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Fresh Views on Stroke Management: Time-Honored Problems and Novel Approaches

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Abstract

Stroke is a major global cause of disability and mortality, and it carries a heavy social cost in terms of disability, mortality, and medical expenses. Recently, there has been a resurgence of interest in disease-modifying treatments and innovative techniques in the acute stroke situation, which has improved patient outcomes and decreased long-term disability. The tenet that "time is brain" has been disproved in recent years, and improved outcomes have resulted from the application of cutting-edge neuroimaging techniques in acute clinical practice. These techniques enable the administration of acute treatments to patients who were previously ineligible based solely on temporal selection. New research on thrombectomy has made it possible to choose stroke patients up to 24 hours after symptoms start by employing sophisticated neuroradiological techniques like magnetic resonance imaging (MRI) and computer tomography perfusion (CTP). Significant therapeutic advancements have also been made possible by the use of newer oral anticoagulants (NOACs) for atrial fibrillation and more efficient acute care of stroke patients in specialized wards (stroke units). We emphasize recent advancements in the diagnosis, treatment, and prevention of acute and chronic stroke problems. In this editorial paper, we synthesize the current knowledge about the major stroke-related breakthroughs and perspectives and their relevance in stroke care. We then go over a few studies that were included in the "Clinical Research on Ischemic Stroke: Novel Approaches in Acute and Chronic Phase" Special Issue.

Keywords: stroke, stroke unit, head CT, CT angiography, thrombectomy.

Introduction

A major cause of mortality and disability globally, stroke will become increasingly more relevant as the absolute and relative number of older people rises due to an increase in life expectancy. This will have a profound effect on healthcare and society. Significant advancements in the treatment and prevention of stroke have occurred during the past few decades, leading to revisions in stroke therapy.

A major barrier to health care and a major factor in sustaining the ability to stay healthy, not only in older age, stroke poses a big challenge to keeping healthy status, which involves maintaining high cognitive and physical functioning, avoiding or at least reducing disease and impairment.

The invention of reperfusion therapies and their use in clinical practice, as well as the recognition of the necessity of managing stroke patients in specialized facilities during the acute phase, were the three largest advancements in the field of stroke care. Additionally, better clinical outcomes were made possible by focusing on a few risk factors and predisposing clinical circumstances, which decreased the incidence and improved the prognosis.

We are currently in an era of rapidly increasing research regarding acute stroke care, following the initial studies of systemic thrombolysis for acute stroke. Our understanding of cerebrovascular disease, and acute stroke in particular, has changed as a result of basic and clinical research, which has accelerated knowledge growth.

When compared to thrombolysis, endovascular thrombectomy for big vessel blockage to intravenous alteplase improved functional independence for a greater number of patients, hence lengthening the duration of acute therapy. But there have been advancements in other areas of stroke management in recent years besides acute care. For instance, it has become clear that antiplatelet medications have a bigger positive impact than previously thought in preventing recurrent ischemic stroke. Other preventive measures for recurrent stroke now include carotid stenting instead of endarterectomy for symptomatic carotid stenosis and direct oral anticoagulants as an alternative to warfarin in patients with atrial fibrillation.

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The rates of stroke-related mortality are decreasing as a result of recently developed stroke management techniques. However, we also observed that the worldwide burden of stroke is rising, leading to significant direct and indirect socioeconomic costs. Stroke survivorship rates, disability-adjusted life-years (DALYs) lost as a result of stroke, and stroke-related fatalities are all rising.

Improved stroke therapy, new developments in acute stroke care, and a more thorough approach to primary and secondary prevention. The best stroke management, however, necessitates addressing individuals at all risk levels. This must be combined with preventative measures, while also considering unhealthy lifestyles and risk factors that are common to other conditions that increase the risk of cerebrovascular accidents, such as diabetes and hypertension.

Advances in basic sciences, radiology, clinical, and therapeutic research have made it possible to effectively manage stroke patients in recent years. This includes enhancing stroke diagnosis and therapy, expanding the time window for stroke treatment, and offering acute stroke therapies to individuals who were not included in earlier trials.

Brain computer tomography (CT) was initially limited to its use in differentiating between ischemic and hemorrhagic stroke. However, it is now also used to evaluate the salvageable ischemic area and large vessel occlusion, which helps select patients more effectively for acute treatment. These developments enhanced the basic idea of "time window." Furthermore, the clinical approach to stroke advanced and focused more on managing the initial days following the beginning of the stroke in addition to acute therapy. As a result, current recommendations suggest the use of specialist stroke units. Although the in-hospital mortality rate for stroke is still high, it has decreased significantly as a result of these advances, primarily because in-hospital complications are avoided. These improvements have also allowed for notable gains in terms of recovery and outcome. These therapeutic advances were actually made possible by more precise management of nutrition, blood pressure, and glucose control in specialized units during the acute phase following a stroke.

This collection of papers presents some of the most popular areas of stroke research, particularly those where notable advancements have been observed recently and where we anticipate rapid future growth in the field.

