

Treatment of cerebral infarction at the stroke unit in Bodø 2011–12

BACKGROUND The regional health enterprises wish to increase the proportion of cerebral infarction patients who receive intravenous thrombolytic therapy. We have identified the reasons why only very few patients received such treatment during 2011–12. We also wished to assess the benefits of ECG telemetry in the examination of the patients.

MATERIAL AND METHOD With permission from the enterprise's own data protection officer, we analysed data for all patients discharged from the stroke unit at the Department of Neurology, Nordland Hospital, after a cerebral infarction (diagnostic code I63) in the period from 1 January 2011 to 30 April 2012.

RESULTS Of a total of 180 patients admitted directly to the stroke unit, only 12 (6.7%) received intravenous thrombolytic therapy. The main reasons why such treatment was not provided include late arrival at the hospital ($n = 91$: 50%) and an unknown time of symptom onset ($n = 60$: 33%). ECG telemetry detected atrial fibrillation in 27 of the 112 patients examined (24%), which meant that anticoagulation treatment was provided to 22 patients who otherwise would have received platelet inhibitors.

INTERPRETATION Half of all patients with cerebral infarction arrived in the hospital too late for provision of intravenous thrombolytic therapy, and in one-third the time of onset could not be determined. In many patients, ECG telemetry led to changes in the choice of secondary prophylaxis.

Next to myocardial infarction and cancer, stroke is the most common cause of illness and death in Norway and other Western countries. Treatment of stroke is therefore a prioritised area for the health authorities. In 2010, the Norwegian Directorate of Health published *National guidelines for treatment and rehabilitation of stroke* (1). Cerebral infarctions account for nearly 85% of all cases of stroke (2).

Meta-analyses based on randomised studies have shown that the clearly most effective measure regarding stroke is to organise the treatment in dedicated stroke units (3). The most effective emergency measure in the case of stroke is early intravenous thrombolytic therapy (4). Despite the documented evidence regarding effect and the widespread attention devoted to such treatment, it is still administered to only very few patients. In its programme, Northern Norway Regional Health Authority has committed itself to increasing this proportion. We therefore wished to identify the reasons why so many patients in our hospital fail to be provided with intravenous thrombolytic therapy. We also wished to assess the benefits of ECG telemetry as a method for detecting periodic arrhythmias that have a bearing on the secondary prophylaxis.

Material and method

The stroke unit at Nordland Hospital, Bodø, is part of the Department of Neurology. Intravenous thrombolytic therapy was intro-

duced in the department in 2003, and significant efforts have been devoted to internal logistics in order to minimise the time spent after the patient has arrived in the hospital (abbreviated «door-to-needle» time).

After having obtained permission from the enterprise's data protection officer, we analysed data for all patients discharged from the department with a cerebral infarction as the main or secondary diagnosis during the period 1 January 2011–30 April 2012. Reports from the hospital's administrative system for patient data (DIPS) were retrieved to identify patients discharged with the diagnoses I63 (cerebral infarction) and I64 (unspecified stroke) in the ICD-10 system. We excluded patients who had been relocated from other hospitals.

We registered the time interval from the onset of symptoms to arrival in hospital, time of admission, whether intravenous thrombolytic therapy had been administered and the reasons why such treatment had not been provided to certain patients. The time of symptom onset was not known for all patients. Some had awoken with symptoms of a stroke, and these were classified as a separate group. Others had been found in a disoriented state, most often at home, with clinical symptoms consistent with a stroke. We categorised these as a separate group, along with patients whose journal did not report the time of onset, generally because the patients failed to recall it. The neurological consequences of the stroke were quantified

Rolf Salvesen

rolf.salvesen@nlsh.no
Department of Neurology
Nordland Hospital Trust

Guttorm Eldøen

Department of Neurology
Molde Hospital Trust

MAIN MESSAGE

The main reasons why intravenous thrombolytic treatment was not administered to patients admitted to the stroke unit in Bodø with a cerebral infarction were late arrival at the hospital and an unclear time of symptom onset.

In many patients, ECG telemetry led to changes in the choice of secondary prophylaxis.

with the aid of NIHSS scores (National Institute of Health Stroke Scale), in which 0 means no neurological findings, while ≥ 20 indicates a very severe stroke.

We also registered and analysed data from long-term recordings of cardiac rhythm and checked whether the patients received anticoagulation treatment as secondary prophylaxis. Some patients had been admitted to other hospitals between their initial admission and final discharge (relocations). Such split admissions were counted as single admissions.

