Induced hypothermia by central venous infusion: Saline ice slurry versus chilled saline

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Objective: **Surface cooling improves outcome in selected comatose survivors of cardiac arrest. Internal cooling with considerable volumes of intravenous cold saline may accelerate hypothermia induction. This study compares core temperatures in swine after central catheter infusions of saline ice slurry (saline with smoothed 100-μm-size ice particles) vs. an equal volume of chilled saline. We hypothesized that slurry would achieve core hypothermia (32–34°C) more consistently and at a faster rate.**

Design: **A total of 11 swine were randomized to receive microparticulate ice slurry, chilled saline infusion, or anesthesia alone in a monitored laboratory setting.**

Interventions: **Intravenous bolus (50 mL/kg) of slurry or chilled 1.5% NaCl saline. Slurry was composed of a 1:1 mixture of ice and distilled H_2O plus NaCl.**

Measurements: **Cerebral cortex, tympanic membrane, inferior vena cava, rectal temperatures, electrocardiogram, arterial blood pressure, and arterial oxygen saturation were recorded for 1 hr after bolus.**

Main Results: **Compared with anesthetized controls, core brain temperatures of the saline and slurry groups dropped by 3.4 ± 0.4°C and 5.3 ± 0.7°C ($p = .009$), respectively. With an infusion rate of 120 mL/min, cooling rates for the saline and slurry groups were −11.6 ± 1.8°C/hr and −18.2 ± 2.9°C/hr, respectively, during the first 20 mins. Four of four animals in the slurry group vs. zero of four animals in the saline group achieved target cortical temperatures of <34°C.**

Conclusions: **Cold intravenous fluids rapidly induce hypothermia in swine with intact circulation. A two-phase (liquid plus ice) saline slurry cools more rapidly than an equal volume of cold saline at 0°C. Ice-slurry could be a significant improvement over other cooling methods when rate of cooling and limited infusion volumes are important to the clinician. (Crit Care Med 2004; 32[Suppl.]:S425–S431)**

KEY WORDS: induced hypothermia; therapeutic hypothermia; cooling; resuscitation; cardiac arrest; swine; slurry; intravenous; saline; core temperature

Cardiac arrest survivors often have severe neurologic sequelae that contribute to their early mortality and poor functional recovery. Induced postresuscitative hypothermia was first reported almost 40 yrs ago as a technique for improving functional outcomes after cardiac arrest (1, 2). The conceptual appeal of such therapeutic hypothermia stemmed primarily from the notion that decreases in core temperature lead to decreased cellular metabolic demand. Cerebral metabolic demand decreases by approximately 6% per degree Celsius (3). Despite this, postresuscitative hypothermia was largely abandoned as a difficult and resource-intensive technique with uncertain clinical benefits.

However, the clinical induction of hypothermia has found widespread acceptance in the perioperative setting during cardiac bypass and certain neurosurgical procedures. In the surgical setting, unlike cardiac arrest, hypothermia is induced before the ischemic insult occurs. Indeed, in the relatively controlled environment of the operating suite, hypothermia induction has been a viable therapeutic option that is protective against conditions of altered blood flow. In addition, hypothermia has also been applied to the treatment of malignant hyperthermia, traumatic brain injury, and acute myocardial infarction (4–7).

Two recent multiple-center, prospective studies of comatose survivors of out-of-hospital cardiac arrest demonstrated improved neurologic outcome at hospital discharge (8) and improved neurologic outcome and mortality rate at 6 months (9) in patients receiving 12–24 hrs of hypothermia (32–34°C) after return of spontaneous circulation. Based on the strength of these findings, the International Liaison Committee on Resuscitation recommended the induction of therapeutic hypothermia for 12–24 hrs in selected comatose survivors after out-of-hospital cardiac arrest with initial ventricular fibrillation (10). The International Liaison Committee on Resuscitation advisory statement calls for the development of hypothermia-induction techniques

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Supported, in part, by NIH/NHLBI through 1RO1 (HL67630) and through a grant from the Laerdal Foundation.

