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Use of Telemedicine and Other Strategies to Increase the Number of Patients That May Be Treated with Intravenous Thrombolysis

Gisele Sampaio Silva · Lee H. Schwamm

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Abstract Stroke is the fourth leading killer in the United States and a leading cause of adult long-term disability. The American Heart Association estimates that only 3% to 5% of patients with acute ischemic stroke are treated with intravenous thrombolysis. A way to improve the rates of treatment with thrombolysis in patients with acute ischemic stroke is the creation of telemedicine stroke networks. Data from many studies support the safety of expanding intravenous tissue plasminogen activator use with the help of telemedicine. In this article we discuss the current evidence for the use of telemedicine within stroke systems of care, the importance of coordinating care within the transferring facilities in the telestroke networks, telestroke economics and applicability, and how to potentially use the telestroke systems to increase recruitment of patients into acute stroke thrombolysis trials.

G. S. Silva
Department of Neurology and Neurosurgery,
Federal University of São Paulo,
São Paulo, SP, Brazil

G. S. Silva
Albert Einstein Neurology Program, Albert Einstein Hospital,
São Paulo, SP, Brazil

L. H. Schwamm
Department of Neurology, TeleStroke and Acute Stroke Services,
Massachusetts General Hospital,
15 Parkman Street WAC 835,
Boston, MA 02114-2696, USA
e-mail: lschwamm@partners.org

L. H. Schwamm
Harvard Medical School,
Boston, MA, USA

G. S. Silva (✉)
Dr Altino Arantes Avenue 741, 81,
04042-033, São Paulo, SP, Brazil
e-mail: giselesampaio@hotmail.com

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Introduction

Stroke is the fourth leading killer in the United States, and a leading cause of adult long-term disability. Approximately 795,000 people experience a stroke each year in the United States [1]. Every minute counts in treating a stroke. The only US Food and Drug Administration approved treatment for acute ischemic stroke—intravenous (IV) thrombolysis with tissue plasminogen activator (tPA)—must begin as soon as possible after symptom onset to be effective [2, 3]. Ideally, treatment should begin within 3 h of the onset of stroke signs or symptoms; however, evidence suggests that treatment may be safely provided up to 4.5 h after symptoms onset [3, 4].

Unfortunately, the American Heart Association estimates that only 3% to 5% of patients with acute ischemic stroke are treated with IV thrombolysis [5–7]. The barriers that prevent patients from receiving proper treatment within this critical time frame are fairly well documented: lack of community awareness of stroke signs and symptoms, a shortage of neurologists in the community setting, and long distances between primary receiving hospitals and tertiary care or stroke-capable hospitals [5, 6, 8]. One way to improve the rates of treatment with thrombolysis in patients with acute ischemic stroke is the creation of telemedicine stroke networks [9••, 10•]. Data from many studies support the safety of expanding IV tPA use with the help of telemedicine [9••, 11–13]. Other strategies to increase the number of patients that may be treated with IV thrombolysis are 1) the use of advanced neuroimaging to improve patient selection for treatment of patients presenting beyond the classic therapeutic time window of 3 or 4.5 h; and 2) treatment with neuroprotective drugs and the use of more fibrin-specific thrombolytic drugs [14–18]. In the present article, we focus on the use of telemedicine to improve thrombolysis in acute ischemic stroke.

Telemedicine has been defined broadly as "the use of telecommunications technologies to provide medical information and services" [19]. The World Health Organization defines telemedicine as the delivery of health care services, where distance is a critical factor, by all health care professionals, using information and communication technologies for the exchange of valid information for diagnosis, treatment, and prevention of disease and injuries, research and evaluation, and for the continuing education of health care providers, all in the interests of advancing the health of individuals and their communities [19]. Telemedicine is definitely not a new concept. In the early 20th century, electrocardiograms and electroencephalograms were transmitted over analogue telephone lines. Medical advice service for seacraft via Morse code and radio was established in 1920. In the 1960s, expensive two-way closed circuit television systems were used to transmit radiographs and evaluate patients [20]. Technology is rapidly evolving and some of these changes have made a new delivery system for medical care possible. No longer do the patient and the doctor need to be in the same room or even the same state for the doctor to deliver high-quality care. Nowadays, cheap, computer-based solutions are being used for videoconferencing and transmission of clinical data from hospitals or patient homes, or even from inaccessible sites such as airplanes, ships, and geographically remote areas [10•, 19, 20].

