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Mobile Stroke Units: Current Evidence and Impact

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Abstract

Purpose of Review Several approaches have been developed to optimize prehospital systems for acute stroke given poor access and significant delays to timely treatment. Specially equipped ambulances that directly initiate treatment, known as Mobile Stroke Units (MSUs), have rapidly proliferated across the world. This review provides a comprehensive summary on the efficacy of MSUs in acute stroke, its various applications beyond thrombolysis, as well as the establishment, optimal setting and cost-effectiveness of incorporating an MSU into healthcare systems.

Recent Findings MSUs speed stroke treatment into the first "golden hour" when better outcomes from thrombolysis are achieved. While evidence for the positive impact of MSUs on outcomes was previously unavailable, two recent landmark controlled trials, B_PROUD and BEST-MSU, show that MSUs result in significantly lesser disability compared to conventional ambulance care.

Summary of Review Emerging literature prove the significant impact of MSUs. Adaptability however remains limited by significant upfront financial investment, challenges with reimbursements and pending evidence on their cost-effectiveness.

Keywords Mobile stroke unit · Prehospital · Acute ischemic stroke · Hemorrhagic stroke

Introduction

Stroke is a devastating neurologic emergency affecting approximately 800,000 patients annually [1] as the fifth leading cause of death and a leading cause of serious long-term disability in the USA [2]. Stroke results in burdensome societal costs secondary to patients' hospital stay, rehabilitation, long-term care and loss of workforce. Timely treatment of acute ischemic stroke with intravenous thrombolysis and endovascular thrombectomy (EVT) is of utmost importance. The crucial factor in determining stroke outcomes is the time to reperfusion. The 2019 American Heart Association/American Stroke Association (AHA/ASA) guidelines on acute stroke management state: "patients should be transported rapidly to the closest available certified primary stroke center or comprehensive stroke center (Class I; Level of Evidence A)" and "systems should be designed, executed and monitored to emphasize expeditious assessment and treatment" [3].

Several approaches have been developed to improve prehospital workflow optimization in an attempt to improve time to treatment [4]. Data from Get with the Guidelines registry show that despite substantial efforts, patients arriving within the thrombolysis window did not significantly increase from 2003 to 2009 [5]. It is estimated that 15–60% of acute ischemic stroke patients arrive at a hospital within 3 h of symptom onset and only 10.6% are treated within 90 min [6]. Golden hour thrombolysis (i.e., within 60 min from symptom onset) is associated with the best outcomes including early discharge to home and disability freedom [7] and yet, only 1.4% are treated within 60 min [6]. It is estimated that ~ 1.9 million neurons are lost every minute in ischemic stroke patients with large vessel occlusion (LVO) [8]. Every 10 minutes of time saved in initiating EVT is estimated to result in an average gain of 39 days of disability-free life [9]. A recent study indicates that the rate of neurons lost per minute is highly variable, ranging from < 35,000 in slow progressors to > 27 million in fast progressors [10]. The highly time sensitive nature of intravenous thrombolysis

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is clearly depicted by the numbers needed to treat for an excellent outcome (modified Rankin scale [mRS] of 0–1) – 4.5, 9 and 14.1 for patients treated at 0–1.5, 1.5–3 and 3–4.5 hours of symptom onset, respectively [11]. Nearly 25% of stroke patients have LVO and yet, only a minority of patients receive timely EVT [12, 13].

One reason for low rates of reperfusion therapy is the delay in presentation to hospital. Over the last two decades, the concept of Mobile Stroke Units (MSUs) has been proposed and implemented across the world for timely delivery of acute stroke care. This review focusses on the current available evidence on MSUs.

Vehicle of Treatment: Mobile Stroke Units

The concept of a MSU, first proposed in 2003 and established in 2008 in Germany, was developed to optimize prehospital stroke care [14, 15]. As a mobile emergency room, a MSU involves a specially equipped ambulance with a computed tomography (CT) scanner for multimodality images including CT angiography (CTA), point-of-care (POC) laboratory for blood analysis according to thrombolytic criteria, a specialized stroke team and appropriate assessment tools and medication [16]. Upon dispatch, an interdisciplinary team, consisting of paramedics, technicians, nurses and physicians, which can include Telemedicine, is brought directly to the patient and can perform a complete diagnostic workup in parallel workflow, saving crucial time. A MSU can initiate direct treatment, provide comprehensive prehospital notification, and ensure correct triage of the patient to the most appropriate level hospital [17, 18]. Currently more than 32 centers worldwide have inaugurated MSU programs.

