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Authors
LACK OF EFFECT OF INDUCTION OF HYPOTHERMIA AFTER ACUTE BRAIN INJURY

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ABSTRACT

Background  Induction of hypothermia in patients with brain injury was shown to improve outcomes in small clinical studies, but the results were not definitive. To study this issue, we conducted a multicenter trial comparing the effects of hypothermia with those of normothermia in patients with acute brain injury.

Methods  The study subjects were 392 patients 16 to 65 years of age with coma after sustaining closed head injuries who were randomly assigned to be treated with hypothermia (body temperature, 33°C), which was initiated within 6 hours after injury and maintained for 48 hours by means of surface cooling, or normothermia. All patients otherwise received standard treatment. The primary outcome measure was functional status six months after the injury.

Results  The mean age of the patients and the type and severity of injury in the two treatment groups were similar. The mean (±SD) time from injury to randomization was 4.3±1.1 hours in the hypothermia group and 4.1±1.2 hours in the normothermia group, and the mean time from injury to the achievement of the target temperature of 33°C in the hypothermia group was 8.4±3.0 hours. The outcome was poor (defined as severe disability, a vegetative state, or death) in 57 percent in the hypothermia group and 27 percent in the normothermia group and an 18 percent increase (i.e., difference between the hypothermia and normothermia groups), respectively, in the percentage of patients who had a favorable outcome. On the basis of these data, we initiated a larger trial of moderate hypothermia in patients with severe brain injury in October 1994 through May 1998 and report the results here.

METHODS

Study Subjects

The National Acute Brain Injury Study: Hypothermia was a prospective, multicenter, randomized trial with a planned sample size of 500 patients. The protocol and consent procedures were approved by the institutional review board of each participating center. In the second year of the trial, a waiver of consent, implemented in compliance with federal regulations, was approved for use if the family of a patient with brain injury could not be located. Written informed consent was obtained from legally authorized representatives for 62 percent of the patients, and consent was waived for 38 percent of the patients. A patient safety and monitoring board reviewed data on complications and mortality each month and evaluated the data every six months against preset rules for stopping the trial.

A total of 392 patients were enrolled, with 193 patients randomly assigned to standard treatment and 199 to standard treatment plus hypothermia. Eighty-eight percent of the patients were enrolled at 5 of the 11 centers participating in the trial: the University of Texas–Houston Health Science Center, St. Louis University, the University of California at Davis, the University of Pittsburgh, and Indiana University at Indianapolis. Enrollment was stopped in May 1998 by the patient safety and monitoring board on the basis of an interim analysis showing that the probability of detecting a treatment effect was less than 0.01 if the trial expanded to include 500 patients.

The criteria for inclusion in the trial were an age of 16 to 65 years, a nonpenetrating head injury, and a score on the Glasgow Coma Scale of 3 to 8 after resuscitation. A score on the Glasgow Coma Scale of 15 signifies normal mental status, and a score of 8 or less signifies coma. A score of 5 to 8 denotes flexor withdrawal or purposeful response to pain, 4 denotes extensor posturing, and 3 de-
notes no motor response. Patients were excluded if they had a score of 3 with unreactive pupils, a life-threatening injury to an organ other than the brain, a systolic blood pressure of less than 90 mm Hg after resuscitation, oxygen saturation of less than 94 percent after resuscitation, bleeding, pregnancy, or known preexisting medical conditions (e.g., severe heart disease) or if the examiners were unable to initiate cooling within six hours after injury. Enrolled patients were stratified at randomization according to study center and initial score on the Glasgow Coma Scale.