Telemedicine is a way to facilitate the distribution of heath to places with shortages of professionals with specialized skill sets. More specifically, telemedicine can speed up diagnosis and the delivery of care for emergencies and allow health care providers located in geographically dispersed locations to receive assistance from specialists located in major health care centers. Telemedicine is showing itself to be an effective way to treat patients who may not be able to make it into the doctors' office, and many groups are beginning to see the advantages of delivering care in this manner [19–21]. The use of telemedicine has many important advantages: increased access to specialty care at lower costs and convenience for both patients and providers, and it can reduce inpatient utilization [22, 23]. In the increasingly likely scenario of health care reform and creation of networks of accountable care organizations, telemedicine may play a critical role in coordination of care and avoidance of hospital readmissions.

In this article we discuss the current evidence for the use of telemedicine within stroke systems of care, the importance of coordinating care within the transferring facilities in the telestroke network, telestroke economics and applicability, and how to use the telestroke systems to increase recruitment of patients into acute stroke trials.

Current Evidence for the Use of Telemedicine Within Stroke Systems of Care

Although using telemedicine in the acute ischemic stroke setting seems appealing, in the era of evidence-based medicine, data that support this practice should be available to reinforce the utility of telestroke. Technology itself cannot provide care, but when used to facilitate care delivery technology can help health care professionals and their patients make better treatment decisions [9••, 10•]. Recently, a review of the evidence for the use of telemedicine within stroke systems of care was published [9••]. Some important questions about telestroke practice include the following: accuracy of the neurologic evaluation in the acute stroke setting; feasibility and reliability of remote assessment of neuroimaging in acute stroke; and feasibility and effectiveness of telemedicine consultation for enabling and providing recommendations in favor of, or against, the use of IV tPA [9••]. Current evidence based recommendations from the American Heart Association for these questions are summarized in Table 1.

Coordinating Care with the Transferring Facility

Telestroke systems of care can operate on a "hub and spoke" model (stroke neurologists at the tertiary center "hub" communicate with "spoke" community hospital emergency departments [EDs] using videoconference), but also spokes can receive neurology coverage from a for-profit company and have a back-up tertiary hospital not related to the teleconference process that can receive patients after tPA treatment [10•, 24, 25]. Regardless of the model used, coordinating care with the transferring facility is of extreme importance because there are risks of adverse outcomes when patients are transferred in the early hours after thrombolysis and blood pressure or other factors are not well controlled.

When good coordination exists between facilities involved in the telestroke process, communication can be established prior to emergencies, parties can agree on the parameters of the interaction, expectations can be set on both sides, and structural elements can be put in place to facilitate success [26, 27]. Structural aspects and thoughtful preparation at both the referring ("spoke") and receiving

Table 1 Recommendations for the use of telemedicine within stroke systems of care

Question	Recommendation
What is the reliability of performing the neurologic examination using telestroke networks in the hyperacute phase?	When an NIHSS bedside assessment by a stroke specialist is not immediately available for patients in the acute stroke setting, the NIHSS telestroke examination administered by a stroke specialist using HQ-VTC is recommended. This assessment is comparable to an NIHSS bedside assessment (Class I, Level of Evidence A).
How reliable is remote assessment of neuroimaging in acute stroke?	1. Teleradiology systems[a] are recommended for review of brain CT scans in patients with suspected acute stroke (Class I, Level of Evidence A).
	2. Stroke specialists or radiologists evaluation of brain CT scans using teleradiology systems[a] is useful for identifying exclusions for treatment with tPA in the acute stroke setting (Class I, Level of Evidence A).
	3. Teleradiology systems[a] within a telestroke network can be effective in supporting imaging interpretation in time for thrombolysis decision making (Class I, Level of Evidence B).
What is the effectiveness of telestroke networks for supporting thrombolysis decision making in patients with acute ischemic stroke?	When onsite stroke specialist is not immediately available, it is recommended that a stroke specialist using HQ-VTC provide a medical opinion supporting thrombolysis decision making in patients with acute ischemic stroke (Class I, Level of Evidence B).