Results

During the period of study, 242 patients were discharged from the stroke unit with acute cerebral infarction as their main diagnosis (163). None were registered with the diagnosis unspecified stroke (164). Of these 242, altogether 180 had been admitted directly to the stroke unit, while 62 had been relocated from other hospitals. This analysis includes those 180 patients who had been directly admitted to the stroke unit. Of these, 175 patients were resident in the Salten district, three were foreign citizens and two were resident in other municipalities in Nordland county. Men accounted for 59% of the patients. Average age was 72.7 years – for men 70.4 years (range: 39–96 years) and for women 75.5 years (48–95 years). Five patients died during their hospitalisation.

Altogether 96 patients (53%) were admitted between 8 a.m. and 4 p.m. and 14 patients (8%) between midnight and 8 a.m. Table 1 shows the distribution of patients with regard to the time interval from the onset of symptoms to admission. A total of 29 patients were admitted within four hours of the onset of symptoms.

Intravenous thrombolytic therapy

12 patients with cerebral infarction out of a total of 29 who were admitted within the possible time window received intravenous thrombolytic therapy. Before their treatment, these had NIHSS scores ranging from 2 to 23 – five had a score of 2–5, two had a score of 7–8, four had a score of 13–17 and one had a score of 23.

The reasons why intravenous thrombolytic therapy was not administered were the too long interval between the onset of symptoms and the arrival in hospital ($n = 91$), unknown time of onset of symptoms ($n = 35$) and that the patient had awoken with symptoms of a stroke ($n = 25$). As regards the 17 patients who did not receive thrombolytic therapy in spite of being within the time window, five were in spontaneous recovery, four were treated with anti-coagulants, three had CT findings deemed to be contraindications, and two had minor neurological outcomes. (NIHSS = 1) (Table 2).

Cardiac rhythm diagnostics

Atrial fibrillation was known in advance or detected by ECG upon admission in 24 patients. ECG telemetry was undertaken in 112 of the 175 patients who were discharged alive (64%). Telemetry findings led to anticoagulation therapy being administered to 22 patients.

A total of 51 patients (29%) were discharged with a diagnosis of atrial fibrillation (in 27 of them this was detected by telemetry), of whom 37 with anticoagulation therapy. Of those who did not receive such treatment, four suffered from an existing or previous severe haemorrhage, four suffered from dementia and four had major stroke sequelae with an NIHSS score ranging from 17 to 23.

Anticoagulation therapy

Of 175 patients discharged alive, 48 (27%) received anticoagulation therapy at the time of discharge. In 11 of these patients no atrial fibrillation had been detected. Four had suffered a deep vein thrombosis and/or a pulmonary embolism, in two patients echocardiography findings indicated such treatment, two had a known left-ventricle aneurysm and in the three remaining patients other causes were detected (known valve disorder, mechanical heart valve, pulmonary arteriovenous malformation).

Discussion

As a general goal, whenever there is a suspicion of a stroke, the patient should be admitted to a stroke unit in a hospital as soon as possible after the onset of symptoms (1). To be able to receive intravenous thrombolytic therapy, the patient must be admitted no later than four hours after the first symptom has occurred. In our group of patients, this precondition was met by approximately every sixth patient.

Approximately every fifth patient had been found with signs of a stroke, or there were other reasons why the time of the first symptom could not be determined. Almost as many had awoken with symptoms or signs of a stroke. These two groups, which accounted for approximately one-third of the patients, were not provided with thrombolytic therapy since the symptoms might have persisted for so long that the treatment would have been associated with an excessive risk of complications.

If modern diagnostics using perfusion CT or advanced MRI methods can provide a definite estimate of the presence of a penumbra zone (an area of the brain with critically reduced perfusion, but in which the nerve cells remain intact) which can be saved with the aid of revascularisation, a larger number of patients in this group could be provided with thrombolytic therapy. Herein lies a potential for increasing the number of patients treated.

Table 1 Time from symptom onset to admission to hospital for 180 patients admitted to the Stroke Unit, Nordland Hospital, Bodø, in the period 1 January 2011–30 April 2012.

Time from symptom onset to admission	Number	(%)
0–4 hours	29	(16%)
4–8 hours	13	(7%)
8–24 hours	13	(7%)
> 24 hours	65	(36%)
Unclear time of onset or found with signs of stroke	35	(19%)
Awoke with symptoms	25	(14%)
Total	180	(100%)

Table 2 Number of patients provided with intravenous thrombolytic therapy and the reasons why such treatment was not provided in patients admitted to the Stroke Unit, Nordland Hospital, Bodø, within four hours of symptom onset.