Current Evidence

Thrombolytic Preliminary Studies

The first MSU trial conducted in Germany demonstrated that prehospital management of stroke significantly improved time to treatment without safety concerns: symptom onset to treatment was 72 min (vs 153 min, $p=0.0011$) with 57% of MSU patients receiving golden hour thrombolysis as compared to 4% of patients treated with standard management [16]. Similar results were shown in the Pre-Hospital Acute Neurological Treatment and Optimization of Medical care in Stroke (PHANTOM-S) study [19], with mean symptom onset to treatment time of 102.7 min (vs 118.5 min; $p<0.001$). Furthermore, there was significantly higher rate of thrombolysis in the MSU group (33% vs 21.1%; $p<0.001$) with a nearly sixfold higher proportion of golden hour thrombolysis. Shortly thereafter, MSUs were launched in the USA, with the first MSU established in Houston, Texas [20].

Shorter time to treatment have also been shown in observational studies with median symptom onset to thrombolysis of 98 min in Houston, Texas [17], 73 min in Berlin, Germany [21], 97 min in Cleveland, Ohio [22], 95 min in Toledo, Ohio [23], 101 min in Oslo, Norway [24] and 96 min in Melbourne, Australia [25•] (Table 1) [26]. Despite a densely populated New York City, MSU implementation resulted in a shortened dispatch-to-thrombolytic time by 29.7 min (95% CI: 6.9–52.5; $p=0.01$) [27].

Thrombolytic Efficacy Studies

While there was reason to believe that earlier reperfusion therapy could lead to better functional outcomes, data on long-term outcomes were scarce until 2021. An observational registry as an ad-hoc continuation of PHANTOM-S trial showed no significant difference in functional independence between MSU and conventional ambulance care despite significant time gains and higher rates of golden hour thrombolysis. However, acute ischemic stroke patients treated via MSU care had significantly lower rates of severe disability (90 day mRS 0–3: 83% vs 74%, p 0.004) and lower rates of 3-month mortality (6% vs 10%, $p=0.022$) [21]. No significant difference in favorable functional outcomes and mortality at 3 months were noted on comparing cohorts from Berlin MSU registry and SITS-EAST registry [28].

Two recent landmark trials have emerged: The Berlin Pre-hospital Or Usual Delivery of stroke care project (B_PROUD) [29, 30] and Benefits of Stroke Treatment Using a Mobile Stroke Unit (BEST-MSU) [17, 31]. B_PROUD is the first large, controlled trial with blinded outcome assessment comparing MSU with Emergency Medical Services (EMS) and Emergency Department (ED)-based standard care. Between February 2017 and May 2019, 16,964 alerts were screened and 1543 tissue-plasminogen activator (tPA)-eligible patients were enrolled: 749 MSU vs 794 standard care, 12.8% of patients in MSU group were treated within 60 min (vs 4% in the standard care). Patients treated in the MSU group had significantly less disability (adjusted common OR 0.71; 95% CI: 0.58–0.86, $p<0.001$), higher rates of discharge to home and significantly improved quality of life. Post hoc analysis further demonstrated that shorter times were associated with excellent outcomes, as shown by the highest adjusted common OR of 3.25 (95% CI: 1.72–6.13) for patients treated within 60 min. There was no difference in symptomatic intracranial hemorrhage between the two groups (adjusted OR: 1.2; 95% CI: 0.66–2.19) [32••].

These positive findings were confirmed with BEST-MSU [33••], a prospective comparative effectiveness multicenter study of MSU vs standard management by EMS.

