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Insights on the Trends and Future of Vascular Neurology

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Abstract

Over the last several decades, advances have been made in vascular neurology, including advancements in stroke diagnosis, treatment, prevention, and rehabilitation. Furthermore, the individuals who are providing the care represent a different cohort than those who were caring for stroke patients 30 years ago, because it has become increasingly important to make quick decisions for acute interventions and a larger workforce is required to provide the many complex aspects of stroke care. Before one can speculate about its future direction, one must understand the field's history. The remainder of this special issue focuses on vascular neurology in a post-thrombectomy era, highlighting some of the recent massive changes in the last few decades and introducing future opportunities and challenges. The management and care of ischemic strokes continues to rely on thrombolysis and thrombectomy, but the way care is delivered, who provides it, how they are trained, where they are provided, and how data are used to inform early management decisions will likely change in the coming years.

Keywords: Vascular neurology, Stroke patients, Acute ischemic stroke, Cerebrovascular disease, Neuroimaging

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Introduction

In the past decades, acute ischemic stroke patient care has advanced more rapidly than in many clinical fields: this disease has evolved from one that was primarily treated by internal medicine physicians to one where vascular neurologists treat it; from being a disease that was primarily treated by internal medicine physicians, As a result, it has evolved from a disease with few treatments and no urgency in its management to a disease in which "Time is Brain" and acute evaluations have become an integral part of the management process; from evaluation in hospitals to early evaluation via telemedicine, mobile stroke units have also become available; it has also shifted from being the second leading cause of death in the United States to the fifth [1]. How will the next 30 years be? By improving primary and secondary prevention, will stroke be eliminated? What are the primary sites where stroke care is provided by emergency medicine doctors or in the field? Does precision medicine allow optimal selection of treatment protocols both for acute care and secondary prevention of ischemic stroke? Throughout this issue, novel developments have been made within stroke care (with a focus on ischemic stroke), which indicates new hope for stroke management and stroke care in the future. In no way will stroke disappear as a disease, but advances in prevention, diagnosis, treatment, and rehabilitation will enable a broader population to be reached and stroke's severe disability to be minimized [2-4].

It's Time to Act Urgently in Stroke Care

In the years before 2000, stroke was treated without any sense of urgency, and treatment changes were often not made after tPA was tested in the NINDS tPA trial [5]. Despite the tPA trial demonstrating efficacy in reducing 3-month outcome, when intravenous tPA was given to appropriate patients within 3 h, and showing a safe treatment profile, emergency medicine communities were reluctant to support treatment, but the emergency medicine community did not embrace the trial results until the data of the tPA trial were reanalyzed to include baseline ischemic stroke severity imbalance. After that, the trial became a key component of acute ischemic stroke evaluation and treatment. Earlier stroke trials confirmed data from the ECASS-III trial, which extended the IV tPA time window to 4.5 h in 2008 [6].

It has become increasingly important to evaluate ischemic stroke patients immediately as more data suggests that every minute counts, as explained in several studies published during 1993 - 1995 [7]. A reduction of 15 min in treatment delay provides an additional one month of disability-free life for every additional minute of door-to-needle time saved. According to one estimate, every additional minute of door-to-needle time saved results in 1.8 days of extra healthy life; reducing door-to-needle time is associated with lower in-hospital mortality and fewer hemorrhagic conversions [8]. In public health messaging, this urgency is emphasized, and American Heart Association/American Stroke Association guidelines emphasize it as well: "Time to treatment is strongly associated with outcomes," as a Class 1, level of evidence A recommendation: "Treatment should be initiated as soon as possible within the above-mentioned timeframes" [9-11] (Figure 1).

How Are Stroke Patients Evaluated and Treated?

