Mobile Stroke Units and Telemedicine for Delivering Acute Stroke Treatment in Resource Rich and Poor Environments and to Vulnerable Populations

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Abstract

Despite decades of effort to improve acute stroke delivery, acute stroke treatment rates remain low. Innovative strategies have been developed to overcome some of the barriers that exist in acute stroke treatment delivery. These include Mobile Stroke Units (MSU) with or without telemedicine (TM) capability and TM alone. The MSU brings the hospital to the stroke patient by equipping an ambulance with a CT scanner for brain imaging, point of care laboratory capability (POC), and a Vascular Neurologist either on board (OB-VN) or via TM (TM-VN). A MSU with or without TM can facilitate faster evaluation and treatment decisions, earlier administration of therapy, and more accurate triage of the patient to the appropriate facility. In studies to date, MSUs with TM are feasible, improve patient care including vulnerable underserved populations, and may be cost-effective. These innovative approaches could be generalizable in improving stroke care in different settings ranging from urban to rural to under-resourced. However, in under-resourced regions major barriers to delivering acute stroke treatment with or without a MSU are non-availability of expertise, equipment and supplies including tPA drug, insufficient emergency transport systems, and other socio-economic issues.

Further research is required to provide more conclusive evidence on improved outcome and cost-effectiveness in settings where MSUs, with or without TM may be most useful.

Key Words: acute stroke, mobile stroke unit, prehospital, emergency medical service, telemedicine, thrombolysis, stroke management

Introduction

Cerebrovascular disease remains a major healthcare problem. Stroke causes 5.5 million deaths and the loss of 49 million disability-adjusted life years worldwide each year. In developing countries, it is assuming increasing importance with 2/3 of all stroke-related deaths now happening in these regions. (1) Approximately 795,000 people in the United States have a stroke each year, of which about 610,000 are a first attack. 6.4 million Americans are stroke survivors. (2)

The only FDA-approved medical therapy for acute ischemic stroke (AIS) is intravenous tissue plasminogen activator (tPA) within the first 4.5 hours from known symptom onset. Successful treatment is very time dependent. A meta-analysis of major multicenter thrombolysis trials showed that the number needed to treat (NNT) to achieve one additional excellent non-disabled outcome rapidly increases from 4-5 in the first 90 minutes after symptom onset to 9 with treatment between 90-180 minutes, and to more than 14 between 181 and 270 minutes. (3) Despite decades of efforts to improve acute stroke treatment delivery, data extracted from hospital-based databases report rates of tPA treatment ranging from 3.4% to 9.1%. (4-5)

One contributing factor to this low treatment rate is that many AIS patients are taken to hospitals where there are no specialists available who are specifically trained in Vascular Neurology. Many patients with AIS live in areas without ready access to Acute Stroke Ready Hospitals (ASRH), primary stroke centers (PSC) or/and Comprehensive stroke Centers (CSC).

In rural areas, available ASRHs, PCSs, and CSCs are often located at a far distance; available Vascular neurologist (VN) in these areas are scarce and timely delivery of treatment becomes challenging.

In developing countries, treatment of AIS with tPA is more an exception than standard medical care. Major barriers to delivery of acute stroke treatment are non-availability of resources (including emergent CT head or even tPA), lack of knowledge, insufficient transport, and socio-economics. (6-7)

New strategies for improving acute stroke care delivery are being developed. These include mobile stroke units (MSUs) with and without telemedicine (TM), and TM alone. The aim and scope of this paper is to review the current state of these innovative treatment delivery systems and opportunities for use of these modalities in various settings. We also hypothesize the clinical and cost-effectiveness of these innovative approaches in both resource rich and resource poor environments.

Mobile Stroke Units:

The concept of MSUs developed in 2003 with realization that "bringing the emergency room to acute stroke patients" can facilitate faster evaluation and treatment decisions, earlier administration of acute therapies, and more accurate triage of patients to the appropriate facilities. (8)

A MSU is an ambulance that contains all the necessary tools for evaluation and treatment of AIS patients along with standard emergency care equipment. MSUs contain imaging equipment, point of care (POC) laboratory testing, appropriate medications needed for stabilizing and treating AIS patients (eg., tPA), and an interdisciplinary team consisting of a VN either on board or via TM, paramedics, a nurse, and a CT technologist.

