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CASE REPORT

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Pre-hospital thrombolysis of ischemic stroke in the emergency service system—A case report from the Treat-NASPP trial

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1 | INTRODUCTION

Acute stroke is a critical medical emergency and it should be tended to by early recognition and rapid triage to the correct level of care.[1] In-hospital, stroke is managed by neurologists and stroke-specialists, and cerebral images are assessed by radiologists for a mutual evaluation and coherent final diagnosis of the patient. In the pre-hospital setting, anesthesiologists trained in pre-hospital critical care provide advanced treatment to acute trauma and medical conditions.[2] Even when stroke is suspected, more than 50% of strokes are misclassified upon dispatch and turn out to be something else,[3] and it is therefore mandatory that the health care provider arriving at the scene is qualified to respond to a number of conditions that are potentially life threatening. At the same time, when stroke does occur, diagnosis and appropriate treatment should be administered without delay, as the outcome is strictly time-dependent.[4] This represents a potential conflict, as the delay to hospital admittance and specialist treatment introduces a unfavorable time-to-treatment delay for stroke patients.[5,6]

The feasibility of a Norwegian MSU with CT-imaging in the pre-hospital setting has been confirmed,[7,8] but thrombolytic stroke-treatment administered by a critical care physician was up until now never done. This case is the first description of pre-hospital thrombolysis of ischemic stroke performed by a critical care physician in an MSU-system. The concept of introducing acute stroke-treatment in the pre-hospital phase of physician-manned critical care, may pave the way for a more efficient, widespread and time-conservative treatment of one of the most time-sensitive groups of patients in our systems. We will in the ongoing trial[9] which the patient described here is part of, use this model to also investigate the possibility of pre-hospital triage to the correct level of care for patients in need of neurosurgery, endovascular intervention, thrombolysis or other specific treatments.

2 | PATIENT INFORMATION

A 78 years old male with symptoms of stroke was met by the MSU 35 minutes after onset of symptoms. He had risk factors associated with cerebrovascular disease including arterial hypertension, coronary heart disease, and congestive heart failure. The patient had stopped smoking more than 3 months ago, had a cardiac pacemaker and he was medicated with acetylsalisylic acid, bisoprolol,

We adhere to the EQUATOR-guidelines for reporting of case reports.
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amiodarone, bumetamide, potassium chloride, lercanidipine, levothyroxine and ramipril.

3 | CLINICAL FINDINGS

The patient arrived in the MSU 39 minutes after symptom onset, and the clinical examination in the MSU revealed a left sided hemiparesis, left sided central facial paresis and dysarthria with an NIHSS score of 9. The clinical evaluation was performed by the critical care physician, and the CT scan was initiated based on this. CT images (Figure 1) were assessed by the MSU-physician and transferred to the hospital by teleradiology. Blood markers measured in the MSU showed Hb value (g/100 mL) 12.8, thrombocyte value (10^{-9}/L) 137 and glucose value (mmol/L) 7.7.

4 | DIAGNOSTIC ASSESSMENT

The patient was diagnosed using both clinical and advanced diagnostics. An NIHSS score was conducted by the critical care physician followed by blood work and a CT-scan. The tentative diagnosis was set to cerebral ischemia, and based on the medical history delivered over the phone by the neurologist in ward, interpretation of CT-images and consulting with the neurologist on duty, no contraindications against thrombolytic treatment were found. Decision to initiate thrombolytic treatment was made 54 minutes after symptom onset.

5 | THERAPEUTIC INTERVENTION

The tPA bolus (8 mg) was administered by the critical care physician in the MSU, 56 minutes after symptom onset (onset-to treatment, OTT) and 17 minutes after the patient arrived in the MSU (door-needle-time, DNT) (see timeline Figure 2). tPA infusion was initiated and ongoing during transportation to the hospital, and the total tPA dosage was 81 mg. Cerebral CT angiography at the local hospital detected an occlusion of the middle cerebral artery (M2), and the patient was transferred to an intervention center for evaluation of thrombectomy. During transportation the patient had a clinical recovery, and at arrival the NIHSS score was 1 due to a discrete central facial paresis. A repeated cerebral CT angiogram revealed that the M2 occlusion had dissolved, and the patient was returned to the primary hospital the following day.

6 | FOLLOW-UP AND OUTCOMES

Upon arrival at the local hospital, the patient had an NIHSS score of 6. Two hours post tPA the NIHSS score was 1, which was also the score at 24 hours and at discharge. The mRS baseline was 1, mRS at day 1 and at discharge was 2. The Barthel Index was 100 at baseline, day 1 and at discharge. The cerebral CT scan 24 hours after thrombolysis, was without cerebral hemorrhage. Cerebral MRI was not conducted due to the patient having a pacemaker. The patient was discharged to home after 7 days in the hospital with a final diagnosis of cerebral infarction. Clopidogrel and atorvastatin were added to the medication list. By follow-up day 90 mRS score was still 2 and Barthel Index score 100.

