

Pre-hospital treatment of stroke – time is brain

In emergency treatment of stroke, *time* is of the essence for the outcome. Current guidelines give rise to a loss of time that restricts the opportunities for effective treatment. To save lives and health, pre-hospital interventions must be included as an active part of the treatment chain. The air ambulances should be equipped with a CT scanner for telemedical transfer of CT images for diagnostics at the nearest stroke unit.

Approximately 15 000 Norwegians suffer strokes each year, and this figure is likely to increase by 50 % over the next 20 years due to an ageing population. Stroke is the third most common cause of death in this country (1). In 2010, a total of 3 180 people succumbed to stroke, while in comparison 3 340 deaths were caused by heart infarctions (2). Even when no lives are lost, many will develop serious and lasting sequelae.

Altogether 85–90 % of the strokes are brain infarctions, in which a thrombus occludes a cerebral artery and causes ischaemic damage in the artery's distal supply area (3). The remaining 10–15 % are brain haemorrhages. With the aid of diagnostic imaging, in the form of a CT or an MR scan, brain infarctions can be distinguished from brain haemorrhages.

In the case of a brain infarction, a *cause-oriented treatment*, i.e. re-establishment of local cerebral circulation, must be initiated as soon as possible, since a reversible ischaemically affected area (a penumbra volume) will exist for the first few hours after the infarction has occurred. Cause-oriented treatment includes intravenous drug-based thrombolysis, invasive removal of the occluding thrombus, or a combination of the two. In the case of a brain haemorrhage, cause-oriented treatment may imply an emergency neurosurgical intervention. The loss of brain cells in the case of cerebral ischaemia has been estimated at approximately 1.7 million brain cells per minute (4). The effect of reperfusion declines rapidly over time, while the risk of complications increases (5). After 240–300 minutes from the onset of symptoms, the positive effect of reperfusion approaches zero (5, 6). The proportion of brain-infarction patients who will benefit from thrombolytic treatment decreases dramatically with each minute that elapses from the onset of symptoms.

The national guidelines

Current national guidelines presuppose that cause-oriented treatment of strokes take place in hospitals on the basis of a brain scan undertaken after hospitalisation. Intravenous thrombolytic treatment should be undertaken under the auspices of the hospital's stroke unit, invasive thrombectomy in specialised stroke units in the university hospitals and neurosurgical interventions in departments of neurosurgery (1).

With regard to the pre-hospital stage, the guidelines state that: «Rapid identification of patients with acute stroke and immediate hospitalisation in a hospital with a stroke unit are important to provide optimal emergency treatment, including thrombolysis (level 1a). (...) If the regular general practitioner/casualty clinic or other health service agencies are the first to be contacted in the case of a suspected stroke, their key task is to expedite a rapid hospitalisation, if necessary without a prior examination, since such an examination will often serve to delay hospitalisation» (1).

The Minister of Health has the ambition that 20 % of patients with brain infarction should be provided with thrombolytic treatment before 270 minutes have passed from the onset of symptoms. Only very few hospitals come close to reaching this goal, and the national average is around 5 %. There are wide variations in thrombo-

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lysis frequency, i.e. the number of patients who receive cause-oriented treatment. In 2011, the Directorate of Health introduced thrombolysis frequency for brain infarction as a «national quality indicator» (7).

The low and disparate figures have a number of explanations. The patients may be unfamiliar with the symptoms of stroke, or else they delay raising the alarm, the A&E centres and the medical emergency centres may give varying priorities to calls, and the geographic and demographic characteristics of this country render it difficult to provide timely cause-oriented treatment. A decentralised hospital structure with a variable intramural skills profile contributes to the variations in the provision of treatment.

Pre-hospital stroke treatment

To obtain a real clinical benefit from active re-canalisation in the case of a brain infarction, the first 90 minutes are crucial (5). The number needed to treat (NNT) to achieve one improved outcome after treatment with intravenous recombinant human tissue plasminogen activator (r-tPA, alteplase) has been reported to be < 4 within 90 minutes, but as many as 45 after 271–360 minutes (5).