Patient Care

Intracranial pressure was monitored in all patients. All patients received 5 to 10 mg of intravenous morphine each hour for at least 72 hours. Intravenous vecuronium was administered to patients in the normothermia group as needed for respiratory management and for 72 hours to all patients in the hypothermia group to prevent shivering. Patients who had hypothermia on admission were not actively rewarmed. Increased intracranial pressure (a level of more than 20 mm Hg) was treated sequentially with intravenous vecuronium, ventricular drainage, hyperventilation with the arterial pressure of carbon dioxide maintained at more than 30 mm Hg, and mannitol until serum osmolality reached 315 mOsm per kilogram. Barbiturate coma was induced according to a published protocol in patients whose intracranial pressure remained high. Cerebral perfusion pressure (the difference between mean arterial pressure and intracranial pressure) was maintained at or above 70 mm Hg by intracranial pressure control and the administration of intravenous fluids and vasopressors to increase blood pressure. Dehydration was avoided; the use of arterial and Foley catheters was specified, and central lines were optional. Temperature was measured continuously in the urinary bladder through the use of Foley catheters with thermistors. Overall treatment was consistent with the recommendations of Bullock et al. A loading dose of 18 mg of intravenous phenytoin per kilogram of body weight was followed by 300 mg of phenytoin administered once a day for seven days. Potassium was given as needed to maintain normal serum concentrations during the period of hypothermia. Fluids containing glucose were used only for parenteral nutrition. Nutritional support by either the enteral or the parenteral route was started 48 hours after injury in the normothermia group and 72 hours after injury in the hypothermia group.

For the patients in the hypothermia group, cooling began immediately after randomization; the goal was to achieve a target bladder temperature of 33°C within eight hours after injury. Cooling procedures included the application of ice, gastric lavage with iced fluids, and the use of room-temperature air in the ventilator circuit. After the target temperature was reached, temperature-control pads incorporated into a kinetic treatment table (Roto-Rest, Kinetic Concepts, San Antonio, Tex.) were used to maintain a temperature of 32.5°C to 34.0°C for 48 hours. A rate of rewarming no faster than 0.5°C per two-hour period was used. The body temperatures of the patients in the normothermia group were maintained at 37.0°C.

Study Outcome

The primary outcome measure was the assessment of patients according to the five-category Glasgow Outcome Scale, which was conducted six months after the injury by examiners who were unaware of the patients’ treatment-group assignments. Good recovery and moderate disability were designated as favorable outcomes; severe disability, a vegetative state, and death were designated as poor outcomes. Good recovery according to the Glasgow Outcome Scale is defined as functional independence with minor disability, and moderate disability is defined as functional independence with more substantial disability. Severe disability is defined as functional dependence. Patients in a vegetative state are awake but noncommunicative. The results of nine neurobehavioral and neuropsychological tests recommended for brain-injury trials (the Neurobehavioral Rating Scale–Revised, the Disability Rating Scale, the Galveston Orientation and Amnesia Test, the Selective Reminding Test, the Rey-Osterrieth Complex Figure Test, the Symbol Digit Modalities Test, Trail Making Test B, the Controlled Oral Word Association Test, and the Grooved Pegboard Test) were also determined six months after the injury.

Data Collection

Temperature, heart rate, mean arterial pressure, intracranial pressure, cerebral perfusion pressure, urine output, volumes and types of intravenous fluid administered, laboratory values, and doses of selected medications were recorded for 96 hours after admission. All patients were evaluated daily, and 67 complications were recorded. The results of the Therapeutic Intervention Scoring System, which quantifies the number and intensity of interventions in patients in intensive care units, were recorded daily so that any bias in the clinical management could be detected.

Statistical Analysis

The primary outcomes were analyzed by the intention-to-treat method. Data on acute care and outcomes were transmitted to the Biostatistics Center at the Medical College of Virginia. Only the study biostatistician was aware of each patient’s treatment-group assignment, but the patient safety and monitoring board had access to data grouped according to treatment.

Post-randomization variables were analyzed for differences between the hypothermia and normothermia groups with the use of multivariate analysis with adjustment for age, and Glasgow coma scores on admission when appropriate. Some simple categorical data were analyzed by two-sided chi-square or Fisher’s exact tests. Comparisons for some simple continuous variables were performed with two-sided t-tests. All data are expressed as means ±SD.

RESULTS

The characteristics of the patients in the hypothermia and normothermia groups were similar at the time of enrollment (Table 1).