	Number
Intravenous thrombolytic therapy	12
No intravenous thrombolytic therapy provided	17
Under recovery in the emergency ward	5
Anti-coagulation therapy	4
Pathological CT findings	3
Minor neurological findings	2
Poor general condition	1
Uncertain early diagnosis	1
Poor logistics	1

Intravenous thrombolytic therapy

Approximately 7% of the patients were provided with intravenous thrombolytic therapy. This is far lower than current professional and health-policy ambitions. The clearly most important reason for this small proportion is that the patient arrived in the hospital too late for such treatment to be provided, whereas in several other patients the time of symptom onset was unclear, or the patient had awoken with symptoms of stroke. Poor intra-hospital logistics were the reason in only one patient, who had been admitted to another department and was not assessed quickly enough.

In seven patients we refrained from providing intravenous thrombolytic therapy because the patient was in recovery or had only minor neurological findings. Because stroke symptoms tend to fluctuate at the most acute stage, opinions differ regarding the treatment of such patients. In Sweden, the proportion of patients with a «minor stroke» (an NIHSS score of 5 or less) who received thrombolytic therapy increased from 22 % in 2007 to nearly 29 % in 2010 (5). In our group of patients, five had an NIHSS score of 5 or less. Hospitals in which a high proportion of the patients were provided with intravenous thrombolytic therapy were also more liberal in their treatment of mild strokes.

A Swiss study found that intravenous thrombolytic therapy had the best effect in patients with minor and moderate stroke (6). On the other hand, Huisa and collaborators found that a good clinical result 90 days after minor strokes (an NIHSS score of 5 or less) did not occur more frequently in the group that had been provided with intravenous thrombolytic therapy than in the group that had not been given such treatment (7). In the IST-3 study, in which 612 patients with a cerebral infarction were randomised, the effect of intravenous thrombolytic therapy was uncertain for an NIHSS score of 0–5 and poorer for an NIHSS score of 6–24 (8).

The current tendency seems to be towards treating more patients with minor outcomes. In our study, patients who were recovering, but still had a tangible findings, were as a rule not provided with intravenous thrombolytic therapy. It is a general experience that many patients who have a fluctuating status at the acute stage will end up with significant outcomes, and there are many reasons to question this practice.

From Oslo University Hospital Ullevål, it is reported that in 2010 more than 20 % of all patients with a cerebral infarction were provided with «reperfusion therapy» (9), which is a very high number in any context. This is a selected group of patients, because stroke patients in other local hospitals in Oslo were only rarely provided with intravenous thrombolytic therapy, as relevant candidates are mainly relocated to Ullevål Hospital.

Approximately 14 % of our cerebral infarction patients had awoken with symptoms. This concurs with other studies, in which the proportion ranges from 8 % to 28 %. A large population-based study undertaken in the USA also found that approximately 14 % of the patients had awoken with symptoms of stroke (10). In our department, we have undertaken perfusion CT in selected patients since 2003. In a recently published patient series from Spain, 29 patients in whom the perfusion CT indicated the presence of a penumbra zone were provided with intra-

venous thrombolytic therapy without an approved indication, mostly because of an unknown or too early symptom onset. The results and the risk of haemorrhage were approximately identical to those in other studies of intravenous thrombolytic therapy (11). No randomised studies are available. With regard to this group of patients, it is reasonable to expect that the treatment strategy will change in the near future.

Anti-coagulation therapy

Our goal is that all patients with a cerebral infarction or TIA with no known atrial fibrillation or another known indication for anti-coagulation therapy should be examined with the aid of long-term telemetric registration of their heart rhythm. The reasons why this examination was foregone in some patients included absence of any therapeutic consequence or insufficient capacity, since the stroke unit only had telemetric equipment for one patient at its disposal during this period. The capacity has since been doubled.

Atrial fibrillation was detected in approximately one in four patients. Nearly every fifth patients had their secondary prophylaxis changed from platelet inhibitors to anti-coagulation therapy after findings made by ECG telemetry, which accordingly is an examination with potential therapeutic consequences. Most likely, the proportion of patients who have their secondary prophylaxis changed will be even larger after long-term monitoring and with a structured analysis algorithm for telemetric data (12). A German study found that the most likely cause of approximately 30 % of all first-time cerebral infarctions is cardiac embolism, and that one-third of these are related to atrial fibrillation which was unknown prior to hospitalisation in the stroke unit (13).

