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Advances in the Stroke System of Care

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Opinion statement

The stroke system of care is undergoing significant evolution. There are promising data to suggest that with new technologies and approaches, primary prevention and community education will become easier and more accessible, and will allow people to have greater participation in their own healthcare. The evidence-based primary and comprehensive stroke center concepts have been translated into robust, rapidly growing certification programs. The continued dissemination of improved EMS routing protocols allows for better allocation of patients to stroke centers, even as we confront the challenge of further improving prehospital recognition of stroke. National quality improvement initiatives help to ensure that patients directed to stroke centers receive evidence-based treatment, which has resulted in improved stroke care and better clinical outcomes. In remote areas, the use of technologies such as telemedicine to extend the reach of vascular neurologists has resulted in increased administration of time-sensitive thrombolytic therapy and better patient outcomes, although greater efficiency within the stroke system will likely be needed to realize the potential benefits of endovascular therapy. System-level paradigms for aggressive medical management promise to lessen the burden of recurrent stroke. Finally, further integration of rehabilitation programs into stroke centers and coordination with community-based rehabilitation services is needed to ensure the best possible outcome for stroke patients.

Introduction

Each year in the United States, 800,000 people experience a stroke, including 610,000 first-ever and 185,000 recurrent strokes. Someone has a stroke approximately every 40 seconds, and on average, someone dies from a stroke every four minutes.[1]. Despite documented benefits of timely treatment with intravenous tissue plasminogen activator (t-PA), recent data show that only 3.4–5.2 % of acute stroke patients in the U.S. receive thrombolytic treatment [2], and less than one-third of patients treated with intravenous t-PA have door-to-needle times of less than 60 minutes [3]. Stroke continues to be a leading cause of serious long-term disability, with a total direct and indirect cost of $36.5 billion in 2010 [1]. Six months after stroke, almost half of all elderly stroke survivors have moderate to severe neurological deficits [4]. By five years after stroke, only about half of patients are alive, and approximately 40 % of survivors are disabled [5, 6].

More efficient and tightly integrated systems for stroke care are needed. In 2005, an American Heart Association (AHA) task force on the development of stroke systems described the fragmentation of stroke care, defined the key components of a stroke system, and recommended methods for encouraging the implementation of stroke systems of care [7]. The task force defined seven key components of the Stroke Systems of Care Model (SSCM): 1) primordial and primary prevention; 2) community education; 3) notification and response of emergency medical services; 4) acute stroke treatment; 5) subacute stroke treatment and secondary prevention; 6) rehabilitation; and 7) continuous quality improvement (CQI) activities. It is helpful to think of a system of care as a bridge between clinical trial evidence/national guidelines and improved processes of care/patient outcomes. The focus of this review will be on recent advances in the stroke system of care that have facilitated implementation, compliance, and integration of evidence-based care (Table 1).

Primordial and primary prevention

Despite the persistence of significant stroke-related morbidity and mortality, there is some reason for optimism. Compared to prior decades, there has been an accelerated rate of decline in stroke mortality in the United States since the 1970s [1]. This effect seems to be primarily attributable to improved control of hypertension related to both clinical hypertension treatment as well as public health strategies and programs to reduce blood pressure in the hypertensive population. The result of these interventions has been a decline in mean systolic blood pressure (SBP) among the U.S. adult population from 131 mmHg in 1960 to 122 mmHg in 2008 [8•]. Control of diabetes mellitus and dyslipidemia as well as the implementation of smoking cessation programs appear to have contributed to the decline in stroke mortality as well. As a result, stroke has fallen from the third to the fourth leading cause of death in the United States. [8•].

While there have been great improvements in controlling hypertension, currently only 81.5 % of patients with hypertension are aware that they have it, 74.9 % are being treated, and 52.5 % are under control [9]. Where do we go from here? To improve blood pressure control, system-level approaches will be needed. A successful system-level approach to improve blood pressure control is illustrated in the experience of Kaiser Permanente Northern California [10•]. From 2001 to 2011, hypertension control increased from 44 % to 87 % by means of a multifaceted approach that included a comprehensive electronic hypertension registry, development and sharing of performance metrics, evidence-based guidelines, medical assistant visits for blood pressure measurement, and single-pill combination pharmacotherapy.