Temperature

Cooling was begun in the hypothermia group immediately after randomization. The mean time from injury to randomization was 4.3±1.1 hours in the hypothermia group and 4.1±1.2 hours in the normothermia group. The mean time from injury to the achievement of the target body temperature of 33°C in the hypothermia group was 8.4±3.0 hours, and the mean temperature in this group during the first 48 hours was 33.2±1.0°C. Hypothermia was maintained for 47.2±3.0 hours, and the rewarming period was 18.1±7.0 hours. Nine patients assigned to the hypothermia group did not receive hypothermia, in violation of the protocol. The mean body temperature after 96 hours in the normothermia group was 37.2±0.8°C; 35 percent of the patients in this group had a temperature of 35.0°C or less at some time during the first 16 hours after injury.

There was no significant relation between the time to reach the target temperature and the outcome. The effect on outcome of the length of time required to reach the target temperature was examined according to quartiles. In the first (lowest) quartile, the mean time to reach the target temperature was 5.3±1.2 hours, and the proportion of patients with poor outcomes was 64 percent. Later initiation of cooling was not associated with a higher proportion of poor outcomes (second quartile, 71±0.3 hours and 62 percent;
Throughout the first 96 hours, the percentage of patients with an intracranial pressure of more than 30 mm Hg was lower in the hypothermia group (P=0.02). The percentage of patients with very high intracranial pressures (more than 30 mm Hg) was lower on day 2 (P=0.002) and day 3 (P=0.03) in the hypothermia group, but this difference did not persist through day 4. The Therapy Intensity Level, 25 which measures the intensity of therapy for high intracranial pressure, was slightly but significantly higher in the hypothermia group than in the normothermia group on day 3 during rewarming (Table 3).

### Laboratory Data

There were small but statistically significant differences in the mean values for certain laboratory tests during the first 96 hours after randomization. Patients assigned to hypothermia had higher arterial blood pH values, hemoglobin concentrations, and hematocrit values. There was also a slight prolongation of prothrombin and partial-thromboplastin times and lower platelet counts in the hypothermia group. The patients

### Medical Treatment

The doses of study medications, cumulative fluid balance, nutritional support, Therapeutic Intervention scores, and percentage of days with complications are shown in Table 2. The hypothermia group had a higher cumulative fluid balance, a greater use of vasopressors, a lower dose of vecuronium, and a higher percentage of days with complications than the normothermia group. Also, in the hypothermia group, mean arterial pressure was lower on days 3 and 4 during and after rewarming, the number of patients with a mean arterial pressure of less than 70 mm Hg was higher on day 4, mean cerebral perfusion pressure was higher on day 1 and lower on days 3 and 4, and the proportion of patients with a cerebral perfusion pressure of less than 50 mm Hg was lower on day 1 and higher on day 4 than in the normothermia group (Table 3).

Mean intracranial pressure did not differ significantly between the two treatment groups on any day.
*Induction and maintenance of hypothermia occurred on days 1 and 2, rewarming occurred on day 3, and post-rewarming treatment occurred on day 4.

†The Therapy Intensity Level was designed to quantify the effects of therapy on the analysis of levels of intracranial pressure — for example, to distinguish between levels of intracranial pressure maintained with sedation alone and the same levels achieved with barbiturate coma. It is a 16-point scale with values ranging from 0 to 15, with higher values indicating more treatment. This score was calculated every 24 hours according to the therapies used during that period.

‡Cerebral perfusion pressure equals the mean arterial pressure minus the intracranial pressure.

