Higher Prehospital Priority Level of Stroke Improves Thrombolysis Frequency and Time to Stroke Unit

The Hyper Acute SStroke Alarm (HASTA) Study

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Background and Purpose—Early initiated treatment of stroke increases the chances of a good recovery. This randomized controlled study evaluates how an increased priority level for patients with stroke, from level 2 to 1, from the Emergency Medical Communication Center influences thrombolysis frequency, time to stroke unit, and whether other medical emergencies reported negative consequences.

Methods—Patients aged 18 to 85 years in Stockholm, Sweden, with symptoms of stroke within 6 hours were randomized from the Emergency Medical Communication Center or emergency medical services to an intervention group, priority level 1, immediate call of an ambulance, or to a control group with standard priority level, that is, priority level 2 (within 30 minutes). Before study start, an educational program on identification of stroke and importance of early initiated treatment was directed to all medical dispatchers and ambulance and emergency department personnel.

Results—During 2008, 942 patients were randomized of which 53% (n = 496) had a final stroke/transient ischemic attack diagnosis. Patients in the Emergency Medical Communication Center randomized intervention group reached the stroke unit 26 minutes earlier than the control group (P < 0.001) after the emergency call. Thrombolysis was given to 24% of the patients in the intervention group compared with 10% of the control subjects (P < 0.001). The higher priority level showed no negative effect on other critical ill patients requiring priority level 1 prehospital attention.

Conclusion—This randomized study shows negligible harm to other medical emergencies, a significant increase in thrombolysis frequency, and a shorter time to the stroke unit for patients with stroke upgraded to priority level 1 from the Emergency Medical Communication Center and through the acute chain of stroke care. (Stroke. 2012;43:2666-2670.)

Key Words: acute care ■ acute stroke ■ emergency medical service ■ organized stroke care ■ RCT thrombolysis ■ stroke unit

A cute treatment may limit the detrimental effects of an ischemic stroke in patients presenting at the hospital early after symptom onset.1-5 The earlier the treatment is started, the better the chance of a positive result.2 Hence, it is crucial that patients arrive as early as possible to the hospital to enable optimal treatment at arrival. Moreover, arriving at the hospital by ambulance with early prenotification to the emergency department (ED) has been shown to increase the chance of receiving thrombolyis.6-8 At the Emergency Medical Communication Center (EMCC), a life-threatening condition is responded to as a priority level 1, an immediate ambulance and prenotification to the ED. At the EMCC in Stockholm, Sweden, in 2008, like in other parts of Sweden still in 2011, acute stroke was prioritized as level 2, that is, ambulance arrival at scene within 30 minutes unless no priority 1 alarms required that ambulance. The priority could be increased at the scene if stroke within 3 hours were suspected, because at the time of the study, in 2008, thrombolytic therapy was given within 3 hours of stroke onset.2 Each year, approximately 5500 patients in the Stockholm area have a stroke/transient ischemic attack. The operative argument against upgrading the priority of all suspected

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stroke was a concern that such a large patient group may obstruct emergency medical service (EMS) for patients with other life-threatening conditions. This study was performed to clarify if an upgrade in priority level from the EMCC and further through the acute chain of care for patients with suspected stroke within 6 hours would result in (1) unproportional interference with medical safety of other prioritized transports; (2) more patients arriving to a stroke unit (SU) within the first 6 hours after stroke onset; and (3) a higher proportion of patients with ischemic stroke given thrombolysis.

Methods
The study was performed in Stockholm county (2 million inhabitants), Sweden, in 2008 and involved the EMCC, EMS, ED, and all SUs in the 7 emergency hospitals within the area. Nurses answered the calls to the EMCC and evaluated the need of care and all ambulances were manned by nurses. Meetings and education of the EMCC, EMS, and ED personnel preceded the start of the study. The study randomized all patients to an upgraded priority (“intervention,” priority level 1) or standard priority (“control,” priority level 2). The inclusion and randomization of the patients was performed by the EMCC, EMS, and ED personel preceded the start of the study. The study randomized all patients to an upgraded priority (“intervention,” priority level 1) or standard priority (“control,” priority level 2). The inclusion and randomization of the patients was performed by the EMCC and the Face–Arm–Speech–Time (FAST) test was used as a tool of identification. All calls interpreted by the EMCC nurse to concern patients with suspected stroke were checked against the criteria for the study, that is, suspected stroke with symptom onset within 6 hours; age between 18 and 85 years; previous independence in activities of daily living; and no other acute condition requiring a priority level 1. The medical dispatchers obtained sealed envelopes containing randomized group information. Inclusion at scene by the EMS was allowed in patients in whom stroke had not initially been suspected by the EMCC (Figure 1).