[a]Approved by the US Food and Drug Administration or an equivalent organization.

Adapted from Schwamm et al. [9••]; see the full document for definitions of levels of evidence for therapeutic and diagnostic recommendations and classifying levels of agreement.

HQ-VTC high-quality videoconferencing; *NIHSS* National Institutes of Health Stroke Scale; *tPA* tissue plasminogen activator.

("hub") facilities are critical to the success of a telestroke interaction. Components that are important in the remote spoke hospital include the following: 1) National Institutes of Health Stroke Scale (NIHSS) awareness and ideally certification for all staff who will be referring patients for possible thrombolysis (free online training is available at www.NIHSS.org); 2) the ability to have images made available for remote viewing using the full DICOM (Digital Imaging and Communications in Medicine) data set rather than just flat image files (eg, JPEG or other compressed image formats); 3) having tPA on formulary and readily accessible to the ED staff, and having an approved IV tPA protocol in place with clear inclusion and exclusion criteria; and 4) standard order sets for administering tPA, controlling blood pressure, and monitoring for deterioration during and after the tPA infusion [10•, 28]. At the receiving hub hospital, aspects that are important include the following: 1) stroke center certification or the equivalent ideally by an independent body; 2) continuous quality improvement with periodic review of procedures, outcomes, and complications; 3) coordination with Emergency Medical Services (EMS) to ensure a smooth transition of care and appropriate stroke detection and patient triage; 4) a clear procedure for contacting and activating the telestroke team; 5) a dedicated telestroke program to support the activities of the telestroke team, the clinical and regulatory interface to spoke sites, and the accountability for care after treatment decision making; and 6) tertiary care services for patients with advanced stroke and/or requiring admission to a neurocritical care unit [25, 28].

Certain key data should be collected, verified, and available for the discussion of a patient eligibility for thrombolysis to assure good clinical management. These include the exact time that the patient was last known to be normal and when symptoms were first detected, current medications especially any antithrombotic therapy, the NIHSS score or another measure of stroke disability, the most recent vital signs, information regarding key exclusion criteria such as possible seizure, intoxication, migraines, or psychiatric disease, the premorbid functional status of the patient, and any previously expressed wishes for limitations on care delivery [25, 27, 29]. The transfer process should include the definition of medications and treatments to be given prior to transfer and treatment goals and expectations for the transfer, and the transfer of health care provider information, including notes and laboratory results in a manner that can be easily viewed at the hub site. With the advent of teleradiology and PC-based image viewers, imaging is now frequently stored on portable media such as CD or DVD and sites should develop methods to ensure that such media can be read at the receiving site [27, 30].

Patients treated using telestroke can be transferred by air or ground, and when by ground by basic or advanced life support providers depending on the patient and local regulations. Weather conditions at any particular time must be factored into the best and safest decisions for patient transport [31]. During transfer of critically ill patients or those requiring hemodynamic management, it is important that EMS or nursing staff have the relevant critical care competencies and experience, that approved and appropriate parenteral blood pressure medications be available, and that stroke-specific protocols are used [10•, 31]. The transferring staff should be alert to the signs of hemorrhagic transformation, which include deterioration in the level of consciousness, increased weakness, headache or vomiting, and increased blood pressure or pulse [32]. Other rare complications of tPA use such as orolingual angioedema (occurs in ~1 to 5% of patients treated) should also be familiar to the acute stroke transfer personnel [33, 34].