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>DAY 1</th>
<th>DAY 2</th>
<th>DAY 3</th>
<th>DAY 4</th>
<th>DAYS 1–4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HYPO-</td>
<td>NORMO-</td>
<td>P VALUE</td>
<td>HYPO-</td>
<td>NORMO-</td>
</tr>
<tr>
<td>Mean arterial pressure</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (mm Hg)</td>
<td>95.5 92.6 0.003</td>
<td>93.4 95.2 0.06</td>
<td>92.4 95.8 &lt;0.001</td>
<td>92.4 96.2 &lt;0.001</td>
<td>93.1 94.6 0.05</td>
</tr>
<tr>
<td>Patients in whom pressure was ever &lt;70 mm Hg (%)</td>
<td>31 40 0.08</td>
<td>18 11 0.06</td>
<td>15 8 0.07</td>
<td>18 8 0.006</td>
<td>53 51 0.75</td>
</tr>
<tr>
<td>Intracranial pressure</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (mm Hg)</td>
<td>15.7 17.1 0.20</td>
<td>15.6 17.7 0.19</td>
<td>16.2 16.1 0.91</td>
<td>16.3 16.5 0.83</td>
<td>18.1 17.9 0.85</td>
</tr>
<tr>
<td>Patients in whom pressure was ever &gt;30 mm Hg (%)</td>
<td>23 32 0.06</td>
<td>14 28 0.002</td>
<td>16 26 0.03</td>
<td>21 29 0.06</td>
<td>41 39 0.02</td>
</tr>
<tr>
<td>Therapy Intensity Level†</td>
<td>4.9 5.3 0.21</td>
<td>5.2 5.0 0.80</td>
<td>5.3 4.3 0.005</td>
<td>4.5 3.8 0.06</td>
<td>5.0 4.6 0.21</td>
</tr>
<tr>
<td>Cerebral perfusion pressure‡</td>
<td>79.9 74.8 0.003</td>
<td>78.0 78.0 1.00</td>
<td>76.3 79.7 0.003</td>
<td>76.1 79.8 0.01</td>
<td>75.2 76.6 0.37</td>
</tr>
<tr>
<td>Mean (mm Hg)</td>
<td>22 31 0.06</td>
<td>18 13 0.20</td>
<td>11 9 0.73</td>
<td>15 8 0.07</td>
<td>44 42 0.75</td>
</tr>
<tr>
<td>Patients in whom pressure was ever &lt;50 mm Hg (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
in the normothermia group had higher mean serum potassium concentrations and white-cell counts. Significantly more patients in the hypothermia group had serum creatinine concentrations of more than 2.5 mg per deciliter (221 µmol per liter; 8 percent vs. 0.3 percent, P=0.05). There were no differences between groups for any other laboratory value. All mean values were within their respective normal ranges.

Complications

Ten percent of the patients in the hypothermia group and 3 percent of those in the normothermia group had critical hypotension (a mean arterial pressure of less than 70 mm Hg associated with organ failure) for two or more consecutive hours (P=0.01). Bradycardia associated with hypotension for two or more consecutive hours occurred in 16 percent of the patients in the hypothermia group and 4 percent of the patients in the normothermia group (P=0.04). The percentage of hospital days on which any complication was recorded was 78±22 percent for patients in the hypothermia group and 70±29 percent for patients in the normothermia group (P=0.005).

Outcome

Outcome data were obtained for 385 patients (98 percent). However, data on age or Glasgow coma score were missing or inaccurate for 17 patients, and therefore outcome data adjusted for age and Glasgow coma score were analyzed for 368 patients. There were no differences between the hypothermia and normothermia groups in the primary outcome measure; 57 percent of the patients in both groups had a poor outcome (severe disability, vegetative state, or death) (Table 4). Mortality was 28 percent in the hypothermia group and 27 percent in the normothermia group. The outcome data unadjusted for age and Glasgow coma score in 385 patients were no different from the outcome data adjusted for age and Glasgow coma score in 368 patients. There were no significant differences between the two groups in the results of the neurobehavioral and neuropsychological tests at six months (data not shown).

The effects of hypothermia were evaluated in subgroups of patients for all independent variables present on admission and known to influence outcome (older age, low Glasgow coma score, compressed cisterns on computed tomographic scans, and surgical hematoma).20-24 For patients in the two treatment groups with Glasgow coma scores of 3 or 4 and 5 to 8, there were no differences in rates of poor outcome or death. In both treatment groups, the outcome was more often poor in patients over 45 years of age than in those who were 45 or younger (P=0.001). There were more poor outcomes in patients over 45 years of age in the hypothermia group than in patients over 45 in the normothermia group (88 percent in the hypothermia group vs. 69 percent in the normothermia group, P=0.08), but mortality was not higher (Table 4). The patients over 45 years of age in the hypothermia group also had more days with complications while they

### Table 4. Rates of Poor Outcome and Death Six Months after Severe Brain Injury in Patients Treated with Induction of Hypothermia or Normothermia.

