Organizing regional networks to increase acute stroke intervention

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Objectives: *Acute ischemic stroke is the second leading cause of death worldwide and the leading cause of adult disability in the United States (US). Thrombolytic therapy was proved effective, and approved for use, in the US by the Food and Drug Administration in 1996, yet 8 years later just 3–4% of stroke victims in the US are treated with tissue plasminogen activator. In order to understand how this figure can be substantially improved, it is important to evaluate the available therapies and systems of care, delineate the critical steps and the existing barriers in the process for successful intervention, and thoroughly understand the key components in the highly successful interventional stroke programs, especially regionalization of care.*
Methods: *A review of the available literature was carried out and interventional stroke data from the Mid America Brain and Stroke Institute at Saint Luke's Hospital (SLH) in Kansas City, Missouri, was analysed.*
Results: *There are several treatment strategies available for acute stroke intervention and more are likely to be developed. There is increasing interest in organizing and standardizing care for stroke. The steps in the process for successful intervention are understood and progress is being made in several areas of the country, but challenges remain in public education, directing emergency transport to 'stroke ready' hospitals and linking stroke experts to primary care providers. The Kansas City regional network linking primary care hospitals to the stroke team at SLH has been highly successful in substantially increasing the number of patients receiving acute stroke intervention.*
Discussion: *The stage is set for many more stroke victims to receive acute interventional therapy. However, these patients must present to hospitals equipped and staffed to render this therapy. Most stroke victims will go or be taken to the closest medical facility. Organizing regional networks linking primary care hospitals and physicians to comprehensive stroke centers staffed, and capable of providing the entire spectrum of acute stroke intervention will be essential in substantially increasing the number of stroke victims who actually receive acute interventional therapy. This article summarizes the evolving solutions to this challenge with specific data from the successful regional network developed around the Mid America Brain and Stroke Institute at Saint Luke's Hospital in Kansas City, Missouri, USA.* [Neurol Res 2005; **27**: S9–S16]

Keywords: Embolectomy; regional stroke networks; stroke intervention; tissue plasminogen activator

INTRODUCTION

Stroke is the second leading cause of death worldwide and the leading cause of adult disability in the United States (US). In 1999, 4.4 million people worldwide died from stroke[1]. Acute ischemic stroke (AIS) represents 85% of all strokes. There are now acute therapies for ischemic stroke that dramatically improve outcomes, but the management of AIS is a time-critical process involving multiple providers of care. This article discusses available therapies and infrastructures for stroke care, the status of the essential links in the chain of stroke intervention and the evolving trend toward regionalization of care to increase the number of patients treated. The experience at the Mid America Brain and Stroke Institute (MABSI) at Saint Luke's Hospital (SLH) in Kansas City, Missouri, is summarized as an example of a successful regional network working together to provide stroke interventional therapy to any patient reaching a medical facility in time. It is possible that the Kansas City experience may serve as a model for other cities and regions across the country and throughout the world.

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ACUTE STROKE INTERVENTION

Intravenous (i.v.) tissue plasminogen activator was approved by the Food and Drug Administration (FDA) in the US for treatment of AIS in 1996. Subsequent analyses of the use the i.v. tPA (Activase, Genetech, Inc. South San Francisco, California, USA) both in clinical

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trials and clinical practice indicate that this intervention benefits patients with AIS when the National Institute of Neurological Disorders and Stroke (NINDS) protocol is followed carefully[2–5]. A recent meta-analysis of 15 studies involving 2639 patients treated with i.v. tPA revealed comparable safety and clinical outcomes to the data published in the NINDS Stroke Trial in 1995[6,7]. In addition, treatment with i.v. tPA is cost-effective. It has been estimated that treating 1000 stroke victims with i.v. tPA in the US could save $4.5 million US dollars, in Canada $3.8 million Canadian dollars and in Finland $6.5 million euros[8]. Despite practice guidelines from multiple national organizations stating that i.v. tPA is the standard of care[9–11], only 3–4% of patients with AIS receive this drug in the US[12].