The emergence of self-monitoring programs and mobile health tools is an exciting trend. McManus et al. [11•] found that patients who were ran-

Table 1. Advances in the Stroke System of Care

System Component	Advance
Primordial and Primary Prevention	System-level paradigms for hypertension management Self-monitoring programs Mobile health
Community Education	Focus on culturally tailored educational campaigns to change behavior
Notification and Response of Emergency Medical Services	EMS stroke center routing protocols New models of EMS medical control for stroke
Acute Stroke Treatment	Growth of primary and comprehensive stroke center certification Growth of telestroke networks Recognition of the need for improved triage for endovascular therapy
Subacute Stroke Treatment and Secondary Prevention	Growth of primary and comprehensive stroke center certification Growth of telestroke networks System-level paradigms for aggressive medical management
Rehabilitation	Incorporation of rehabilitation into comprehensive stroke centers
Continuous Quality Improvement Activities	Growth of primary and comprehensive stroke center certification Growth of national quality improvement programs

domized to self-monitoring of blood pressure combined with individualized self-titration algorithms saw a decrease of 9.2 mmHg in systolic and 3.4 mmHg in diastolic blood pressure compared to standard care at the 12-month office visit. Patients took their blood pressure twice every morning for the first week of each month, and used a paper-based individualized three-step plan to increase or add antihypertensive medications. In light of the ongoing expansion of technology, studies have recently looked at mobile phone applications as a way to aid patients in managing their own health. Hallberg et al. [12] described the development and preliminary evaluation of an interactive mobile phone-based system aimed at supporting patients in self-management of their hypertension.

Community education

The central purpose of educating the public to recognize stroke symptoms is to prompt an immediate and adequate reaction (i.e., calling emergency medical services [EMS]). Mass media interventions have had partial success in raising public awareness of stroke symptoms, but they are expensive, and have had limited impact on behavior [13, 14]. Unfortunately, there appears to be a discrepancy between theoretical stroke knowledge and an individual's reaction in a real-life situation. Teuschl and Brainin reviewed studies of prehospital delay, knowledge of stroke symptoms, and educational interventions among stroke patients [15], and found that the single largest component of prehospital time delay was decision delay (time from noticing the symptoms to call for help). Median decision delays ranged from 38 minutes to four hours, and accounted for 45 % of prehospital time. Help-seeking behavior was more related to perceived severity of symptoms rather than to symptom knowledge. Importantly, the person seeking medical help was rarely the patient. EMS was activated by less than 7% of patients, compared to 40–66 % of bystanders. The presence of a bystander, and bystanders noticing the symptoms and making the decision to call EMS, significantly reduced time delay.

The mixed results of mass media stroke awareness campaigns has prompted a new emphasis on a culturally tailored approach recognizing social context and health-literate educational materials, and on desired outcomes of behavioral change and stroke preparedness [16]. An individual's preparedness to take action requires that they recognize the warning signs of stroke, call EMS, facilitate a dialogue about stroke, and navigate the emergency medical system and emergency department. Of particular interest is the emergence of culturally tailored school-based programs that have sought to test whether "child-mediated stroke communication" could improve stroke literacy among children and their parents [17, 18].

Notification and response of EMS

There has been substantial progress in the ability of the EMS to accomplish the goal of getting the right patient to the right place at the right time. EMS stroke recognition has been associated with shorter door-to-physician assessment times in the emergency department [19]. Pre-notification has been linked to additional benefits in time to physician assessment, time to CT scan performance, time to thrombolytic therapy, and likelihood of administration of thrombolytic therapy [19–21].

A major recent advance is the development of EMS protocols to route suspected stroke patients to designated stroke centers. In 2000, counties in Alabama and Texas first began routing acute stroke patients to stroke-designated hospitals [22•]. The first study of the impact of stroke center designation and selective triage of acute stroke patients to stroke centers was reported by Gropen et al [23]. In this study, acute stroke patients were selectively triaged to 14 hospitals in Brooklyn and Queens that met Brain Attack Coalition (BAC)-based primary stroke center (PSC) criteria [24]. From baseline to re-measurement, t-PA utilization increased from 2.4 % to 5.2 %, and the stroke-unit admission rate increased from 16 % to 39 %. Since then, there has been rapid development of primarily state-based EMS stroke patient routing protocols. The U.S. population covered by routing protocols has increased substantially, from 1.5 % in 2000 to 53 % in 2010 [22•].

