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ORIGINAL ARTICLE

Ultraearly thrombolysis by an anesthesiologist in a mobile stroke unit: A prospective, controlled intervention study

Karianne Larsen[1,2] | Henriette S. Jæger[1,2] | Lars H. Tveit[3,4] | Maren R. Hov[1,4,5] | Kjetil Thorsen[1] | Jo Røislien[1,6] | Volker Solyga[3] | Christian G. Lund[4] | Kristi G. Bache[1,2]

[1]The Norwegian Air Ambulance Foundation, Oslo, Norway

[2]Institute of Basic Medical Sciences, University of Oslo, Oslo, Norway

[3]Department of Neurology, Østfold Hospital Trust, Grålum, Norway

[4]Department of Neurology, Oslo University Hospital, Oslo, Norway

[5]Faculty of Health Sciences, Oslo Metropolitan University, Oslo, Norway

[6]Faculty of Health Sciences, University of Stavanger, Stavanger, Norway

Correspondence
Karianne Larsen, The Norwegian Air Ambulance Foundation, Box 414 Sentrum, 0103 Oslo, Norway.
Email: karianne.larsen@norskluftambulanse.no

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Abstract

Background: Acute stroke treatment in mobile stroke units (MSU) is feasible and reduces time-to-treatment, but the optimal staffing model is unknown. We wanted to explore if integrating thrombolysis of acute ischemic stroke (AIS) in an anesthesiologist-based emergency medical services (EMS) reduces time-to-treatment and is safe.

Methods: A nonrandomized, prospective, controlled intervention study. Inclusion criteria: age ≥18 years, nonpregnant, stroke symptoms with onset ≤4 h. The MSU staffing is inspired by the Norwegian Helicopter Emergency Medical Services crew with an anesthesiologist, a paramedic-nurse and a paramedic. Controls were included by conventional ambulances in the same catchment area. Primary outcome was onset-to-treatment time. Secondary outcomes were alarm-to-treatment time, thrombolytic rate and functional outcome. Safety outcomes were symptomatic intracranial hemorrhage and mortality.

Results: We included 440 patients. MSU median (IQR) onset-to-treatment time was 101 (71–155) minutes versus 118 (90–176) minutes in controls, $p = 0.007$. MSU median (IQR) alarm-to-treatment time was 53 (44–65) minutes versus 74 (63–95) minutes in controls, $p < 0.001$. Golden hour treatment was achieved in 15.2% of the MSU patients versus 3.7% in the controls, $p = 0.005$. The thrombolytic rate was higher in the MSU (81% vs 59%, $p = 0.001$). MSU patients were more often discharged home (adjusted OR [95% CI]: 2.36 [1.11–5.03]). There were no other significant differences in outcomes.

Conclusions: Integrating thrombolysis of AIS in the anesthesiologist-based EMS reduces time-to-treatment without negatively affecting outcomes. An MSU based on the EMS enables prehospital assessment of acute stroke in addition to other medical and traumatic emergencies and may facilitate future implementation.

KEYWORDS
acute stroke, anesthesiologists, emergency medical services, mobile stroke unit, thrombolysis

Clinical Trial Registration-URL: https://clinicaltrials.gov. Identifier: NCT03158259.

INTRODUCTION

The emergency medical services (EMS) provides urgent prehospital treatment, stabilization and transportation in medical and traumatic emergencies, but diagnostic limitations lead to insufficient ability to detect and treat acute ischemic stroke (AIS). AIS is utterly time critical where small reductions in time to intravenous thrombolysis (IVT) lead to better outcomes [1–3] but still a minority of AIS patients receive IVT and the treatment is rarely administered in the more effective time window – the golden hour [4]. Mobile stroke units (MSU) are ambulances equipped with a computed tomography (CT) scanner and staffed with a stroke team which enables prehospital assessment of stroke [5,6]. MSUs are generally set up with an onboard stroke physician as the decision maker or a non-physician team relying on telemedical evaluation by an in-hospital stroke physician [5,7]. The different staffing models report time reductions, better outcomes and both increased thrombolytic rates and golden hour treatment [5,7,8].

The Norwegian Acute Stroke Prehospital Project (NASPP) was inspired by the Norwegian Helicopter Emergency Medical Services (HEMS), a nationwide anesthesiologist-staffed air ambulance service, and staffed the MSU with an anesthesiologist trained in prehospital critical care, a paramedic-nurse and a paramedic. Acute stroke assessment was added to the worklist of the physician-based EMS and the feasibility of such a model was explored. The study showed that the prehospital anesthesiologists effectively could interpret cerebral CT scans and use the National Institutes of Health Stroke Scale (NIHSS), both with good agreement with in-hospital specialists [9,10]. Treat-NASPP, the follow-up study, added IVT to the procedure.