Intra-arterial (i.a.) infusion of thrombolytic agents within 6 hours of symptom onset has been shown to be effective in reestablishing flow in cerebral artery occlusions[13,14] with improved clinical outcomes over placebo at 90 days[15]. Combining i.v. with i.a. tPA has been shown to be as safe and effective as i.v. therapy alone in a non-randomized trial[16]. A larger randomized trial of i.v. tPA versus the combination of i.v. and i.a. tPA has been proposed and will be reviewed by NINDS for support. Despite the fact that i.a. thrombolytic therapy is not approved by the FDA, stroke centers are offering i.a. thrombolysis with tPA, expanding the time window to 6 hours after symptom onset. Practice guidelines recognize the benefit in i.a. thrombolysis, but note the challenge of getting large numbers of patients to a relatively small number of hospitals offering this option[10].

Mechanical embolectomy is also being used for AIS. The Merci®Retriever (Concentric Medical, Mountain View, California, USA) was cleared by the FDA for removal of clots from intracerebral arteries in August, 2004. The clinical trial testing the Merci Retriever allowed patients to be treated up to eight hours after symptom onset[17]. The retriever can be used in combination with tPA. Expanding the treatment window from three hours for i.v. tPA to 6 or 8 hours with i.a. thrombolysis or mechanical embolectomy could dramatically increase the number of patient with AIS who are eligible for treatment. However, it is clear that eight years after approval of i.v. tPA, still only 3–4% of patients receive treatment. The potential for treating large numbers of stroke victims will not be realized unless patients make it to a hospital ready, willing and able to provide the full spectrum of stroke intervention options.

STROKE CENTERS

Professional organizations interested in improving access to stroke intervention therapy came together in a collaborative effort known as the Brain Attack Coalition (BAC). Realizing that stroke care bears significant similarities to trauma, they established and published the criteria for Primary Stroke Centers[18]. The Joint Commission for Accreditation of Hospitals Organization (JCAHO) now offers Primary Stroke Center Certification. The Stroke Center at Saint Luke's Hospital in Kansas City received its certification in 2004. Hundreds of hospitals in the US have expressed interest in pursuing this certification. The BAC is now in the process of finalizing and publishing the criteria for Comprehensive Stroke Centers and it is anticipated that at some point in the future certification will be offered for this more complex level of stroke care. Comprehensive stroke centers are those that have interventional neuroradiologists as part of a stroke team that is available 24 hours a day, 7days a week to mobilize quickly, and utilize the advanced intra-arterial and mechanical embolectomy techniques described above.

REGIONAL STROKE NETWORKS

Much of the population of the world is distributed in medium to large urban and suburban centers surrounded by small rural towns supporting the area farms and ranches. Acute stroke strikes as an emergency. Patients will naturally seek care at the closest medical facility. The logical goal should be that every hospital, large or small, have an organized approach to stroke. Small organizations must decide if they can muster the resources to safely administer i.v. tPA. Relationships and communication between small hospitals and hospitals with organized stroke centers will be the keys to success. Models for the delivery of stroke care are emerging and most involve a regional organization of care around a large urban center[19–21].

LINKS IN THE CHAIN OF SUCCESSFUL STROKE INTERVENTION

Public education

Successful stroke treatment depends on early arrival of patients. Unlike acute coronary events, most patients with AIS do not experience pain and because the brain is the affected organ, the stroke victim may not be able to process what is happening. It is imperative, therefore, that education about stroke symptoms and the importance of accessing Emergency Medical Services (EMS) be provided not just to the 'at risk' population, but to everyone, including large employers[22]. The American Stroke Association, National Stroke Association, VHA Stroke Sense Program and countless local providers have excellent programs focused on stroke education for the public. Though there remains a great deal of work to be done, in and around Kansas City, Missouri, more people are becoming aware that stroke treatment is time dependent and they are arriving at emergency rooms anticipating that treatment will be offered.

Emergency medical services

Providers of Emergency Medical Services play a key role in the success of acute stroke intervention. While on the scene, they can obtain important information about the time of onset and perform a quick neurological assessment, such as the Cincinnati Prehospital Stroke Scale (CPSS) that tests arm strength, facial

symmetry and speech. The CPSS and the Los Angeles Prehospital Stroke Screen (LAPSS) have demonstrated excellent reproducibility among pre-hospital personnel and physicians, and good validity in identifying stroke victims who may be candidates for interventional therapy[23,24]. Training programs for EMS providers now include stroke education for these purposes. If a stroke is suspected, the EMS crew can pre-notify the hospital of arrival time so that personnel in the emergency department can be ready for possible acute intervention.