Table 1 Comparison of times to treatment in prehospital MSU settings across the world

	Study site	Sample size	Catchment area	Alert to tPA times – Median (IQR)	Onset to tPA times – Median (IQR)	Rate of thrombolysis	Golden hour thrombolysis	Call to groin puncture – Median (IQR)	Onset to groin puncture – Median (IQR)
EUROPE Walter et al. 2012 [16]	Homburg, Germany	53 MSU vs 47 EMS	~30 km around Saarland University hospital	38 (34–42) vs 73 (60–93); p < 0.0001	72 (53–108) vs 153 (136–198). MD 80 (40–115); p = 0.0011	23% vs 17%; p = 0.3	57% vs 4%		
Ebinger et al. 2014 [19]	Berlin, Germany	3213 MSU vs 2969 EMS	~16 min radius from base, population 1.3 million	51.8 vs 76.3*; p < 0.001	102.7 (93.9–11.5) vs 118.5(111.8–125.2)*; p 0.003	32.6% vs 21%; p < 0.001	31% vs 5%; p < 0.01		
Kunz et al. 2016 [21]	Berlin, Germany	305 MSU vs 353 EMS	~16 min radius from base, population 1.3 million	46 (39–53) vs 76 (64–93); p < 0.0005	73 (53–120) vs 112 (85–175); p < 0.0005		37% vs 4%; (p < 0.0005)		
Helwig et al. 2019 [41]	Homburg, Germany	63 MSU vs 53 optimized EMS care		50.1 (10.1) vs 84.9 (30.2)#; P < 0.001				109 (114) vs 183 (84); p = 0.46	
Larsen 2021 [24]	Norway	166 MSU vs 274 EMS	~10 min from base	53 (44–65) vs 74 (63–95); p < 0.001	101 (71–155) vs 118 (90–176); p = 0.007	81% vs 59%; p = 0.001	15.2% vs 3.7%; p = 0.005		
Ebinger et al. 2021 [32••]	Berlin, Germany	749 MSU vs 794 EMS	2 MSUs covering 94% of Berlin area		95 (60–149) vs 110 (80–165); p = 0.003	67% vs 48.1%	12.8% vs 4% (OR 2.96; 95% CI 1.93—4.53)	136 (117–160) vs 125 (110–154)	170 (137–216) vs 157 (126–228); OR 0.12 (-0.16 to 0.4)
USA Cerejo et al. 2015 [18]	Cleveland, Ohio	5 MSU vs 5 EMS	Cleveland city limits, estimated population 390,113						Door to Groin puncture: 93 (75–116.5) vs 200 (185–223)
Itrat et al. 2016 [60]	Cleveland, Ohio	100 MSU vs 53 EMS		32 (24–47) vs 58 (53–68); p < 0.001					
Taqui et al. 2017 [22]	Cleveland, Ohio	100 MSU vs 53 EMS	Cleveland city limits, estimated population 390,113	55.5 (46–65) vs 94 (78–105); p 0.0006	97 (61–144) vs 122.5 (110–176); p 0.0485		25% vs 0%		
Bowry et al. 2015 [17]	Houston, Texas	24 MSU		47* (37–60)	98 (47–265)* MSU		33%		175 (140–224)* MSU
Czap et al. 2020 [44]	Houston, Texas	40 MSU CT/CTA vs 84 MSU CT							Door to groin puncture: 41 (30–63.5) vs 94.5 (69.8–117.3) P < 0.001

Table 1 (continued)

	Study site	Sample size	Catchment area	Alert to tPA times – Median (IQR)	Onset to tPA times – Median (IQR)	Rate of thrombolysis	Golden hour thrombolysis	Call to groin puncture – Median (IQR)	Onset to groin puncture – Median (IQR)
Grotta et al. 2021 [33••]	Multicenter	617 MSU vs 430 EMS		46 (39–55) vs 78 (66–93)	72 (55–105) vs 108 (84–147)	97.1% vs 79.5%		141 (116–171) vs 132 (114–160)	166 (131–202) vs 163 (134–209)
Alexandrov et al. 2021 [45•]	Memphis, Tennessee	402 MSU				33%	31.5%		112 (90–139)
Kummer et al. 2019 [27]	New York City, New York	66 MSU vs 19 EMS	Cornell and Columbia catchment areas	61.2 (15.27) vs 91.6 (39.2)#; p = 0.001	101 (46.5) vs 143.9 (49.9)#; p = 0.04	43.9% vs 47.4%; p = 0.48			
Lin et al. 2018 [23]	Toledo, Ohio	105 MSU	~ 15 min from base	53 (42–59)	105 (52–128.8)		30%		
AUSTRALIA Zhao et al. 2020 [25•]	Melbourne, Australia	100 MSU vs 153 EMS	20 km radius, population 1.7 million		95 (69–128) vs 143.5 (107.5–196)			119.5 (103.3–137.3) vs 170 (120.5–227.5)	148 (120.3–210.5) vs 234.5 (157.8–287.5)
Fatima et al. 2020 [26]	Meta-analysis	6065 MSU vs 15,232 EMS		62 (38–75) vs 75 (61–110)*; p = 0.03	62.02 vs 110.5*				