The aim of Treat-NASPP was to explore if IVT administered by an anesthesiologist in an MSU reduces time-to-treatment and is safe [11]. We hypothesized that the model reduces onset-to-treatment time (OTT) with ≥15 minutes without negatively affecting outcomes [11].

METHODS

Treat-NASPP is a single-center, nonrandomized, prospective, controlled intervention study conducted in Southeast Norway, Østfold county, comparing AIS treatment in an MSU with standard in-hospital care. The county covers about 4000 km^2 (1550 miles^2), has approximately 300 000 residents and one primary stroke center (PSC). The largest city in the county, Fredrikstad, has about 83 000 inhabitants. The nearest comprehensive stroke center (CSC) is in Oslo, 90 km (55 miles) north of the PSC. The county has five ambulance stations situated from 7 to 50 km (5 to 31 miles) from the PSC. As a precaution against delay, the MSU was only allowed to enroll patients situated ≥10 minutes driving distance from the PSC (Figure S1). The MSU was based at the ambulance station in Sarpsborg, which is within the 10-minute exclusion zone and the station closest to the PSC (Figure S1).

Trial design

The MSU enrolled patients consecutively on weekdays 08:00 hours to 20:00 hours (on-hours) 2 weeks per month except during maintenance, weekends and public vacations due to logistical and economical limitations. Controls were recruited by ordinary ambulances weekdays, 08:00 hours to 20:00 hours, 2 weeks per month when the MSU was not operative, except weekends and vacations. A lower enrollment than expected led to a deliberate change in procedure where (i) inclusion in both groups was extended to all weekdays from February 2018, (ii) control group inclusion also in weekends and vacations from April 2018 and (iii) a 24–7 inclusion in the control group from January 2019. After the changes in February 2018, both the intervention group and control group enrolled weekdays 08:00 hours to 20:00 hours, but the MSU enrollment was prioritized. Control patients were included in MSU on-hours if the MSU was preoccupied or not operative.

Inclusion criteria were age ≥18 years, nonpregnant and stroke symptoms lasting ≤4 h. The emergency medical communication center (EMCC) used the Norwegian Index of Emergency Medical Assistance as a decision tool for the appropriate response [12]. The MSU was always dispatched in parallel with an ordinary ambulance due to the known inaccuracy in stroke code dispatches [13] and to effectively cooperate between the five ambulance stations without causing prehospital delay. The rendezvous approach was applied when appropriate.

Intervention

An MSU (Mercedes Sprinter) equipped with a CT scanner (CereTom® eight-slice mobile CT; Samsung NeuroLogica), a ventilator (LTV 1200; Carefusion, Diacor AS), a defibrillator (Lifepak 15; Physio Control) and a point-of-care laboratory (pocH-100i Automated Hematology Analyzer). Hemochron Jr (ITC Edison) and CoaguChek Pro II (Roche Diagnostic, Alere™) measured international normalized ratio. Meytec (Werneuchen) used telecommunication by 4G for transmission of images and data from the CT.

The Treat-NASPP MSU was staffed like the nationwide HEMS with an anesthesiologist trained to provide prehospital critical care to critically ill patients including acute stoke. The additional team members were a paramedic-nurse and a paramedic. The 11 participating anesthesiologists had median (IQR) 14 (12–15) years of clinical training, 10 (8–13) years anesthesiology training and 2 (0–9) years of prehospital work experience. The anesthesiologists work with medical emergencies in the HEMS and/or in intensive care units. In-hospital anesthesiologists are involved in the reception of critically ill patients arriving in the emergency department and the participating anesthesiologists have experience in treating medical and traumatic emergencies including stroke.

The EMS in Norway is a government funded, non-physician-based system where ambulances are staffed with two paramedics [14]. The education of ambulance personnel is either (i) a 3-year

bachelor program in Paramedic Science, (ii) a 2-year high school education along with 2 years EMS practice or (iii) ambulance worker authorization of nurses after 2 years work in the EMS and completion of compulsory advanced life support courses. Regarding the MSU, the first two groups are referred to as paramedics and the third group referred to as a paramedic-nurse since they have different work tasks.