Since the approval of t-PA, the AHA has recommended the use of prehospital stroke screens by EMS personnel. Improvement of prehospital stroke recognition is even more critical in the current environment of stroke patient routing protocols. While a number of prehospital stroke screens have been developed and validated, the most studied prehospital stroke screen is the Cincinnati Prehospital Stroke Scale (CPSS) [25, 26]. The largest examination of the CPSS was conducted by Ramanujam et al., who reported on 440 patients with a discharge diagnosis of stroke, noting 44 % sensitivity in EMS impression of stroke [27]. Recently, Gropen et al.[28] found that stroke was missed more frequently by EMS in patients without motor signs and in patients with moderate–severe stroke when the CPSS was not documented. The sensitivity of prehospital screening for patients with moderate–severe stroke might be improved by including additional non-motor signs and by stressing the indications for when screens should be performed.

Clearly, there is a need to improve prehospital stroke recognition, and the greatest opportunity may lie with new models of EMS medical control for stroke. An innovative way to improve prehospital stroke recognition is to leverage the recent advances in mobile videoconferencing technology to enable physicians to participate in prehospital stroke assessment (mobile telestroke). Mobile telestroke has the potential to facilitate performance and interpretation of the prehospital stroke scale, more accurate prehospital stroke identification, better EMS triage decisions, instantaneous pre-notification, and ultimately, more rapid ED evaluation and treatment of stroke patients. There are limited data regarding the use of mobile telestroke. The first two-way ambulance-based telemedicine system for stroke assessment reported in the literature was the TeleBAT system, developed by the Maryland Brain Attack Team [29, 30]. While the TeleBAT system was limited by the technology available at the time (1996 to 1999), reports in the last couple of years suggest that mobile telestroke may be feasible in many areas in the near future [31, 32].

Acute stroke treatment

Based on the work of the BAC [24, 33], the Joint Commission started its program of PSC certification in 2003 and comprehensive stroke center (CSC) certification in 2012. As of August 2014, the Joint Commission had certified 1,051 PSCs and 77 CSCs, while other agencies had certified 124 PSCs and 14 CSCs [34–36]. As noted above, this is increasingly reflected in the organization of prehospital stroke care in which patients are preferentially diverted or transferred to the nearest PSC, as well as the increasing number of networks with a hub CSC and associated spokes, including both PSCs and non-stroke center acute care facilities. A recently recognized challenge to the delivery of stroke care is the shortage of vascular neurologists and the inability of vascular neurology fellowships to keep pace with the expansion of the stroke care infrastructure —a shortage that is particularly noticeable in rural communities [37].

Fortunately, the geographical disparity in vascular neurologists and other physicians involved in the delivery of stroke care has been mitigated by the rapid increase in telestroke networks serving rural communities and small hospitals. A recently published survey of programs in the U.S. [38•] revealed a significant increase in mean number of spokes per hub from 2007 to 2009. In 65.5 % of hubs, over 80 % of the spoke sites were rural, and in 51.7 % of hubs, more than 80 % of the spokes were small hospitals (0–99 beds). A recent scientific statement from the ASA found compelling (class I, level of evidence A) evidence that the NIHSS telestroke examination is comparable to an NIHSS bedside assessment, and that review of brain CT scans by stroke specialists or radiologists using teleradiology systems approved by the FDA is useful for identifying exclusions for thrombolytic therapy [39]. Telestroke has been shown to result in correct acute stroke treatment decisions more often than telephone-only consultation [40], increased patient access to t-PA in hospitals using telestroke [41], and comparable three-month patient outcomes at hubs and spokes [42, 43]. Despite the rapid growth of telestroke networks, however, there remain significant barriers to program growth, including the inability to obtain physician licensure, lack of program funds, and lack of reimbursement [38•].

