# Bringing Emergency Neurology to Ambulances: Mobile Stroke Unit

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Semin Respir Crit Care Med 2017;38:713–717.

## Abstract

Ischemic stroke results from blocked arteries in the brain, with earlier thrombolysis with intravenous tissue plasminogen activator (tPA) and/or mechanical thrombectomy resulting in improved clinical outcomes. Mobile Stroke Unit (MSU) can speed up the treatment with tPA and facilitate faster triage for patients to hospitals for mechanical thrombectomy. The first registry-based MSU study in Germany demonstrated faster treatment times with tPA using a MSU, a higher proportion of patients being treated within the first "golden hour," and a suggestion of improved 3-month clinical outcomes. The first multicenter, prospective, randomized clinical trial comparing MSU versus standard care was started in 2014 after the launch of the MSU in Houston, TX, demonstrating the feasibility and safety of MSU operation in the United States, and reliability of telemedicine to evaluate stroke patients for tPA eligibility. Although conclusive evidence from clinical trials to support MSUs as being cost effective and improving clinical outcomes is still needed, there are a myriad of other clinical and research applications of MSUs that could have profound implications for managing patients with neurological emergencies.

**Keywords**
- stroke
- thrombectomy
- telemedicine
- thrombolysis
- prehospital
- ambulance
- neurological emergencies

## Background

A blocked artery in the brain can often lead to irreversible cell death resulting in an ischemic stroke with major disability or death.[1,2] Permanent damage to brain tissue (infarct core) occurs within minutes, with adjacent regions consisting of areas of brain where blood flow and oxygen are compromised (ischemic penumbra), but still salvageable. Timely reperfusion of this penumbra is the mainstay of a "time-is-brain" approach for treating such strokes, with the ultimate goal of treatment consisting of faster and complete restoration of blood flow of occluded arteries to save brain cells from irreparable injury.

The standard treatment for acute ischemic stroke involves the administration of intravenous tissue plasminogen activator (IV tPA) within 4.5 hours of symptom onset, and/or with intra-arterial mechanical thrombectomy for selected patients with large vessel arterial occlusions.[3] Not only is earlier recanalization associated with improved outcomes[4–10] but there is a 15% incremental decrease in chances of a good clinical outcome for every 30-minute reperfusion delay with intra-arterial treatment.[10]

Despite the potential for IV tPA to improve outcomes for patients with ischemic strokes, however, only a limited number of patients are able to receive such treatment in a timely manner.[11,12] While reasons for this discrepancy are complex, major obstacles include time delays in patients' arrival to hospitals capable of administering such treatment.[13,14] In some estimates, the median door to needle

**Issue Theme** Advancements in Neurocritical Care and Emergency Neurology; Guest Editors: David Y. Hwang, MD, FNCS, and David M. Greer, MD, MA, FCCM, FAHA, FNCS, FAAN, FANA



**DOI** https://doi.org/10.1055/s-0037-1607994.
**ISSN** 1069-3424.

time in stroke center emergency rooms in the United States is approximately 60 minutes,[15] with most patients being treated beyond 2 hours.[16] Given the direct relationship of improved outcomes with faster treatment times with IV tPA,[4–9] minimizing delays in the triage, evaluation, and treatment of patients is vital.

Hospital notification by emergency medical system (EMS) units prior to hospital arrival is key to faster triage and treatment of stroke patients, leading to more efficient mobilization of medical teams and initiation of hospital procedures.[17] Administrative delays in the triage process of stroke patients in the emergency room often offset this potential time savings, however, irrespective of the time needed to conduct a history and physical, obtain a computed tomography (CT) scan, and initiate treatment with IV tPA.

Considering the association between faster tPA administration (within the first 60 minutes after symptom onset, the "golden hour") and a higher frequency of discharge home (rather than to a nursing facility or other institutions[18]) and better outcomes at discharge,[19] optimization of stroke care is imperative. The use of specially equipped ambulances in the prehospital setting is one way to facilitate the earlier treatment of stroke patients. While studies have reported the feasibility of telestroke assessment in ambulances with regard to various time metrics related to thrombolysis and triage,[20,21] evidence to support the impact on clinical outcomes and health care cost savings has been lacking.