After admission to the ED, patients randomized to the control group were treated according to routine unless meeting criteria for thrombolysis. In such cases, they were treated as fast as possible and rushed to the SU. However, patients randomized to the intervention group were, regardless of whether meeting thrombolysis criteria or not, prioritized by the hospital personnel for fast admission to the SU. No other differences in the care of the patients were made. Interim analysis was scheduled in the study protocol to identify any unproportional interference with other medical needs. This was made through a review of reported incidences to the EMCC.

Power
The sample needed to detect a difference between the groups was calculated using the Altman’s nomogram for sample size. On a significance level of 0.05 with a power of 80%, it was estimated that 600 patients were required to detect a 10% difference in arrival to SU within 6 hours and 1800 patients to detect a 50% increase in thrombolytic therapy (from 50–75 patients yearly during 2 years) between the groups. However, the study was prematurely stopped when the interim analysis showed no negative effects for other emergency patients, resulting in an increased priority level of standard care for acute stroke in the county.

Statistics and Data Analysis
Data were analyzed with PASW Statistics, Version 18 (IBM Corporation, Somer, NY) and significance level set to 5%, 2-sided. The continuous variables obtained had a nonnormal distribution; thus, to test for significance, the Mann-Whitney test was used. For categorical data, the χ² and Fisher exact test were used to test significance.

The results of thrombolysis and SU care, only relevant for included patients with an actual diagnosis of stroke or transient ischemic attack, were analyzed separately for these patients. Stroke was classified as International Classification of Diseases codes I61, hemorrhagic stroke; I63, ischemic stroke; or I64, unspecified stroke.

Interim analysis was scheduled in the study protocol to identify any unproportional interference with other medical needs. This was made through logistic regression was used for categorical data, and analysis of variance for continuous data.

The study was approved from the Regional Ethical Review Board (EPN: 2008/383-31/4) without need of consent from the participating patients.

Results
Inclusion started May 19, 2008, and closed November 15, 2008, when an interim analysis revealed no case of interference with other medical needs since initiation of recruitment. During the 6 months, 942 patients were randomized to either the intervention group (n=488) or to the control group (n=454).

Demographics
A majority of the patients, 56% (n=523), were men. The median age was 71 years (range, 22–93 years). EMCC randomized 71% (n=667) of the patients. EMS randomized 25% (n=233) of the patients for whom intervention started when the ambulance unit was at scene (Figure 1). In 4% (n=42), data were missing.

Timeframe
For patients randomized by the EMS, no significant differences in delay between intervention and control groups were observed (Table). In contrast, those randomized by the EMCC to intervention had significantly faster pass through the chain of care both pre- and in-hospital (Table) with a 13-minute shorter delay between call and arrival at the hospital (median time; P<0.001), 3-minute shorter delay between call and dispatch (P<0.001), and 6-minute shorter to ambulance arrival at the scene (P<0.001).

The in-hospital time, from the ED to the SU, was 20 minutes faster in the EMCC intervention group (P=0.010). For patients receiving thrombolysis, door-to-needle time did not differ significantly between the intervention and control
groups, \( P = 0.751 \) and \( P = 0.086 \) in the EMCC and EMS randomized groups, respectively.

### Final Diagnosis, Thrombolysis Frequency, and Time to SU

Almost half of the patients, 47\% (\( n = 446 \)), were discharged from the hospital with a nonstroke diagnosis, 34\% (\( n = 316 \)) diagnosed as ischemic stroke, 5\% (\( n = 46 \)) as hemorrhagic stroke, and 14\% (\( n = 134 \)) as transient ischemic attack.

A majority of the patients in the study, 84\% (\( n = 686 \)), arrived at the hospital within 3 hours from onset and there was no difference between patients in the intervention and control groups (\( P = 1.000 \)).

Thrombolysis was given to 24\% (\( n = 60 \)) of the patients in the intervention group compared with 10\% (\( n = 24 \)) in the control group (\( P < 0.001 \); Figure 2). Seventy-one percent of all patients with a stroke/transient ischemic attack diagnosis at discharge were treated in a SU and of these, 88\% and 85\% in the intervention and control groups, respectively, arrived there within 6 hours of symptom onset (\( P = 0.423 \)). In the intervention group, a higher proportion of patients arrived at the SU within 3 hours from onset, 61\% compared with 46\% (\( P = 0.008 \)) in the control group.