Imaging in the Mobile Stroke Unit:

Multimodal imaging equipment (non-contrast CT, CTA, and CT perfusion) is installed in the ambulance and is of the same design as portable CT scanners in intensive care units: portable, accumulator-driven and radiation-shielded. (9) Images produced are sufficient to evaluate for hemorrhages and early changes of acute ischemic infarction. Most MSUs have reduced size equipment that can fit in standard ambulances which reduces costs and improves accessibility on narrow roads or high traffic environments. (10) These units mostly utilize a Ceretom®, Neurologica/Samsung, Boston, USA model which is efficient for CTA evaluation of proximal anterior circulation large vessel occlusions. However these models are limited in that they are unable to visualize neck vessels and aortic arch (11); A different scanner, Somatom Scope®, Siemens, Erlangen, Germany used in Memphis, Tennessee, USA allows for more complete visualization of these vessels as well as high resolution imaging. Its drawback is that a larger scanner requires a considerably larger vehicle with more power generators and may not be well tolerated in certain urban environments.

Prehospital point-of-care laboratory:

Based on AHA guidelines, certain laboratory tests are recommended for evaluation of AIS (i.e. international normalized ratio (INR), platelet count, hemoglobin and glucose levels), although it is not necessary to wait for the results prior to tPA administration to avoid delays in the treatment. (12)

All MSUs use POC laboratory testing as it is faster, can be done simultaneously with patient evaluation, and does not delay treatment. A study with 200 consecutive patients evaluated reliability of POC laboratory testing. The results of most POC laboratory tests (except aPTT and INR moderate agreement) revealed good agreement with results from a standard centralized hospital laboratory. Furthermore, this strategy reduced door-to-therapy decision times from 84±26 to 40±24 min ($p<0.001$).(13)

Staff on board:

The on board disciplinary team usually includes at least one paramedic, nurse and CT technician. There has traditionally been a physician presence on the MSU especially in earlier iterations, but new evidence has demonstrated the feasibility and safety of remote neurologists making decisions via TM. There is a move to transition to remote TM neurologists to save costs and for more efficient utilization of VN manpower. The MSU in Houston has used two systems: an FDA approved and HIPAA compliant RP-Xpress (In Touch Health, Santa Barbara, CA) technology that allows bidirectional audio and video communication using a fisheye camera capable of 6xzoom with hypercardioid microphone and speaker, and a Maxlife TM solution that uses multiple high definition IP based cameras with PTZ camera control. A substudy of The Benefits of Stroke Treatment Delivered Using a Mobile Stroke Unit (BEST-MSU) study tested inter-rater agreement for tPA eligibility between a TM-based VN (TM-VN) and on-board VN (OB-VN). The study showed 98% satisfactory connectivity and 88% agreement between the TM-VN and OB-VN on the tPA treatment decision (k=0.73). (14) This is the same agreement as was found between two VN evaluating patients in person in the Emergency Department, (15) demonstrating the feasibility and accuracy of utilizing TM on the MSU. Further study to determine if the TM consultation can be carried out just as quickly as with the OB-VN is underway.

Telemedicine without Mobile Stroke Unit:

Technically speaking, TM encompasses healthcare provided remotely via any form of telecommunication (for example fax, telephone, webcam). (16) For AIS patients, remote consultation via real-time, two-way audio-visual communication ("Telestroke") has been found to be superior to telephone consultation in terms of tPA treatment decision making. (17)

Telestroke physicians provide consultation to distant hospitals via either a 'hub-and-spoke' model or a 'distributed' model. In the hub-and-spoke model, a central 'hub', which can be any Stroke Center, is connected to community hospitals with the goal of providing support in treatment decisions and transferring patients to appropriate PSCs or CSCs when necessary for continued evaluation and treatment. In the 'distributed' model, the teleconsultant is often affiliated with a third party employer which provides services on a contractual basis with the originating hospital site. (18)

