ORIGINAL ARTICLE

Targeted Temperature Management for Cardiac Arrest with Nonshockable Rhythm

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ABSTRACT

BACKGROUND

Moderate therapeutic hypothermia is currently recommended to improve neurologic outcomes in adults with persistent coma after resuscitated out-of-hospital cardiac arrest. However, the effectiveness of moderate therapeutic hypothermia in patients with nonshockable rhythms (asystole or pulseless electrical activity) is debated.

METHODS

We performed an open-label, randomized, controlled trial comparing moderate therapeutic hypothermia (33°C during the first 24 hours) with targeted normothermia (37°C) in patients with coma who had been admitted to the intensive care unit (ICU) after resuscitation from cardiac arrest with nonshockable rhythm. The primary outcome was survival with a favorable neurologic outcome, assessed on day 90 after randomization with the use of the Cerebral Performance Category (CPC) scale (which ranges from 1 to 5, with higher scores indicating greater disability). We defined a favorable neurologic outcome as a CPC score of 1 or 2. Outcome assessment was blinded. Mortality and safety were also assessed.

RESULTS

From January 2014 through January 2018, a total of 584 patients from 25 ICUs underwent randomization, and 581 were included in the analysis (3 patients withdrew consent). On day 90, a total of 29 of 284 patients (10.2%) in the hypothermia group were alive with a CPC score of 1 or 2, as compared with 17 of 297 (5.7%) in the normothermia group (difference, 4.5 percentage points; 95% confidence interval [CI], 0.1 to 8.9; P=0.04). Mortality at 90 days did not differ significantly between the hypothermia group and the normothermia group (81.3% and 83.2%, respectively; difference, –1.9 percentage points; 95% CI, –8.0 to 4.3). The incidence of prespecified adverse events did not differ significantly between groups.

CONCLUSIONS

Among patients with coma who had been resuscitated from cardiac arrest with nonshockable rhythm, moderate therapeutic hypothermia at 33°C for 24 hours led to a higher percentage of patients who survived with a favorable neurologic outcome at day 90 than was observed with targeted normothermia. (Funded by the French Ministry of Health and others; HYPERION ClinicalTrials.gov number, NCT01994772.)

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*Lists of the investigators in the HYPERION trial and the members of the Clinical Research in Intensive Care and Sepsis (CRICS) Group are provided in the Supplementary Appendix, available at NEJM.org.

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In accordance with the 2015 guidelines of the International Liaison Committee on Resuscitation (ILCOR),[1] targeted temperature management with a target of 32°C to 36°C (moderate therapeutic hypothermia) is currently advocated for all patients with coma after successful resuscitation from cardiac arrest. Trial results published in 2013, however, showed inconclusive effects of this treatment in the 19% of patients who had cardiac arrest with a nonshockable rhythm (asystole or pulseless electrical activity),[2] and the use of hypothermia subsequently decreased in this situation.[3-5] Two retrospective case-series studies suggested beneficial effects of hypothermia on both neurologic outcomes and survival among these patients,[6,7] two showed no effect,[8,9] and two suggested harm.[10,11] This uncertainty requires resolution, because nonshockable rhythms now predominate among patients with cardiac arrest[12] and are associated with a poor prognosis, with only 2 to 15% of patients having good neurologic outcomes,[2,13,14] as compared with nearly 65% of patients who have cardiac arrest with a shockable rhythm.[15] Finally, data on moderate therapeutic hypothermia are limited in patients with cardiac arrest due to noncardiac causes or in those with in-hospital cardiac arrest. The objective of the Therapeutic Hypothermia after Cardiac Arrest in Nonshockable Rhythm (HYPERION) trial was to assess whether moderate therapeutic hypothermia at 33°C, as compared with targeted normothermia (37°C), would improve neurologic outcome in patients with coma who had been successfully resuscitated after cardiac arrest with nonshockable rhythm.

Methods

Trial Design

We conducted this investigator-initiated, open-label, blinded-outcome-assessor, pragmatic, multicenter, randomized, controlled trial in 25 intensive care units (ICUs) in France (11 in university hospitals and 14 in community hospitals). The trial rationale and design have been described previously.[16] The research protocol (available with the full text of this article at NEJM.org) was approved by the appropriate ethics committees and French data-protection authorities.