Stroke patients have traditionally been treated by internal medicine clinicians; however, the evolution of this model varies widely between countries. Although interventions and evaluation times continued to

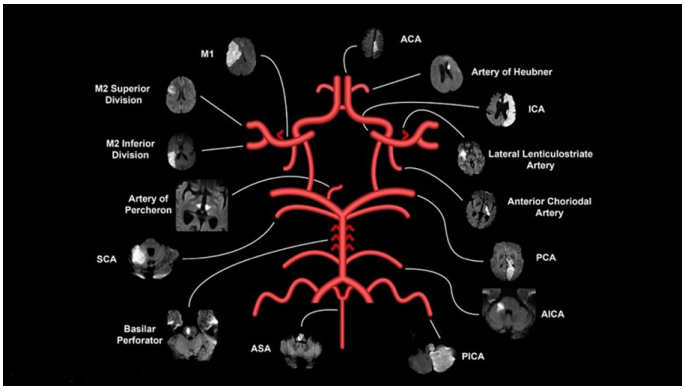

Figure 1: Diagram of brain (Source: Jeremy Heit on X).

change, stroke-specialized internists continued to care for most stroke patients, despite a shortage of neurologists in the United Kingdom [6, 12-16]. A new ABPN-certified Vascular Neurology fellowship began, to maximize training and expertise in cerebrovascular disorders, in contrast to the United States, where the field of vascular neurology emerged as a response to clinical needs.

The question of who is best suited to manage acute stroke care in particular has been the subject of debate, with some leading experts suggesting that neurologists are best suited to manage strokes because they have detailed knowledge of cerebrovascular disease and pathology. However, another expert argues that in order to provide stroke care, internists need to be familiar with comorbidities and aspects of disease [17]. No matter what, general internists and general neurologists are likely not adequately trained to make the kind of life-or-death decisions required when managing stroke patients [18].

There are many factors to consider when evaluating stroke patients, including not only those who are capable of managing blood pressure, making decisions on tPA or thrombectomy, or optimizing secondary prevention, but also those who are trained in evaluating stroke patients for diagnostic purposes [19]. There are often stroke mimics, accounting for one-third to nearly half of stroke alerts in some hospital series, and the rate is predicted to rise [20-22]. A careful neurologic examination is crucial to determining true stroke patients and to exclude mimics, even if neuroimaging fine-tunes a diagnosis. Transient ischemic attacks, which may represent an important opportunity to prevent secondary strokes, are not reliably diagnosed by emergency medicine physicians, despite the fact that they are estimated to represent most of the strokes diagnosed by emergency medicine physicians [23-24]. Additionally, mimics are often caused by other neurological conditions, so a neurologic evaluation is important to rule out both stroke and any other neurological illness [25].

Even mimics who are given tPA generally do well, with few complications, and lower hemorrhage rates than those with an ischemic stroke, in consideration of who might be best positioned to make decisions about an initial diagnosis and consideration for tPA [26]. The decision-making process involving further advances in stroke has become more complex as factors like unknown onset times, thrombectomy, and most recently, evidence that thrombectomy is beneficial for patients with basilar thrombosis [27-29]. Since basilar thrombosis presents atypically and is more frequently missed in the emergency department, the risk of misdiagnose increases, resulting in the denial of treatment for patients. In order to guide diagnostic considerations, decision-making, and management, it is essential for a well-trained clinician to evaluate the stroke patient [6, 30].

The need for specialty-trained stroke clinicians will likely exceed the number of available specialists, although there is considerable value in having these clinicians. The number of patients who were hospitalized with acute ischemic stroke from 1998 through 2000 was 60% when they were seen by a combination of a generalist and a neurologist, 17% when they were seen by only a neurologist, and 18% when they were seen by only a generalist [31]. Approximately 67% of patients with ischemic stroke were seen by a non-vascular neurologist and only 19% by a vascular neurologist, according to an updated Medicare analysis evaluating claims from later years (2009 - 2021) [32-34].

A growing number of stroke patients are being treated by hospitalists, and it is likely that going forward, fewer stroke patients will be treated by neurologists, particularly vascular neurologists. Hospitalists reported consulting a neurologist only 40% of the time for ischemic stroke patients in a survey [35]. It will be crucial to adapt to this changing landscape by establishing clear pathways for stroke education, identifying circumstances where neurologic consultation is particularly necessary, and establishing team-based collaborative care [36].