Standard treatments and monitoring during the transfer of tPA-treated patients include the following: strict "nothing by mouth" (ie, NPO) including medications or nutrition/hydration, airway management, oxygen if necessary to keep oxygen saturation greater than 92%, IV fluids (maintenance of a normal circulating blood volume with regulation of metabolic parameters within physiologic ranges is desirable), and telemetry (general agreement supports the use of cardiac monitoring to screen for atrial fibrillation and other potentially serious cardiac arrhythmias that would necessitate in route diversion to the nearest facility and/or emergency cardiac interventions) [35]. Protocols should be in place to address rare but life-threatening adverse events such as use of antihistamines, corticosteroids, and assessment of airway patency in orolingual angioedema [33], use of anticonvulsants for recurrent seizures and stopping the tPA infusion (if still running) until hemorrhagic transformation can be excluded, and use of pre-approved antihypertensive agents to keep blood pressure below 180/105 mm Hg [35]. Neurologic deterioration should always prompt the question of hemorrhagic transformation; therefore, medical control should be contacted to arrange for emergency neuroimaging and blood tests upon hospital arrival [35].

Pre-arrival notification by EMS may increase the number of patients who receive timely IV or intra-arterial thrombolysis [10•, 36]. Upon arrival, a complete report, especially as relates to changes in route, is very important as well as delivery of all documents and discs. Continuous feedback and quality improvement suggestions from the tertiary hub hospital to the remote spoke hospital should be given in a timely manner [30].

Telestroke Economics and Applicability

Licensing and credentialing are time consuming and expensive. There is no national level medical licensing and credentialing that is available for doctors, so every time a new spoke gets added to a telestroke network the physicians have to go through the credentialing process all over again [27, 37]. If the spoke is in another state or region, then the physician may also be required to go through the process of being licensed in that state or region [37]. In cross-border areas in European countries or in North America this may represent an insurmountable obstacle.

Reimbursement and lack of funding or reimbursement are other barriers to the successful implementation of a telemedicine program. Telemedicine in the United States is only reimbursed when the initiating site is in an underserved area, almost always in a rural county or census area defined by Medicare. Lack of access to acute stroke care in more urban or metropolitan areas is not addressed in current Medicare definitions of underserved regions. Other coding or reimbursement guidelines designed for assessing in-person traditional encounters may limit reimbursement (eg, the need for a complete physical examination, or presence at the "bedside" or "face to face," often limits codes in the acute stroke setting to those with low levels of reimbursement) [27]. In prior hospital billing rules for telemedicine, either the accepting or the receiving hospital got paid for the telemedicine consult, but not both parties, and this was often determined by who filed first. Despite increased reimbursement for thrombolysis, these higher-value diagnosis-related group (DRG) payments are only paid to hospitals that deliver the tPA and admit the patient. This means that spoke sites that participate in tele-thrombolysis and transfer the patient to a hub hospital only get the outpatient ED-based reimbursement for tPA drug costs and physician evaluation, and unless the hub hospital provides additional intra-arterial thrombolysis or thrombectomy, it only gets paid for the DRG of a routine stroke admission. Although the Center for Medicare adopted an administrative code for tracking purposes (v45.88: status post administration of tPA in a different facility within the last 24 h prior to admission to current facility), it currently provides no additional reimbursement for these cases to either facility. This remains an important impediment to increasing access to IV tPA care and may inadvertently drive increased use of catheter-based procedures [28, 38, 39•, 40].

Developing a feasible business model that will allow for long-term sustainability of telestroke programs has been a challenge. In some cases the hub fully funds the program and provides the spoke with the necessary equipment and consultations at no charge. Sometimes this is done with federal or local grants, but many programs use capital budget funds and hope that spoke sites will subsequently purchase the services to offset costs [40, 41].