***Values expressed as Mean (95% CI); #Values expressed as Mean (SD)**

From August 2014 to August 2020, the BEST-MSU study screened 10,443 alerts and enrolled 1,047 tPA-eligible acute ischemic stroke patients across 7 US sites: 617 in the MSU group and 430 in EMS group. Time from symptom onset to tPA treatment was shorter in the MSU group compared to EMS (72 vs. 108 min, $p<0.001$). 97.1% of all tPA eligible patients received tPA in the MSU group (vs 79.5% in the EMS group); 32.9% of MSU patients were treated within the first "golden" hour of symptom onset vs 2.6% with EMS management. Importantly, MSU management also resulted in significantly less disability at 90 days compared to EMS management (mean utility-weighted mRS score 0.72 vs. 0.66; $p=0.002$). Four patients treated with thrombolysis on a MSU would avert severe disability or death in one, and nine patients treated would result in one completely free of disability. Improved outcomes with MSUs were likely due to faster stroke treatment, particularly within the first hour.

Taken together, these landmark trials show that the significant time gains in treatment achieved by MSU care are indeed associated with significantly less disability without increase in mortality or symptomatic secondary intracranial hemorrhage.

Triage, Transport and Treatment of LVO Stroke

In LVO patients, thrombolytics may achieve early recanalization prior to arrival at an endovascular-capable center, obviating the need for EVT [34•]. Early recanalization by ED arrival or emergent angiography occurred in 28% of LVO patients with ultra-early tPA treatment on the Houston MSU without delays in EVT [34•]. These results support continued efforts to administer tPA as quickly as possible on a MSU in all ischemic stroke patients who qualify per guidelines, including those with LVOs. As with tPA, faster EVT reperfusion results in better outcomes [35, 36] and guidelines have called for organized systems of care to improve workflow [3].

Consensus statement on prehospital systems of care [37] recommend that patients with suspected LVO should be routed directly to a comprehensive stroke center (CSC) or thrombectomy capable stroke center (TSC). In case of longer transport times, patients should be transported to a primary stroke center (PSC) or acute stroke ready hospital. As of 2019, there are ~250 CSCs and 50 TSCs in the USA and roughly 56% and 85% can access CSC/TSC within 60 min by ground or air, respectively [38]. Complex interhospital transfers can result in significantly delays up to approximately 143 min in EVT initiation [39, 40] with an increased risk of mortality [40]. In addition to increasing thrombolytic rate and speeding thrombolytic treatment into the first "golden hour," MSUs have the potential to accelerate accurate prehospital triage to the appropriate level center. High variability in prehospital clinical scores could miss about 20% of LVOs or could result in high false positive rate. By bringing imaging to the patient with CT/CTA, MSU can appropriately triage LVO patients to the right center. In a multicenter controlled trial conducted in Saarland, Germany, appropriate triage was accurate in 100% of MSU cases vs 69.8% of optimized EMS care with validated clinical scoring (mean difference: 30%, 95% CI: 17.8–42.5%; $p<0.001$) [41].

In an early published experience of Cleveland Ohio, MSU led to appropriate field triage of LVO patients to CSC with shortened door to groin puncture times as compared to historical controls (93 vs 200 min) [18]. Melbourne MSU also demonstrated significant improvement of time to groin puncture (148 vs 234.5 min) [25•]. [42]. Alternatively, NYC MIST (New York City Mobile Interventional Stroke team) [43] study showed significantly faster door to recanalization times (mean difference 83 min; $p<0.01$) by transferring interventionalist team to TSC for endovascular treatment. Combination of such mobile interventionalist team and MSU rendezvous to the closest regional TSC instead of CSC in densely populated urban areas could potentially further reduce door to recanalization time.