### Sex Aspects

Slightly more men were included in the study, 56\%. The mean age was 70 and 73 years for men and women, respectively. No significant differences in relation to sex were found when analysis was done in the intervention and control groups, respectively, and no interaction based on sex could be found.

### Discussion

This study shows a significant increase in thrombolysis frequency and a shorter time from call to arrival at SU for patients with stroke if the EMCC priority level for patients with suspected stroke is upgraded to priority level 1 and kept through the acute chain of care.

Although 84\% of all patients arrived at the hospital within 3 hours, the time limit for thrombolysis at the time of the

<table>
<thead>
<tr>
<th>Table. Times (min) in the Chain of Care From Symptoms to Stroke Unit</th>
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<tbody>
<tr>
<td><strong>EMCC randomized</strong></td>
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<tr>
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</tr>
<tr>
<td>EMS–call to dispatch</td>
</tr>
<tr>
<td>324 5 0–72 4/7 327 8 0–75 5/14 ( P = 0.001 )</td>
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<tr>
<td>Ambulance–dispatch to arrival at scene</td>
</tr>
<tr>
<td>324 9 0–74 7/13 318 15 0–51 9/22 ( P = 0.001 )</td>
</tr>
<tr>
<td>Ambulance–at scene</td>
</tr>
<tr>
<td>315 14 0–67 10/18 315 13 0–42 9/18 ( P = 0.270 )</td>
</tr>
<tr>
<td>Ambulance–scene departure to hospital</td>
</tr>
<tr>
<td>313 12 0–75 8/18 313 14 0–58 9/20 ( P = 0.013 )</td>
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<tr>
<td>Prehospital–call to hospital</td>
</tr>
<tr>
<td>308 42 17–155 35/51 310 55 10–123 44/68 ( P = 0.001 )</td>
</tr>
<tr>
<td>Hospital–hospital to thrombolysis</td>
</tr>
<tr>
<td>36 58 25–124 46/77 16 57 40–128 48/79 ( P = 0.751 )</td>
</tr>
<tr>
<td>Hospital–hospital to stroke unit</td>
</tr>
<tr>
<td>132 60 15–472 40/106 116 80 11–398 49/121 ( P = 0.010 )</td>
</tr>
<tr>
<td>Stroke chain–call to stroke unit</td>
</tr>
<tr>
<td>129 106 38–527 82/155 116 132 58–458 105/192 ( P = 0.001 )</td>
</tr>
<tr>
<td><strong>EMS randomized</strong></td>
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<tr>
<td>EMS–call to dispatch</td>
</tr>
<tr>
<td>118 5 0–27 2/9 79 5 0–47 3/8 ( P = 0.954 )</td>
</tr>
<tr>
<td>Ambulance–dispatch to arrival at scene</td>
</tr>
<tr>
<td>137 10 0–52 6/17 95 12 0–29 7/17 ( P = 0.581 )</td>
</tr>
<tr>
<td>Ambulance–at scene</td>
</tr>
<tr>
<td>138 17 0–42 9/18 93 16 2–55 12/21 ( P = 0.261 )</td>
</tr>
<tr>
<td>Ambulance–scene departure to hospital</td>
</tr>
<tr>
<td>138 11 0–65 7/20 93 11 0–42 6/15 ( P = 0.128 )</td>
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<tr>
<td>Prehospital–call to hospital</td>
</tr>
<tr>
<td>118 48 21–115 36/65 77 45 20–119 36/56 ( P = 0.081 )</td>
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<tr>
<td>Hospital–hospital to thrombolysis</td>
</tr>
<tr>
<td>23 57 35–206 52/64 8 49 30–68 40/58 ( P = 0.086 )</td>
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<tr>
<td>Hospital–hospital to stroke unit</td>
</tr>
<tr>
<td>73 58 0–412 40/95 50 81 15–452 45/148 ( P = 0.144 )</td>
</tr>
<tr>
<td>Stroke chain–call to stroke unit</td>
</tr>
<tr>
<td>65 117 59–270 93/161 39 122 58–521 89/210 ( P = 0.282 )</td>
</tr>
</tbody>
</table>

EMCC indicates Emergency Medical Communication Center; EMS, emergency medical services.