The trial was supported by independent research grants from the French Ministry of Health, the nonprofit health care institution Centre Hospitalier Départemental Vendée, and the Laerdal Foundation. None of the trial funders had any role in the trial design, the collection or analysis of the data, or the writing of the manuscript. The authors vouch for the completeness and accuracy of the data and for the fidelity of the trial to the protocol.

Patients

Candidates for trial enrollment were 18 years of age or older and had been resuscitated from out-of-hospital or in-hospital cardiac arrest with a nonshockable rhythm due to any cause. Eligible patients had coma (score ≤8 on the Glasgow Coma Scale [GCS]; scores range from 3 to 15, with lower scores indicating poorer function) at ICU admission. In patients who had been sedated before ICU admission, the GCS score that had been determined by the emergency physician just before sedation was used. Exclusion criteria were a no-flow time (from collapse to initiation of cardiopulmonary resuscitation [CPR]) of more than 10 minutes; a low-flow time (from initiation of CPR to return of spontaneous circulation) of more than 60 minutes; major hemodynamic instability (continuous epinephrine or norepinephrine infusion >1 μg per kilogram of body weight per minute); time from cardiac arrest to screening of more than 300 minutes; moribund condition; Child–Pugh class C cirrhosis of the liver (severe hepatic dysfunction); pregnancy or breast-feeding; status of being under guardianship; status of being an inmate at a correctional facility; previous inclusion in another randomized, controlled trial involving patients with cardiac arrest in which the neurologic outcome at 90 days was assessed as the primary end point; lack of health insurance; and decision by the next of kin for the patient not to participate.

According to French law, because the strategies used in both groups were considered to be components of standard care, informed consent for trial participation was not required. However, French data-protection authorities require that patients be given the opportunity to decline that their data be used. Therefore, since the patients had coma, it was required that the closest available relatives receive specific information about trial enrollment. Patients with no available rela-

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tive were included in the trial, were informed as soon as they regained competence, and were asked whether they wanted to remain in the trial; if the answer was negative, they were excluded from the analysis.

RANDOMIZATION AND BLINDING

At each center, eligible patients were randomly assigned in a 1:1 ratio to either moderate therapeutic hypothermia (33°C) or targeted normothermia (37°C). Randomization was conducted with the use of a Web-based system that was accessible 24 hours per day. The randomization sequence was generated by the statistician (who was not involved in the recruitment of patients), with permuted blocks of varying sizes and with stratification according to center and cause of cardiac arrest (presumed cardiac vs. presumed noncardiac).

It was not feasible for the staff who were providing patient care to be unaware of the group assignments. However, the psychologist who assessed the trial outcomes in all patients was unaware of the group assignments.

TARGETED TEMPERATURE MANAGEMENT

The trial protocol involved the standardization of several variables including sedation, neuromuscular blockade,[17] and the management of expected adverse events. Details are provided in the Supplementary Appendix, available at NEJM.org.

In patients who had been assigned to the hypothermia group, hypothermia at 33°C (with a window of ±0.5°C) was induced and then maintained for 24 hours. Each center followed its standard protocol (active internal cooling with a specific device, active external cooling with a specific device, or active external cooling without a specific device). Slow rewarming was then performed at a rate of 0.25 to 0.50°C per hour, to 36.5 to 37.5°C, which was maintained for 24 hours. Sedation was provided according to the standard protocol in each center, with dosage adjustment to obtain a Richmond Agitation–Sedation Scale score of −5 (on a scale from −5 [unresponsive] to +4 [combative]).[18] During rewarming, sedation was tapered when the body temperature rose above 36°C.

In patients who had been assigned to the normothermia group, body temperature was maintained at 36.5 to 37.5°C for 48 hours according to the standard protocol in each ICU. Sedation was given routinely only during the first 12 hours after randomization, in accordance with 2010 ILCOR guidelines.[19]

ASSESSMENT OF NEUROLOGIC PROGNOSIS AND LIFE-SUPPORT WITHDRAWAL

Decisions regarding limitation of treatment followed current guidelines.[1,19] A multimodal assessment of neurologic prognosis was performed, with the contribution of an independent consultant if needed. All patient data that were available on the day of the decision were evaluated. Details on the decision-making process and on implementation of the decision were recorded. Additional information is provided in the Supplementary Appendix.