In reality, there are significant barriers to making this an effective process in most communities. There may be multiple providers of Emergency Medical Services in a given geographical region. Kansas City's situation is even more complex because the metropolitan area spans across the state line between Kansas and Missouri. Each EMS organization has its own policies and procedures regarding transport of patients and hospital destination. Many have a policy of transporting the patient to the closest facility without information as to whether that hospital is prepared to treat acute stroke aggressively. There are frequently political obstacles in the way of designating certain hospitals for stroke care as EMS policy. Many EMS crews, however, are quite aware of the discrepancies in the approach to acute stroke intervention and will direct patients to a particular hospital without official mandate.

Plans for methods to overcome these barriers have been developed in several cities including Houston, Dallas and Birmingham, Alabama[25]. In the city of Birmingham, EMS providers determined the criteria for a 'stroke ready hospital' and educated the hospitals about these criteria. A central dispatch was established where hospitals can call in to report that they are or are not 'stroke ready.' For example, if the CT scanner is only operational during the working day, then the hospital would notify central dispatch that they are not 'stroke ready' after the CT technician leaves for the day. EMS crews who identify a stroke victim can call the central dispatch to determine the closest 'stroke ready' hospital.

In southeastern Ontario, Canada representatives of all groups involved in emergency medical services developed a Regional Acute Stroke Protocol (RASP), whereby ambulance services began bypassing the closest hospital to deliver patients meeting the criteria for the RASP to the Kingston General Hospital, a regional tertiary care provider. At 12 months after initiation, 403 strokes occurred in the region, RASP was activated 191 times and 42 patients received i.v. tPA[20].

Rural communities are experimenting with direct helicopter transport of stroke victims to a tertiary care 'stroke ready' hospital. The Shands-Jacksonville Acute Stroke Program is an example of the success of this approach[26]. When a stroke victim is identified by the rural EMS team, the patient is transported to one of several helicopter landing sites by ambulance and then directly flown to Shands-Jacksonville Hospital for treatment. This resulted in a 38% stroke intervention rate (18/85) for ischemic stroke over a 3-year period. Recently, a stroke victim in rural Kansas was taken by ambulance from his farm to the local baseball field and transported by helicopter directly to the Mid America Brain and Stroke Institute in Kansas City, where he received intra-arterial tPA with a good outcome.

Developing regional networks

Despite the success of direct helicopter transport and regional hospital bypass plans, most stroke victims are likely to present to the closest rural or suburban hospital. Many of these hospitals do not have neurologists or neurosurgeons on staff. There is ongoing controversy among emergency physicians regarding whether they should be responsible for administering i.v. tPA. A report from the Mercy Healthcare System in Sacramento, California found that protocol deviations were much higher (30% compared with 5%) when emergency department (ED) physicians prescribed tPA compared with when neurologists prescribed the drug. However, clinical outcomes were comparable in the two groups[27]. ED physicians at the University of Cincinnati and University of Michigan, among others, have demonstrated great success in safely directing acute stroke intervention with tPA. In general, however, it is likely that most physicians staffing emergency rooms would prefer, at the minimum, to have consultation with a neurologist before administering tPA. So how can this be accomplished?

Telemedicine may be able to play a significant role in some regions[28–30]. At the Medical College of Georgia (MCG), the Remote Evaluation for Acute Ischemic Stroke (REACH) program has proved very successful in increasing i.v. tPA use in rural areas[31]. A rural ED in Georgia can activate a Code REACH that pages the on-call neurologist at MCG. The neurology consultant can perform a NIHSS via the camera in the ED and view the CT head scan. Then, a phone connection with the family is established for discussion regarding treatment options.

In Cincinnati, physicians on the stroke team at the University of Cincinnati are on call for the entire network of hospitals and go to the hospital where the patient presents when a stroke call is initiated[25]. This model presents challenges of manpower, geographic coverage and the number of hospitals that can be served.

A more common model is the one exemplified in the OSF (Sisters of the Third Order of Saint Francis) Stroke Network Experience[19]. The OSF Network was organized in 1997 to improve stroke care in the central Illinois region with a population of 1.5 million people. Twenty hospitals in 23 counties participated. When a stroke victim presented to one of these hospitals, the physician in the emergency department contacted a neurologist at the tertiary care facility, Saint Francis Medical Center (SFMC). In collaboration, a decision was made whether to treat the patient with i.v. tPA. Most patients who received tPA were then transported to SFMC. The results of study indicated that tPA could be safely given in rural and community hospitals without on-site neurology. The overall stroke intervention rate was 6.3%.