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**Figure 2.** Frequency for arriving to the hospital \( >3 \) hours, SU \( <3 \) and \( 6 \) hours, and thrombolytic treatment for patients with final diagnose of stroke/transient ischemic attack. SU indicates stroke unit; TIA, transient ischemic attack.
study, the intervention group had a significantly higher thrombolysis frequency. The proportion of patients arriving to the ED within 2 hours of stroke onset has been reported to be 15% to 18%.11,12 It has been estimated from The Netherlands that 24% of all patients with stroke, instead of the 7% actually treated, would be possible to treat with thrombolysis within 3 hours if delay was avoided.13

Compared with the previous thrombolysis frequency in Stockholm, 4% in 2007,14 there was an increase in both groups. However, the patients with stroke with the highest priority level from the EMCC were more than twice as likely to receive thrombolysis, 24% compared with 10% in the control group. It is difficult to compare the present results with historical data because of the limitations of age (18–85 years) and time window (<6 hours) in Hyper Acute Stroke Alarm (HASTA), but we believe that the increase in thrombolysis frequency in both groups may be due to the extensive education before the study start and the focus on stroke as a result of the study. Patients in the control group identified as possible thrombolysis candidates were upgraded to priority level 1 although remaining in the control group. The priority level did not affect the door-to-needle time for thrombolysis, indicating that other actions need to be taken to cut that delay. The fact that the intervention group arrived earlier to the SU may be one reason for the differences in thrombolytic frequencies. Standard care was given to all patients according to guidelines but several of the participating hospitals had a much higher stroke competence at the SU than at the ED and may have re-evaluated the intervention group earlier, thus making thrombolysis still an option.

Interestingly, the in-hospital time reduction was even greater than the prehospital. In standard care, the priority is re-evaluated and often decreased in the ED when thrombolysis is not indicated, which results in a longer stay in the ED. In the intervention group, the initially given priority level was kept all the way to the SU. The lack of significant differences in in-hospital delay for the EMS randomized group could be an effect of the relatively small number of patients.

SU care is associated with a better outcome and is recommended for patients with stroke of all ages and both sexes.15 Despite this, only 65% of the patients with stroke in Stockholm were initially treated in a SU in 2006 and 74% were treated in a SU at some time during the acute hospitalization.14 In a study from the United Kingdom, the level of SU care has been similar, 78%,16 and the level of SU care in Sweden spanned between 55% and 88% in 2009.14

Approximately half of the randomized patients were diagnosed as a stroke/transient ischemic attack after in-hospital workup, which is in the same range as described in other studies.6,17,18 In this study, the EMCC and EMS were instructed to interpret a positive FAST score as a possible stroke, which may have led to “overdiagnosing” because the EMCC in an ordinary setting may have attributed some of the FAST symptoms to other conditions.

Like in most stroke studies with an upper age limit, a slightly higher proportion of men were included, which is expected because women are older at the time of stroke.14 Older patients were excluded from the study with the rational of not being thrombolysis candidates. This study showed no differences according to sex, which is in agreement with findings from Michigan where no sex differences concerning prehospital or in-hospital delay for patients arriving within 6 hours were found, although they found a longer in-hospital delay for women.19 In a review on sex differences in stroke from 2010, 2 studies were presented showing women to be less likely to receive thrombolysis, whereas 5 studies found no sex differences.20

Recruitment was prematurely terminated after a protocol-defined safety interim analysis at the EMCC. The analysis showed that no harm to other urgent medical needs had been reported and it was agreed that all patients with suspected stroke with onset within 6 hours should be a priority level 1 at the EMCC in Stockholm. Before the HASTA study, there was a concern that a higher priority level for patients with acute stroke would negatively affect other groups of patients requiring priority level 1 prehospital attention. The premature interruption of the study is a limitation because only half of the planned number of patients was recruited.

Conclusion
This randomized controlled study showed that a higher priority level from the EMCC influenced the entire acute stroke chain of care resulting in an increased thrombolysis frequency and faster arrival at the SU. The higher priority level did not interfere with other medical needs and for patients randomized to higher priority by EMCC, the thrombolysis frequency doubled.

Our results support a recommendation that patients with recent onset of stroke symptoms should have the highest priority level throughout the acute stroke chain of care.

Appendix

Scientific Committee of Fighting Stroke (Uppdrag Besegra Stroke)
Nils Wahlgren (chair), Niaz Ahmed, Maaret Castrén, Ulf Eriksson, Jonas Frisén, Ulf Hedlin, Staffan Holmin, Åke Sjöholm, Mikael Svensson, and Mia von Euler.

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Disclosures
None.
References

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