A second model of stroke clinical evaluation that has proven successful and will likely become more prevalent in the future is the use of telemedicine to fill the gaps when specialized stroke clinical evaluation is not possible [37]. A higher reperfusion rate, lower mortality rate, and increased use of alteplase were associated with telestroke compared to no telestroke facility. There is value in telemedicine both for stroke treatment in general and for decisions regarding acute interventions when expert opinion is unavailable locally [38]. The "ideal disease" for telemedicine is stroke because of the short timeframe and ease of video and image access. Furthermore, we need to decide if stroke neurologists should handle telemedicine solely or if other specialists should be trained to provide this service. Telemedicine has been increasingly used in stroke care, yet there are still gaps in access [39].

In the Care of Acute Ischemic Stroke Patients, What Data are Being Analyzed?

Increasing the number of patients who qualify for acute interventions, whether it is based on wake-up strokes or specific imaging criteria, will increase the work burden. Automated systems are likely to be needed in the future to perform initial screenings for eligible patients at a minimum. Increasingly, software that interprets computed tomography (CT) perfusion data perfusion mismatches using artificial intelligence, such as RAPID software and other artificial intelligence systems, allows for faster decision-making and a quicker screening of patients who may be eligible for intervention through automated artificial intelligence. Food and Drug Administration approved and widely used, these approaches have been used in multiple clinical trials to expedite treatment and expand access to care [40-44]. Several clinical trials have been conducted with these approaches. In determining the appropriateness of acute intervention, decision-support tools such as e-ASPECTS can be compared to a clinician-rated ASPECTS score on head CT. In addition to stroke prediction based on risk factors, brainstem infarction prediction based on CT, and thrombolysis optimization tools, machine learning and artificial intelligence-based approaches have a host of other applications [6, 45]. In parallel with these expansions, artificial intelligence is increasingly being used in health care.

Nevertheless, these automated methods don't negate the need for experts to interpret clinical situations and make decisions about appropriate treatment despite their improvement in speed of access to information about potential large vessel occlusions [46]. Moreover, they have their limitations as well. A patient's technical characteristics, scanner characteristics, or some other factor may influence the

accuracy or interpretation of these images, and these automated approaches may add additional information that does not add value and complicate a complex picture [47]. To reduce the likelihood of erroneous artificial intelligence imaging results. The cost of commercial artificial intelligence has also been questioned, with some arguing that large-scale randomized trials should be conducted to determine if there is a benefit equivalent to the cost [48]. The introduction of generative adversarial networks is one of the most concerning developments, because the networks are commonly used to build superficially realistic neuroimages of patients based on orthogonal contrast mechanisms. The proliferation of artificial intelligence tools in medicine will be unavoidable, given the breadth of applications that could be beneficial in stroke along with the exponential growth of machine learning. Vascular neurologists of the future will need to embrace them. It is likely that these tools will continue to be most valuable when used in conjunction with other clinical data and not as a replacement for them in the short term [6, 49, 50].

It may, however, be possible to use artificial intelligence tools to develop more flexible models regarding who and how these decisions are made, and how they are made. Additional considerations include the fact that more data does not always translate into better decisions. The decision-making process may become more complicated before it becomes easier if a clear understanding of the implications of certain findings that can be identified with these automated systems is lacking, as a greater amount of research may be needed to determine best practices if certain incidental artificial intelligence-detected findings occur [51].

Changes in Interventions and Treatments

In order to expedite the decision-making process and increase who can make decisions at least about acute stroke care, new locations have been identified for delivering care or, at the very least, for beginning the diagnostic process [52, 53].

Once hospitalized, stroke patients can receive specialized care in the stroke unit. A study found that these units improved outcomes, particularly for patients with strokes that affected large vessels [54-57]. Emergency departments (or stroke units) make acute stroke decisions, however. For eligible patients, the mobile stroke unit was born as a result of the emphasis on reducing the time to potential treatment [58]. A stroke-trained ambulance (or, more recently, a stroke-trained specialist available via telemedicine) can not only provide acute evaluation, including neuroimaging, but can even initiate thrombolysis for those patients. It has been shown that mobile stroke units have better post-stroke outcomes than traditional ambulances, despite the fact that they are expensive and require extensive resources to ensure optimal availability. Individuals managed initially by mobile stroke units had less disability after 90 days, despite the fact that they were evaluated and transported by traditional ambulances [59, 60].