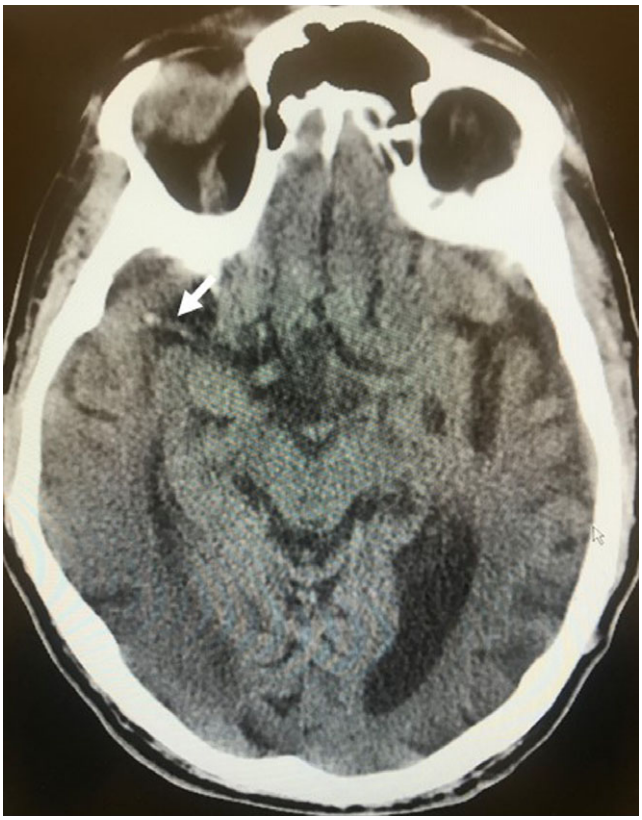

FIGURE 1 MSU CT image with no contraindications against thrombolysis and revealing a hyperdens artery sign of the right middle cerebral artery (arrow)[Colour figure can be viewed at wileyonlinelibrary.com]

7 | DISCUSSION

This case report describes the tenor of the first stroke patient treated in the Norwegian MSU model according to the Treat-NASPP concept.[8,9] This is a concept that includes stroke-care to the list of existing advanced emergency medical services performed by anesthesiologists trained in pre-hospital critical care. The strength of Treat-NASPP is summarized in two major points, namely (a) time saving and (b) patient safety. By training the pre-hospital critical care anesthesiologist to conduct NIHSS, perform a CT scan and interpret the images, and when indicated initiate thrombolytic treatment, it is possible to reduce time from symptom onset to treatment because diagnosis-specific measures are applied before the patient arrives at the hospital. Correct diagnosis already in the pre-hospital phase also opens up for direct transportation to the right level of care.[10] This introduces the opportunity to save time by making severe cuts into the time spent *before* the patient arrives at the hospital. The safety of the patient is ensured by the expertise of the pre-hospital critical care physician with the skills to treat acute medical and traumatic emergencies[11,12] as well as stroke.[8] The neurologist on duty at the