FOLLOW-UP AND OUTCOMES

All surviving patients were followed until day 90 after randomization. The primary outcome was survival with a favorable day-90 neurologic outcome, which was assessed with the use of the Cerebral Performance Category (CPC) scale (scores range from 1 to 5, with higher scores indicating greater disability). For this trial, a favorable neurologic outcome was defined as a CPC score of 1 (good cerebral performance or minor disability) or 2 (moderate disability).[20] The CPC score at 90 days was assessed during a semistructured telephone interview adapted from the validated French version[21] of the 5-item Glasgow Outcome Scale[22] by a single psychologist who was unaware of the group assignments and who had been specifically trained for the trial.[23] The secondary outcomes were mortality, mechanical ventilation duration, length of stay in the ICU and hospital, infections, and hematologic adverse events.

STATISTICAL ANALYSIS

We assumed that 23% of the patients in the hypothermia group and 14% of those in the normothermia group would have a CPC score of 1 or 2 on day 90.[24] We calculated that the trial would need to enroll 584 patients in order for the trial to have 80% power to detect an absolute between-group difference of 9 percentage points in the percentage of patients with the primary outcome, at a two-sided significance level of 5%, and given that two interim analyses were planned.

The results of two interim analyses, performed

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after the inclusion of 200 and 400 patients, were provided to an independent data and safety monitoring board but not to the investigators. The Peto and Haybittle rule[25] was applied, with the significance level set at 0.001 for both interim analyses, and the significance level associated with the final analysis was set at 0.049 to maintain an overall type I error of 5%.

Categorical variables were described with the use of numbers and percentages, and continuous variables with the use of medians and interquartile ranges. To estimate the treatment effect on the primary outcome, we estimated the between-group difference and its 95% confidence interval using a linear model with an identity link function. Missing data were handled by assuming that patients with missing data had died. To assess the consistency of the treatment effect on the primary outcome across prespecified subgroups, differences in percentages and 95% confidence intervals across subgroups were assessed by linear models with identity link functions including interaction terms. An additional analysis was performed with respect to the primary outcome and was adjusted for stratification variables (trial center and cardiac vs. noncardiac cause of arrest) with the use of a linear model with an identity link function.

Secondary outcomes that were expressed as proportions with their 95% confidence intervals were compared between groups. Secondary outcomes that were reported as cumulative incidences were analyzed with the use of the competing-risks approach, with death, ICU discharge, and hospital discharge as the competing risks. Confidence intervals for the secondary efficacy end points were not adjusted for multiplicity, and therefore inferences drawn from these intervals may not be reproducible. We used SAS software, version 9.4 (SAS Institute), and R software, version 3.3.1, for the statistical analyses.

RESULTS

PATIENTS

Of 2723 patients who had been assessed for eligibility between January 26, 2014, and January 12, 2018, a total of 584 underwent randomization, including 3 patients in the hypothermia group who subsequently withdrew consent; therefore, 581 patients (284 patients in the hypothermia group and 297 in the normothermia group) were included in the analysis (Fig. 1, and Table S1 in the Supplementary Appendix). The characteristics of the patients at baseline were evenly balanced between the groups (Table 1 and Table S2). Cardiac arrest occurred in the hospital in 27.4% of the patients and out of the hospital in 72.6%. The cause of cardiac arrest was noncardiac in two thirds of the patients; circulatory shock was present in 58% of the patients.

TEMPERATURE MANAGEMENT

In the hypothermia group, cooling began a median of 16 minutes (interquartile range, 0 to 53) after randomization and was stopped prematurely in 36 of 284 patients (12.7%); reasons are given in Table S3. Cooling was achieved with the use of an intravascular cooling catheter in 43 patients (15.1%) in the hypothermia group and in 44 of 297 patients (14.8%) in the normothermia group; with the use of a dedicated closed-loop surface device in 136 (47.9%) and 101 (34.0%), respectively; and with the use of a basic external cooling device with no closed loop in 105 (37.0%) and 151 (50.8%) (data were missing for 1 patient [0.3%] in the normothermia group) (Table S4). Figure 2 shows the temperature changes over time; the mean (±SD) temperature between 12 and 24 hours after randomization was 33.5±1.1°C in the hypothermia group and 37.0±0.7°C in the normothermia group. Figures S1 and S2 show the lowest and highest temperatures recorded daily after day 3.

