Stroke Severity Determines Body Temperature in Acute Stroke

Gudrun Boysen, MD, DMSc; Hanne Christensen, MD

**Background and Purpose**—Several studies have claimed that temperature on admission is of prognostic significance in acute stroke. Experimental studies showing that hyperthermia increases infarct size have lent credibility to this assumption. The aim of the present study was to test the hypothesis that initial body temperature is of importance for stroke outcome.

**Methods**—This prospective study included 725 consecutive patients, 584 with cerebral infarcts and 141 with intracerebral hemorrhages, admitted to an acute stroke unit within 6 hours of stroke onset. Time of stroke onset and time of admission were recorded. Body temperature was measured on admission and every 2 hours during the first 24 hours. Patients were divided into 2 groups on the basis of stroke severity on admission: Scandinavian Stroke Scale Score (SSS) ≤25 was defined as major stroke, and SSS >25 was defined as mild to moderate stroke.

**Results**—On admission, mean body temperature was normal. In the major stroke patients, body temperature started to rise 4 to 6 hours after stroke onset. At 10 to 12 hours after stroke onset, increased body temperature was found to be related to poor outcome. In mild to moderate stroke, there was no significant rise in temperature. Initial temperature >37.5°C was not related to stroke severity or stroke outcome.

**Conclusions**—In major stroke, a significant rise in temperature occurred hours after stroke onset. Severe infarcts and intracerebral hemorrhages caused temperature to rise, whereas initially increased temperature had no influence on stroke severity. Elevated body temperature on admission within 6 hours of stroke onset had no prognostic influence on stroke outcome at 3 months. *(Stroke. 2001;32:413-417.)*

**Key Words:** body temperature ▪ cerebral infarction ▪ hyperthermia ▪ intracerebral hemorrhage ▪ outcome

The prognostic influence of initial body temperature on acute stroke was recently the subject of a meta-analysis of 9 studies with 3790 patients.¹ From these data, Hajat et al¹ concluded that pyrexia after stroke onset was associated with a marked increase in morbidity and mortality. The exact time lag between stroke onset and temperature measurement was not well described in all studies.

The aims of the present study were to test the hypothesis that initial temperature is of significance for stroke outcome and to describe the time course of body temperature in acute stroke.

**Subjects and Methods**

This work is a prospective study based on 725 consecutive patients admitted to an acute stroke unit from its establishment in February 1998 to March 2000. The unit admits patients within 6 hours of stroke onset from a well-defined urban region comprising a population of 600,000 inhabitants. The patients were discharged to their own homes or, when in need of longer-term care, to stroke rehabilitation units on day 7. Risk factors and clinical and paraclinical findings were recorded on special forms by the attending doctors and nurses, and a clinical database was created from this material. Cerebral computerized tomography (CT) was performed and described routinely on admission with a Picker 5000. Early CT signs of stroke registered were early hypodensity, dense artery sign, focal cerebral edema, hemorrhagic transformation, and intracerebral hemorrhage. Follow-up was scheduled 3 months after stroke onset in the outpatient department or by telephone interview.

Aspirin 150 mg/d plus dipyridamole retarded formulation 400 mg/d was standard antiplatelet treatment after cerebral infarction in the unit starting after the CT scan. Anticoagulant treatment was prescribed in atrial fibrillation and, in some cases of stroke in progression, after individual consideration. No patients were treated with thrombolysis. Fifty-nine patients were included in randomized, placebo-controlled trials with either low-molecular-weight heparin or neuroprotective substances. So far, none of these treatments have shown beneficial effect. Neurological deficits were assessed with the Scandinavian Stroke Scale (SSS)² on admission and on days 2, 4, and 7.

Nurses assessed motor function and speech; reported vital values, including body temperature, every 2 hours for the first 24 hours and every 4 hours for the next 24 hours; and recorded the values on a special form. Vital values were registered within minutes of hospital arrival. Body temperature was measured as a tympanic temperature with First Temp Genius 3000A thermometers. The precision of this particular device has been validated in a number of studies, most of which found the thermometer accurate, reproducible, and highly correlated to pulmonary artery, esophageal, or rectal temperature.³⁻⁹ A Norwegian study reported that it was imprecise and generally gave too high readings,¹⁰ and one study concluded that the measured

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temperatures were generally too low compared with rectal temperatures. Patients with body temperature >37°C were treated with paracetamol 1 g; this treatment did not exclude any patients from this study.