MSU management did not increase or expedite EVT in BEST-MSU [33••] or B-PROUD [32••]. Time from symptom onset to EVT did not differ between groups (BEST-MSU: 166 vs 163 min; B-PROUD: 170 vs 157 min, p=0.12). Demonstration of LVO by CTA was often deferred to after ED arrival in both trials, eliminating the opportunity for MSU to speed up this triage process. In a study published earlier [44], implementation of onboard CTA and early notification to the receiving endovascular team in Houston MSU demonstrated reduction of in-hospital delays and improvement of door to groin puncture time by 54 min (41 min vs 94.5) [44]. Availability of high-resolution CTA imaging including the aortic arch in the Memphis MSU enabled ED bypass entirely in 41% of patients requiring thrombectomy [45•]. Structured team approach of different healthcare professionals working in parallel further helps to achieve very short treatment times.

Intracerebral Hemorrhage

Intracerebral hemorrhage (ICH) accounts for 10–15% of all strokes, but it results in a disproportionately high risk of morbidity and mortality [46, 47]. ICH volume is a strong predictor of outcome [48]. Given that hematoma expansion usually occurs early in the course of the symptoms, prompt treatment is an important step in improving outcomes. Patients with ICH were less frequently delivered to a hospital without neurosurgery when transported by a MSU (11.3% vs 43%, $p<0.01$) [42]. Identification of ICH with imaging on a MSU allows blood pressure management with intravenous antihypertensives available onboard [49] as well as effective triage to the appropriate centers with neurosurgical services. Coagulopathy can be assessed using POC labs and reversed with available agents, including Vitamin K, Tranexamic acid, activated Factor VII, Idarucizumab, prothrombin concentrate complex and andexanet alfa [50, 51]. MSUs are the ideal platform to study the hyperacute phase of hemorrhagic stroke and to investigate new pharmacological approaches. There are two ongoing clinical trials investigating the effect of recombinant factor VIIa (FASTEST: rFVIIa for Acute Hemorrhagic Stroke Administered at Earliest Time; www.clinicaltrials.gov NCT03496883) and tranexamic acid (STOP-MSU: Stopping Haemorrhage With Tranexamic Acid for Hyperacute Onset Presentation Including Mobile Stroke Units; www.ClinicalTrials.gov NCT03385928) on ICH in the ultra-early time window of two hours from symptom onset. For patients with subarachnoid hemorrhage on CT [52], performing CTA on site can aid with the early identification of an aneurysm [53]. These initial scans allow for the bypass of the PSC and the ED, with the patients potentially taken to a pre-notified angiography suite directly for appropriate intervention.

MSU Operations

Establishing MSU is a complex task and it requires a coordinated approach in order to reap the maximum benefits. Technical design and configuration of MSU largely depends on the manufacturer and size of ambulance and CT scanner. Majority of MSUs utilize a portable 8-slice, 5-mm CT scanner on a standard 12-foot ambulance and few units boast a 16-mm high-resolution CT scanner in a larger ambulance [45•]. Bigger CT scanners allow for imaging of aortic arch and neck vessels at the expense of requiring more space, trouble with navigating the roads and the need of onboard power generation. Portable CT scanner images have yielded similar diagnostic accuracy with a proven radiation profile compared to standard CT scans [45•, 54, 55]. Basic POC laboratory tests including blood cell counts, electrolytes, renal function, coagulation tests and blood gas analysis are recommended to be available onboard to aide in determining tPA eligibility, with similar results from centralized hospital laboratories [16, 56].

Most MSUs operate on a shift basis to capture the most acute stroke patients but do not yet cover 24/7 due to inadequate reimbursement. MSU teams are typically comprised of registered nurse with Advanced Cardiac Life Support training, licensed paramedic, licensed CT technician and a physician. Staff should be trained to provide optimal care on board and local regulations should be considered to meet the requirements for training and liability. Different physician staffing models have been successfully utilized including onboard vascular neurologists, telemedicine-based vascular neurologists, critical care physicians or anesthesiologists [57–59]. Telemedicine-based models, which can cut staffing costs, have been shown to be highly reliable with comparable time metrics and low rates of technical failure [22, 57, 60].