FOLLOW-UP AND OUTCOMES

On day 90, of the 284 patients who had been assigned to the hypothermia group and were included in the analysis, 29 had a CPC score of 1 or 2, as compared with 17 of the 297 patients who had been assigned to the normothermia group (10.2% vs. 5.7%; difference, 4.5 percentage points; 95% confidence interval [CI], 0.1 to 8.9; P=0.04) (Table 2 and Fig. 3). The effect of the intervention was consistent across prespecified subgroups (Fig. S3). Similar results were obtained in the analysis that was adjusted for stratification variables (between-group difference, 4.9 percentage points; 95% CI, 0.5 to 9.3; P=0.03).

The number of patients who died within 90 days was 231 in the hypothermia group and 247 in the normothermia group (81.3% vs. 83.2%; difference, –1.9 percentage points; 95% CI, –8.0 to 4.4). Neither the duration of mechanical ven-

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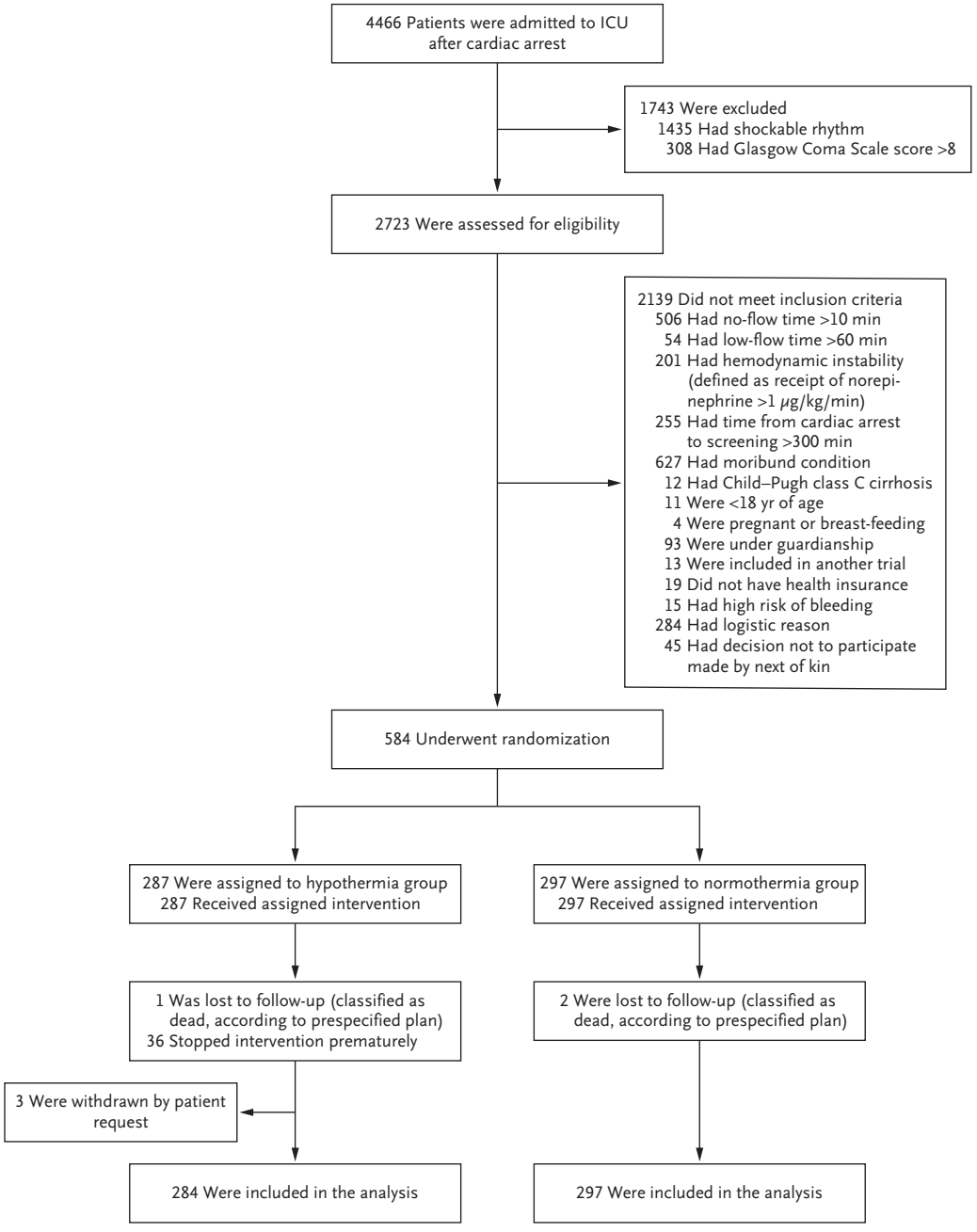

