

Editorial

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Time is the key factor in brain survivability in acute stroke treatment.¹ The therapeutic effects of intravenous recombinant tissue Plasminogen Activator (IV rtPA) are highly dependent on time.¹⁻³ Stroke patients presenting within the first 60 minutes, or the golden hour, are the most likely to benefit from recanalization therapy.¹⁻³ Thus, making rapid clinical and imaging evaluation of stroke patients of upmost importance and very difficult to complete within the golden hour time window. Based on Get with the Guidelines-Stroke Program (April 2003 to October 2009), less than one-third of patients treated with IV rtPA have door-to-needle times of less than 60 minutes.⁴

However, the delivery of care to a stroke victim is complex and involves pre-hospital and in-hospital stages. Once the patient arrives in a hospital, the recommended door-to-needle time is less than 60 mins.⁵ Despite combined efforts to streamline procedures in hospitals to provide treatment as soon as possible, most places are challenged to stay within this time window.^{4,6} In fact, most patients are still treated with considerable delay and very few of them receive intravenous tissue Plasminogen Activator (tPA) within 90 mins after symptom onset.⁶ While the number needed to treat in order to achieve a modified Rankin Scale (mRS) of 0-1 is only 4.⁵ when treatment is provided within 90 mins, it raises to 9 between 90 and 180 mins and exceeds 14 by 4.5 h.²

The majority of the delay in treating these patients is related to prehospital delay. Rapid triage of such patients could lead to faster treatment with acute therapies such as IV rtPA. To increase the number of patients treated within the golden hour, Mobile Stroke Units (MSUs) have emerged as the potential mitigation of this problem and as the future of acute stroke treatment. Currently, MSUs have emerged in Germany as well in the Unites States in Houston and Cleveland.

The MSU concept offers a remedy to the "time" dilemma in acute stroke management. Stroke patients can be triaged at the scene and taken directly to comprehensive stroke centers without delay and bypassing potential delays in subsequent transfers. Acute stroke patients could also receive prompt imaging in the Mobile Stroke Unit, which in turn would lead to faster triaging of patients and their care. However, the MSU is more than just a mobile CT scanner; it also provides a platform for point of care laboratory testing, telemedicine, and acute management of stroke including the prompt administration of systemic thrombolysis.

This strategy was first proposed in Germany in 2003⁷ and shown to be feasible in 2010.⁸ In 2012, Walter et al reported findings from a single-center prospective randomized trial involving 100 patients in Saarland, Germany.⁹ They demonstrated a 50% reduction in the delay to a therapy decision regarding IV tPA administration. The median alarm to-therapy decision time of 35 minutes and the symptom-onset-to-needle time of 72 min were shorter than all other reported time limits for stroke management. In 2014, Ebinger et al reported on a similar model implemented in Berlin, Germany.¹⁰ The study included 6182 patients who were randomized to weeks with and without availability of the mobile stroke ambulance. Compared to control

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weeks, there was a reduction by 25 minutes from mean-alarm to treatment time. In addition, the rate of tPA administration was 33% during MSTU weeks, compared to 21% during control weeks.

MSUs could also allow for patients with suspected large-vessel occlusion to be specifically triaged to specialized stroke centers that offer endovascular treatment.¹¹ Most recently the Cleveland MSU group was able to demonstrate this concept and the effectiveness in the MSU in the rapid triage of patients with Acute Ischemic Stroke (AIS) from large vessel occlusions to a facility with interventional capabilities thereby saving precious time spent in inter hospital transfers.¹² In their study they were able to show that the time from door to groin puncture, and the first picture to groin puncture was shorter by almost one-half in the Mobile stroke treatment units (MSTUs) group when compared to Emergency Medical Systems (EMS)/private transport. Moreover, the MSU could allow for organization of further specialized treatments and etiology-specific blood pressure management already in the pre-hospital phase of stroke management.^{8,13-14} The latter could be specifically clinically relevant because there are indications that differential adjustment of blood pressure can be beneficial for patients with ischemic stroke (tolerating higher blood pressure values) or hemorrhagic stroke (reducing elevated blood pressure).¹¹

In addition, the implementation of the MSU has made the management of hemorrhagic stroke faster, with earlier blood pressure reduction based on the most recent guidelines.¹⁵ Having intravenous antihypertensive medications on board the MSU with experienced medical personnel familiar with their use and titration makes the hyper acute management of hemorrhagic stroke potentially more effective. Because hemorrhage enlargement occurs more frequently early in the course of intra cerebral hemorrhage,¹⁶⁻¹⁸ the MSU might be a useful venue for testing out new therapies to limit bleeding. The Cleveland MSU group recently applied this principle, and they were able to initiate warfarin reversal within 57 minutes of EMS dispatch, with an MSTU door-to-needle time of 40 minutes.¹⁹ This new treatment paradigm combining a fast-acting reversal agent with remote physician evaluation, on-site imaging, and laboratory testing for the first time affords ultra early reversal of warfarin effect. If earlier time to antihypertensive or coagulopathy reversal treatments benefits in preventing hematoma expansion, the MSU might have an important role in delivering and showing the efficacy of early hemorrhagic stroke treatment.

The next step needed is to address the generalizability of such units. Each state, municipality, and collaborating EMS agency might have different requirements for ensuring accountability, licensing, radiation safety, and insurance. The reality is that emergency medical systems (EMS) Germany as in rural Ocala, Florida. How much time can be saved by use of MSUs in the United States where traffic patterns, distances, market forces, and local regulations differ from Germany, is also likely to be location-specific and differ between urban and rural areas. Furthermore, most cities in Germany have a highly developed emergency care system with specifically trained doctors on ambulances,²⁰ which is not the case in the United States. Implementing MSUs across various cities in the Unites States would require many MSUs, cooperation of various different kinds of EMS systems/personal, and exceptional coordination within the system to overcome logistical issues. Furthermore, deployment of an MSU in a rural or ex-urban area would require different organization.

The cost-effectiveness of the MSU also still needs to be studied and compared with other strategies of remotely triaging stroke patients including the use of telestroke alone.²¹ Financial sustainability will be a major issue and the biggest barriers to this ground-breaking approach in acute stroke treatment will be logistical and financial. The advantages of the MSU have to be weighed against the costs of the project, including expenses for investments, staff, and consumables. Other issues, besides staffing, that will determine net costs include the design of the MSU and reimbursement for drugs, transport, and physician services. Judicious attention to cost control will be needed when making the case for MSU coverage by healthcare payers. A health economic analysis needs to be carried out as part of the MSU trials.

In summary, logistical and financial barriers remained to be solved. In addition, more clinical studies are needed to explore the long-term clinical outcomes in patients. Even in light of these obstacles, MSUs have the potential to be the future of acute stroke treatment.

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