Inter-rater reliability of the stroke examination is very good when comparing in-person and TM evaluations. (19-20) One pilot study evaluated 41 patients: no examination was interrupted because of technical reasons and the weighted kappa ranged from 0.85 to 0.99. (19)

Interpretation of the neuroimaging necessary to make the tPA decision has also demonstrated excellent inter-rater reliability between the hub teleconsultant to neuro-radiologist and spoke radiologist to neuro-radiologist (kappa 0.92 and 0.89, respectively). (21)

Providing acute stroke care via TM has repeatedly been demonstrated to be reliable and safe, (22-23) and to be cost effective. (24) A study was conducted to evaluate cost-effectiveness of the telestroke system by developing a network model with 1 hub and 7 spokes over a 5 year period and it predicted that 45 more patients would be treated with tPA and 20 more with endovascular treatment per year compared with a model without a TM network. Each spoke had $109 080 in cost savings but the hub had expenses of $405 121. If there are at least 4 spokes there is a net cost saving for the network. However, cost effectiveness varies between different models and is very sensitive to available resources, in particular spoke to hub transfer rates and number of endovascular treatments.

The UT Teleneurology Program was formally initiated in 2010. This hub-and-spoke network now consists of 17 spokes at distances ranging from ten to 200 miles from the hub. Telestroke consultants are trained in Neurology and provide 24/7 coverage for spokes. Some spokes are located in medically underserved areas, while others are not. Spoke hospitals vary in number of hospital beds, amount and availability of in-house Neurology coverage, and stroke center certification levels. From 2012 to 2015 the number of telemedicine consults increased from 510 to 2254 per year and continues to increase exponentially. Excluding telephone consultation consults, the number increased from 327 to 1473. The number of patients treated with tPA per year increased from 93 to 346 over the same time period with a tPA treatment frequency range of 22.5 to 28.4%.

Is the most effective setting for these modalities Mobile Stroke Unit with or without telemedicine or telemedicine alone without the Mobile Stroke Unit

A major question is whether prehospital acute stroke treatment delivery via MSUs is generalizable and whether it is cost effective in improving stroke care in different settings, ranging from urban to rural to developing countries. Regional barriers to delivery of acute stroke treatment need to be identified and the use and generalizability of the MSU model should be assessed accordingly. In some rural regions, a TM approach may be more feasible and has already demonstrated improvement in the numbers of patients being treated. (25) While MSUs covering multiple sites within a large urban area may be feasible and cost effective, in a rural community this may not be the case. The added advantages of expedited triage to appropriate PSCs and CSCs based on potential eligibility for endovascular thrombectomy (ET) may be moot in underserved sparsely populated communities without resources for such treatments.

Urban areas:

MSUs seem most advantageous in urban resource rich areas because they can offer faster accessibility and delivery of tPA with the goal of treating patients within the "golden hour" of symptom onset, and also better triaging of patients to CSCs for endovascular treatment, both possibly resulting in better outcomes.

Faster treatment-goal of "golden hour"

Most MSU studies have demonstrated significant reduction in delays before treatment. For example, in the study from Houston, Texas, USA mean symptom onset-to-treatment time was 98min (47-265mins) (26); in Cleveland, Ohio a case series study showed median alarm to treatment of 64mins (IQR, 58.3-72.5) (27); the PHANTOM-S (Pre-Hospital Acute Neurological Therapy and Optimization of Medical Care in Stroke) study showed median symptom onset to treatment time of 81min (IQR 56-129min). (28) These are much faster treatment times than what has been reported in clinical practice with median symptom onset-to-treatment times of 140min (110-165mins). (29) The MSU trials have shown that MSUs can break the "golden hour" limit. The Houston MSU program treated 31% of their patients within 60 minutes of symptom onset. (30) In the PHANTOM-S trial, treatment was within 60 mins in 31% of the patients. (31)