## The Mobile Stroke Unit Concept

Fassbender et al in Homburg, Germany, first proposed[22] and performed[23] the Mobile Stroke Unit (MSU) concept (ambulance equipped with a CT scanner, laboratory testing, telemedicine [TM] connection to the hospital, and appropriate medication on-board [OB] the MSU) enabling the prehospital diagnosis and treatment of stroke in a relatively rural setting. Results from their study demonstrated that prehospital management achieved a median symptom onset-to-therapy decision time of 56 minutes (vs. 104 for hospital-based intervention, $p < 0.0001$) and a median symptom onset-to-treatment time of 72 minutes (vs. 153, $p = 0.0011$) without any concerns of safety resulting from the use of a MSU. More than 50% of patients had a time-to-therapy decision within the first "golden hour" from stroke symptom onset.[24]

Similar trends in safety and time savings (time from initial call to treatment) were seen in the Pre-Hospital Acute Neurological Treatment and Optimization of Medical care in Stroke (PHANTOM-S) study undertaken in an urban environment by the Stroke Emergency Mobile Unit (STEMO) group in Berlin, Germany[25] with an increased likelihood for discharge home for patients who received thrombolysis within the first 60 minutes from stroke onset.[18] An observational, registry-based comparison of 3-month functional outcomes using modified Rankin scale (mRS) scores suggested a beneficial effect of prehospital thrombolysis using the MSU, compared with standard hospital-based administration of tPA (odds ratio [OR]: 1.40, 95% confidence interval [CI]: 1.00–1.97; $p = 0.052$ for mRS $\leq 1$), with a time saving of $\sim$30 minutes to the initiation of thrombolysis.[26] The STEMO group is currently conducting a prospective study employing a city-wide coverage scheme consisting of several MSUs working in conjunction with local EMS services of the fire department.

Following the successes of establishing and operating the first MSUs in Germany, the earlier treatment of ischemic strokes became a reality in the United States with the launch of the first MSU in Houston, TX, in May 2014.[27] Following the initial "run-in" phase,[28] the reliability of a TM-based vascular neurologist (VN) to determine tPA eligibility compared with an OB neurologist was established,[29] along with demonstrable radiation safety of operating a portable CT scanner (radiation levels were also found to be within normal limits in the MSUs in Germany).[30] A prospective, multicenter, cluster-randomized comparative effectiveness trial (Benefits of Stroke Treatment Delivered Using a MSU compared with standard management by emergency medical services) is currently ongoing, which is expected to answer relevant questions regarding clinical benefit and cost effectiveness, including poststroke health care utilization and fixed costs of introducing and operating an MSU.[31] The initial establishment in Houston was followed by the implementation of similar MSU programs across various other sites including Cleveland, Denver, Memphis, Toledo, New York City, New Jersey, Pennsylvania, Phoenix, Chicago, Los Angeles, and Indianapolis, with plans to launch similar programs globally in cities such as Paris (France), Edmonton (Alberta, Canada), and Melbourne (Australia).

## The Nuts and Bolts of Setting Up a Mobile Stroke Unit

The MSU itself is a standard ambulance that is fitted with a portable CT scanner, and consists of all necessary equipment needed for the acute evaluation and treatment of a stroke patient. The MSU team can be composed of either an OB- or TM-based VN, a nurse skilled in stroke management, a paramedic, and a CT technologist. While the first prehospital thrombolysis projects relied on physician-staffed ambulances,[23,25,27,28] the group in Cleveland showed that a model using solely a TM VN on a MSU is feasible and associated with a low technical failure rate (all technical delays were <1 minute without affecting patient care). The replacement of an OB VN with a TM VN might not only lead to savings in personnel costs but could also facilitate the simultaneous operation of multiple MSUs by a single TM VN in geographically distinct areas.[21] Subsequently, the Houston team demonstrated the reliability between an OB VN and a TM VN in making clinical decisions regarding to tPA eligibility,[29] which was demonstrably comparable to two VNs seeing the same patient in an emergency department.[32] Time-to-tPA decision (OB: 18 minutes [interquartile range, IQR: 14–23] vs. TM: 21 minutes [IQR: 16–26], $p = 0.05$) and initiation of tPA bolus were equivalent (OB: 23 minutes [IQR: 19–30] vs. TM: 24 minutes [IQR: 19–28]), $p = 0.70$, with 95% CI ($-2.18$ to 3.24) between an OB VN and a TM-based VN on the MSU.