Operating MSUs require an understanding of the organization of prehospital emergency care locally as MSU services work best in close collaboration with the dispatch center and EMS. A standard dispatch center algorithm must be established with constant quality monitoring to identify potential stroke patients. Several different algorithms have been tried in the past and no single scale has been shown to possess high sensitivity and specificity which underlines the importance of continuing education [41, 61, 62]. Each staff member needs to carry specific responsibilities. Adequate communication with the EMS crews aids with the rendezvous approach. Standardized treatment algorithms must be created for common clinical situations including managing tPA complications and prenotification to receiving hospitals. Procedures must be implemented for handovers at the site of initial contact and hospital arrival [63]. Before launching an MSU, triage algorithms must be created based on patient diagnosis, patient preference, medical coverage, and other local regulations. The MSU in Colorado has successfully integrated the hospital electronic medical records into the unit [64]. Such incorporation provides clinicians access to previous encounters, laboratories and radiographic studies with seamless transfer of information.

Cost Effectiveness

The adaptability of MSU worldwide depends on its cost-effectiveness and long-term clinical benefits. It involves a significant financial investment with initial set-up ranging approximately from $600,000 to $1,000,000, with widely varying operational costs between $500,000 and 1,000,000 annually based on staffing and shifts [65–67]. There are several ways to improve cost efficiency in the future including reduction of onboard personnel, use of existing ambulance design to build lower cost models [20], improvement of stroke identification algorithms for more precise MSU dispatch and expansion of its use to treat other emergencies including head trauma/hemorrhage [68]. However, data suggest that MSUs are cost-effective as early thrombolysis can mitigate costs associated with prolonged hospitalization, rehabilitation, disability and loss of work.

Using data from Saarland MSU, Dietrich et al. [67] calculated estimated benefit–cost ratios for different staffing scenarios and operating distance as direct cost savings in relation to operational costs of MSU based on specific local assumptions of incidence rates, population density, costs, etc. Cost efficiency (benefit–cost ratio ≥ 1) was achieved at ~ 10 mile operating distance. As the staffing size decreased and population density increased, higher cost–benefit ratios were attainable—2.16 at 26.88 miles, 6.85 at 40.55 miles and to a maximum of 16.13 at a population density of 3,500 inhabitants per sq.km. Cost-efficiency was also demonstrated in rural regions at a population density as low as 274 inhabitants per sq.mile, where the medical value might be especially high.

Using PHANTOM-S trial results, Gyrd-Hansen et al. deduced that the annual expected health gain of 18 cases of avoided disability would be equivalent to 29.7 Quality-Adjusted-Life-Year (QALY) that resulted in cost effectiveness ratio of €32,456 per QALY [65]. Similarly, the Melbourne MSU experience calculated an estimated avoided loss of 16.9 Disability-Adjusted-Life-Year (DALY) and 27.94 DALYs with earlier access to thrombolysis and EVT respectively. Utilization of MSU was estimated to cost $30,982 per DALY avoided [69]. Modeling of a representative cohort of 1000 ischemic stroke patients based on parameter values derived from published literature, Sriudomporn et al. [70•] showed that MSUs averted roughly $11 million & 651 DALYs relative to standard EMS care. It would result in a cost of $17, 498 per DALY averted. All of these values fall below the assumed average US willingness-to-pay threshold of $50,000-$100,000 per QALY [71]. While these results help further clarify the cost-effectiveness of a MSU, these analyses are also limited by the numerous medical and payer systems in which a MSU would be functional [72].

Most of the above-mentioned MSU cost-effectiveness were estimated using models and retrospective data. BEST-MSU is the first trial gathering prospective data on cost efficiency by following all patients and measuring healthcare utilization for a full-year post-stroke [33••] and that should allow better insights. One should note that historically, implementation and coverage of medical decisions have always been based on clinical evidence rather than on explicit cost-effectiveness criteria. Currently in the USA, there is no reimbursement for MSU specialized services or for thrombolytics and other drugs administered. Recent data demonstrating improved clinical outcomes should lead payers (Medicare and other private insurance companies) to reimburse for MSU services, enabling them to become financially self-sustaining.