Increase number of patients treated

Furthermore, being able to evaluate patients early provides the opportunity to evaluate more patients within the 3-4.5 hour window for effective tPA treatment. A trend towards increasing the number of patients treated from 17% to 23% has been documented in one MSU trial (9), and from 21% to 33% in another. (28) Thus far, however, MSU studies have not convincingly found better clinical outcomes despite such faster treatment. In a cohort of patients treated with tPA on the Berlin MSU between 2011-2015, there was no increase in 90 day MRS score of 0 or 1 (p=0.14) compared to non-randomized standard management controls. However, when adjusted for baseline differences between the groups the results were significantly better in the MSU cohort. (32) Given the uncertainty about the magnitude of benefit, clinical outcomes are being studied more rigorously in ongoing MSU trials.

Appropriate triaging

It is important to triage patients to an appropriate PSC or CSC so that they can receive further evaluation and treatment in a timely matter. ET is a highly effective intervention for approximately 20% of tPA candidates who harbor large clots and consequently do not often respond to tPA. ET is currently only available consistently at CSCs. As with tPA, results with ET are highly time-dependent with better outcomes with quicker intervention post stroke onset. Studies have shown that the so called "drip and ship" model of giving tPA at a PSC before shipping the patient to a CSC has led to significantly delayed tPA to ET skin puncture times when compared with those directly admitted to a CSC. In the Interventional Management of Stroke III study, time from tPA bolus to skin puncture was 105 minutes in transferred patients vs 83 minutes in patients treated directly at a CSC (p<0.0001). (33) The MSU provides a unique opportunity for the VN, either via TM or on-board, to examine the patient and treat with tPA if indicated as well as pre-notify the hospital with an accurate history and plausible diagnosis. As the MSU is equipped with CTA capability that allows visualization of large vessel occlusions responsive to ET, it is perhaps possible to bypass the ED and directly transport the patient to the ET suite for intervention, potentially drastically minimizing delays.

Cost-effectiveness:

With the potential improvements in acute stroke treatment delivery offered by MSUs, the question still remains whether it is cost-effective to operate and maintain. There have been only two studies that evaluated the cost-effectiveness of these units. The studies showed that costs depend on the staff configuration, including the presence of the OB-VN vs TM-VN, as well as distance traveled, population density, and configuration of the unit (e.g. it is cheaper if a standard ambulance is the basis of unit). (10) Dietrich et al (34) did a 1-year cost benefit analysis and showed that the benefit-cost ratio was 1.96 even in the research setting and with 2 OB-VN. This benefit-cost ratio improved when switching the OB-VN to a TM-VN, and with higher population density and optimum operating distance. The benefit-cost ratio became between 2·16 and 6·85 in those circumstances. Gyrd-Hansen et al (35) modeled cost-effectiveness based on the PHANTOM-S study results. The estimated net annual cost was €963,954. A higher frequency of tPA administration within a shorter time interval resulted in an annual health gain of avoidance of 18 cases with disability which calculated to be 29 more quality adjusted life years. This estimate met the European standard threshold for cost-effectiveness. However, further studies are needed to evaluate prospectively the cost of maintaining a MSU.

When evaluating the various aspects of the MSU, it seems that in an urban setting, and implementing TM would be most advantageous and cost-effective. Telestroke alone is a plausible option although it does not avoid delays resulting from transferring the patient to a tertiary center.

Rural areas in developed countries:

In rural areas the MSU with TM could be a clinically effective and cost-effective tool in treating acute stroke patients assuming the availability of wireless networks and well-trained first responders to identify stroke symptoms. As discussed above, problems that exist in rural areas are long distances, lack of resources, and VN availability. A MSU with TM could rendezvous with a regular ambulance en route and evaluate, treat, and triage patients appropriately, saving substantial time.

Telestroke alone has shown that spokes in underserved areas improve the number of patients treated and allow for the safe transfer of patients to appropriate hub centers. However an MSU with TM called to the scene could be a better alternative by providing faster treatment on scene rather than at the spoke ED, and avoiding transfer delays by directly transporting the patient to the distant hub.