The other financial issue that hospitals face is the inability, in many cases, to bill third party and government payers for telemedicine consultation. Although some states have favorable policies that allow for billing, few programs are able to bill insurance companies for the consultations. For example, Louisiana has a law that requires insurance companies that are licensed and regulated by the state to pay for telemedicine consults [41, 42]. What this shows is that for the telemedicine programs to be successful long term, insurance rules and regulations need to catch up to rapidly evolving technology. Physician and other providers also need to be fairly compensated for their time or many will not be interested in participating.

Recruiting Patients into Acute Stroke Thrombolysis Trials

"Drip and ship," the use of remote tPA followed by transfer, is increasing in popularity [9••]. Telestroke is widening the net of hospitals capable of delivering initial acute stroke thrombolytic therapy. This might negatively impact novel acute stroke clinical trials seeking to treat patients before they receive thrombolysis, by providing a disease modification therapy prior to enrollment. Conversely, telestroke can be used as a potential tool to increase enrollment in acute stroke trials, especially if consent could be applied prior or during transfer to a tertiary center [43].

A pilot study during interhospital helicopter transfer included 100 patients to evaluate the role of IV ranitidine to prevent aspiration pneumonia in acute stroke. In this trial, starting consent at an outside ED saved 59 min in initiating the study procedures [44]. In the FAST-MAG (Field Administration of Stroke Therapy—Magnesium Phase 3 Clinical Trial) pilot trial, ambulances were equipped with consent forms and dedicated trial cell phones. Investigators consented patients on scene, with a legal representative via cell phone. Twenty patients were enrolled and none withdrew consent. Compared with patients enrolled in prior studies using standard in-hospital consent, prehospital consent procedures reduced time from paramedic arrival on-scene to start of study agent, and did not prolong the on-scene to ED arrival time [45].

Clinical care of acute stroke is partially growing by building care networks. Therefore, research networks should parallel clinical networks. Broadening of the co-investigator pool can increase the ability to enroll patients in acute stroke trials. This will require full training of local investigators, certification of local health care professionals in basic stroke assessment and disability scales, certification of transport personnel, and revamping the process for institutional review board approval and individual patient consent via telephone or remote consent via telemedicine [24, 36]. Offering the option to participate in a clinical trial for community hospitals might be seen as an enhancement of the level of care. Wider adoption of remote consent might increase the number of patients to be enrolled in acute trials, especially those offering novel therapeutics or alternatives to traditional tPA time windows [43]. Further discussions for exception from informed consent in high-risk patients should be considered to increase acute stroke trial enrollment overall and via telemedicine.

Conclusions

An important part of the application of a new technology depends on human factors and the ability to apply the new technology in a variety of scenarios, from research proof-of-concept environments to real-time acute stroke interventions. Because telestroke is not a treatment modality but rather a technology that may enable the delivery of previously validated interventions, many of the studies on this topic assessed agreement between observers using traditional versus telemedicine-enabled methods of performing key tasks in the delivery of acute stroke care [27].

Some very important issues involving telestroke have to be resolved to assure sustainability and growth of these programs that increase access to care and reduce disparities based on geography or economic circumstance. Reimbursement needs to reflect modern practice patterns and future cost-saving innovations. Alternatives of how to monetize these transactions in the absence of third party payment for services should be developed. Having national level polices for credentialing and licensing would simplify procedures and allow for better access to care, especially for patients residing in states or regions that are neurologically underserved.

Thus, telestroke is a powerful tool to increase the numbers of patients that may be treated with IV thrombolysis, especially when used within the context of a stroke system of care network. Beyond increasing thrombolysis rates, telestroke can help to improve stroke treatment in patients not eligible for IV tPA by helping to select patients appropriate for intra-arterial procedures or those with more severe strokes such as intracerebral hemorrhages, malignant middle cerebral artery, and brainstem strokes who might benefit from an urgent transfer to a hospital with neurocritical care capability. It can also promote early inclusion of patients in clinical trials that extend the window for thrombolysis.

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