Re: New Research in the Field of Stroke: Therapeutic Hypothermia After Cardiac Arrest

To the Editor:

We read with interest the article by Dietrich et al 1 on therapeutic hypothermia after cardiac arrest. Deeply grateful for considering the results of the 2 randomized clinical trials published in a recent issue of *The New England Journal of Medicine* 2,3 as landmark studies in the field of cerebral resuscitation, we regret that the authors still have concern with regard to mild therapeutic hypothermia and its possible beneficial effects in victims of cardiac arrest from other causes. Please allow us to emphasize 2 important facts with regard to this new emerging therapy in the field of global cerebral ischemic stroke.

For the purpose of showing a statistical significant benefit by keeping the study efforts within realistic limits, it was necessary to enroll patients with very strict inclusion criteria. Otherwise, resuscitative hypothermia would have been a loser, as many other therapies already tried for resuscitation. 4 This would have consequently been followed by losing many more primary cardiac arrest survivors. In this regard, please be so kind as to consider that we have assessed 3551 patients for eligibility and finally randomized 275 and not 136 as stated (Figure). 2

Even if the study by Hachimi-Idrissi et al 5 has enrolled only 30 patients (Table), they were able to show a numerical benefit for victims of cardiac arrest not so carefully selected as in the HACA trial and with other causes and primary rhythms. 6 In addition, many pathomechanisms also valid for the period after resuscitation have been proven sensitive to intra- and postischemic temperature reductions independently of the experimental design. 1

Thus, we think that therapeutic hypothermia has the necessary support from preclinical data and from 3 well-designed clinical studies and therefore should be considered as standard in comatose survivors of cardiac arrest.

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Randomized Clinical Trials of Therapeutic Hypothermia After Cardiac Arrest

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<tr>
<th>N</th>
<th>Age, y</th>
<th>Cause</th>
<th>Rhythm</th>
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<tbody>
<tr>
<td>HACA</td>
<td>275</td>
<td>18–75</td>
<td>Cardiac</td>
</tr>
<tr>
<td>Bernard et al</td>
<td>77</td>
<td>&gt;18 (&gt;50 for females)</td>
<td>All</td>
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<tr>
<td>H-Idrissi et al</td>
<td>30</td>
<td>&gt;18</td>
<td>Cardiac</td>
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VF indicates ventricular fibrillation; VT, ventricular tachycardia; PEA, pulseless electrical activity.


Response

We appreciate the interest in our Emerging Therapies article on therapeutic hypothermia after cardiac arrest. 1 As we emphasized in this short review, the 2 randomized clinical trials published in a recent issue of *The New England Journal of Medicine* 2,3 provide compelling evidence for therapeutic hypothermia improving outcome in this patient population. We thank you for bringing to our attention the study by Hachimi-Idrissi and colleagues 6 in which the results of selective head cooling in cardiac arrest patients were reported. We apologize to the authors for incorrectly stating that the total enrollment of patients in the HACA trial was 136, when a total of 275 were actually randomized. In the review, we attempted to stress the importance of injury severity on therapeutic strategies, including hypothermia. Experience in experimental cerebral ischemia and traumatic brain injury models has demonstrated that injury severity is a critical factor in determining degrees of protection. We agree that hypothermic therapy should be considered in other patient populations afflicted with acute neurological injury. However, many critical scientific questions remain unanswered concerning the use of hypothermia, including mechanisms of protection, therapeutic windows, cooling levels and duration, rewarming procedures, as well as gender considerations.

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Stroke. 2003;34:e103; originally published online July 17, 2003;
doi: 10.1161/01.STR.0000083469.51522.0C

The online version of this article, along with updated information and services, is located on the
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