The primary focus of effective acute stroke treatment has been shown to be the timely and accurate assessment of large vessel occlusion and the salvageable ischemic area in acute stroke patients. To achieve this, advanced neuroimaging equipment and software tools that are based on CT or MRI are required.

Numerous instruments have been suggested, and this area of study is expanding quickly. In comparison to the widely used six-point classifications of multiphase CTA, Verdolotti et al. [1] assessed the efficacy of a new semi-automatic post-processing program (ColorViz FastStroke, GE Healthcare, Milwaukee, WI, USA) in the evaluation of collateral circulation. 86 patients with anterior ischemic stroke symptoms who underwent multiphasic CTA and ColorViz were examined independently by two neuroradiologists. Their initial findings suggested that this technology might perform as a diagnostic tool on par with CTA. Furthermore, it can shorten the evaluation period, enabling the quick appraisal of supporting vessels.

Because they enable a quicker differential diagnosis between small vessels and large vessel occlusion (LVO) and enrollment in acute treatment schemes, including mechanical thrombectomy, neuroradiological tools in the evaluation of acute stroke are even more crucial.

While a number of methods can be employed singly or in combination, mechanical thrombectomy has recently emerged as the accepted treatment for individuals with acute ischemic stroke (AIS) brought on by left ventricular outflow (LVO). These methods' primary goal is to achieve full and quick vascular recanalization while avoiding problems. Direct aspiration and stent retrievers are used in these procedures; nevertheless, operator preference and anatomical assessment are the primary determinants of technique selection. Making the optimal decision is tough, though, because comparing head-to-head results can be tricky. This clinical problem has been the subject of numerous studies, but no answers have yet been found. The procedural efficacy of the stent retriever technique with a Solitaire FR stent and the direct aspiration technique employing a Penumbra ACETM aspiration catheter was compared in a retrospective research with 76 patients [2]. The equivalent clinical effects shown by the results point to the potential utility of both procedures, albeit perhaps in different settings.

Although posterior strokes can sometimes be deadly, anterior circulation strokes have always been the focus of clinical research for acute stroke reperfusion treatments.

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Anterior circulation has long been a focal point for thrombolysis and thrombectomy in cases of acute stroke. For this reason, the most widely used stroke-related scales in clinical practice today are designed for anterior circulation and are either completely uninformative or of limited use for posterior circulation. However, 20–40% of all ischemic strokes are posterior circulation strokes. Studies have shown that treating stroke in the posterior circulation can be beneficial. Although there are now no special clinical measures for treating posterior stroke, it is likely that in the near future, posterior stroke treatment will also be introduced. Adam's Scale of Posterior Stroke (ASPOS), a new seven-item scale designed specifically to measure the severity of posterior circulation strokes, was proposed by Wisniewski et al. [3]. They created a prospective observational research with 126 patients who had ischemic strokes of the posterior circulation. In order to evaluate the validity and reliability of ASPOS and look into its predictive value, four researchers who had previously received ASPOS training randomized the stroke severity using the ASPOS tool and other appropriate stroke scales (the Israeli Vertebrobasilar Stroke Scale—IVBSS, the Glasgow Coma Scale—GCS, the National Institute of Health Stroke Scale—NIHSS, or the Barthel Index—BI). They said that ASPOS is a legitimate and trustworthy instrument with the potential to be utilized for further predictive purposes in addition to selecting patients for particular therapies more precisely.

Though their application in clinical practice is rather restricted, there is growing interest in the use of novel biomarkers that can predict the fate of strokes. In contrast to glycated hemoglobin (HbA1c), Kim et al. [4] investigated the effects of glycated albumin (GA) on short-term functional outcomes in 1163 acute-infection patients from two hospitals. The results were examined using the modified Rankin Scale (mRS) at three months. The higher GA group (GA > 16%) exhibited a 1.4-fold increased chance of having an unfavorable mRS after correcting for several variables, indicating that GA level may be a novel predictive biomarker for short-term stroke outcome in comparison to HbA1c.

The potential hemorrhagic transformation (HT) of ischemic stroke, and specifically symptomatic hemorrhagic transformation (sHT), is a hot topic in stroke research. A complication of AIS is hemorrhagic transformation, which can occur spontaneously from ischemic lesions or be produced or encouraged by reperfusion therapy. One potentially fatal side effect of acute ischemic stroke is known as symptomatic hemorrhagic transformation (sHT) (AIS). Although there is currently no known signal associated with sHT, early detection of people at elevated risk of sHT may have clinically significant ramifications. Świtońska et al. investigated the relationship between neutrophil-to-lymphocyte ratio (NLR) at admission and sHT since AIS causes a strong immune system activation and even more HT. They discovered that NLR can predict sHT in patients with AIS undergoing revascularization [5].