The degree of handicap was assessed by the modified Rankin Scale (mRS) as a cutoff point because patients with lower scores were all nonambulant with other severe deficits. We called this group the major stroke group and because patients with lower scores were all nonambulant with other severe deficits on admission. SSS was missing in 111 patients. However, we obtained information on all patients as to whether they were alive or dead at 3 months.

The patients were divided into 2 groups on the basis of stroke severity on admission. SSS ≤25 was selected as a cutoff point because patients with lower scores were all nonambulant with other severe deficits. We called this group the major stroke group and those with SSS >25 the mild to moderate stroke group. Deteriorating stroke was defined as a deterioration of the neurological deficit of ≥2 points lasting >4 hours.

Statistical analysis was done with SPSS 9.0 for Windows. Non-parametric methods (Spearman’s ρ, Kolmogorov-Smirnov’s z test, multinomial logistic regression) were performed on ordinal scale data. Parametric methods (t test) were used for continuous data.

The Scientific-Ethical Committee found that the study was not of such a biomedical kind that it was within its coverage. The committee had no objections to the study or its conduct.

Results

Of the 725 stroke patients, 584 (median age, 76 years) had cerebral infarctions, and 141 (median age, 74 years) had intracerebral hemorrhages (Table 1). Patients were admitted early after stroke onset, 50% within 2 hours. In 35 patients (5.3% of patients with cerebral infarction, 5.0% of those with intracerebral hemorrhage), body temperature exceeded 37.5°C on admission. These patients did not differ as to age, stroke severity, stroke outcome, or stroke diagnosis (Table 2).

In 10 of these patients, a diagnosis of acute infection was made on admission; in 7, alcohol withdrawal symptoms were diagnosed; 2 patients died from cerebral herniation within hours of admission; and in 16 patients, body temperature decreased within hours, and no probable cause of the fever was found. Twelve of these patients were treated with paracetamol on admission.

In total, 316 patients (44%) were given ≥1 dose of paracetamol within 18 hours of stroke onset on this indication. One hundred fifty-nine patients (22%) had ≥1 temperature measurement exceeding 37°C without receiving paracetamol. In the group of patients with a peak temperature exceeding 37°C, we compared patients who actually received paracetamol with patients not receiving paracetamol and found that the peak temperature was higher in patients receiving paracetamol (37.6°C versus 37.4°C in patients not receiving paracetamol; P<0.001, t test). We also found that the mean temperature over the first 18 hours in patients receiving paracetamol was higher (36.9°C versus 36.7°C; P=0.002, t test). We found no differences as to age, stroke severity, or outcome.

In 88 patients, body temperature exceeded 38°C at some time point during the first 2 days. In 16% of these patients, clinical signs of infection required treatment with antibiotics within the first 2 days of stroke onset. Deteriorating stroke occurred in 19% of patients with infarctions and 43% of patients with intracerebral hemorrhages. Patients who deteriorated had more severe strokes, higher mortality, and significantly (P=0.042, t test) lower body temperature on admission (Table 3). Mean temperature on admission in patients who died within 7 days (36.5°C) or 3 months (36.5°C) tended to be lower than in survivors (36.6°C; P=0.086, t test).

In 93 patients, body temperature on admission was <36°C. These patients had more severe strokes than patients with higher temperature (median SSS on admission, 24 versus 37; P<0.001, Kolmogorov-Smirnov’s z test). The 7-day fatality rate was higher in patients with lower body temperature on admission (21% versus 10%; P=0.002, χ²). No difference was found in survivors at 3 months.

To demonstrate a possible relationship between body temperature in the first hours after stroke onset and outcome at 3 months, we performed multiple Spearman correlation tests of mRS, including death versus body temperature at admission. Table 3. Patients With Admission Temperature >37.5°C and ≤37.5°C

<table>
<thead>
<tr>
<th>Temperature &gt;37.5°C</th>
<th>Temperature ≤37.5°C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>74 (65–80)</td>
</tr>
<tr>
<td>SSS on admission</td>
<td>37 (20–46)</td>
</tr>
<tr>
<td>mRS at 3 mo, including deceased</td>
<td>4 (2–6)</td>
</tr>
<tr>
<td>Kolmogorov-Smirnov’s z test P=0.840</td>
<td>3 (2–6)</td>
</tr>
</tbody>
</table>

Values are medians and 25th and 75th quartiles.