Figure 1. Screening, Randomization, and Follow-up of the Patients.

Scores on the Glasgow Coma Scale range from 3 to 15, with lower scores indicating poorer function. No-flow time was defined from collapse to the initiation of cardiopulmonary resuscitation (CPR), and low-flow time as from the initiation of CPR to the return of spontaneous circulation. ICU denotes intensive care unit.

tilation nor the length of stay in the ICU differed substantially between the two groups among patients who survived or among those who died (Table 2). Additional details on neurologic outcomes and sources of follow-up information are provided in Table 2, Figure 3, and Table S5. There were no significant differences between the groups in the proportion of patients who

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Table 1. Baseline Characteristics of the Patients in the Groups Treated with Moderate Therapeutic Hypothermia (33°C) or Targeted Normothermia (37°C).*

Characteristic	Hypothermia (N=284)	Normothermia (N=297)
Age — yr		
Median	67.1	67.2
Interquartile range	56.9–76.3	57.8–76.1
Male sex — no. (%)	185 (65.1)	188 (63.3)
Charlson comorbidity index†		
Median	4.0	4.0
Interquartile range	2.0–6.0	2.0–6.0
Chronic heart disease — no. (%)	162 (57.0)	180 (60.6)
Chronic pulmonary disease — no. (%)	97 (34.2)	107 (36.0)
Location at cardiac arrest — no. (%)		
Place of residence	138 (48.6)	157 (52.9)
Public place	73 (25.7)	54 (18.2)
Hospital	73 (25.7)	86 (29.0)
Bystander-witnessed cardiac arrest — no. (%)	274 (96.5)	273 (91.9)
Bystander-performed CPR — no. (%)	200 (70.4)	207 (69.7)
First monitored rhythm — no. (%)		
Asystole	221 (77.8)	241 (81.1)
Pulseless electrical activity	33 (11.6)	36 (12.1)
Unknown, not shocked	30 (10.6)	20 (6.7)
Cause of cardiac arrest — no. (%)		
Asphyxia	158 (55.6)	162 (54.5)
Cardiac cause	79 (27.8)	79 (26.6)
Anaphylaxis	4 (1.4)	5 (1.7)
Neurologic cause	7 (2.5)	6 (2.0)
Pulmonary embolism	10 (3.5)	12 (4.0)
Other medical cause	20 (7.0)	22 (7.4)
Trauma	1 (0.4)	2 (0.7)
Drug poisoning	1 (0.4)	7 (2.4)
Drowning	4 (1.4)	2 (0.7)
Glasgow Coma Scale score at enrollment‡		
Median	3.0	3.0
Interquartile range	3.0–3.0	3.0–3.0
Circulatory shock — no. (%)§	159 (56.0)	180 (60.6)
Duration from cardiac arrest to randomization — min		
Median	232.5	219.0
Interquartile range	178.0–276.5	170.0–266.0
Body temperature at inclusion — °C		
Median	35.5	35.4
Interquartile range	34.6–36.4	34.4–36.5

* The characteristics of the patients at baseline were evenly balanced between the groups. Percentages may not total 100 because of rounding. CPR denotes cardiopulmonary resuscitation.
† In the Charlson comorbidity index, each comorbidity category is weighted from 1 to 6, on the basis of adjusted risk of death or resource use, and the sum of the weights produces the score for the patient. A score of 0 indicates an absence of known coexisting conditions, and higher scores indicate higher risks of death and greater resource use.
‡ Scores on the Glasgow Coma Scale range from 3 to 15, with lower scores indicating poorer function.
§ Circulatory shock was defined as a systolic blood pressure of less than 90 mm Hg for at least 30 minutes or impaired end-organ perfusion (cool extremities, mottling, or urine output <30 ml per hour).

