therapy and in ruling out the stroke mimics. After initial physical examination, the only tests that should

lead to decide their eligibility for rtPA are non-contrast CT (NCCT) head and serum glucose level, as hypoglycemia mimics an acute ischemic stroke. However, other tests including blood counts, metabolic panel, coagulation panel, cardiac enzymes and, electrocardiogram, are important but should, in general, not delay in the initiation of treatment.

The level/class of evidence and role of NIHSS and various neuroimaging modalities used in evaluating an acute ischemic stroke as shown in Table 1.

The perfusion studies (CTP and MRP) are Level 3/ Class IIb and may aid in providing further information in diagnosis, management, and prognostic assessment, but their use still remains limited to special situations.[31,32,33.] The initial evaluation with NIHSS followed by CT or CT followed by NIHSS are both accepted protocols that are practiced by different institutions. The CTA has proven beneficial in rapidly selecting patients for thrombectomy in anterior circulation large vessel occlusions, it is likely to be inclusive as part of the initial stroke imaging protocols[31,34] at most institutes. The other key measures and evaluations that need to be observed in acute ischemic stroke patients are as summarized in Table 2.[35]

Stroke education is crucial to the creation of stroke awareness, so the endorsement of stroke specific education in communities and primary care settings would benefit influencing the stroke performance outcome measures. Rapid entry into the health care system is required to achieve rapid thrombolysis in eligible patients. rapid thrombolysis in eligible patients.

Blood Pressure Management

Blood pressure management is very critical in patients with acute ischemic stroke. The International Stroke Trial with 17,398 of ischemic stroke has shown high and low blood pressures are independent prognostic factors for a poor outcome. This study even found a U-shaped relationship between baseline systolic blood pressure and death or dependency.[36] In theory, the "permissive hypertension" in acute ischemic stroke patient is to enhance perfusion and prevent hemorrhagic conversion.[37] The recommended systolic and diastolic blood pressure before administration of IV rtPA in eligible patients is <185 mm HG and 110 mm HG respectively.[34,35] After administration of IV rtPA the blood pressure should be controlled below 180/105, besides monitoring for every 15 minutes for 2 hours, then every 30 minutes for 6 hours, and lastly for every 60 minutes for 24 hours.[38,39] Blood pressure management and adherence to guidelines is crucial, as the pressures either too low or high can influence outcomes.

Thrombolytic Therapy

The intravenous recombinant tissue plasminogen activator (rtPA) is the only proven Level of Evidence 1, Class A recommendation approved by Food and Drug Administration for treatment within three hours of symptom onset, in patients with ischemic stroke.[40,41] The initial studies that have used the first generation thrombolytic Streptokinase and Urokinase have proven ineffective for treating patients with ischemic stroke.[42]

The pioneer study, "National Institute of Neurologic Disorders rtPA Stroke Study," showed the efficacy of thrombolytic when administered within three hours of symptom onset, with minimal or no disability three months

Table 3
Checklist for Inclusion and Exclusion Criteria for Thrombolytic Therapy

STROKE TEAM – RAPID EVALUATION

1. TIME PATIENT LAST KNOWN WELL: _____
2. TIME OF PATIENT ARRIVAL TO FACILITY: _____

Pre-Admission Blood Thinners & Plaque Stabilizers:

Antiplatelet therapy:	Aspirin [ ]	Plavix [ ]	
Anticoagulation:	Coumadin [ ]	Lovenox [ ]	Other: _____
Statin:	Yes [ ]	No [ ]	Which: _____

Cerebral Vascular Risk Factors:

Hypertension	Yes [ ]	No [ ]
Hyperlipidemia	Yes [ ]	No [ ]
Smoking	Yes [ ]	No [ ]
Atrial Fibrillation	Yes [ ]	No [ ]
Age >60 years	Yes [ ]	No [ ]
Diabetes	Yes [ ]	No [ ]

Exclusion Criteria for Tissue Plasminogen Activator (tPA)