One of the main considerations in the design of a MSU is the configuration and placement of the CT scanner. Portable CT scanners (CereTom, NeuroLogica–Samsung Corporation, Danvers, MA; Somatom Scope, Siemens, Erlangen, Germany) can be installed across the back wall of the MSU, with special brackets to lock the CT scanner in place during transport. Depending on the type of CT scanner and space allocation, additional enhancements are generally necessary to make the power and charging circuitry more robust, including an upgrade to the standard OB generator to provide additional power for operating the CT scanner. Eligible patients for tPA are positioned on a gurney which is then raised to align the patient's head with the scanner when performing the CT scan. A standard 8-slice, 5-mm configuration is obtained for each patient and is available for immediate viewing on a portable laptop by the OB VN or readily transmittable to the TM VN and destination hospital via a cloud-based picture archiving and communication system.[27] Direct comparison of CereTom images with those from a standard clinical CT scan have shown a high comparability of CereTom images in terms of diagnostic accuracy and reliability versus a standard clinical CT scanner.[33] To safeguard radiation exposure and ensure certainty of obtaining quality CT images, the MSU requires staffing a CT technologist. As a cost-saving measure, CT technologists can be cross-trained as emergency medical technicians to assist the MSU paramedic/nurse when an OB VN is not available and/or can become also highly skilled in other forms of imaging modalities. Essential point-of-care testing, including fingerstick glucose, international normalized ratio, and creatinine, is readily obtainable and accessible on the MSU, without causing any treatment delays.

Establishing MSUs can be a challenging venture and requires prudent financial investment. The ideal structure and operational design of the MSU will depend on regional/local terrains, bureaucratic regulations, as well as available economic resources.[27] Monetary costs to build and fully equip a functional MSU are estimated to be between $600,000 and $2 million. Although currently available cost-effectiveness studies suggest that the expenditure pays off in the long run,[34,35] the predictive utility is limited. It is anticipated that future research will provide more robust cost-effectiveness analyses.[28,31]

## Applications beyond Tissue Plasminogen Activator

Although reducing time to thrombolysis is a key goal of MSUs, the potential benefits of earlier assessment and MSU intervention are far more expansive. Given recent evidence from clinical trials showing the efficacy of endovascular therapies (ETs) for large vessel strokes,[36–38] it is vital for triage processes in stroke care to be modified in a manner that promotes efficient triage of ET-eligible patients directly to stroke centers with ET capability. Considering the reduced probability of intra-arterial treatment for every minute of transfer delay to an ET capable hospital,[39] the identification of patients with large vessel occlusions and/or salvageable penumbra using CT angiography and perfusion on the MSU can save time in the field by bypassing initial transport to non-ET facilities, expedite laboratory testing by using point-of-care testing,[40] facilitate faster administration of IV tPA, and shorten times to intra-arterial therapy.[41] The benefits of