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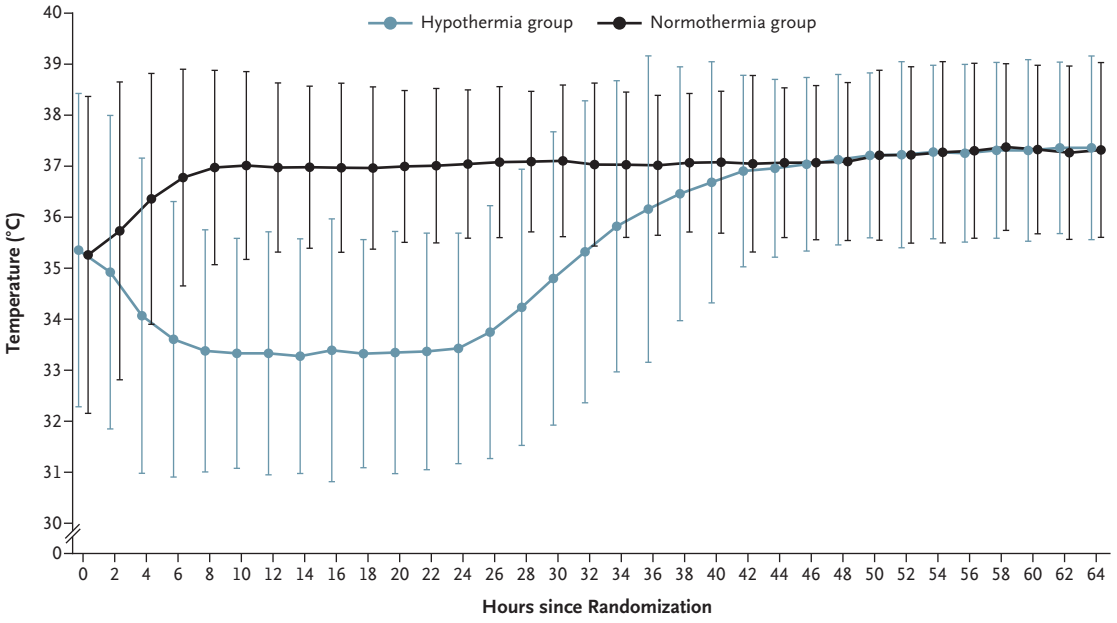

Figure 2. Mean Body Temperature during the Intervention in the Groups of Patients Who Had Been Randomly Assigned to Hypothermia (33°C) or Normothermia (37°C).

I bars indicate ±2 standard deviations; 95% of the recorded values were within the bars. The bars are shown slightly offset at each time point for better visibility.

had any of the prespecified serious adverse events (Table S6). Figure S4 shows the changes between day 0 and day 7 in the Sequential Organ Failure Assessment (SOFA) score (scores range from 0 to 20, with higher scores indicating more severe organ dysfunction).

CAUSES OF DEATH

Of the 581 patients, 478 (82.3%) died during follow-up. Table S7 reports the causes of death. The most common cause of death was withdrawal of life support, which occurred in 143 of 231 patients (61.9%) in the hypothermia group and in 161 of 247 patients (65.2%) in the normothermia group. Figure S5 and Table S8 provide details about the methods used to assess neurologic prognosis, and Figure S6 shows the time from randomization to withdrawal of life support.

DISCUSSION

In this open-label, multicenter, randomized, controlled trial with blinded outcome assessment, the targeting of a temperature of 33°C in patients who had cardiac arrest with nonshockable rhythm significantly improved survival with a favorable day-90 neurologic outcome as assessed with the use of the CPC scale, as compared with targeted normothermia. Overall mortality at 90 days did not differ significantly between the two groups. We detected no significant harmful effects of hypothermia at 33°C as compared with targeted normothermia.