All MSU personnel completed a 2-day stroke assessment course and an NIHSS certification [15]. The anesthesiologists completed a 2-day course in cerebral CT assessment relying on the validation done in the previous NASPP study [10,16]. The course included interpretation of CT scans regarding contraindications for IVT, CT calibration, conduction of CT scans and radiation safety. As a daily start-up routine, the anesthesiologist conducted a CT calibration, a CT quality assurance and a CT scan of a head phantom which was sent teleradiologically to the in-hospital radiographer as a safety check of technical systems, image quality and the teleradiology system. A green light in the front of the MSU indicated good 4G connectivity. In case of connectivity problems, the anesthesiologist could try to resend the images, move the MSU to a place with better connectivity or abort mission and transport the patient to the PSC.

The paramedic, who was the MSU driver, planned the meeting point if it was a rendezvous dispatch and prepared for reception of the patient by leveling the MSU, preparing the stretcher and assisting the paramedic-nurse. The paramedic-nurse prepared for blood sampling and medication before the patient arrived. The paramedic-nurse drew blood samples, measured vital signs, administered medication if indicated and assisted the anesthesiologist. The anesthesiologist checked vital signs, medical history and NIHSS. If indicated, a cerebral CT scan and blood analysis were conducted. CT images were transferred for a second interpretation by the on-call radiologist, and the on-call neurologist was conferred for a final agreement on IVT indication. Tissue plasminogen activator (tPA) was administered according to in-hospital procedures. From November 27, 2017 a direct triage algorithm agreement with the CSC was established to further reduce time-to-treatment in both cerebral hemorrhages and large vessel occlusions (LVO). Patients with non-traumatic subarachnoid hemorrhage (SAH) or surgically available intracranial hemorrhage (ICH) in benefiting patients (evaluating frailty, prognosis, hematoma size and location) were transported directly to the CSC. All patients with NIHSS ≥6 or aphasia and a non-contrast cerebral CT without hemorrhage were considered as possible LVO and were evaluated for direct transportation to the CSC (Figure S2).

Control

Controls were initially recruited by 10 paramedics working in ordinary ambulances. Due to a lower recruitment than expected, this group was increased to 63 in November 2018. All completed a 2-day course in acute stroke assessment and an NIHSS certification [15]. The course was based on the training program for prehospital personnel validated in NASPP, [9] and the training was done to optimize the control group. In November 2018, low recruitment led to a deliberate change in procedure where all other ambulance personnel in the county (n = 230) could enroll patients.

Outcomes

The primary outcome was to determine the difference in OTT between the intervention and control group. A power analysis (two-sample, two-sided, power 0.80) determined a sample size of 86 thrombolyzed patients in each group to confirm a 30-minute difference in OTT [10,11].

Secondary outcomes were alarm-to-treatment time (ATT), thrombolytic rate and functional outcome (modified Rankin Scale [mRS]). The thrombolytic rate was defined as the proportion of patients with a final hospital diagnose of cerebral ischemia (AIS, transient ischemic attack [TIA]) receiving IVT within the 4.5-h time window. TIA was included in the thrombolytic rate as all patients had ongoing stroke symptoms at time of inclusion and when IVT was initiated. If symptoms resolved within 24 h and radiological workup was negative, a TIA diagnosis was registered at the PSC. The PSC did not have a routine for registering averted strokes.

As mRS at discharge was rarely registered, discharge-to-home was used as a surrogate. The follow-up mRS was collected by a telephone interview 3 months (±1 week) after IVT. The registrars were certified in mRS assessment and blinded for study group [17].

Safety endpoints included symptomatic intracranial hemorrhage (SICH), serious adverse events (SAE) and mortality three months after IVT. An SAE was defined as complications following IVT leading to death, intensive care treatment, transfusion or surgery. SICH was defined as local or remote parenchymal hemorrhage type 2 on the 22–36 h post-treatment scan, combined with a deterioration in NIHSS of ≥4 from baseline or the lowest NIHSS between baseline and 24 h or leading to death SITS-MOST, [18] or a significant worsening of symptoms linked to the cerebral bleeding [11]. Safety parameters were reported to an external safety committee of two experienced neurologists. The committee was blinded for study group and could stop the study if they found evidence for an unacceptable increase in SICH (>4%) or deaths [11].

Statistical methods

Data were run through intention-to-treat analyses in IBM SPSS Version 27 and R 4.0.3. A significance level of 0.05 was used. Continuous variables were skewed and compared with Mann–Whitney U test. Categorical variables were compared using Pearson's Chi-squared test or Fisher exact test.