THE KANSAS CITY REGIONAL NETWORK EXPERIENCE

The Stroke Center at the Mid America Brain and Stroke Institute (MABSI)

In 1992, SLH in Kansas City took care of approximately 250 ischemic stroke patients. They were distributed throughout the hospital and generally admitted by primary care physicians with some neurological consultation. A more organized approach to care of stroke patients was undertaken to facilitate communication among all of disciplines involved, and to standardize the prevention of deep vein thrombosis, aspiration pneumonia and urinary tract infections. Eight beds on the neuroscience unit were designated as the Stroke Center, and a part time nurse co-ordinator and medical director were appointed. At about the same time, an interventional neuroradiologist joined the staff and raised the possibility of using intra-arterial urokinase for severe strokes caused by middle cerebral or basilar artery occlusions. Four such cases were done in 1993 with excellent outcomes. The number of cases gradually increased and by the end of 1998 a total of 83 patients had been treated with i.a. urokinase for acute stroke and were reported in an abstract at the American Stroke Association International Stroke Meetings[32]. Initially, several neurologists on the Saint Luke's Hospital staff declined to be involved in acute stroke intervention so two separate call schedules were set up in the emergency department, one for stroke and one for general neurology. Eventually, through retirement or relocation of some of the neurologists, the remaining group all agreed to participate in stroke call and there was no longer any need for two call schedules. The on-call neurologist covers all neurological emergencies, including stroke. There is no resident coverage for the neurology service.

The University of Cincinnati invited SLH to join their network of collaborating hospitals in the NINDS trial of i.v. tPA. As a result of participation in this trial, systems for rapid response were put in place at SLH and the stage was set for aggressive stroke intervention. Information about the trial was distributed to metropolitan and regional emergency departments, and EMS providers in the region. For the first time, the stroke team was not just taking care of the patients who happened to present to the facility, but was actively encouraging that stroke victims in the entire region be transferred in to SLH. The database developed for stroke intervention cases in 1995 documented that, indeed, increasing volumes of patients with acute stroke were being transferred from other hospitals in the region to the stroke team at SLH.

A systems approach to stroke treatment

A pro-active plan to further increase acute stroke intervention in the region was undertaken. Nurses and physicians in regional community hospital emergency rooms were contacted and educational opportunities, both formal and informal, were offered by the MABSI physicians and nurses. A packet of information was developed and distributed to regional hospitals that included a flow sheet designed for use in community hospital emergency rooms (*Figure 1*) along with a list of stroke interventions available at the SLH stroke center, including i.v. tPA or combined i.v. with i.a. tPA using a 3 hour window, i.a. tPA using a 6 hour window and, beginning in 2002, the Merci Retriever with an 8 hour window.

Facilitating transfers in an efficient manner was a primary goal. A transfer team, staffed by nurses knowledgeable regarding stroke treatment, was established. Named the 'Doctor's One Call' program, one of its main advantages is that a referring emergency room only has to make one phone call. The calls are answered by the transfer team nurse 24 hours a day, 7 days a week. Key questions are asked regarding time of onset and CT head scan results. The transfer team nurse then pages the neurologist on call for stroke and patches through to the caller from the referring emergency department. The two physicians decide together what to do for the patient. If the patient is still within the 3 hour window and meets the eligibility criteria, the decision will often be made to administer i.v. tPA, generally at the lower dose of 0.6 mg/kg described in the EMS Bridging Trial[33] and then transport the patient to Saint Luke's Hospital. Often the MABSI neurologist will also speak to the family and/or patient on the phone in the referring emergency department to verify time of onset, to describe initially what interventions might be available when the patient arrives at SLH and to obtain a cell phone number so that communication with the family can be reestablished as soon as the patient arrives at SLH by ambulance or helicopter. The MABSI neurologists then communicates the plan back to the transfer team nurse who makes all the transfer arrangements, requests that laboratory reports be faxed when available, verifies that the CT head scan will accompany the patient and notifies the interventional radiology team if they are going to be needed. Even in the middle of the night, the entire interventional team can be activated within 30 minutes. The MABSI neurologist generally meets the patient on arrival in the emergency department and makes the decision regarding further intervention. If the patient is a candidate for a research protocol, a research nurse is also called in. Once the intervention is complete, either the neurologist, the interventional neuroradiologist or the nurse co-ordinator communicates the results back to the referring emergency department staff. An effort is made to also communicate the results back to the EMS crews. If time permits, an ambulance or helicopter crew might stay until the completion of the intervention to see how the case turns out.