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Total No.</th>
<th>No. (% with Poor Outcome*)</th>
<th>Relative Risk (95% CI†)</th>
<th>P Value</th>
<th>No. (% with Poor Outcome)</th>
<th>Relative Risk (95% CI†)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients‡</td>
<td>368</td>
<td>102 (57)</td>
<td>1.0 (0.8–1.2)</td>
<td>0.99</td>
<td>108 (57)</td>
<td>1.0 (0.7–1.4)</td>
<td>0.79</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>190</td>
<td>141 (74)</td>
<td>1.0 (0.7–1.4)</td>
<td>0.79</td>
<td>53 (28)</td>
<td>1.0 (0.7–1.4)</td>
<td>0.79</td>
</tr>
<tr>
<td>Normothermia</td>
<td>178</td>
<td>61 (34)</td>
<td>1.0 (0.7–1.4)</td>
<td>0.79</td>
<td>48 (27)</td>
<td>1.0 (0.7–1.4)</td>
<td>0.79</td>
</tr>
<tr>
<td>Patients with Glasgow coma scores of 3–4 on admission</td>
<td>87</td>
<td>50 (59)</td>
<td>1.1 (0.8–1.4)</td>
<td>0.64</td>
<td>37 (43)</td>
<td>1.1 (0.8–1.4)</td>
<td>0.64</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>50</td>
<td>39 (78)</td>
<td>1.1 (0.8–1.4)</td>
<td>0.64</td>
<td>22 (44)</td>
<td>1.1 (0.8–1.4)</td>
<td>0.64</td>
</tr>
<tr>
<td>Normothermia</td>
<td>37</td>
<td>27 (73)</td>
<td>1.1 (0.8–1.4)</td>
<td>0.64</td>
<td>13 (35)</td>
<td>1.1 (0.8–1.4)</td>
<td>0.64</td>
</tr>
<tr>
<td>Patients with Glasgow coma scores of 5–8 on admission</td>
<td>281</td>
<td>140 (49)</td>
<td>0.9 (0.7–1.2)</td>
<td>0.55</td>
<td>69 (49)</td>
<td>0.9 (0.7–1.2)</td>
<td>0.55</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>140</td>
<td>69 (49)</td>
<td>0.9 (0.7–1.2)</td>
<td>0.55</td>
<td>30 (21)</td>
<td>0.9 (0.7–1.2)</td>
<td>0.55</td>
</tr>
<tr>
<td>Normothermia</td>
<td>141</td>
<td>75 (53)</td>
<td>0.9 (0.7–1.2)</td>
<td>0.55</td>
<td>32 (23)</td>
<td>0.9 (0.7–1.2)</td>
<td>0.55</td>
</tr>
<tr>
<td>Patients &gt;45 years old</td>
<td>52</td>
<td>26 (51)</td>
<td>1.3 (1.0–1.7)</td>
<td>0.08</td>
<td>23 (44)</td>
<td>1.3 (1.0–1.7)</td>
<td>0.08</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>26</td>
<td>23 (88)</td>
<td>1.3 (1.0–1.7)</td>
<td>0.08</td>
<td>10 (38)</td>
<td>1.3 (1.0–1.7)</td>
<td>0.08</td>
</tr>
<tr>
<td>Normothermia</td>
<td>26</td>
<td>18 (69)</td>
<td>1.3 (1.0–1.7)</td>
<td>0.08</td>
<td>10 (38)</td>
<td>1.3 (1.0–1.7)</td>
<td>0.08</td>
</tr>
</tbody>
</table>

*Poor outcome was defined as severe disability, vegetative state, or death and was adjusted for age and Glasgow coma score on admission.

†Values indicate the relative risk in the hypothermia group as compared with the normothermia group. CI denotes confidence interval.

‡Data are presented for 368 patients because outcome data were missing for 7 patients and Glasgow coma score on admission, age, or both were missing for 17 patients.
were hospitalized (82±21 percent of days in the hypothermia group vs. 55±29 percent of days in the normothermia group, P=0.002).

Effect of Hypothermia at the Time of Hospitalization

Retrospective analysis of body temperature on admission showed that temperatures of 35.0°C or less had an adverse effect on outcome; however, temperatures above 35.0°C had no effect (Table 5). Factors that adversely affect outcome in patients with severe brain injury were more prevalent in the subgroup with hypothermia on admission than in the subgroup with normothermia on admission; these factors included a higher mean age, a higher Injury Severity Score, and a higher percentage of patients with prehospital hypotension. Other factors not known to affect the outcome after brain injury that were associated with hypothermia on admission were a positive test for blood alcohol, a higher volume of fluid administered before hospitalization, and admission in the winter (Table 5). The mean length of time from injury to admission was the same in both groups.