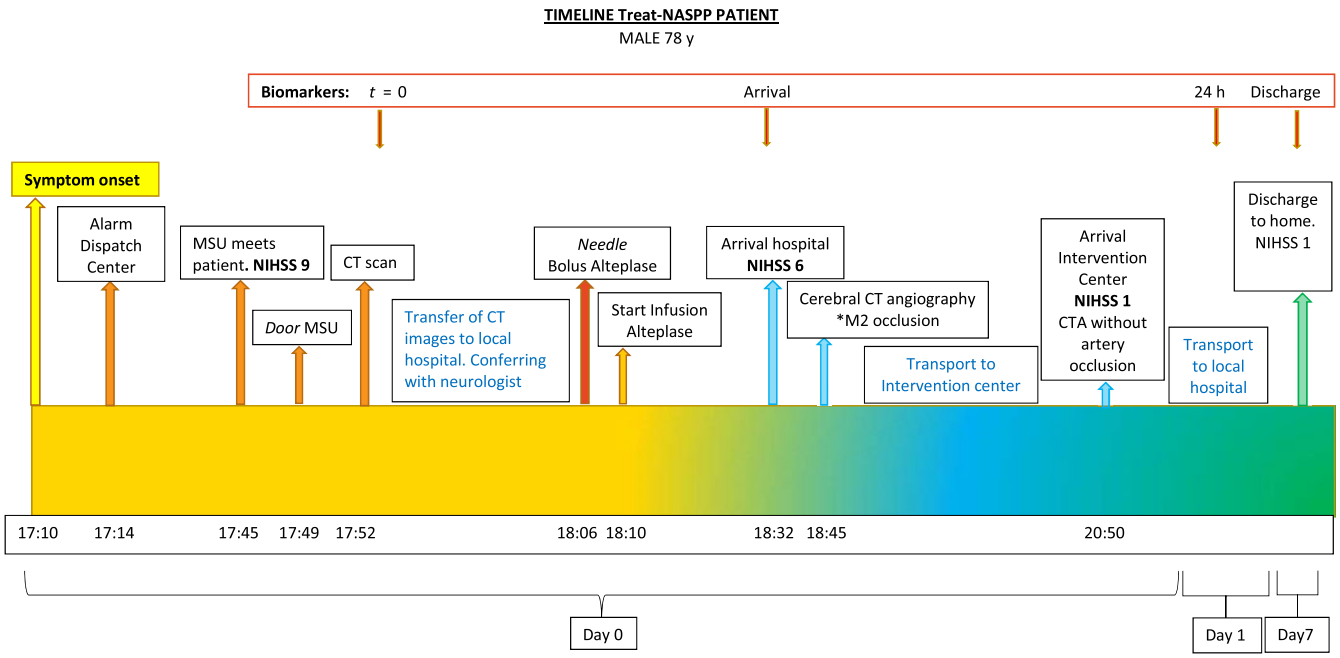

FIGURE 2 Timeline Treat-NASPP patient

hospital, who is currently consulted as a safety precaution, must be seen as a benefit in such early phase of the trial,[9] but with a clear expectation that the critical care physician will be autonomous with accumulating, supporting evidence[7,8,10] and experience. Early pre-hospital diagnosis, triage and intervention is made possible through the MSU with its specially trained crew, the CT scanner and the point of care laboratory. The pre-hospital critical care physician is specialized to handle conditions that require immediate lifesaving treatment, like respiratory failure, cardiac arrest and severe traumatic injuries, and this is a great advantage in a pre-hospital setting.

Efforts have been made to improve the conditions and decrease in-hospital time for stroke patients,[13-15] and the highly specialized hospitals have door-to-needle times of less than 15 minutes. This urges the need to look at pre-hospital stroke care, because the time from symptoms of stroke occur to treatment starts (OTT), is the time that really matters.

The idea of an MSU was introduced more than a decade ago[16] and MSUs are operational in different models and health systems around the world (summarized in[17]). Stroke patients are successfully treated pre-hospitally in the MSU ,[1,6,18-20] with median time gains up to more than 40 minutes from alarm to therapy decision.[19] The previously described systems rely on models dedicated solely to acute stroke care, as they are run by in-hospital stroke specialists. This is a system which may be difficult and expensive to implement, and the pre-hospital environment requires wide knowledge of pre-hospital emergency care other than stroke. The main difference between the Norwegian MSU model and what is previously described, is the use of existing emergency services. The Norwegian MSU is staffed with a critical care physician, a paramedic and a nurse paramedic. The pre-hospital setting, where a variety of acute medical situations need to be handled, is the normal working environment for the critical care physician and the rest of the MSU-team, and they are additionally trained in specialized acute stroke evaluation and treatment.[8] The Norwegian MSU is therefore not strictly a specialized stroke ambulance, but rather an advanced emergency medical service prepared to handle traumatic cerebral conditions, acute medical conditions and trauma, as well as stroke.

An earlier study of the Norwegian MSU-model showed that the inter-rater agreement between the pre-hospital critical care physician and the in-hospital radiologists was excellent and the door-to-decision time was in median 10 minutes.[8] In the case presented in this article, the door MSU-to-CT scan was only 3 minutes (see timeline, Figure 2). Fourteen minutes passes with transfer of the images and decision-making in cooperation with the in-hospital neurologist, which results in a door-to-needle time of 17 minutes. If the entire process of CT-scanning and interpretation of the images is made by the critical care physician alone, a door-to-treatment time of 10 minutes is realistic.[8] The results so far indicate that this is feasible and will be the procedure of the future in our system. When leaving the diagnostics and decision to the pre-hospital critical care physician, the potential of further time-saving increases. This would be in line with the idea of creating feasible stroke identification systems that are possible to implement in the existing pre-hospital health care services, where health- and life-saving stratification and treatment of all stroke-patients in a safe and timely manner is the norm.

For our patient, with a door-to-needle time of 17 minutes, and an OTT time of only 56 minutes, we are looking at a patient treated within the golden hour – the time span shown to result in the best outcome.[21,22] This is rarely achieved with the conventional ambulance and in-hospital treatment, as the time at the pick-up scene,

driving distance and time to hand-over the patient, have to be considered as well. Early decision-making and early onset of treatment is mandatory to improve the prognosis and outcome for stroke patients,[4] and accumulating evidence strongly suggest that the Norwegian MSU model contributes to this achievement.