Approximately 27 % of the patients were discharged with anti-coagulation therapy, in most cases because of atrial fibrillation. It is far from obvious that all cerebral infarctions in patients with paroxysmal atrial fibrillation are caused by cardiac embolism, for example in the case of lacunar infarctions. Most professional communities agree, however, that anti-coagulation therapy is more effective than platelet inhibitors as prophylaxis in patients with atrial fibrillation and a CHA₂DS₂-VASc score of at least 2 (this score is used to assess the risk of a new ischemic event) (13). Atrial fibrillation with an associated need for anti-coagulation therapy is particularly common among older patients (14). Some of our patients in this group were not provided with anti-coagulation therapy, most frequently because of an existing or a previous haemorrhage, major stroke sequelae, dementia or advanced age.

Conclusion

Only 6.7 % of all patients admitted to the stroke unit at Nordland Hospital with a cerebral infarction during 2011–12 were provided with intravenous thrombolytic therapy. The most common reasons for not providing such treatment included too late arrival in the hospital and an unclear time of symptom onset. Atrial fibrillation was detected with the aid of ECG telemetry in nearly one-fourth of those examined, which caused a change of secondary prophylaxis in approximately one-fifth of the patients examined.

Rolf Salvesen (born 1952)

is a specialist in neurology, Senior Consultant and Professor II at the Department of Clinical Medicine, University of Tromsø.

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

Guttorm Eldøen (born 1951)

is a specialist in neurology and otorhinolaryngology and Senior Consultant.

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

References

1. HelseDirektoratet. Nasjonal retningslinje for behandling og rehabilitering ved hjerneslag. 04/2010. IS-1688. www.helseDirektoratet.no (3.6.2013).
2. Feigin VL, Lawes CM, Bennett DA et al. Stroke epidemiology: a review of population-based studies of incidence, prevalence, and case-fatality in the late 20th century. *Lancet Neurol* 2003; 2: 43–53.
3. Stroke Unit Trialists' Collaboration. Organised inpatient (stroke unit) care for stroke. *Cochrane Database Syst Rev* 2007; 4: CD000197.
4. Lees KR, Bluhmki E, von Kummer R et al. Time to treatment with intravenous alteplase and outcome in stroke: an updated pooled analysis of ECASS, ATLANTIS, NINDS, and EPITHET trials. *Lancet* 2010; 375: 1695–703.
5. Stecksén A, Asplund K, Appelros P et al. Thrombolytic therapy rates and stroke severity: an analysis of data from the Swedish stroke register (Riks-Stroke) 2007–2010. *Stroke* 2012; 43: 536–8.
6. Ntaios G, Faouzi M, Michel P. The effect of thrombolysis on short-term improvement depends on initial stroke severity. *J Neurol* 2012; 259: 524–9.
7. Huisa BN, Raman R, Neil W et al. Intravenous tissue plasminogen activator for patients with minor ischemic stroke. *J Stroke Cerebrovasc Dis* 2012; 21: 732–6.
8. Sandercock P, Wardlaw JM, Lindley RI et al. The benefits and harms of intravenous thrombolysis with recombinant tissue plasminogen activator within 6 h of acute ischaemic stroke (the third international stroke trial [IST-3]): a randomised controlled trial. *Lancet* 2012; 379: 2352–63.
9. Reichenbach AS. Tverrfaglig behandling ved hjerneslag. *Tidsskr Nor Legeforen* 2011; 131: 2220.
10. Mackey J, Kleindorfer D, Sucharew H et al. Population-based study of wake-up strokes. *Neurology* 2011; 76: 1662–7.
11. Cortijo E, Calleja AI, Garcia-Bermejo P et al. Perfusion computed tomography makes it possible to overcome important SITS-MOST exclusion criteria for the endovenous thrombolysis of cerebral infarction. *Rev Neurol* 2012; 54: 271–6.

>>>

12. Kallmünzer B, Breuer L, Hering C et al. A structured reading algorithm improves telemetric detection of atrial fibrillation after acute ischemic stroke. *Stroke* 2012; 43: 994–9.
13. Palm F, Kleemann T, Dos Santos M et al. Stroke due to atrial fibrillation in a population-based stroke registry (Ludwigshafen Stroke Study) CHADS(2), CHA(2) DS(2) -VAsc score, underuse of oral anticoagulation, and implications for preventive measures. *Eur J Neurol* 2013; 20: 117–23.
14. Gur AY, Tanne D, Bornstein NM et al. Stroke in the very elderly: characteristics and outcome in patients aged ≥ 85 years with a first-ever ischemic stroke. *Neuroepidemiology* 2012; 39: 57–62.

Received 17 December 2012, first revision submitted 27 March 2013, approved 3 June 2013. Medical editor: Petter Gjersvik.