MABSI STROKE INTERVENTIONS: 2000–2004

Interventional data

Stroke volumes and interventional data are summarized in *Table 1*. The total number of ischemic strokes admitted to the Mid America Brain and Stroke Institute from January, 2000 through September, 2004 was 1694. Annualizing the 2004 data brings the total to approximately 1800.

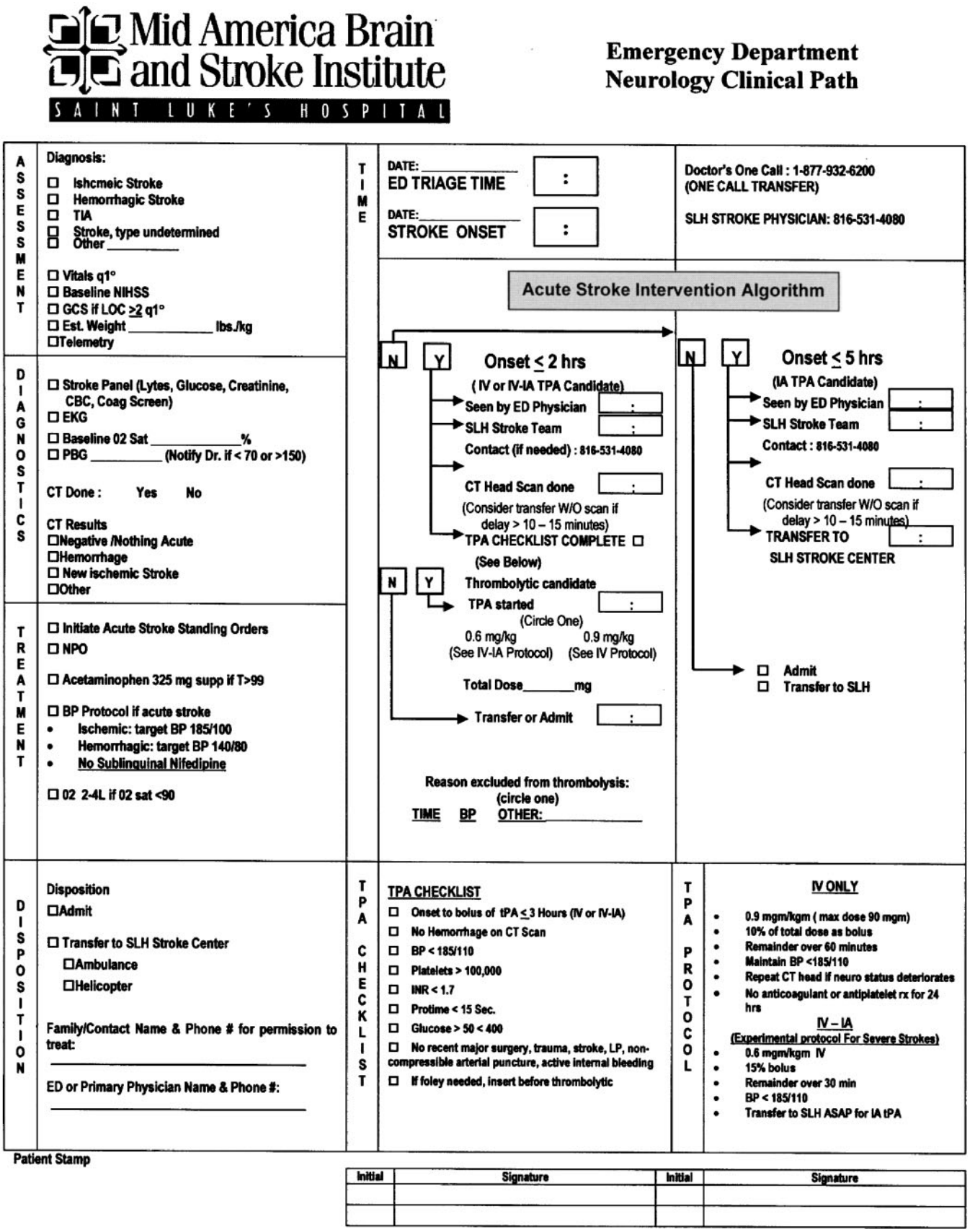

Figure 1: Emergency department flow sheet and checklist for primary care hospitals treating and/or referring patients with acute stroke to Saint Luke's Hospital Stroke Center