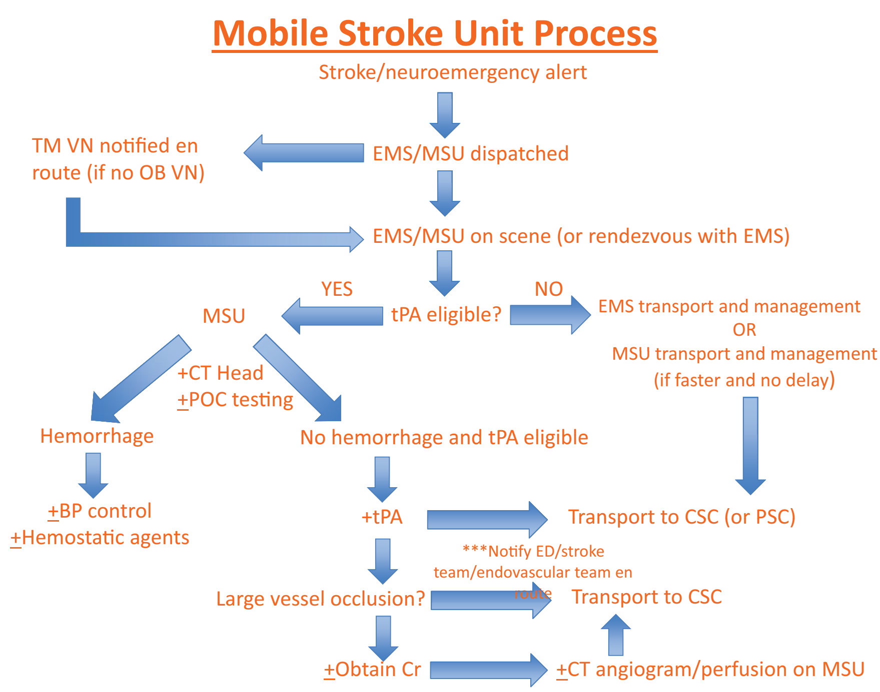


**Fig. 1** Algorithm of MSU work flow and triage. Cr, creatinine; CSC, comprehensive stroke center; CT, computed tomography; EMS, emergency medical services; MSU, Mobile Stroke Unit; OB VN, on-board vascular neurologist; POC, point of care; PSC, primary stroke center; TM VN, telemedicine vascular neurologist; tPA, tissue plasminogen activator.

MSU triage are not only applicable to patients needing ET but are also applicable to virtually any ischemic stroke patient who can benefit from care in hospitals with dedicated stroke units and patients with intracerebral hemorrhages (ICHs) to centers with neurosurgical expertise.[42] Beyond stroke, efficiency in prehospital triage may also be helpful in patients with head trauma[43] and other acute neurological emergencies (i.e., status epilepticus) by having patients being diverted to hospitals with expertise in neurological emergencies and critical care. Streamlined triage processes (►**Fig. 1**) are thus an integral feature of the MSU paradigm.

MSUs also allow for the rapid management of patients with ICH. Since hemorrhage enlargement occurs more frequently early in the course of ICH,[44,45] the MSU provides an avenue to promptly administer intravenous antihypertensive medications to control blood pressure and/or other hemostatic agents (i.e., prothrombin complex concentrate for warfarin-associated hemorrhages) and antidotes for specific agents (i.e., idarucizumab for dabigatran) to treat coagulopathies that are associated with ICHs.

MSUs are also an instrumental tool for research spanning broad domains, including biomarkers,[46,47] neuroimaging,[48] and cerebral physiology (via the use of noninvasive cerebral blood flow monitoring devices).[49] The effects of earlier administration of time-sensitive, adjunctive neuroprotective therapies with tPA, along with other hemostatic agents for ICH (i.e., tranexamic acid, factor VIIa) can also be potentially investigated. Dedicated teams, ideally with proficiency in both clinical care and research, will have an invaluable resource given the unique opportunities offered by MSUs.

## Future Directions

The optimal setting (e.g., rural vs. urban) where MSUs can have maximal impact will need to account for innumerable factors, including local EMS systems and protocols, cooperation between hospitals, environmental landscapes, and population dynamics. In urban settings, the proficiency of MSU operations will likely depend on the success of integrating the MSUs within EMS response algorithms and the interplay between EMS responders and hospital systems with differing capabilities of managing stroke patients (i.e., comprehensive stroke centers vs. primary stroke centers, hospitals with neurosurgery, and/or neurocritical care expertise). Significant reductions in time to decision can be made by utilizing a "rendezvous model" in rural settings, where instead of having to wait for patients to be transported to the closest stroke center (which may be distant and require prolonged travel times), MSUs can travel out to meet the incoming ambulance, thereby leading to reductions in time to treatment. This rendezvous approach can also be applied to urban areas and expand the service areas of these units from their base of operation.[28] Ultimately, the diagnosis of the patient, stroke severity, patient preference, and possibly other region/country-specific rules and regulations will dictate the feasibility of operations of a particular MSU.

One of the keys to the widespread application and success of MSUs will be the standardization of MSU processes and operations across the world. The Prehospital Stroke Treatment Organization (PRESTO) was thus organized in 2016 as a collaboration of international medical providers to improve patient outcomes and promote research across the various spheres of stroke care in the prehospital setting. By facilitating the expansion of MSU programs worldwide, PRESTO can establish a global and cohesive network of stroke care that can link patients, public/municipal resources, and providers alike. On a worldwide scale, MSUs hold great promise with the potential to improve patient outcomes and provide more cost-effective medical care.[50]

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