There have been five recently published randomized trials of endovascular therapy for the treatment of acute ischemic stroke [44–48]. Two of the studies reported superior angiographic and three-month clinical outcomes with stent retriever devices compared to the corkscrew-shaped Merci Retriever [44, 45]. The SYNTHESIS Expansion study [46] compared endovascular treatment to intravenous t-PA. Among the 165 patients who received endovascular treatment, at a median time of 3 hours 45 minutes from stroke onset to treatment, 109 were treated with intra-arterial t-PA, and a device was added in 56 patients (including a stent retriever in 23 patients). Outcomes at three months were similar, indicating that endovascular therapy was not superior to intravenous t-PA. The Interventional Management of Stroke (IMS) III trial [47] compared 222 patients randomized to intravenous t-PA with 434 patients randomized to t-PA plus endovascular therapy (including stent retrievers in five patients). The mean length of time from stroke onset to start of intravenous t-PA was 2 hours 2 minutes, and the mean time from stroke onset to groin puncture was 4 hours 9 minutes. The IMS III trial failed to show a benefit in functional outcome with the use of additional endovascular therapy compared to intravenous t-PA alone.

The primary factors that have been cited for the failure of recent clinical trials to prove the benefit of endovascular therapy include the use of older devices, inadequate rates of near-complete or complete recanalization based on the Thrombolysis in Cerebral Infarction (TICI) scale, and delay to treatment, as well as patient selection factors including the inclusion of patients with milder deficits and patients with no evidence of demonstrated proximal large-vessel occlusion on MR or CT angiography [49–51]. What implications do these studies have for the stroke system of care? They certainly reaffirm the importance of a continued focus on increasing access to timely intravenous t-PA and stroke units. They also provide information that will strengthen future trials of endovascular therapy. The IMS III, SYNTHESIS Expansion, and MR RESCUE trials all demonstrated substantial delays in triage and initiation of endovascular treatment [46–48]. Analysis of the IMS III data [52] revealed that important delays occurred in the length of time from intravenous t-PA initiation to groin puncture (median 84 minutes) and from the start of endovascular therapy to reperfusion (median 85 minutes). The use of CTA angiography was associated with a reduction in delay. As there is strong evidence to suggest that a good clinical outcome following successful reperfusion is highly time-dependent [53], improving our ability to rapidly identify and triage those patients who may benefit from endovascular therapy will be critical. The median length of time from arrival to start of endovascular treatment for acute ischemic stroke patients is a recommended metric for measuring quality of care in comprehensive stroke centers [54]. Recent consensus guidelines have advised a door-to-groin puncture time of less than 120 minutes [51].

Subacute stroke treatment and secondary prevention

The dramatic growth of stroke centers and networks has provided the infrastructure necessary to improve access to acute stroke therapies. Stroke centers also form the basis for subacute stroke treatment and initiation of efforts to prevent stroke recurrence. A key feature of stroke centers, both primary and comprehensive, is the stroke unit. The most recent Cochrane meta-analysis of organized inpatient care for stroke was published in 2013, included 28 trials and 5,855 participants, and continues to demonstrate that patients treated in stroke units compared to alternative venues are more likely to be alive, independent, and living at home one year after stroke [55], benefits that are possibly related to the prevention and treatment of post-stroke complications [56].

Just as telemedicine has improved access to t-PA for stroke patients in rural areas, it has the potential to extend the reach of vascular neurologists to provide stroke unit care. A model of decentralized care with a telemedicine-supported stroke unit (or "telestroke unit") is exemplified in the TeleMedical Project for integrative Stroke Care (TEMPiS) in southeast Germany. Initial data from 2003–2005 showed that implementing systems of specialized stroke units, continuing education, and telemedicine in five community hospitals offered long-term benefits for stroke patients treated in TEMPiS hospitals compared to patients treated in five matched control hospitals [57]. Subsequently, Müller-Barna et al. evaluated the sustainability of the TEMPiS project from 2003 to 2012, by which time the network comprised two hubs and 15 spokes [58]. In addition to 24/7 availability of telestroke consultation for thrombolysis, the hubs also provide a teleconsultation team of five to seven full-time vascular neurologists available 24/7 for follow-up care, and assist the spokes through the formation of a multidisciplinary stroke team, standardized protocols, continuing training, and an ongoing quality improvement program, with audits, a stroke registry, benchmarking, and certification procedures. The number of patients with stroke and TIA treated in telestroke unit hospitals increased substantially, from 19 % to 78 %, between February 2003 and December 2012. Further research into the outcomes for patients treated in telestroke units compared to those transferred to PSCs or CSCs is warranted.