1.	Evidence of an acute intracranial hemorrhage	Yes [ ]	No [ ]
2.	Major Early CT signs of infarction	Yes [ ]	No [ ]
3.	Another stroke, serious head trauma, intracranial surgery in the past 3 months	Yes [ ]	No [ ]
4.	Intracranial neoplasm, AVM, or an aneurysm	Yes [ ]	No [ ]
5.	Uncontrolled hypertension (systolic >185, diastolic >110)	Yes [ ]	No [ ]
6.	Rapidly improving or minor symptoms	Yes [ ]	No [ ]
7.	Symptoms suggesting subarachnoid hemorrhage	Yes [ ]	No [ ]
8.	History of intracranial bleed	Yes [ ]	No [ ]
9.	Major surgery in the past 14 days	Yes [ ]	No [ ]
10.	Known bleeding disorder	Yes [ ]	No [ ]
11.	GI or GU bleed in the past 3 weeks	Yes [ ]	No [ ]
12.	Arterial puncture at a non-compressible site in the past 7 days	Yes [ ]	No [ ]
13.	Seizure at the onset of stroke	Yes [ ]	No [ ]
14.	Pt >15, INR >1.7	Yes [ ]	No [ ]
15.	Heparin within the past 48 hours and elevated aPTT	Yes [ ]	No [ ]
16.	Use of direct thrombin inhibitors or direct factor Xa inhibitors with elevated sensitive laboratory tests (such as aPTT, INR, platelet count, and ECT; TT or appropriate factor Xa activity assays)	Yes [ ]	No [ ]
17.	Platelet count <100,000	Yes [ ]	No [ ]
18.	Serum Glucose <50mg/dL or >400mg/dL	Yes [ ]	No [ ]
19.	MI in the past 3 months	Yes [ ]	No [ ]

Exclusion Criteria of IV tPA within 3 to 4.5 hours

1.	Age >80 years	Yes [ ]	No [ ]
2.	Severe stroke (NIHSS>25)	Yes [ ]	No [ ]
3.	Taking an oral anticoagulant regardless of INR	Yes [ ]	No [ ]
4.	History of both diabetes and prior ischemic stroke	Yes [ ]	No [ ]

after treatment with a single IV dose of 0.9mg/Kg.[43] This study has shown favorable outcome in patients who were less than 75 years old and those with a NIHSS score less than 20, but patients >75 years still benefit within three hour symptom onset.[34] The more rapid the time to presentation and evaluation, the greater the benefit of thrombolysis:

1) Patients who received treatment within the first 90 minutes had a more favorable outcome at 3 months compared to patients who were treated between 90 and 180 minutes.[41,44]

2) For every 15 minute delay in treatment there is an estimated 4% reduction in the probability of good functional outcome.[45]

3) Every minute delay in treatment from symptom onset would result in loss of 1.8 days of extra healthy life.[46] Inclusion and exclusion criteria for treatment with rtPA are shown in Table 3. These must be reviewed with the patient or patient representative, and consent should be dscussed, all within this time frame.

The extended use of IV tPA in the 3- to 4.5-hour window is a recommendation but not an approved treatment by Food and Drug Administration. Given its off-label use, the consent to treat is generally required obtained from the patient or family member and need to be documented. It is based on the study of European Cooperative Acute Stroke Study III (ECASS III), which showed a favorable outcome in 821 ischemic stroke patients when treated with either rtPA or placebo within this time frame.[47] The analyses of several other clinical trials have failed to show any beneficial effect in administering rtPA within 4.5 to 6 hour symptom onset.[48]

The mild or resolving neurological deficits or with NIHSS score <4 should never be excluded on the basis of score, as several studies suggested poor outcome, progression of symptoms, or residual disability after failing to receive rtPA[49]. In fact, the more common medico-legal issue is failure to administer IV tPA with resulting functional impairment from stroke rather than from complications of tPA.

The other observant symptoms such as aphasia, gait problems, hemianopia, and large vessel occlusions on MRI should not be excluded, from treatment with tPA, as it has proven beneficial.