Table 2. Patients With Admission Temperature >37.5°C

| Age, y              | 77 (69–84)          |
| SSS on admission    | 23 (8–38)           |
| mRS at 3 mo, including deceased | 6 (4–6) |

Values are medians, 25th and 75th quartiles, or mean and 95% confidence intervals. t test P=0.042.
Different time points (Table 4). Correlation was found between lower temperature and less favorable outcome on admission within 6 hours of stroke onset. At 8 hours after stroke onset and later, a significant correlation between higher temperature and less favorable outcome was demonstrated. In patients admitted within 2 hours of stroke onset, no correlation was found between body temperature on admission and outcome.

Cerebral Infarctions

A rise in body temperature was observed in some patients. This rise in body temperature was related to initial stroke severity and started 4 to 6 hours after stroke onset in the major stroke patients (Figure 1). No change in temperature was observed in the patients with mild to moderate strokes (Figure 2).

To evaluate factors with possible influence on stroke outcome, we performed a multinomial logistic regression test of SSS on admission, age, sex, prestroke mRS, history of atrial fibrillation, p-glucose, and body temperature on admission versus mRS at 3 months as a measure of outcome. The following factors reached significance in this model: Older age ($P<0.001$), low SSS on admission ($P<0.001$), and high prestroke mRS ($P=0.001$) negatively affected outcome in this model. The model significance was $P<0.001$. The explanatory value of the model was moderate ($R^2=0.468$, Cox and Snell).

In 65% of cases, the first dose of antiplatelet therapy was given on the day of admission, usually 8 to 12 hours after stroke onset.

Intracerebral Hemorrhages

A substantial rise in body temperature was also observed in these patients within the first 12 hours. In the major stroke group (Figure 3), mean body temperature started to rise 4 to 6 hours after stroke onset and rose 1°C. In the moderate hemorrhagic stroke patients, an uncertain tendency toward an increase was observed (Figure 4).

To evaluate factors with possible influence on stroke outcome, we performed a multinomial logistic regression test of SSS on admission, age, sex, prestroke mRS, history of atrial fibrillation, p-glucose, C-reactive protein, and body temperature on admission versus mRS at 3 months as a measure of outcome. The following factors contributed in this model: Low SSS on admission ($P<0.001$), older age, and high body temperature on admission ($P=0.001$) negatively affected outcome. The model significance was $P<0.001$. The explanatory value of the model was moderate ($R^2=0.425$, Cox and Snell).

Different time points (Table 4). Correlation was found between lower temperature and less favorable outcome on admission within 6 hours of stroke onset. At 8 hours after stroke onset and later, a significant correlation between higher temperature and less favorable outcome was demonstrated. In patients admitted within 2 hours of stroke onset, no correlation was found between body temperature on admission and outcome.

**TABLE 4. Correlations Between mRS for All Patients at 3 Months, Including Death and Temperature at Different Time Points After Stroke Onset**

<table>
<thead>
<tr>
<th>Time Point</th>
<th>Spearman's $\rho$</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admission</td>
<td>-0.113</td>
<td>0.007</td>
</tr>
<tr>
<td>6–8 h after onset</td>
<td>0.070</td>
<td>0.137</td>
</tr>
<tr>
<td>8–10 h after onset</td>
<td>0.111</td>
<td>0.018</td>
</tr>
<tr>
<td>10–12 h after onset</td>
<td>0.172</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>12–14 h after onset</td>
<td>0.119</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>14–16 h after onset</td>
<td>0.236</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>16–18 h after onset</td>
<td>0.210</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Figure 1.** Mean body temperature in 166 patients with severe cerebral infarction, SSS $\leq 25$ on admission.