Cardiac arrest with nonshockable rhythm usually occurs outside the hospital, is often due to noncardiac causes, and is associated with a poorer neurologic prognosis than cardiac arrest with shockable rhythm. In two pioneer trials comparing hypothermia with normothermia in patients with cardiac arrest with shockable rhythm, neurologic outcomes were good in 26% and 39% of patients who were treated with normothermia.[26,27] In a post hoc analysis[2] of the TTM (Target Temperature Management 33°C versus 36°C after Out-of-Hospital Cardiac Arrest) trial by Nielsen et al.,[28] hypothermia did not improve

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Table 2. Neurologic Outcomes and Hospitalization Characteristics.*

Outcome	Hypothermia (N=284)	Normothermia (N=297)	Difference or Hazard Ratio (95% CI)
CPC score of 1 or 2 on day 90 — no. (%)	29 (10.2)	17 (5.7)	4.5 (0.1 to 8.9)†
CPC score distribution on day 90 — no. (%)			
CPC score of 1	16 (5.6)	11 (3.7)	
CPC score of 2	13 (4.6)	6 (2.0)	
CPC score of 3	22 (7.7)	31 (10.4)	
CPC score of 4	1 (0.4)	0	
CPC score of 5	231 (81.3)	247 (83.2)	
Loss to follow-up	1 (0.4)	2 (0.7)	
Death by day 90 — no. (%)	231 (81.3)	247 (83.2)	−1.9 (−8.0 to 4.4)†
Death in the ICU — no. (%)	222 (78.2)	236 (79.5)	0.93 (0.78 to 1.10)‡
Duration of mechanical ventilation — days			
Median	4.5	4.0	
Interquartile range	2.0 to 7.0	2.0 to 7.0	
Length of stay in ICU — days			
Median	4.0	4.0	
Interquartile range	2.0 to 7.0	2.0 to 6.0	
Survival to ICU discharge — no. (%)	62 (21.8)	61 (20.5)	1.07 (0.75 to 1.52)‡
Duration of mechanical ventilation — days			
Median	11.0	10.0	
Interquartile range	6.0 to 24.0	4.0 to 27.0	
Length of stay in ICU — days			
Median	6.0	6.0	
Interquartile range	4.0 to 18.0	2.0 to 21.0	
Survival to hospital discharge — no. (%)	56 (19.7)	50 (16.8)	1.19 (0.81 to 1.74)‡

* The primary outcome was survival with a favorable neurologic outcome, assessed on day 90 after randomization with the use of the Cerebral Performance Category (CPC) scale. CPC scores range from 1 to 5, with higher scores indicating greater disability; a CPC score of 5 indicates death. For this trial, a favorable neurologic outcome was defined as a CPC score of 1 (good cerebral performance or minor disability) or 2 (moderate disability).[20] Confidence intervals for secondary efficacy end points were not adjusted for multiplicity, and therefore inferences drawn from these intervals may not be reproducible. ICU denotes intensive care unit.

† Differences between percentages in the analyses of CPC score of 1 or 2 on day 90 and death by day 90 are shown in percentage points.

‡ The hazard ratios were estimated with the use of competing-risk models. Hazard ratios in the analyses of survival to ICU or hospital discharge indicate the likelihood of survival to that time point rather than likelihood of death.

survival or neurologic outcomes in the group with nonshockable rhythms. Improvements in outcomes after cardiac arrest with shockable rhythm[29] may make cardiac arrest with nonshockable rhythm the situation that is most likely to benefit from hypothermia.