Additionally, this model stressed the importance of prehospital care in addition to using a mobile stroke unit for early thrombolysis. Other acute interventions and neuroprotective treatments have also been evaluated in this setting, though many of them have been unsuccessful or even harmful, such as FAST-MAG and nitroglycerin [61]. Possibly this model, of delivery of early interventions prehospitally, will continue to be used as a way of testing treatments most promising when commenced very early after stroke onset. As well as enabling early diagnosis in ambulances, mobile stroke units can also facilitate in-hospital treatments including thrombectomy, paving the way for improvements in patient care in the future [6, 62-65].

The ability to provide stroke care to underserved communities is a major obstacle to stroke care delivery. Due to cost and efficiency limitations that are particularly problematic in regions with low stroke populations, mobile stroke units are unlikely to be able to adequately access these regions. There will continue to be a need for telemedicine to deliver care to a variety of communities, and particular caution is needed to prevent further disparities from developing (high-resource communities have access to mobile stroke units and improving therapy options, while low-resource communities lack these units and the relevant therapy options). However, an increase in telemedicine is unlikely to solve the problem of improving access to care globally. One study of 75 countries found that mechanical thrombectomy access was less than 3% on average, but improved access would only address a relatively small proportion of stroke-related inequities [66].

Changes in Training and Specialization

Currently, there is a noticeable shift in vascular neurology trainees in the United States, with more individuals wishing to undertake both vascular neurology and neurointerventional radiology training. Having training in stroke seems like an advantage for future neuro-interventionists, but many vascular neurologists are likely to primarily focus on acute interventions rather than diagnosis, secondary prevention, rehabilitation, and other important aspects of stroke management [67, 68]. As vascular neurologists can handle the entire spectrum of stroke diagnosis and care, this model (training vascular neurologists as interventionalists) may be optimal. Given the increasing number of patients eligible for thrombectomy, if we plan to increase our need for vascular neurologists with additional interventional training), it is essential to ensure that all other aspects of stroke care remain in the hands of stroke-trained doctors, and a shift to an interventional specialty may lead to a loss of these other important stroke care aspects [69]. In order to emphasize the value of each of these career paths, perhaps a two-track stroke fellowship option would be necessary (interventional stroke vs stroke). This shift towards an intervention-based fellowship model will also need to be examined in order to understand how it might impact the already significant disparities in frequency of women and physicians from underrepresented groups [70].

The increasing use of telemedicine is another key consideration in the training of future vascular neurologists; this will form a major part of stroke care in the future, and telemedicine consultants have shown that with greater experience with telemedicine consults, they are able to improve care and shorten page-to-needle times [71, 72].

Neurologists are expected to be in short supply by 19% by 2025 in the United States, and vascular neurologists will likely face a similar shortage. There were only 209 vascular neurology fellowship positions in 2022, according to the National Resident Matching Program; 15% of these fellowship positions remained unfilled in 2022, and the percent of neurology residents who pursued vascular neurology decreased from 19% in 2014 to 15% in 2017 [73, 74]. It may be necessary to increase the number and size of fellowship programs as stroke patients and patients eligible for acute interventions increase.

Future Directions in Stroke Care

Increasing eligibility for thrombolysis or thrombectomy has been a major focus of recent ischemic stroke research, either by expanding the time window or improving care delivery. These interventions will be more accessible to more patients, but the majority of stroke patients will not be eligible due to the size of their strokes (too small or too big), the time it took them to reach the emergency department, or certain comorbidities [75, 76]. In addition, there are many individuals who live in communities that do not have a primary stroke center, a comprehensive stroke unit, or a mobile stroke unit, as well as

telecommunications systems that are not well-established enough to allow access to equity in stroke care [77-78].

In the event of stroke symptoms, fewer individuals might delay a visit to the emergency room by improving public health messaging and education, and system-level improvements may also improve the number of patients eligible for acute interventions by reducing door-to-needle times or eliminating other barriers [79]. It is important for future stroke research to continue to focus on improving acute treatment, rehabilitation strategies, and secondary prevention strategies, even though many patients will not qualify for these therapies. As a result of these system-level issues in stroke care, disparities exist both globally and, in the United States, when it comes to stroke prevention, care, and recovery. To prevent these disparities and provide broader access to optimal stroke care, it is critical to continue investigating the nature and extent of these issues in stroke systems of care [80-83].