Over that 5 year period, there was a 50% increase in overall volume of ischemic strokes, with the major increase occurring between 2003 and 2004. Stroke intervention, including i.v., i.a., i.v.+i.a. thrombolysis, with or without mechanical retrieval, increased from 16.1% (49/304) in 2000, to 29.1% (99/340) in 2004, with an overall intervention rate of 21.6% over the 5 years. In all of these years, a minimum of two-thirds of the patients who received intervention were transferred from another hospital with an average transfer rate for interventions of 73.2% over the 5 years. In 2002, 83.1% of the patients who received interventional therapy were transfer cases. The MABSI neurologists and the regional hospital emergency department physicians have become comfortable in working together to decide who should receive i.v. tPA prior to transfer. Every effort is made to adhere strictly to the NINDS tPA protocol inclusions and exclusions[7]. The checklist on the ED flow sheet serves as a reminder of the important inclusions and exclusions (*Figure 1*). On average, about half (51.9%) the patients transferred for intervention received i.v. tPA prior to transfer. The EMS Bridging dose of tPA at 0.6 mgm/kgm with a 15% bolus[33] is initiated in the referring ED and the rest of the i.v. dose is administered over the next 30 minutes while in transport by ambulance or helicopter. In one case where the patient had a basilar artery occlusion and the patient met all eligibility criteria, the referring ED did not have tPA available. The helicopter crew initiated the i.v. therapy on board under the phone supervision of a MABSI neurologist.

The hospital network

The number of hospitals in the referral network has gradually increased in the 5 years to a total of 47 in 2004. Fourteen of the 47 are in the Kansas City metropolitan area and 33 are in a regional circumference of approximately 150 miles in all directions. The size of the referring hospitals ranges from 15 to 586 beds. Intravenous tPA has been initiated by the emergency department physicians in even the smallest of the hospitals. In the first three-quarters of 2004, the number of patients transferred from a single institution varied. A few hospitals sent just one patient during the 9 month period and one hospital transferred 32 patients in the same time frame. There were several hospitals in the network that transferred 10–25 patients.

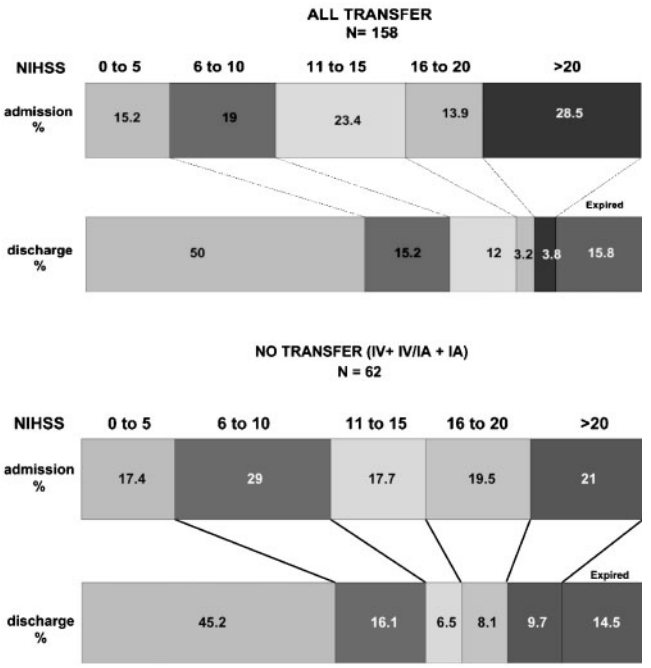

Figure 2: Comparison of admission and discharge NIHSS and mortality rates in stroke patients who were transferred (All Transfers) versus those who presented to Saint Luke's Hospital (No Transfers)