Modified Rankin Scale (mRS) was analyzed as an ordinal scale (0–6) and dichotomized where mRS 0–2 was defined as favorable outcome (functionally independent). Associations between study group and outcomes were tested in adjusted and unadjusted binary logistic regression. Predictors were selected by univariate analysis and clinical evaluation. These predictors (age, sex, study group, initial NIHSS,

baseline mRS, atrial fibrillation, LVO, hypertension, EVT) were used in a stepwise logistic regression to find the best model. When forward and backward regression resulted in different models, we used Akaike information criterion to select the optimal model (see Table 3).

Ethics

The Regional Ethics Committee approved the study protocol (Ref. 2016/974) [11]. Written informed consent was obtained from the participating person or a legally authorized representative.

RESULTS

The study started May 15, 2017 and terminated March 27, 2020 after reaching the required sample size. Follow-up was finalized in June 2020. The MSU included 166 patients in 456 operative days (Figure 1), and 86% were rendezvous dispatches. Direct triage was performed in 19 patients (Figure S2). Technical problems (n = 2) and disrupted teleradiological connectivity (n = 4) hindered prehospital CT evaluations in six cases. The control group included 274 patients in 771 study-operative days (Figure 1).

The MSU patients were median (IQR) 72 (57–83) years and 40% were females (Table 1). The control patients were median (IQR) 72 (60–81) years and 49% were females (Table 1). The baseline characteristics were balanced except for initial NIHSS (Table 1). The median (IQR) scene-to-hospital time was 20 (15–30) minutes in the MSU group and 20 (13–27) minutes in the controls, p = 0.036 (Table 1).

The median (IQR) OTT was 101 (71–155) minutes in the MSU (n = 92) versus 118 (90–176) in controls (n = 107), p = 0.007 (Table 2). The median (IQR) ATT was 53 (44–65) minutes in the MSU versus 74 (63–95) in controls, p < 0.001 (Table 2). The thrombolytic rate was 81% in the MSU versus 59% in controls, p = 0.001) (Table 2). Ten of the MSU patients received in-hospital IVT (Table S1).

Ultraearly thrombolysis ≤60 minutes after symptom onset was four-fold higher in the MSU (15.2% vs 3.7%, p = 0.005), which corresponds to a relative risk (95% CI) of 4.1 (1.4–11.9) (Table 2, Figure 2). A sensitivity analysis for patients outside the exclusion zone showed a 13-fold higher golden hour rate in the MSU (15.2% vs 1.2%, p = 0.001), which corresponds to a relative risk (95% CI) of 12.9 (1.7–96.3) (Table 2). Forty-two percent of the MSU patients had an OTT ≤90 minutes compared to 25% in the controls, p = 0.010 (Table 2, Figure 2). Sensitivity analyses for on-hour patients and patients situated outside the exclusion zone are presented in Table 2.