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REFERENCES

1. Audebert HJ, Saver JL, Starkman S, Lees KR, Endres M. Prehospital stroke care: new prospects for treatment and clinical research. *Neurology*. 2013;81(5):501-508.
2. Langhelle A, Lossius HM, Silfvast T, et al. International EMS systems: the Nordic countries. *Resuscitation*. 2004;61(1):9-21.
3. Leathley MJ, Jones SP, Gibson JM, et al. "Can you send an ambulance please?": a comparison of callers' requests for emergency medical dispatch in non-stroke and stroke calls. *Emerg Med J*. 2014;31 (e1):e25-e28.
4. Meretoja A, Keshtkaran M, Saver JL, et al. Stroke thrombolysis: save a minute, save a day. *Stroke*. 2014;45(4):1053-1058.
5. Morris DL, Rosamond W, Madden K, Schultz C, Hamilton S. Prehospital and emergency department delays after acute stroke: the Genentech Stroke Presentation Survey. *Stroke*. 2000;31(11):2585-2590.
6. Ebinger M, Winter B, Wendt M, et al. Effect of the use of ambulance-based thrombolysis on time to thrombolysis in acute ischemic stroke: a randomized clinical trial. *JAMA*. 2014;311(16):1622-1631.
7. Hov MR, Nome T, Zakariassen E, et al. Assessment of acute stroke cerebral CT examinations by anaesthesiologists. *Acta Anaesthesiol Scand*. 2015;59(9):1179-1186.
8. Hov MR, Zakariassen E, Lindner T, et al. Interpretation of brain CT scans in the field by critical care physicians in a mobile stroke unit. *J Neuroimaging*. 2018;28:106-111.
9. Bache KG, Hov MR, Larsen K, Solyga VM, Lund CG. Prehospital advanced diagnostics and treatment of acute stroke: protocol for a controlled intervention study. *JMIR Res Protoc*. 2018;7(2):e53.
10. Hov MR, Ryen A, Finsnes K, et al. Pre-hospital ct diagnosis of subarachnoid hemorrhage. *Scand J Trauma Resusc Emerg Med*. 2017;25 (1):21
11. Reid BO, Rehn M, Uleberg O, Kruger AJ. Physician-provided prehospital critical care, effect on patient physiology dynamics and on-scene time. *Eur J Emerg Med*. 2018;25:114-119.
12. Sollid S, Rehn M. The role of the anaesthesiologist in air ambulance medicine. *Curr Opin Anaesthesiol*. 2017;30(4):513-517.
13. Puolakka T, Kuisma M, Lankimaki S, et al. Cutting the prehospital on-scene time of stroke thrombolysis in helsinki: a prospective interventional study. *Stroke*. 2016;47(12):3038-3040.
14. Kalnins A, Mickelsen LJ, Marsh D. Decreasing stroke code to CT time in patients presenting with stroke symptoms. *Radiographics*. 2017;37(5):1559-1568.
15. Assis ZA, Menon BK, Goyal M. Imaging department organization in a stroke center and workflow processes in acute stroke. *Eur J Radiol*. 2017;96:120-124.
16. Fassbender K, Walter S, Liu Y, et al. "Mobile Stroke Unit" for hyperacute stroke treatment. *Stroke*. 2003;34(6): e44.
17. Fassbender K, Grotta JC, Walter S, Grunwald IQ, Ragoschke-Schumm A, Saver JL. Mobile stroke units for prehospital thrombolysis, triage, and beyond: benefits and challenges. *Lancet Neurol*. 2017;16(3):227-237.
18. Walter S, Kostpopoulos P, Haass A. Bringing the hospital to the patient: first treatment of stroke patients at the emergency site. *PLoS ONE*. 2010;5(10):e13758.
19. Walter S, Kostopoulos P, Haass A, et al. Diagnosis and treatment of patients with stroke in a mobile stroke unit versus in hospital: a randomised controlled trial. *Lancet Neurol*. 2012;11(5):397-404.
20. Weber JE, Ebinger M, Rozanski M, et al. Prehospital thrombolysis in acute stroke: results of the PHANTOM-S pilot study. *Neurology*. 2013;80(2):163-168.
21. Advani R, Naess H, Kurz MW. The golden hour of acute ischemic stroke. *Scand J Trauma Resusc Emerg Med*. 2017;25(1):54.
22. Kim JT, Fonarow GC, Smith EE, et al. Treatment with tissue plasminogen activator in the golden hour and the shape of the 4.5-hour time-benefit curve in the national united states get with the guidelines-stroke population. *Circulation*. 2017;135(2):128-139.

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