Safety and outcomes

Given this very aggressive approach to stroke intervention, it was important to evaluate whether the outcomes in patients who were transferred were comparable to patients who presented primarily to the ED at Saint Luke's Hospital. Data from January 2000 to June 2003 was presented in an abstract at the American Stroke Association International Stroke Meeting, February, 2004[34]. A total of 220 patients had acute thrombolytic stroke intervention of some type. One-hundred-and-fifty-eight were transferred (designated All Transfer in *Figure 2*) and 62 came to Saint Luke's primarily (designated No Transfer in *Figure 2*). Hospital mortality rates were no different in the two groups and good outcomes as defined by a National Institutes of Health

Table 1: Summary of ischemic stroke volume, intervention rate and transfer rate by year at the Mid America Brain and Stroke Institute at Saint Luke's Hospital

Case volume by year	Ischemic strokes	Stroke interventions	Transferred interventions	i.v. tPA prior to transfer
2000	304	49 (16.1%)	32 (65.3%)	19 (59.4%)
2001	338	55 (16.3%)	43 (78.2%)	20 (46.5%)
2002	340	83 (24.4%)	69 (83.1%)	32 (46.4%)
2003	372	80 (21.5%)	58 (72.5%)	30 (51.7%)
2004 (thru Q3)	340	99 (29.1%)	66 (66.7%)	38 (57.6%)
2004 (annualized)	453	132 (29.1%)	88 (66.7%)	51 (57.6%)
Actual total (thru Q3 2004)	1694	366 (21.6%) (mean)	268 (73.2%) (mean)	139 (51.9%) (mean)

Table 2: Acute stroke interventions by year and type of intervention at the Mid America Brain and Stroke Institute at Saint Luke's Hospital

Interventions by year and type	% i.v. tPA	% i.v.+i.a. tPA	% i.a. tPA	% Retriever	% Retriever+i.v. and/or i.a. tPA
2000 (n=49)	45.3%	22.6%	32.1%	0%	0%
2001 (n=55)	23.3%	31.7%	45.0%	0%	0%
2002 (n=83)	34.9%	15.0%	38.4%	4.7%	7.0%
2003 (n=80)	26.5%	9.7%	19.3%	10.8%	33.7%
2004 (thru Q3) (n=99)	30.0%	8.9%	14.7%	6.8%	39.6%

Stroke Scale (NIHSS) of 0–5 at discharge (average length of stay was 5 days) were no different. The severity of strokes in the two groups was quite similar as defined by NIHSS on presentation (*Figure 2*). By these measures, the transfer protocol seemed to be effective and safe.

Types of interventions

The modes of stroke intervention changed as new options became available and these are summarized by year in *Table 2*. Prior to the spring of 2002, tPA in the various delivery protocols was the only form of treatment used. The data from 2000 and 2001 indicates that intra-arterial therapy was used in 32–45% of the cases, i.v. tPA in 23–45% of the cases, with the remainder receiving a combination of the two. Once the mechanical retriever became available, the percentage of patients receiving i.a. tPA alone or the combination of i.v.+i.a. tPA dropped dramatically in favor of a combined approach using tPA and the retriever for embolectomy. In the first three-quarters of 2004, 39.6% (39/99) of stroke intervention cases utilized i.v. and/or i.a. tPA in combination with the Merci Retriever. The percentage of patients receiving i.v. tPA alone has not changed significantly over the past 4 years, constituting between one quarter and one third of the cases (*Table 2*). These are the patients with milder symptoms or those whose symptoms have cleared by the time of arrival to SLH and, therefore, do not need further interventional treatment. It is of interest that the majority of these patients received only 0.6 mgm/kgm of i.v. tPA, raising the possibility that the lower dose may be as effective as 0.9 mgm/kgm.

CONCLUSIONS

It is entirely likely that many new drugs and devices will be developed for acute stroke intervention. Much attention has been directed to developing stroke teams and centers in hospitals, but it is clear from the Kansas City experience that it is just as important to develop a regional network of medical facilities working together to offer the best treatment available to every patient. The safety and feasibility of primary care hospitals administering i.v. tPA has been demonstrated by us and others[19,35]. The Saint Luke's Hospital stroke intervention cases would be only one-third the number without transfers from the regional network. To realize the potential to treat a substantial number of stroke victims, systems will need to continue to evolve to ensure that patients in all types of geographical settings will have access to interventional treatment. Many models for regionalization of care are in development or are already working well. Although challenging, the future looks very bright.

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