In addition to assessing acute outcomes of stroke patients, further research is also needed to evaluate the long-term effects of different types of strokes, regardless of whether acute interventions were available. In the Determinants of Incident Stroke Cognitive Outcomes and Vascular Effects on Recovery (DISCOVERY) study, participants with ischemic stroke, hemorrhagic stroke, and subarachnoid hemorrhage are being recruited, with an emphasis on those from disparities populations. In the long term, post-stroke cognitive outcomes are evaluated in light of preexisting conditions and stroke itself [84, 85].

In the last few decades, a significant advance has been made that will likely shape the field for the foreseeable future: it has become increasingly clear that managing stroke patients requires carefully considering the patient's medical history, stroke subtype, and stroke location. A patient's health may also be influenced by genetics, subtle neuroimaging features of the stroke, and underlying cerebrovascular disease, among other characteristics [6, 85]. A study conducted in China showed that Chinese patients with minor strokes or TIAs with the CYP2C19 platelet dysfunction allele received ticagrelor plus aspirin vs clopidogrel plus aspirin, with a lower rate of recurrent stroke in those treated with ticagrelor, highlighting the importance of genetically determined treatment. It is also a form of precision medicine to consider specific imaging features of an acute stroke patient, which could be expanded with additional imaging assessment. Our precision-based approaches to patient care will likely be enhanced by advances in technology that incorporate all of the available data, using machine learning methodologies. Medications are not prescribed exactly the same way for every patient, and a precision medicine-based approach might help us decide which antiplatelets, which antihypertensives, which statins, and maybe even what acute interventions are best for each patient. Future research should consider these considerations as well in order to prevent strokes as soon as possible.

Rehabilitation

In order for rehabilitation to be most effective, it must be offered early and use procedures that are similar to those used in real-life use by the impaired limbs. A shared framework for research priorities in rehabilitation has been established by experts in this field of research [86]. In terms of stroke recovery, therapeutic options range from more traditional approaches to brain stimulation and robotics-based approaches as well as pharmacological interventions such as small molecules, growth factors, and monoclonal antibodies. Telerehabilitation also shows promise as an alternative to conventional face-to-face therapy, as it has been found to be as effective or even more effective [87].

The Next Decades

Over the next decades, stroke care will evolve in many ways. In the pre-hospital setting, care will likely be routinely delivered, with additional agents reaching broader populations. In stroke care and rehabilitation, medical professionals and in particular vascular neurologists - may be replaced to some extent by automated decisions up to a certain point; it is likely that doctors will not be replaced entirely. It will continue to be a major cause of disability, and stroke risk factors will still exist. Genetics, metabolism, or other factors that guide the best management for an individual may be incorporated into a precision-based approach of most optimal medications for prevention; this may even extend to acute interventions, where certain imaging features, metabolic characteristics, or genetic makeup may make one therapy less effective. To ensure equitable access to a broad community of stroke patients, multidisciplinary teams will be needed to apply and interpret these advancements [88].

Our goal should be to keep vascular neurology an exciting field for future trainees, despite the expected advances and modifications in how care is delivered. It is also necessary to continue training clinicians about acute strokes, clot retrieval, secondary prevention, and directing patients to appropriate early rehabilitation in order to comprehend the subtleties of acute stroke presentation and diagnosis. In addition to remaining excited about potential discoveries in stroke and cerebrovascular disease, the top future investigators (physician-scientists and scientists) need to remain focused on this field [89].

Among the topics covered in this collection are issues relating to secondary prevention of stroke, disparities in stroke intervention access, and reperfusion injury and outcome in minor strokes. They reflect important changes or changes in stroke care in the coming decades [6, 90]. Stroke research has made significant progress due to thrombectomy, however there is still much to be done in optimizing stroke care, improving its delivery, and identifying priorities for future studies. We anticipate the next generation of clinicians and researchers will continue to be engaged in some of the exciting areas covered in this issue of neurotherapeutics.

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Conflict of Interest

None.

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