Stroke patients face a significant risk of recurrent stroke and associated morbidity and mortality. Over 10 years of follow-up in an Australian cohort, the risk of first recurrent stroke was six times greater than the risk of first-ever stroke in the general population. Additionally, the 30-day case fatality after a first recurrent stroke was 41 %, which was about twice as high as the case fatality after a first-ever stroke. The authors stressed the need for effective stroke prevention strategies to be "implemented early, monitored frequently, and maintained long term after first-ever stroke" [59]. Yet the literature suggests that in a broad variety of contexts, only about one-third of patients with chronic illness have excellent medication adherence (perfect or with some timing irregularity) [60]. Bushnell et al. studied patient, provider, and system-level factors influencing continuation of prevention medications, noting that about one-third of stroke patients discontinued one or more secondary prevention medications within one year of hospital discharge [61]. Interestingly, the majority ceased taking these medications based on post-discharge healthcare provider recommendations. Independent predictors of one-year medication persistence and adherence included fewer medications prescribed at discharge, adequate income, having an appointment with a primary care provider or neurologist, and greater understanding of why medications were prescribed and their side effects. Hence, the literature suggests that system-level barriers contribute significantly to poor medication adherence.

Fortunately, system-level interventions can improve medication adherence, risk factor control, and recurrent stroke risk. In 2005, Chimowitz et al. reported high rates of recurrent stroke in patients with symptomatic intracranial disease randomized to warfarin versus aspirin in the Warfarin-Aspirin Symptomatic Intracranial Disease (WASID) trial [62]. In 2011, Chimowitz and colleagues reported the results of the Stenting vs. Aggressive Medical Therapy for Intracranial Arterial Stenosis (SAMMPRIS) trial, which randomly assigned patients with symptoms related to 70-99 % intracranial stenosis to aggressive medical management, with or without angioplasty and stenting [63]. SAMMPRIS showed higher morbidity in the stenting arm than expected, with a 30-day rate of stroke or death of 14.7 %, prompting discontinuation of the study. Notably, there was also lower morbidity in the medical arm than expected, with a 30-day rate of stroke or death of 5.8 %, half the rate of recurrent events compared to a matched group of WASID patients. What was the difference? In WASID, patients received standard risk factor management, with targets based on national guidelines. In SAMMPRIS, risk factor management was multimodal and protocol-driven, including antiplatelet therapy, intensive management of vascular risk factors, and a lifestyle modification program [63]. Derdeyn et al. recently published three-year follow-up SAMMPRIS data confirming the shorter-term results that intracranial angioplasty and stenting in combination with aggressive medical management confer no greater benefit than aggressive medical management alone [64•]. Interestingly, the study also showed a low risk of stroke beyond one year in the medically treated patients, perhaps related to stabilization of vulnerable plaque or improvement in collateral blood flow.

Rehabilitation

The last decade has seen important advances in our understanding of the "black box" of post-stroke rehabilitation processes and outcomes, starting with the multicenter Post-Stroke Rehabilitation Outcomes Project (PSROP) [65]. This observational study established that better outcomes were associated with earlier initiation of rehabilitation, more time per day spent in higher-level rehabilitation activities such as gait, upper extremity control, and problem solving, use of newer psychiatric medications, and enteral feeding [66].

A significant development has been the inclusion in AHA CSC metrics and Joint Commission CSC criteria that a CSC should explicitly involve appropriate members of the rehabilitation team (including physical therapists, occupational therapists, speech-language pathologists, and physicians specializing in physiatry or having specific expertise in stroke rehabilitation) [54, 67]. However, as pointed out by Bagherpour et al. [68], CSCs often lack rehabilitation programs. Potential benefits of integration of rehabilitation programs into CSCs include improved continuity of multidisciplinary care, access to psychological care, earlier comprehensive discharge planning, accelerated hospital discharge, and a coordinated transition to home-based rehabilitation for selected stroke patients.

