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.

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, in need of long-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
temperatures were generally too low compared with rectal temperatures. Patients with body temperature $>37^\circ C$ 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) at 3 months; death was rated as 6. mRS at 3 months was not performed systematically until July 1998, and in total, mRS 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 $\leq 25$ 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 $\geq 2$ points lasting $>4$ hours.

Statistical analysis was done with SPSS 9.0 for Windows. Non-parametric methods (Spearman’s $\rho$, 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 $37.5^\circ C$ 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 $\geq 1$ dose of paracetamol within 18 hours of stroke onset on this indication. One hundred fifty-nine patients (22%) had $\geq 1$ temperature measurement exceeding $37^\circ C$ without receiving paracetamol. In the group of patients with a peak temperature exceeding $37^\circ C$, we compared patients who actually received paracetamol with patients not receiving paracetamol and found that the peak temperature was higher in patients receiving paracetamol ($37.6^\circ C$ versus $37.4^\circ C$ 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 ($36.9^\circ C$ versus $36.7^\circ C$; $P=0.002$, $t$ test). We found no differences as to age, stroke severity, or outcome.

In 88 patients, body temperature exceeded $38^\circ C$ 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 ($36.5^\circ C$) or 3 months ($36.5^\circ C$) tended to be lower than in survivors ($36.6^\circ C$; $P=0.086$, $t$ test).

In 93 patients, body temperature on admission was $<36^\circ C$. 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%; $P=0.002$, $\chi^2$). 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, $r=0.042$.

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**Table 1. Patients Characteristics**

<table>
<thead>
<tr>
<th></th>
<th>Cerebral Infarctions (n=584)</th>
<th>Intracerebral Hemorrhages (n=141)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, y</td>
<td>76 (67–82)</td>
<td>74 (63–81)</td>
</tr>
<tr>
<td>Male sex, %</td>
<td>53 (n=584)</td>
<td>51 (n=141)</td>
</tr>
<tr>
<td>Median SSS on admission</td>
<td>39 (22–48)</td>
<td>20 (8–32)</td>
</tr>
<tr>
<td>SSS≤25, %</td>
<td>29 (n=573)</td>
<td>60 (n=140)</td>
</tr>
<tr>
<td>3 mo mortality, %</td>
<td>19 (108 of 584)</td>
<td>48 (67 of 141)</td>
</tr>
<tr>
<td>mRS at 3 months in survivors</td>
<td>2 (2–4)</td>
<td>3 (2–4)</td>
</tr>
</tbody>
</table>

Values are medians, 25th and 75th quartiles, or %.

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**Table 2. Patients With Admission Temperature >37.5°C and ≤37.5°C**

<table>
<thead>
<tr>
<th></th>
<th>Temperature &gt;37.5°C (n=35)</th>
<th>Temperature ≤37.5°C (n=612)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>74 (65–80)</td>
<td>76 (66–82)</td>
</tr>
<tr>
<td>SSS on admission</td>
<td>37 (20–46)</td>
<td>34 (19–47)</td>
</tr>
<tr>
<td>mRS at 3 mo, including deceased</td>
<td>4 (2–6)</td>
<td>3 (2–6)</td>
</tr>
</tbody>
</table>

Kolmogorov-Smirnov’s $z$ test $P=0.840$

Values are medians and 25th and 75th quartiles.

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**Table 3. Patients With and Without Deteriorating Stroke**

<table>
<thead>
<tr>
<th></th>
<th>Deteriorating Stroke (n=171)</th>
<th>Not Deteriorating Stroke (n=554)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>77 (69–84)</td>
<td>76 (66–82)</td>
</tr>
<tr>
<td>SSS on admission</td>
<td>23 (8–38)</td>
<td>39 (22–48)</td>
</tr>
<tr>
<td>mRS at 3 mos, including deceased</td>
<td>6 (4–6)</td>
<td>3 (2–4)</td>
</tr>
<tr>
<td>Admission temperature (mean), °C</td>
<td>36.4 (36.3–36.5)</td>
<td>36.7 (36.6–36.8)</td>
</tr>
</tbody>
</table>

$t$ test $P=0.042$

Values are medians, 25th and 75th quartiles, or mean and 95% confidence intervals. $t$ test $P=0.0042$.
different time points (Table 4). Correlation was found be-
tween 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 demon-
strated. In patients admitted within 2 hours of stroke onset, no
correlation was found between body temperature on admis-
sion 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 admis-
sion 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 ex-
planatory value of the model was moderate (pseudo-
$R^2=0.468$, 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

### 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 Points After Stroke Onset</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>

Boysen and Christensen Severity Determines Temperature in Acute Stroke

![Figure 1](image1.png)  
**Figure 1.** Mean body temperature in 166 patients with severe cerebral infarction, SSS ≥25 on admission.

![Figure 2](image2.png)  
**Figure 2.** Mean body temperature in 407 patients with mild to moderate cerebral infarction, SSS >25 on admission.

![Figure 3](image3.png)  
**Figure 3.** Mean body temperature in 84 patients with severe intracerebral hemorrhage, SSS ≥25 on admission.
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who experienced a rise in temperature. Schwarz et al,13 in

sured early enough to tell if it was the severe stroke patients

unfavourable outcome. However, temperature was not mea-

in early stroke was strongly correlated to severe stroke and

hours as the first time point and concluded that hyperthermia

correlation coefficients against time from stroke onset with 6

tic marker. They demonstrated this finding by plotting the

that hyperthermia within this period was a negative prognos-

mitted to hospital within 24 hours of stroke onset. They found

course of poststroke hyperthermia. Their patients were ad-

which found elevated temperature in 5.3% of patients with

This is a considerably higher proportion than in our study,

cerebral infarct and intracerebral hemorrhage population.

increase in temperature.13 Castillo et al 14 looked into the time

Intraventricular hemorrhage has been associated with an

probably subsequent necrosis and edema are of importance.

stroke. From this, we assume that the hyperthermia is caused

by the infarct or hemorrhage and that size of the lesion and

were included in the meta-analysis 1 has given a satisfactory expla-

nation 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 investigators15 and axillary temperature was used by

others.14 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 paraceta-

mol in patients with temperatures >37°C probably blunted the

rise in temperature but had no influence on admission tem-

perature. 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 study17 in which intracra-

bral temperature was found to be unaffected by paracetamol.

The present study shows that when temperature is mea-

sured soon enough, only low initial temperature is related to

stroke severity. We assume that low temperature on admission

could be due to exposure in the period from stroke onset

to hospital admission. The severe stroke patients may loose

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.

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