Pre-hospital thrombolytic treatment of heart infarction was introduced in Norway in the early 1990s (8). In the same way, use should be made of the pre-hospital space for diagnostics, high-quality triage and cause-oriented treatment for cases of stroke. Although the pathogenesis is near-identical for heart and brain infarctions, there are some material diagnostic and therapeutic differences indicating that the experience from the 1990s is not directly transferable. Pre-hospital treatment of cerebral ischaemia is wholly dependent on a precise diagnostic differentiation with regard to the nature of the cerebral haemorrhage. Furthermore, in the case of an acute cerebral ischaemia it must be clarified whether this involves a proximal or a distal arterial occlusion in order to select those that should be treated with invasive techniques.

Even though the further development of today's diagnostic tools is based on the premise that stroke treatment takes place in-hospital, research and development efforts are underway in the field of pre-hospital diagnostics on the basis of biomarkers (9), microwaves (10), infrascanning (11) and ultrasound (12). This notwithstanding, diagnostics on the basis of brain scans has the largest potential at the pre-hospital stage. Walters and collaborators have shown that in an area with a short distance to a hospital, the time from the onset of symptoms to thrombolytic treatment can be reduced to < 90 minutes with the aid of an ambulance equipped with a CT scanner and staffed by a neurologist and a neuroradiologist (13). In comparison, rapid transport to a stroke unit for diagnostics and thrombolytic treatment required > 150 minutes. Moreover, it was shown that not only the stroke patients, but all the patients examined were faster and more correctly triaged, resulting in faster specific cause-oriented treatment (13, 14).

It is difficult to envisage that ambulances staffed by neurologists and neuroradiolo-

gists may be possible in Norway. In addition, a ground-based mobile stroke unit will have a limited operative range. The German project clearly demonstrated, however, that telemedical transfer of CT images for parallel diagnostics undertaken in the stroke unit of a hospital is possible (13).

In Norway, we have a well-developed air ambulance service staffed by anaesthesiologists, who with adequate diagnostic tools and with the aid of intravenous thrombolytic drugs will be able to minimise the time from the onset of symptoms to cause-oriented treatment for a large number of stroke patients. This presupposes telemedical diagnostic support from a neurological and neuroradiological medical institution and good procedures for triage of patients for intervention treatment or neurosurgery. The air ambulance has a maximum response time (time from alarm to take-off) of 15 minutes, and can reach the majority of the population in 30 minutes. With a quick alert, it will be realistic to initiate thrombolytic treatment and/or transport of the patient directly to invasive treatment within 90 minutes from the onset of the illness.

Norwegian Air Ambulance Foundation (SNLA) is engaged in the adaptation of a CT scanner to the current air ambulance fleet, and is preparing procedures for pre-hospital cause-oriented stroke treatment. Furthermore, a multi-centre study of pre-hospital diagnostics and thrombolytic treatment of stroke is being planned. This study will make use of ground-based CT-equipped ambulances staffed by an anaesthesiologist and a specialist nurse. The study is part of a comprehensive European research collaboration.

In the case of a stroke, the *time* elapsing

before initiation of cause-oriented treatment is completely crucial for the outcome. In provision of treatment the concern for *time* must take precedence over the concern for hospital organisation. By including the pre-hospital space in the chain of treatment, the ambitions of the Minister of Health can be raised considerably – for the benefit of the stroke patient.

Hans Morten Lossius

hans.morten.lossius@norskluftambulanse.no

Christian Georg Lund

Hans Morten Lossius (born 1959) is a Specialist in Anaesthesiology and Professor of Pre-Hospital Critical Care at the University of Stavanger. He heads the R&D division of the Norwegian Air Ambulance Foundation.

The author has completed the ICMJE form and declares no conflicts of interest.

Christian Georg Lund (born 1961) is an MD, PhD, a Specialist in Neurology at the Department of Neurology, Oslo University Hospital Rikshospitalet. In recent years, he has been especially engaged in introducing active revascularisation in cases of acute brain infarction. The author has completed the ICMJE form and declares no conflicts of interest.

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