Walker et al. recently reviewed different models of community stroke rehabilitation, including multidisciplinary stroke teams, single-discipline home-based therapy, and outpatient facility-based therapy [69]. A recent systematic review suggests some benefits for home-based versus facility-based therapy in terms of patient functional outcome, cost, and caregiver satisfaction [70]. One model of home-based post-stroke rehabilitation care particularly suitable for patients with mild to moderate disability is early supported discharge (ESD). An ESD service provides early assessment in the hospital, coordination of the discharge home, and early rehabilitation at home at an intensity that would have been received in-hospital. A systematic review of all randomized trials of ESD found that it reduced the odds of dependence as well as the length of the hospital stay [71]. While it is clear that stroke rehabilitation care should be provided for a period of time after discharge from the hospital, the relative benefits of the various models are not clear.

Continuous quality improvement

An important advance in the stroke system of care has been the growth of a framework to support ongoing quality improvement. This includes PSC and CSC certification, as CQI is a required component of each. In addition, the growth of national quality improvement programs has had a significant impact. Target: Stroke was launched in 2010 by the AHA/ASA in order to reduce door-to-needle (DTN) times for t-PA administration to less than 60 minutes, and consisted of best-practice strategies including EMS pre-notification, activating the stroke team with a single call, rapid acquisition and interpretation of brain imaging, use of specific protocols and tools, premixing t-PA, a team-based approach, and rapid data feedback [72]. Prior to the intervention, 29.6 % of patients had DTN times of less than 60 minutes, compared to 53.3 % of patients after the intervention. The annual rate of increase in the proportion of patients with DTN times for t-PA administration of ≤60 minutes was1.36 % per four quarters during the pre-intervention period, but increased to 6.20 % per four quarters after the intervention. Overall, the use of t-PA increased from 5.7 % during the pre-intervention period to 8.1 % during the post-intervention period [73•]. In a further analysis, Xian et al. evaluated specific strategies used by Target: Stroke hospitals to reduce DTN times. They found that rapid triage/stroke team notification, single-call activation system, and t-PA stored in the emergency department were independently associated with lower DTN times [74]. Dissemination and integration of successful strategies at hospitals nationwide may improve the timeliness of stroke treatment, resulting in improved clinical outcomes over time.

Programs such as the Joint Commission PSC certification program focus primarily on structural components, setting standards, and self-improvement, but often do not require specific levels of achievement to obtain, maintain, or renew certification or accreditation. This contrasts with the AHA's Get With The Guidelines–Stroke (GWTG-Stroke) Performance Achievement Award (PAA), which is based on achieving specific performance levels on evidence-based measures of process, outcome, safety, and efficacy. Fonarow et al. [75] examined 1,356 hospitals in the GWTG-Stroke Program from 2010 to 2012, and found that programs that were classified as both PAA hospitals and PSCs had higher odds of providing all seven indicated stroke measures compared to hospitals that were classified as either PAA hospitals or PSCs, or hospitals classified as neither a PAA hospital nor a PSC. Conformity was highest for PAA-recognized hospitals regardless of their PSC certification status, intermediate for non-PAA-recognized hospitals with PSC certification, and lowest for hospitals without recognition or certification. Thus, recognition is a more reliable predictor of better-performing hospitals than certification. Hospitals should strive to achieve specific performance levels on evidence-based measures to ensure the best treatment of stroke patients.

Conclusions

The tremendous burden of stroke-related mortality and morbidity in the United States has spurred a dramatic growth in systems of care to address the disparities and fragmentation of stroke care and to bridge the gap between clinical evidence and patient outcomes. Key recent developments in the stroke system of care have included advancements in 1) approaches to primary and secondary stroke prevention that are multifaceted, protocol-driven, yet individualized to allow patients greater opportunities for self-management, 2) an evidence-based framework of certified primary and comprehensive stroke centers, 3) emergency medical service routing protocols to facilitate access of patients to stroke centers, 4) telemedicine networks to improve access for acute stroke patients in rural areas to vascular neurology expertise and thrombolytic therapy, and 5) national continuous quality improvement programs to encourage and reward superior levels of stroke care.

Compliance with Ethics Guidelines

Conflict of Interest
Dr. Matthew Clark and Dr. Toby Gropen each declare no potential conflicts of interest.

Human and Animal Rights and Informed Consent
This article does not contain any studies with human or animal subjects performed by any of the authors.

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