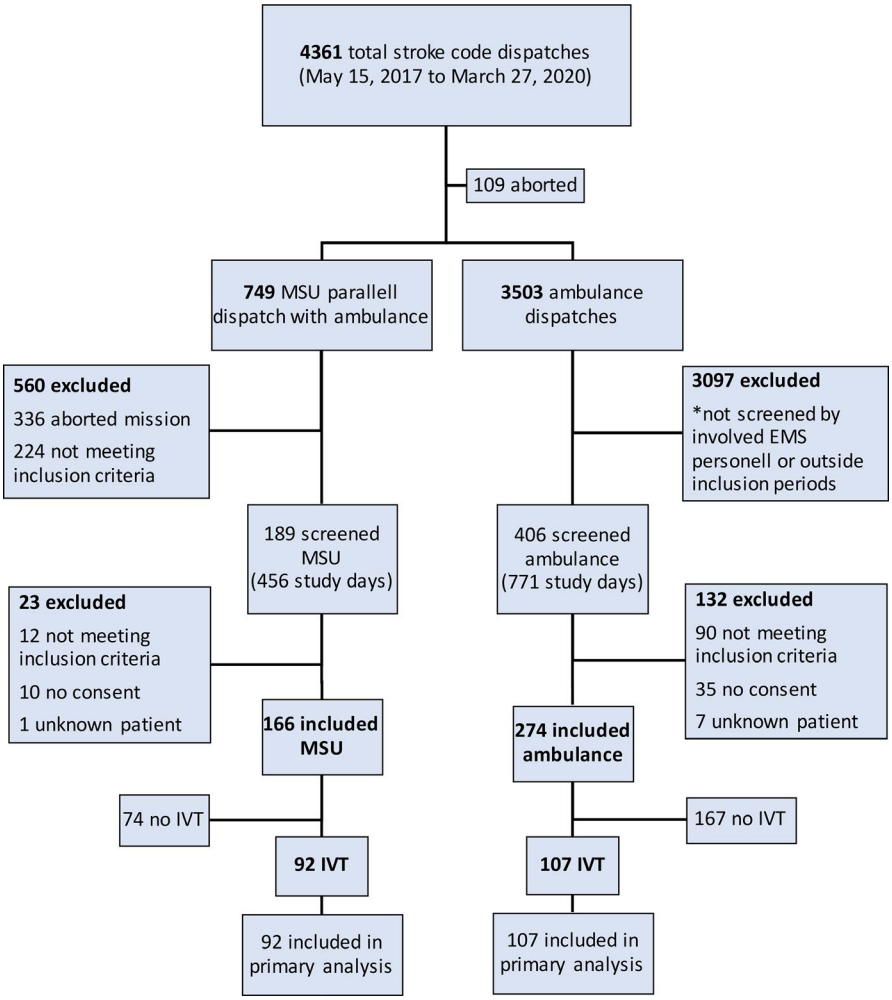

FIGURE 1 Study flow chart showing enrollment in the intervention and control group. EMS, emergency medical services; IVT, intravenous thrombolysis; MSU, mobile stroke unit

TABLE 1 Baseline characteristics, time intervals and discharge information compared between the mobile stroke unit and the controls

Baseline characteristics	MSU (*n* = 166)	MP	Control (*n* = 274)	MP	*P* value
Females, %, *n*	40 (66)		49 (135)		0.052
Age, years, median (IQR)	72 (57–83)		72 (60–81)		0.620
Thrombolysis, % (*n*)	55 (92)		39 (107)		0.001
Comorbidities					
Heart disease, % (*n*)	32 (53)		40 (109)		0.098
Hyperlipidemia, % (*n*)	23 (37)	4	17 (46)	7	0.154
Atrial fibrillation, % (*n*)	13 (21)	1	17 (46)	1	0.245
Hypertension, % (*n*)	55 (92)		56 (153)		0.932
Diabetes, % (*n*)	13 (22)	1	16 (43)	1	0.490
Smoking, % (*n*)	18 (28)	13	19 (47)	29	0.827
Cerebrovascular disease, % (*n*)	28 (47)		28 (77)		0.962
Stroke severity					
NIHSS, median (IQR)	4 (2–8)	3	2 (1–6)	13	<0.001
NIHSS 0–5, % (*n*)	65 (106)	3	73 (190)	13	0.090
NIHSS 6–14, % (*n*)	23 (37)	3	20 (53)	13	0.558
NIHSS ≥15, % (*n*)	12 (20)	3	7 (18)	13	0.060
Onset to alarm, min, median (IQR)	43 (13–95)		32 (10–78)		0.057
Alarm-rendezvous, min, median, (IQR)	29 (24–36)	24	NA		
MSU scene[a] to CT, min, median, (IQR)	11 (8–16)	1	NA		
Scene[a] to hospital, min, median (IQR)	20 (15–30)[b]	1	20 (13–27)	3	0.036
Premorbid living home, % (*n*)	95 (154)	3	90 (245)	3	0.131
Discharged home, % (*n*)	67 (108)	4	62 (166)	6	0.323
Survival day 7, % (*n*)	96 (159)		97 (265)		0.613
Survival day 90, % (*n*)	89 (146)	1	92 (252)		0.224
Discharge diagnoses					
AIS, % (*n*)	35 (58)		37 (101)		0.684
TIA, % (*n*)	15 (25)		14 (39)		0.812
ICH, % (*n*)	6 (10)		7 (19)		0.709
SAH, % (*n*)	2 (3)		1 (3)		0.677
Other, % (*n*)	42 (70)		41 (112)		0.790

Abbreviations: AIS, acute ischemic stroke; CT, computed tomography; ICH, intracerebral hemorrhage; IQR, interquartile range; MP, missing patients; MSU, mobile stroke unit; NA, not available; NIHSS, National Institutes of Health Stroke Scale; SAH, subarachnoid hemorrhage; TIA, transient ischemic attack.

[a]Scene is initial patient site or rendezvous site.

[b]As 86% of the MSU dispatches were rendezvous, the actual scene-to-hospital time was longer as the ambulance transportation time from initial patient site to rendezvous site must be considered.

There were no differences in mRS categories (0–6) between the groups at 3 months, $p = 0.637$ (Figure 3). Adjusted odds ratio (OR) for discharge-to-home was higher in the MSU (2.36 [1.11–5.03]). No other significant differences in outcomes were found (Table 3).