**Figure 2.** Mean body temperature in 407 patients with mild to moderate cerebral infarction, SSS $>25$ on admission.

**Figure 3.** Mean body temperature in 84 patients with severe intracerebral hemorrhage, SSS $\leq 25$ on admission.
who experienced a rise in temperature. Schwarz et al., in a study of patients admitted to hospital within 24 hours of stroke onset, found elevated temperature in 5.3% of patients with cerebral infarct and 5% of patients with intracerebral hemorrhage. There is no straightforward explanation of the different results. However, our repeated measurements clearly demonstrate that temperature does rise in both severe cerebral infarction and hemorrhages. Thus, if the initial temperature measurement is done 8 to 10 hours after stroke onset, it might lead to the impression that admission temperature determines stroke severity and not vice versa. At 8 hours after stroke onset, higher body temperature was a negative predictor of outcome 3 months after stroke in our study, which is in accordance with the above-mentioned studies. However, the important difference is that our study documents that initially the body temperature in severe stroke is low or normal and that only later does the severity of the lesion cause body temperature to rise. Neither the earlier studies nor a recently published study that was not included in the meta-analysis has given a satisfactory explanation of the mechanism by which initial temperature should influence the initial severity of the stroke.

Could the difference between our findings and those of others be due to the thermometer, the electronic tympanic device? This is not likely because a similar device was used by some investigators and axillary temperature was used by others. Even if the tympanic thermometer might have a lower reproducibility than the rectal mercury thermometer, this is not likely to have invalidated our data, which included >4000 temperature measurements. Treatment with paracetamol in patients with temperatures >37°C probably blunted the rise in temperature but had no influence on admission temperature. We cannot exclude that treatment with paracetamol in 12 of the 35 patients with initially increased temperature may have had a beneficial effect on outcome. The effect of paracetamol has not been formally studied in stroke patients except in a small study in which intracerebral temperature was found to be unaffected by paracetamol.

The present study shows that when temperature is measured soon enough, only low initial temperature is related to stroke severity. We assume that low temperature on admission is a negative predictor of outcome 3 months after stroke in our study. The severe stroke patients may lose body temperature faster during transportation as a result of a lack of muscle activity.

Stroke severity determines the later rise in temperature. This does not exclude the possibility that a sustained rise in temperature during the first 24 to 36 hours may have a detrimental effect and further aggravate the neurological deficit or that induced hypothermia may be beneficial. This, however, has to be shown in randomized, controlled studies.

**Discussion**

In this study, we could not confirm a negative prognostic influence of elevated body temperature in the first hours after stroke onset on outcome after 3 months. In major stroke patients, we found that low body temperature on admission was a negative prognostic marker. A rise in temperature was found in the major stroke groups, both ischemic and hemorrhagic. This rise occurred hours after clinical manifestation of stroke. From this, we assume that the hyperthermia is caused by the infarct or hemorrhage and that size of the lesion and probably subsequent necrosis and edema are of importance. Intraventricular hemorrhage has been associated with an increase in temperature. Castillo et al. looked into the time course of poststroke hyperthermia. Their patients were admitted to hospital within 24 hours of stroke onset. They found that hyperthermia within this period was a negative prognostic marker. They demonstrated this finding by plotting the correlation coefficients against time from stroke onset with 6 hours as the first time point and concluded that hyperthermia in early stroke was strongly correlated to severe stroke and unfavourable outcome. However, temperature was not measured early enough to tell if it was the severe stroke patients who experienced a rise in temperature. Schwarz et al. in their study of 251 patients with supratentorial intracerebral hemorrhage, did not find that initial body temperature was an independent explanatory prognostic factor, but they did find that increased body temperature during the first 72 hours, which occurred in 91% of patients, was associated with poor outcome. Reith et al. found increased body temperature, >37.5°C on admission within 6 hours of stroke onset without specifying the exact time of the recording, in 25% of a mixed cerebral infarct and intracerebral hemorrhage population. This is a considerably higher proportion than in our study, which found elevated temperature in 5.3% of patients with cerebral infarcts and 5% of patients with intracerebral hemorrhage. There is no straightforward explanation of the different results. However, our repeated measurements clearly demonstrate that temperature does rise in both severe cerebral infarction and hemorrhages. Thus, if the initial temperature measurement is done 8 to 10 hours after stroke onset, it might lead to the impression that admission temperature determines stroke severity and not vice versa. At 8 hours after stroke onset, higher body temperature was a negative predictor of outcome 3 months after stroke in our study, which is in accordance with the above-mentioned studies. However, the important difference is that our study documents that initially the body temperature in severe stroke is low or normal and that only later does the severity of the lesion cause body temperature to rise. Neither the earlier studies nor a recently published study that was not included in the meta-analysis has given a satisfactory explanation of the mechanism by which initial temperature should influence the initial severity of the stroke.

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**References**


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