The doubts over administering rtPA to patients on novel oral anticoagulants (NOAC) dabigatran, rivaroxaban, apixaban, edoxaban, factor Xa inhibitors stems from the difficulty in measuring their effects. The accurate measurement of dabigatran through thrombin time (TT) or ecarin clotting time (ECT) and factor Xa inhibitors is not available in most emergency departments. Currently, there are no well-accepted guidelines on the time of last dose to the safety of rtPA administration, and these cases are approached individually, and often with the consultation of a clinical pharmacist.

The rtPA infusion should be stopped in patients who develop new neurological deficits after initiation of the drug with strong consideration for a STAT CT of the head. Approximately 6% of patients receiving thrombolytic develop symptomatic intracerebral hemorrhage.50 Neurosurgical consultation should be sought for any evident surgical management should hemorrhage be present. The other watchful conditions for acute neurological worsening are cerebral edema, stroke progression, recurrent stroke and seizures. The treatment to reverse coagulation consist of administering platelets (6-8U), cryoprecipitate with factor VIII and consideration of recombinant factor VIIa and fresh frozen plasma (FFP).51 Different institutes have different protocols and there is little evidence-based data to guide treatment.52,34 Other conditions to be considered with acute neurological worsening are cerebral edema, stroke progression, recurrent stroke and seizures.

Several studies that have used third and fourth generation thrombolytics (Tenecteplase, Reteplase, Desmoteplase and Ancrod) have failed to show any benefits in treating patients with acute ischemic stroke.[42]

The rtPA has proven very beneficial, when administered within three hours of symptom onset. In fact a common medico legal issue is, patient not getting IV tPA and having functional impairment from stroke and not from complications of tPA.

The emergence or reporting of newer symptoms and worsening clinical condition should dictate, discontinuation of infusion and reassessment of the patient.

Endovascular Therapies

The benefit of IV rtPA in large proximal vessel occlusions is limited and in some studies up to 57% to 58% patients die or become dependent, regardless of treatment with IV rtPA.[42,53] This has driven the search for more diagnostic and treatment approaches that can achieve higher rates of recanalization in less time with minimal risk to the patient. The 11th commandment in stroke treatment previously was "thou shall reserve endovascular therapy in the most desperate cases." The advancements in neuroimaging (CTA/CTP/MRP) have broadened the investigations and use of various endovascular therapies. The success of intra-arterial thrombolysis (IA) was well established with Prolyse in Acute Cerebral Thromboembolism II (PROACT II) study which showed 66% recanalization and 40% good neurological outcomes.[54] The Recanalization using Combined intravenous Rt-PA

and Neurointerventional ALgorithm for acute Ischemic StrokE (RECANALISE) study of intracranial occlusions showed 52% and 87% of recanalization at 24 hours but no significant difference in a mRS (modified Ranklin scale)at 90 days.[55] However, the use of IA with microcatheter is advantageous in delivering high concentrations of thrombolytics with reduced systemic exposure. Currently, the optimal dose of rtPA for IA treatment is not well established and is not approved by FDA.[56]

Theoretically, mechanical stent-retriever devices expedite recanalization, revascularization of large-artery occlusions with reduced risk of hemorrhage and longer time window for use when compared to thrombolytics.

The successive generations of MERCI (Mechanical Embolus Removal in Cerebral Ischemia) retriever devices that were used in various studies (MERCI pilot, MERCI1 and Multi-MERCI) yielded better recanalization rates which prompted other trials (Intra-arterial Versus Systemic Thrombolysis for Acute Ischemic Stroke [SYNTHESIS], Mechanical Retrieval and Recanalization of Stroke Clots Using Embolectomy [MR RESCUE], Interventional Management of Stroke III [IMS III]), resulting in negative outcome. These trials were heavily criticized for slow recruitment, time to intervention, lack of vascular imaging in selecting appropriate patients and the use of older devices instead of stent retrievers.