DISCUSSION

Introducing IVT in the anesthesiologist-based EMS significantly reduced OTT and increased ultraearly thrombolysis and the thrombolytic rate without any safety concerns compared to in-hospital treatment. This is a report from the first operative MSU in the Nordic countries and one of only a few MSU studies conducted in a nonurban area [19–21].

OTT was 17 minutes shorter in the MSU and more than 40% of the MSU patients were treated within 90 minutes from symptom onset. The time reductions achieved are reliant on: (i) accurate communication and coordination between the MSU, EMCC, ambulances and the PSC, (ii) a well-coordinated stroke team in the MSU and (iii) maintained technical systems. The reported time reductions are clinically relevant as for every 15-minute delay in OTT there is a

TABLE 2 Characteristics and outcomes in thrombolyzed patients

Characteristics and outcomes	MSU(*n* = 92)	MP	Control(*n* = 107)	MP	*P* value
Age, year, median, (IQR)	72 (62–83)		74 (64–82)		0.775
Females, % (*n*)	46 (42)		52 (56)		0.347
Premorbid living home, % (*n*)	95 (86)	1	89 (95)		0.152
Initial NIHSS, median, IQR	4 (3–8)		4 (2–7)		0.178
Days in stroke unit, median (IQR)	4 (2–6)		4 (3–6)		0.875
Discharged home, % (*n*)	69 (63)		59 (62)	1	0.146
OTT, min, median (IQR)	101 (71–155)		118 (90–176)		0.007
ATT, min, median (IQR)	53 (44–65)		74 (63–95)		<0.001
DNT, min, median (IQR)	22 (14–28)		29 (25–36)		<0.001
Alarm-to-CT, min, median (IQR)	38 (31–46)		54 (42–69)		<0.001
Golden hour, % (*n*)	15.2 (14)		3.7 (4)		0.005
OTT ≤90 min, % (*n*)	42 (39)		25 (27)		0.010
Thrombolytic rate, % (*n*)	81 (67)		59 (82)		0.001
Discharge diagnoses[a]					
AIS, % (*n*)	53 (49)		66 (71)		0.060
TIA, % (*n*)	20 (18)		10 (11)		0.064
Other, % (*n*)	27 (25)		23 (25)		0.537
Outcomes					
mRS 0–2 baseline, % (*n*)	84 (76)	2	92 (97)	2	0.081
mRS 0–2 day 90, % (*n*)	70 (64)	1	74 (78)	2	0.536
mRS day 90, median (IQR)	1 (0–3)	1	0 (0–3)	2	0.554
Survival day 7, % (*n*)	97 (89)		98 (105)		0.664
SICH, % (*n*)	2.2 (2)		1.9 (2)		1.000
SAE, % (*n*)	3.3 (3)		2.8 (3)		1.000
Mortality day 90, % (*n*)	8.7 (8)		3.7 (4)		0.143
Sensitivity analyses					
On-hour patients,[b] *n*	MSU, 92		Control, 47		
OTT, min, median (IQR)	101 (71–155)		127 (87–198)		0.023
ATT, min, median (IQR)	53 (44–65)		73 (60–98)		<0.001
DNT, min, median (IQR)	22 (14–28)		27 (22–37)		<0.001
Patients outside exclusion zone,[c] *n*	MSU, 92		Control, 85		
OTT, min, median (IQR)	101 (71–155)		115 (91–181)		0.005
ATT, min, median (IQR)	53 (44–65)		78 (69–98)		<0.001
Golden hour, % (*n*)	15.2 (14)		1.2 (1)		0.001

Abbreviations: AIS, acute ischemic stroke; ATT, alarm-to-treatment time; CT, computed tomography; DNT, door-to-needle time; IQR, interquartile range; MP, missing patients; mRS, modified Rankin Scale; MSU, mobile stroke unit; NIHSS, National Institutes of Health Stroke Scale; OTT, onset-to-treatment time; SAE, serious adverse event; SICH, symptomatic intracranial hemorrhage; TIA, transient ischemic attack.

[a] Sum not 100% due to rounding of numbers.

[b] Patients enrolled weekdays 08:00 hours to 20:00 hours.

[c] The exclusion zone was a 10-minute driving time radius around the primary stroke center where the MSU was not allowed to enroll patients.

decline in functional outcome, [4] and the number-needed-to-treat increases rapidly after the first 90 minutes [1]. In the present study, the MSU patients were more often discharged home (adjusted OR 2.36 [1.11–5.03]), but we found no significant differences in other outcomes (Table 3). The study was not powered for detection of differences in outcome, so the lack of these results could be expected.