Optimal MSU Setting

The optimal setting for MSUs remains uncertain, as it is dependent on several local factors including population density, geography, climate, local EMS protocols, interhospital relationships and local regulations. MSUs have economic viability based on retrospective data both in urban and rural areas. One limitation to MSUs is the limited range of a single unit. In order to expand the MSU catchment area, the Houston MSU proposed an innovative solution with a rendezvous approach where the MSU can meet the EMS crew at a coordinated meeting location en-route to the hospital, doubling the treatment radius. Nearly 50% of all thrombolytics were administered via rendezvous model between 2014 and 2018 without difference in alert to thrombolysis times. [73]. Widening the catchment area may be particularly important in low-density populations regions to help improve the cost efficiency and serve highly underserved remote rural areas. Such a rendezvous concept has extended the operating radius to as much as 250 km in Edmonton, Alberta, Canada [74]. Air-MSUs, customized helicopter with CT scanner, POC laboratory testing and Telemedicine (analogous to MSUs), have been proposed an alternate solution to serve rural areas [75].

Computational simulation models have been used to optimize location and operating boundaries for MSU in Melbourne and demonstrated that the MSU was superior to conventional ambulance in delivering thrombolysis and triaging to TSC thrombectomy up to 76 min from base [76, 77]. Such models can be helpful in consideration of the most efficient placement of future MSU units.

Future Directions and Conclusion

The MSU concept has gained importance in prehospital stroke management and has emerged as a vehicle for improved clinical care and research. Since the launch of the first MSU, there has been a rapid proliferation across the world. The number needed to treat (NNT) for functional independence (mRS 0–1) acute stroke interventions has been reported as 8.4 (NINDS-tPA) [78] and 14 (ECASS III) [79] for thrombolytics and 2.8 (DAWN) [80] and 3.6 (DEFUSE-3) [81] for thrombectomy. For every 100 patients treated with an MSU, 27 will have less disability and 11 more will be disability-free [33••]. MSUs have a compelling NNT for functional independence of 9.4 and 11.6 with BEST-MSU [33••] and B-PROUD [32••], respectively. Given the magnitude of their effect, MSUs are poised to make a significant public health impact on stroke outcomes. MSUs furthermore have the potential to improve functional outcomes beyond ischemic stroke through prehospital reversal of oral anticoagulation or ultra-early blood pressure management in ICH. Adaptability is however limited by significant upfront financial investment and challenges with reimbursements. To facilitate communication, education and support, improve patient outcomes and further stroke research in prehospital care, The Pre-hospital Stroke Treatment Organization (PRESTO) was formed in 2016 as an international consortium of medical practitioners [82].

As experience with MSUs increase, more avenues for its use have emerged. MSUs have been employed in transporting patients with other acute neurological conditions including seizures, traumatic brain injury [68], tumors, and intracranial infections [83]. Early evaluation by a neurologist can lead to appropriate medical management and optimize triage. Widening the scope of MSU in management, triage and transport of patients with emergent non-neurological conditions could potentially expand its role in prehospital care.

MSUs have proven to be a relevant research platform, with new studies planned or underway in the United States, Canada, Japan, Germany, United Kingdom, Spain (global FASTEST; www.clinicaltrials.gov NCT03496883), Norway (Treat-NASPP: Prehospital Advanced Diagnostics and Treatment of Acute Stroke; NCT03158259) and Australia (STOP-MSU; NCT03385928). With early presentation, MSUs offer a unique opportunity to study cellular and molecular ultra-early biomarkers of acute stroke and cerebral inflammation, currently underway at the University of Colorado. Further areas of exploratory research include understanding pathophysiology, role of alternative therapeutic drugs, novel imaging software and neuroprotective agents in hyperacute time window.

The prehospital field of MSUs, a practical but ingenious innovation that brings the stroke center to the patient, has dramatically evolved over the past two decades, with expanding clinical and research applications on the horizon.

Declarations

Conflicts of Interest Grotta receives Research Grant from Genentech, CSL Behring, NIH, PCORI and is Consultant/Advisory Board member at Frazer Ltd. The other authors report no conflicts.

Human and Animal Rights and Informed Consent All reported studies/experiments with human or animal subjects performed by the authors have been previously published and complied with all applicable ethical standards (including the Helsinki declaration and its amendments, institutional/national research committee standards, and international/national/institutional guidelines).

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