The subsequent trials demonstrated better results with stent retrievers, and when using neuroimaging to identifying patients with proximal anterior occlusions. The multi-center MRCLEAN[57] showed independent functional outcome, that was achieved at 90 days with endovascular therapy (33%) and standard care group therapy (19%). Below is the summary of the stent retriever trials that showed recanalization and better clinical outcome with the use of neuroimaging as shown in Table 4.

Endovascular therapies offer a new window of opportunity to treat when last well known is less than 6 hours or in "wake-up" strokes in some special cases. These therapies are only available at a limited number of highly specialized comprehensive stroke centers. These centers provide 24/7 care from a rapid response stroke team, consisting stroke neurologist, neuroendovascular specialistneurosurgeon, neurointensivist, anesthesiologist and nursing. They incorporate well-practiced treatment protocols, inpatient pathways, and provide rapid consultation and transfer services for patients in smaller centers.

Table 4
Summary of Treatment Trials with Endovascular Therapy

Name of trial	No. Of pts.	Mode of Intervention	Time Window (Hour)	Primary endpoint	Imaging selection
MR CLEAN	500	Endovascular treatment (stent retrievers 81.5%) plus usual care (87.1% IVT)	0-6	mRS at 90 days (mRS 0-2)	CT, CTA
ESCAPE	316	Endovascular treatment (stent retrievers 86.1%) plus standard care (72.7% IVT)	0-12	mRS at 90 days (OR for 1 point improvement in mRS)	CT, CTA (good/moderate collaterals), CTA Alberta Stroke Program Early CT score (ASPECTS).
EXTEND-IA	70	Endovascular thrombectomy (Solitaire FR stent retriever) plus IVT < 4.5 h	0-6	Reperfusion 24 h Early neurological improvement	CT, CTA, CT perfusion Core/mismatch-RAPID
SWIFT PRIME	196	Endovascular thrombectomy (Solitaire stent retriever) plus IVT <4.5 h	0-6	mRS shift at 90 days	CT, CTA, CT/MR perfusion, core/ mismatch and ASPECTS.
REVASCAT	206	Endovascular thrombectomy (Solitaire stent retriever) plus usual care (77% IVT)	0-8	mRS shift at 90 days	CT, CTA, ASPECTS.

*IVT=intravenous thrombolysis; mRs=Modified Ranklin scale; FR=Flow restoration

Management of Acute Ischemic Stroke in Ineligible Patients for Thrombolytic Therapy

Complications in Acute Ischemic Stroke Patients

Medical complications in patients with acute ischemic stroke effect clinical outcome and with an extended length of hospital stay.[63] Ingeman et al., study demonstrated that 25% of patients with stroke suffer from medical complications including[64] urinary tract infection (15.4%, pneumonia (9%), and constipation (6.8%). Depression is a disturbing and serious complication that is noted in 30% of patients, either early or in the later stages of stroke[65]. Unfortunately, it is under-recognized. Other complications that need to be remembered are fever, hyper/hypo glycemia and deep vein thrombosis. Patients with large strokes, even those not amenable to thrombolysis or mechanical intervention, are often monitored in an ICU setting as these patients may be at higher risk for intracerebral edema and resultant deterioration caused by mass effect.

Antiplatelet Therapy

Patients who are ineligible for thrombolysis should be administered aspirin immediately (81-325mg).[58] The administration of aspirin within 48 hours of ischemic stroke onset has been shown to reduce death and disability.[59, 60] The combination of clopidogrel and aspirin in selected patients showed better protection from subsequent strokes than aspirin alone in first 90 days without an increased risk for hemorrhage.[61] The long-term use of combination of clopidogrel and aspirin beyond 90 days is not recommended for secondary prevention as it may increase risk for hemorrhage with little therapeutic benefit.[58,62] Clopidogrel is slightly more effective than low dose aspirin in prevention of secondary stroke.