Golden hour treatment gives higher odds of early neurological improvement, complete recanalization and favorable functional outcome [2,4,22] but still in-hospital golden hour treatment is reported to be as low as 1%–2% [4,22,23]. Treat-NASPP confirms that prehospital assessment of acute stroke by an anesthesiologist-based EMS team can increase the golden hour rate. The MSU also followed a

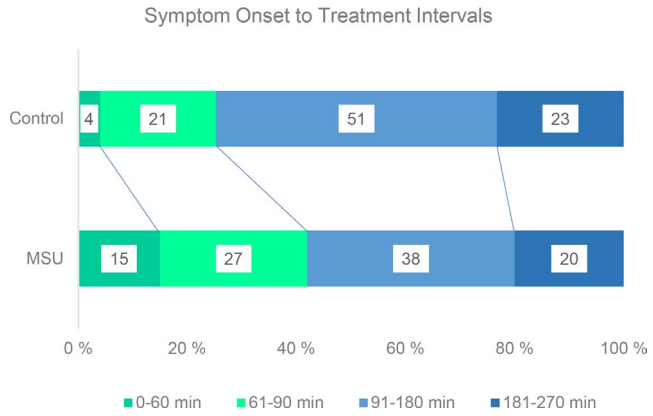

FIGURE 2 Symptom onset to treatment intervals. The proportion of patients treated within each time interval in the mobile stroke unit (MSU) and control group. More patients in the MSU are treated within the first 60 and 90 min after symptom onset. In the control group the sum is not 100% due to rounding of numbers

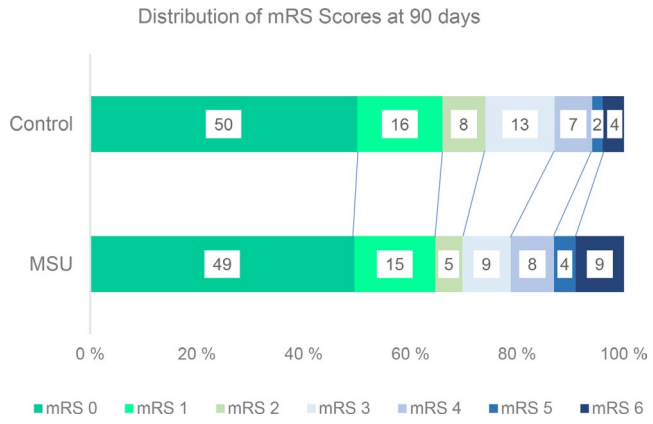

FIGURE 3 Distribution of modified Rankin Scale (mRS) scores for thrombolyzed patients at 90 days. MSU, mobile stroke unit. In the MSU group the sum is not 100% due to rounding of numbers

CSC triage algorithm for hemorrhages and suspected LVO to further reduce time-to-treatment (Figure S2). The accuracy of prehospital triage would increase if cerebral CT angiography was performed on the MSU [24] but this was not available in our study.

The thrombolytic rate in the MSU was significantly higher than in the controls and higher than in other MSU studies [5]. Assessment and treatment in the field increases the possibility that late presenting patients can be treated within the time limit thus increasing the thrombolytic rate.

Stroke mimics were included in our analyses as reports on mimics in other MSU studies are sparse, and as mimics are a real part of hyperacute stroke evaluations (Figure S3). Forty percent of stroke dispatches in Treat-NASPP were for non-stroke patients, which is similar to previous reports [25,26]. The mimic rate of IVT-treated patients were not significantly different between the groups (Table 2). No complications were registered in these patients, which is in line with research showing that IVT in mimics is safe [27]. Regional and liberal indications for IVT may have contributed to both high mimic rates and high thrombolytic rates – a main goal of treating all eligible AIS patients, no lower NIHSS limit, no upper age limit and short door-to-needle time (DNT) [28].

The NASPP studies introduce an alternative MSU model based on the Norwegian nationwide HEMS which may be a benefit in a reality where almost half of stroke code dispatches are for non-stroke patients [13]. A crew that can respond to all medical and traumatic emergencies may also be a benefit in suburban/rural areas where the population and stroke incidence is lower. As a safety precaution the anesthesiologist had to confer with the in-hospital neurologist before initiating tPA and this often led to a decision delay. The future perspective, based upon results from the NASPP and Treat-NASPP studies [9,10] must be that the MSU becomes an autonomous unit with onboard digital access to medical records where the anesthesiologist independently interprets CT images and decides the indication for IVT. Clinical, health economical and geospatial studies will be necessary to develop tailor-made solutions for prehospital treatment of acute stroke.