In our trial, the cardiac arrest occurred outside the hospital in approximately three quarters of the patients, and the presumed cause of cardiac arrest was noncardiac in two thirds of the patients. In a retrospective registry study involving patients with out-of-hospital cardiac arrest, hypothermia was associated with neurologic outcomes at hospital discharge that were poorer than those associated with no specific temperature-management strategy.[11] Another registry study involving patients with in-hospital cardiac arrest in any rhythm showed poorer neurologic outcomes and survival with hypothermia than with no specific temperature-management strat-

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egy.[10] However, no details were supplied about the hypothermia methods, temperatures achieved, or temperature management in patients who did not receive hypothermia. In addition, although propensity-score matching was used, the differences between the two groups suggest missed confounders, such as bystander resuscitation and no-flow duration. Cardiac arrest is a highly heterogeneous entity, and many factors may affect the efficacy of hypothermia. In a retrospective cohort study, the efficacy of hypothermia increased with no-flow duration,[30] although this result was not replicated in a post hoc analysis of the TTM trial.[31]

Moderate therapeutic hypothermia has been shown to improve neurologic outcomes in patients with severe ischemia-reperfusion brain injury.[32,33] We consequently included patients with worse cardiopulmonary-resuscitation characteristics, such as long no-flow and low-flow times and high epinephrine doses, as well as a larger proportion of patients with circulatory shock (58% in our trial vs. 15% in the TTM trial[28]). No-flow and low-flow times are very difficult to determine accurately.[34] It is possible that a global predictor such as the Cardiac Arrest Hospital Prognosis score[35] may prove useful in the future for constituting uniform patient groups.

Moderate therapeutic hypothermia improved the neurologic prognosis but not survival at 90 days, whereas the opposite has been reported for epinephrine.[36] The number needed to treat for one additional patient to survive with a CPC score of 1 or 2 is 22 with hypothermia, as compared with a number needed to treat to prevent one death of 15 with bystander CPR[37] and 112 with epinephrine.[36]

Our trial has several limitations. First, the primary outcome was assessed during a telephone interview rather than a face-to-face interview. Second, a substantial proportion of patients had body temperatures above 38°C, notably after the period of targeted temperature management. We chose 37°C as the target in the control group to avoid hyperthermia during the period of targeted temperature management.[38] Third, we used targeted temperature management for 56 to 64 hours in the hypothermia group and for 48 hours in the normothermia group to avoid rebound hyperthermia.[39] Data to indicate that prolonging targeted temperature management beyond 48 hours may help to prevent or treat neurologic injuries are limited.[15,28] Fourth, patients with missing data were assumed to have died. However, only three patients (one in the hypothermia group and two in the normothermia group) had missing data. Last, the fragility index value of 1 for our trial indicates that an outcome change in a single patient would make the difference in the primary outcome nonsignificant. However, all three patients who withdrew consent were in the hypothermia group. The point estimate for the absolute between-group difference in the frequency of a good outcome of 4.5 percentage points (95% CI, 0.1 to 8.9) in favor of hypothermia as compared with the 5.7% frequency with normothermia is of clinical importance (which is different from statistical significance).[40]

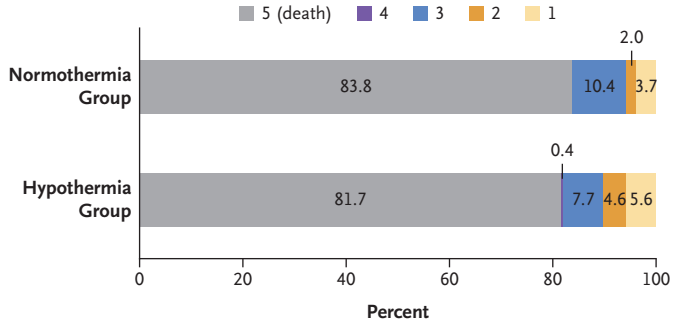

Figure 3. Distribution of Cerebral Performance Category Scores on Day 90 after Randomization.

Cerebral Performance Category (CPC) scores range from 1 to 5, with higher scores indicating greater disability. Patients who were lost to follow-up (one in the hyperthermia group and two in the normothermia group) were assigned a score of 5, indicating death. For this trial, a favorable neurologic outcome was defined as a CPC score of 1 (good cerebral performance or minor disability) or 2 (moderate disability).[20] Percentages may not total 100 because of rounding.

In conclusion, among patients with coma who had been resuscitated from in-hospital or out-of-hospital cardiac arrest with nonshockable rhythm due to cardiac or noncardiac causes, the use of moderate therapeutic hypothermia at 33°C led to a higher percentage of patients who survived with a favorable neurologic outcome at day 90 than was observed with targeted normothermia.

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APPENDIX

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