Developing Countries:

Barriers to delivering effective acute ischemic stroke care in developing countries are multifactorial: prehospital barriers (e.g. lack of transportation, lack of stroke education in the general population), financial constraints, lack of infrastructure (7) and socio-cultural factors.(36) Half of developing countries do not have ambulance services in rural areas. (7) The median time to admission of stroke patients in Gambia and Ethiopia is 8 hrs and 13.5hrs respectively. (7) The proportion of stroke patients that reach a hospital within three hours in Iran and India is 8% and 14.7%. There is also lack of knowledge in many populations regarding signs of stroke symptoms, which results in late arrival times to hospitals. Furthermore, financial constraints are a large hindrance to receiving acute stroke treatment. Only 30% of Iranian stroke patients could pay the cost of tPA with their own savings. A study in south India reported that only 16% of patients arriving at the hospital within three hours were qualified to receive thrombolysis treatment, and none of them received therapy because none of them could afford the drug. (7) Not only are financial constraints a barrier, but resource limitation regarding treatment centers is of concern. In Brazil there are only 20 hospitals that can deliver tPA serving a population of 186 million. In Iran only five university hospitals serve 70 million people, in Pakistan five hospitals serve 160 million, and in Senegal three hospitals serve 10 million people.(36) While public education about stroke symptoms is needed, there is a more urgent need to train nurses, physicians, and technicians, and develop a health care system that provides acute stroke treatment delivery.

Telestroke in this setting could be helpful to improve stroke care delivery. One potential limitation is that telestroke requires good wireless connectivity and the feasibility of this in rural areas is questionable. A MSU with an OB-VN could be a "roving stroke ED" especially in the regions where regular hospital EDs are non-functional and EMS systems are non-existent.

Vulnerable populations: gender, socio-economic status, and baseline disability

In preliminary TM data at UT Houston, there were no gender differences in tPA administration frequency. Additionally, there were no differences in tPA administration frequency or tPA administration time metrics between patients of different racial and ethnic groups. (37) The patients served by Houston MSU are largely minorities (45% African American and 19% Hispanic) since minorities are higher users of the 911 alert system. These groups also have a higher incidence of stroke than Caucasians. Therefore, the MSU can deliver the fastest and most expert possible stroke treatment to patients who are otherwise at high risk and underserved by our current health care system.

Also vulnerable are patients with high premorbid Modified Rankin Scale (mRS), with mRS $\geq$ 2 representing some disability. These patients are routinely excluded from most studies of stroke intervention and information about their outcome after stroke is scarce. Thirty percent of patients treated on the Houston MSU have some pre-existing disability prior to their stroke. Previously published data have shown unfavorable outcome in the majority of patients with baseline disability who receive thrombolytic therapy. (38) The Thrombolysis in Ischemic Stroke Patients (TriSP) (39) cohort study evaluated 7430 tPA-treated patients of whom 489 (6.6%) were dependent. Poor outcome was more apparent in the dependent group. However, after adjusting for age and stroke severity, the odds of poor outcome were actually lower in dependent patients. As a result, the authors concluded that patients with high premorbid mRS score should be treated as aggressively as independent patients. Further evaluation is needed to determine if faster and more efficient delivery of stroke therapy on the MSU will provide better outcomes and shorten hospitalization time for these vulnerable populations.

In conclusion, the MSU together with TM are a progressive innovation which may improve acute stroke therapy delivery in almost all the settings described above. Both require a team approach involving nurses, paramedics, CT techs, and VNs. In order to be successful, education and training patients, EMS dispatchers, and first responders in recognizing the signs and symptoms of stroke is essential. In studies to date, MSUs with TM are feasible, improve patient care, and may be cost-effective. Further research is required to provide more conclusive evidence on improved outcome and cost-effectiveness. Moreover, studies should also examine possible different settings where MSUs, with or without TM may be most useful.

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