TABLE 3 Unadjusted and adjusted outcomes for mobile stroke unit patients

	Univariable		Multivariable	
Variable	**OR (95% CI)**	**MP**	**OR (95% CI)**	**MP**
Binary logistic regression				
mRS 0–2 day 90	0.82 (0.44–1.54)	3	1.07[a] (0.41–2.83)	6
Discharged home	1.54 (0.86–2.77)	1	2.36[b] (1.11–5.03)	9
SICH	1.17 (0.16–8.45)	0	0.95[c] (0.12–7.34)	0
Mortality day 90	2.45 (0.71–8.43)	0	2.07[d] (0.50–8.62)	0

The outcome analyses were conducted for thrombolyzed patients.

Abbreviations: CI, confidence interval; MP, missing patients; mRS, modified Rankin Scale; MSU, mobile stroke unit; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio; SICH, symptomatic intracranial hemorrhage.

[a]Adjusted for age, gender, initial NIHSS, baseline mRS, atrial fibrillation.

[b]Adjusted for age, initial NIHSS, baseline mRS, hypertension, large vessel occlusion.

[c]Adjusted for initial NIHSS.

[d]Adjusted for age, initial NIHSS.

Treat-NASPP has limitations and a nonrandomized study is more susceptible to bias. Control patients were recruited also in the MSU's off-hours (Table 2). As the MSU had a 10-minute exclusion zone from the PSC (Figure S1) and most dispatches were rendezvous, the time reductions and recruitment were affected (Table 2). Low inclusion rates in both groups were due to few operative periods, enrollment based on too few paramedics working in on-off periods and a suburban/rural area with few stroke dispatches. Training ambulance personnel in acute stroke assessment could impact the results in the control group. Follow-up mRS was a prespecified secondary outcome, but the study was underpowered for this endpoint. This study provides mainly safety data and the findings cannot be generalized to anesthesiologists (or other specialists) without specific training.

The Treat-NASPP MSU model, with an anesthesiologist-based EMS team, reduces time to thrombolytic treatment and increases ultraearly thrombolytic therapy in AIS without negatively affecting functional outcomes or safety outcomes. Utilizing the existing physician-based EMS enables prehospital assessment of acute stroke in addition to other medical and traumatic emergencies and may facilitate future implementation in prehospital emergency care systems.

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CONFLICT OF INTERESTS

None.

AUTHOR CONTRIBUTIONS

Karianne Larsen: Conceptualization (supporting); Data curation (lead); Formal analysis (lead); Investigation (lead); Methodology (supporting); Project administration (lead); Visualization (lead); Writing-original draft (lead); Writing-review & editing (lead). **Henriette S. Jæger:** Data curation (supporting); Investigation (supporting); Methodology (supporting); Project administration (supporting); Writing-original draft (supporting); Writing-review & editing (supporting). **Lars H. Tveit:** Data curation (supporting); Investigation (supporting); Project administration (supporting); Writing-original draft (supporting); Writing-review & editing (supporting). **Maren R. Hov:** Conceptualization (lead); Formal analysis (supporting); Funding acquisition (lead); Investigation (supporting); Methodology (supporting); Project administration (supporting); Supervision (supporting); Validation (lead); Visualization (supporting); Writing-original draft (supporting); Writing-review & editing (supporting). **Kjetil Thorsen:** Formal analysis (lead); Methodology (supporting); Writing-original draft (supporting); Writing-review & editing (supporting). **Jo Røislien:** Conceptualization (supporting); Formal analysis (lead); Methodology (lead); Writing-original draft (supporting); Writing-review & editing (supporting). **Volker Solyga:** Conceptualization (supporting); Data curation (supporting); Investigation (supporting); Project administration (supporting); Validation (supporting); Writing-original draft (supporting); Writing-review & editing (supporting). **Christian G. Lund:** Conceptualization (lead); Investigation (supporting); Methodology (supporting); Project administration (lead); Supervision (supporting); Validation (supporting); Writing-original draft (supporting); Writing-review & editing (supporting). **Kristi G. Bache:** Conceptualization (lead); Formal analysis (supporting); Funding acquisition (lead); Investigation (lead); Methodology (lead); Project administration (lead); Supervision (lead); Validation (lead); Visualization (supporting); Writing-original draft (supporting); Writing-review & editing (supporting).

DATA AVAILABILITY STATEMENT

Study data are available from the corresponding author upon reasonable request.

ORCID

Karianne Larsen https://orcid.org/0000-0001-5580-4231

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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