There were differences in the pattern of body temper-
Hypothermia is a result of more severe brain injury. This finding might suggest that spontaneous hypothermia in patients who have normothermia on admission is not beneficial, and that re-warming of patients who have hypothermia on admission is detrimental. Supporting this argument is the finding that hypothermia on admission was associated with a greater severity of injury and worse outcomes than was normothermia on admission. This finding might suggest that spontaneous hypothermia is a result of more severe brain injury.

An alternative interpretation is that the very early cooling in patients who have hypothermia on admission is crucial to achieving a neuroprotective effect. In the hypothermia group, the time from the injury to the achievement of the target temperature was only slightly less in the patients who had hypothermia on admission. These patients, however, had significantly lower temperatures in the first eight hours than the patients who had normothermia on admission. The results indicate that brain-injured patients who have hypothermia on admission should not be re-warmed, but that induced hypothermia that reaches a target temperature eight hours after injury did not prevent a poor outcome in patients with severe head injury.

Supported by grants from the National Institutes of Neurological Disorders and Stroke (NIH RO1 NS32786-06) and from Kinetic Concepts (San Antonio, Tex.). Dr. Clifton has served as a consultant to Gaymar Industries, a manufacturer of temperature-control blankets.

We are indebted to the members of the patient safety and monitoring board — Mary Ellen Cheung, Ph.D., National Institute of Neurological Disorders and Stroke; William Clarke, Ph.D., University of Iowa; Sureyya Dikmen, Ph.D., University of Washington; Daniel Hanley, M.D., Johns Hopkins University; Sidney Starkman, M.D., University of California at Los Angeles; Michael Walker, M.D., National Institute of Neurological Disorders and Stroke; and Byron Young, M.D., University of Kentucky.

REFERENCES


Table 6. Body Temperature on Admission and Outcome Six Months After Severe Brain Injury in Patients Treated with Induction of Hypothermia or Normothermia.

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Temperature on Admission</th>
<th>No. (%) with Poor Outcome</th>
<th>Relative Risk (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤35.0°C</td>
<td>&gt;35.0°C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All patients‡</td>
<td>102</td>
<td>264</td>
<td>0.8 (0.6–1.0)</td>
<td>0.09</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>62</td>
<td>127</td>
<td>38 (61)</td>
<td>0.09</td>
</tr>
<tr>
<td>Normothermia</td>
<td>40</td>
<td>137</td>
<td>31 (78)</td>
<td>1.01 (0.8–1.3)</td>
</tr>
<tr>
<td>Patients ≤45 years old</td>
<td>81</td>
<td>33</td>
<td>0.7 (0.5–1.0)</td>
<td>0.02</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>48</td>
<td>33</td>
<td>25 (52)</td>
<td>1.01 (0.8–1.3)</td>
</tr>
<tr>
<td>Normothermia</td>
<td>33</td>
<td>118</td>
<td>25 (76)</td>
<td>1.01 (0.8–1.3)</td>
</tr>
<tr>
<td>Patients &gt;45 years old</td>
<td>21</td>
<td>31</td>
<td>1.1 (0.8–1.5)</td>
<td>0.60</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>14</td>
<td>12</td>
<td>13 (93)</td>
<td>1.3 (0.9–2.0)</td>
</tr>
<tr>
<td>Normothermia</td>
<td>7</td>
<td>19</td>
<td>6 (86)</td>
<td>0.12 (0.0–1.0)</td>
</tr>
</tbody>
</table>

*Poor outcome was defined as severe disability, vegetative state, or death and was adjusted for age and Glasgow coma score on admission.
†Values indicate the relative risk in the hypothermia group as compared with the normothermia group. CI denotes confidence interval.
‡Data are presented for 366 patients because temperature on admission was missing for 2 patients, outcome data were missing for 7 patients, and Glasgow coma score on admission, age, or both were missing for 17 patients.

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