The current guidelines suggest that stroke patients be treated in units specifically designed for stroke care. However, because some patients require critical care both before and after the treatment, thrombectomy has introduced new problems. Stroke patients may face additional risks due to management in an intensive care unit, which is linked to a poor prognosis [6]. 158 AIS patients who had undergone thrombectomy and were hospitalized to a neuro-intensive care unit (NICU) were the subjects of a prospective cohort research designed to evaluate the variables associated with functional outcomes such as independence (mRS < 2). While older age and hemorrhagic transformation were linked to 6-month independence, IVT and nasogastric tube removal were associated with better outcomes at 3 months. These findings suggest that acute stroke patients with LVO who require NICU management soon after IAMT may exhibit specific clinical factors that influence both short- and long-term prognosis [7]. These findings raise the possibility that nutrition and most likely dysphagia are related to short-term outcomes. Dysphagia is a pertinent subject in the treatment of acute stroke. Indeed, there is evidence that people with AIS have less force while coughing, which is connected to a higher risk of aspiration, and that reflexive coughing is compromised when certain brain regions are affected. This subject was examined in a retrospective MRI research by Bo Lee et al. [8].

Researchers discovered that patients with AIS exhibited a weak cough flow when lesions in the inferior parietal and temporal lobes, as well as the superior and mid-temporal gyrus, were linked to a weak peak cough flow during voluntary coughing. Other brain regions affected by AIS included the sub-gyral frontal lobe, the superior longitudinal gyrus, and the posterior corona radiata. The findings of this study may help identify and more accurately evaluate patients who are susceptible to aspiration pneumonia due to impaired cough function.

Blood pressure management in acute stroke patients is another significant issue that is still far from resolving and become even more difficult with the introduction of IAMT. In actuality, there is ongoing discussion on the best ways to treat elevated blood pressure in patients with acute cerebrovascular disorders who report to the emergency room, even with the abundance of evidence regarding preventive and therapeutic measures that can be

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implemented. Cantone et al.'s review [9] offers an up-to-date and pertinent analysis of the present management of hypertensive crises in patients undergoing cerebrovascular accidents, as well as the hotly contested problems surrounding this condition. Additionally, they concentrate on the administration of time-dependent stroke treatments, like mechanical thrombectomy and intravenous thrombolysis.

The field of antithrombotic treatments has advanced significantly in the last few years. For atrial fibrillation-related cardioembolic stroke, new oral anticoagulants have been released following the introduction of clopidogrel as an alternate antiplatelet treatment. However, clopidogrel resistance has given rise to certain worries. High platelet reactivity in clopidogrel-treated individuals may make acute stroke patients' prognosis worse, according to prior research. Wisniewski et al. [10] demonstrated that the dynamics of platelet reactivity over time predict the clinical course and prognosis of stroke better than a single value in a prospective, single-centre observational research that enrolled 74 AIS patients.

The most frequent risk factor for cardioembolic stroke, the most severe ischemic stroke subtype, is non-valvular atrial fibrillation (NVAF). Even while preventative antithrombotic therapies saw some advancements with the advent of NOACs, acute antithrombotic therapies saw minimal progress, and there is disagreement over the ideal time to begin or resume anticoagulant medication therapy. Edoxaban was administered during acute stroke in observational prospective uncontrolled research [11] that included 75 elderly AIS patients with mild disability. After three months of treatment with early Edoxaban dosing, they saw two severe gastrointestinal bleedings and eleven minor bleedings, but no symptomatic brain haemorrhage or recurrent stroke. Due to the limited sample size, these results should be validated in a larger trial; however, they do indicate that Edoxaban, when taken early after an acute stroke, appears to be safe in certain patients who have had a cardioembolic stroke.

Lastly, there is ongoing discussion over the contribution of vascular risk factors to the long-term effects of stroke, including cognitive impairment. One of the main impairments that stroke survivors experience is post-stroke cognitive impairment (PSCI). Numerous glucose indicators, including haemoglobin A1C, hyperglycaemia, glycaemic variability, and glucose dynamics, have drawn a lot of attention due to their possible role as risk factors for PSCI in both diabetic and non-diabetic individuals. In an observational retrospective study, Lee et al. [12] examined this matter because post-stroke hyperglycaemia is often observed in acute ischemic stroke patients and because it is linked to poor functional and cognitive outcomes. They evaluated the relationship between the glycaemic gap upon admission and PSCI in ischemic stroke patients. They showed that, three months after a stroke, an elevated glycaemic gap is significantly linked to PSCI, with a preference for frontal and memory domain dysfunctions. They came to the conclusion that, in addition to glycaemic control status at the time of stroke onset, hyperglycaemia should be taken into account for the prediction of cognitive outcome following ischemic stroke.

Although there are still a lot of unanswered questions in the field of acute and post-stroke therapy, we concentrated on the most promising research areas in this Special Issue in the hopes that they may lead to important therapeutic advancements in the care of stroke patients in the next years.
To sum up, we hope that the research presented in this Special Issue will pique curiosity about more fundamental and applied studies on cerebrovascular illnesses, advancing the search for improved acute care that will improve stroke recovery and lessen the social and medical burden on stroke victims.

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