Anticoagulants

The use of anticoagulants and antithrombotic in acute ischemic stroke patients is declining as the studies on the use of heparin and other anticoagulants remain inconclusive.[66,67] Although newer anticoagulants such as direct thrombin inhibitors-dabigatran, and Factor Xa inhibitors-apixaban and rivaroxaban are equally or more effective than warfarin, data of their use in acute ischemic settings limited. Atrial fibrillation is still the most common indication and adds an overall risk of stroke of 5% per year.[68] The treatment with oral coagulants in these patients can often be started within one to two weeks after acute ischemic stroke.[69]

Rehabilitation in Acute Ischemic Stroke

The rehabilitation measures incorporating goal-targeted therapies hasten the recovery with considerable benefits, when compared to the natural recovery. Previous studies endorse early mobilization and intense neuro-rehabilitation for better functional outcomes.[70] The common impairments resulting from ischemic stroke are motor impairment, speech and language, swallowing, vision, sensation and cognition. The rehabilitation in these patients is a step wise and a progressive goal oriented process with an aim to reach their optimal physical, cognitive, emotional, communicative or social functional level.[71]

The last decade witnessed significant increases in the number of clinical trials with anticipated interventions that can enhance stroke rehabilitation phase. The advances in Brain–Computer Interface (BCI) devices, enabled their use into various clinical trials and have demonstrated gain in functional outcomes.[72] The potential of other therapies including motor imagery (MI),[73,74] virtual reality (VI),[75] robotic assisted training (RAT),[76] and drug augmentation of exercise training with amphetamines[77] in improving functional outcomes are on the horizon. Continued research is anticipated and needed.

These rehabilitation measures need to be established, optimized, and quantified for which they are being intervened and with cyclical reassessments to achieving the targeted functional outcomes.

Stem Cell-Based Therapies for Acute Ischemic Stroke

Stem cell-based therapies are an emerging new direction as potential regenerative or protective treatments for ischemic stroke. The Stem Cell Therapies as an Emerging Paradigm in Stoke (STEPS) committee suggests and establishes guidelines for preclinical and clinical trials. Studies in preclinical ischemic stroke models, have shown promising functional improvement with therapies that used embryonic stem cells (ESC), pluripotent stem cells (iPSC), neural stem cells (NSC), mesenchymal stem cells (MSC), and mononuclear cells (MNC) cell types.[78,79] The advances and understanding from basic researches empowered the translation of using various stem cell therapies in patients with ischemic stroke. However, the clinical trials in patients have shown limited benefit, needing more studies to establish the safety and efficacy of these cell therapies. So far MSCs are considered the only treatment to improve neurological function in stroke patients.[80] There are several ongoing clinical trials using adult stem cells to treat patients with ischemic stroke. See http://clinicaltrials.gov.

Conclusion

The telestroke has proven instrumental and effective in supporting awareness in rural and remote areas, and has increased the use of rtPA in rural areas by a factor of 2-6. Telemedicine has opened new frontiers in aiding community hospitals in triaging and providing treatment to complex acute ischemic stroke patients. Additionally, EMS and mobile stroke units have furthered accessibility to high-quality care in time for the better outcome. The designations for primary and comprehensive stroke centers with 24/7 dedicated stroke teams, advanced in providing complex medical care in acute settings, have expanded.

The current use of neuroprotectants, such as IV magnesium, was shown to be safe to use in mobile stroke units, with hope for advancement on near the horizon. The advancement of neuroimaging as a diagnostic tool is a significant factor in the development of endovascular therapeutics and expanded and judicious use of perfusion imaging may expand future stroke therapies.

The development of newer thrombolytics targeted towards fibrin specificity, rapid onset of action, and shorter half-life can be safe and effective in treating patients with AIS. The development of reversal agents for the newer oral anticoagulants can improve safety of these agents when used in an extended care setting.

Additionally, stem cell based therapies are emerging as a new therapeutic approach and as a potential restorative therapy. Technological advances are transforming neurorehabilitation interventions through BCI, MI, VR and RAT and may offer more promising outcomes.

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Disclosure

None reported.

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