Terry Vanden Hoek and Ken Kasza share first authorship of this article on the basis of their major contributions in working with Dr. Becker in the conception, planning, and execution of the experiments; David Beiser is second author for taking primary responsibility for writing the manuscript, analyzing data, and modeling the heat transfer.

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DOI: 10.1097/01.CCM.0000134259.59793.B8

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that are rapid, convenient, and minimally invasive.

Hypothermia Induction Methodologies: Surface and Internal Cooling

Each method for inducing hypothermia represents a different compromise among invasiveness, cooling rate, temperature control, and ease of use. Minimally invasive surface cooling techniques such as ice packs, forced-air cooling mattresses and blankets, and cooling caps have been used in clinical studies of patients with cardiac arrest (8, 9, 11, 12). In the Hypothermia After Cardiac Arrest study, the median time from return of spontaneous circulation to target core temperature (32–34°C) was 8 hrs (interquartile range, 4–16 hrs), with typical cooling rates of <1°C/hr (9). Some surface methods used in these studies require minimal equipment (e.g., ice packs) and can be initiated by paramedics. Others, such as cooling mattresses/blankets, require specialized equipment.

Internal cooling techniques such as endovascular cooling catheters have been developed to address the induction, maintenance, and rewarming phases of hypothermia. Such catheters have demonstrated rapid cooling rates in human-sized swine (4.5°C/hr) and nonhuman primates (6.3°C/hr) (13, 14). Recently, the Cool-MI study utilized endovascular cooling catheters for inducing hypothermia in awake, but sedated, patients in the setting of acute ST-segment elevation myocardial infarction (4). Although more invasive, this approach provides faster cooling rates and more precise temperature control than surface cooling. Other internal cooling techniques reported include the use of hemodialysis (15). Internal cooling techniques provide faster cooling; however, some of this advantage is lost because additional time is required for the set-up and placement of catheters and support equipment before cooling is initiated.

Recent studies have demonstrated that an intravenous bolus of chilled single-phase crystalloid fluid can quickly induce hypothermic core temperatures (16–19). Infusion of a large-volume bolus (40 mL/kg) of chilled saline via a femoral catheter produced an average 2.5°C decrease in core temperature within approximately 30 mins (17). One study of comatose out-of-hospital cardiac arrest survivors demonstrated an average 1.7°C decrease in bladder temperature after a bolus (30 mL/kg) of chilled (4°C) lactated Ringer's (given via peripheral or via central catheter). In addition, the group demonstrated a significant increase in mean arterial pressure. Despite the large bolus volume, none of the postarrest patients developed clinical or radiographic evidence of pulmonary edema (16).

The cooling rates achieved by intravenous chilled saline seem quite rapid, yet the large bolus volumes required to reach hypothermic temperatures remain a potential concern given the variation in cardiopulmonary dysfunction that may occur after return of spontaneous circulation. In addition to cardiac arrest, other resuscitation settings may require high cooling potential with limited fluid volumes. For example, recent strategies proposed for the treatment of hemorrhagic shock or traumatic brain injury include the use of hypertonic saline or the induction of mild hypothermia. Both strategies may attenuate inflammation associated with global ischemia/reperfusion (7, 20). However, higher sodium loads and concerns of diluting clotting factors or increasing edema limit the volume of saline that can be given.

Development of a Saline Slurry for Intravenous Application

We tested a microparticulate slurry (MPS) coolant originally developed by Argonne National Laboratory for industrial cooling applications. MPS, a two-phase fluid composed of smooth globular ice particles of <100 μm in diameter suspended in a liquid carrier medium (Fig. 1), has an inherent thermodynamic advantage over liquid saline, stemming from the energy required to melt ice in solution. For ice solutions, this so-called latent heat of fusion is approximately 80 cal/g solution. Accordingly, it requires 74 kcal of energy to melt and warm a 1000-mL sample of slurry composed of a 1:1 mixture of ice and saline from 0 to 34°C. By contrast, warming a similar sample of saline requires only 34 kcal.

A proprietary procedure for chemically and thermally smoothing individual

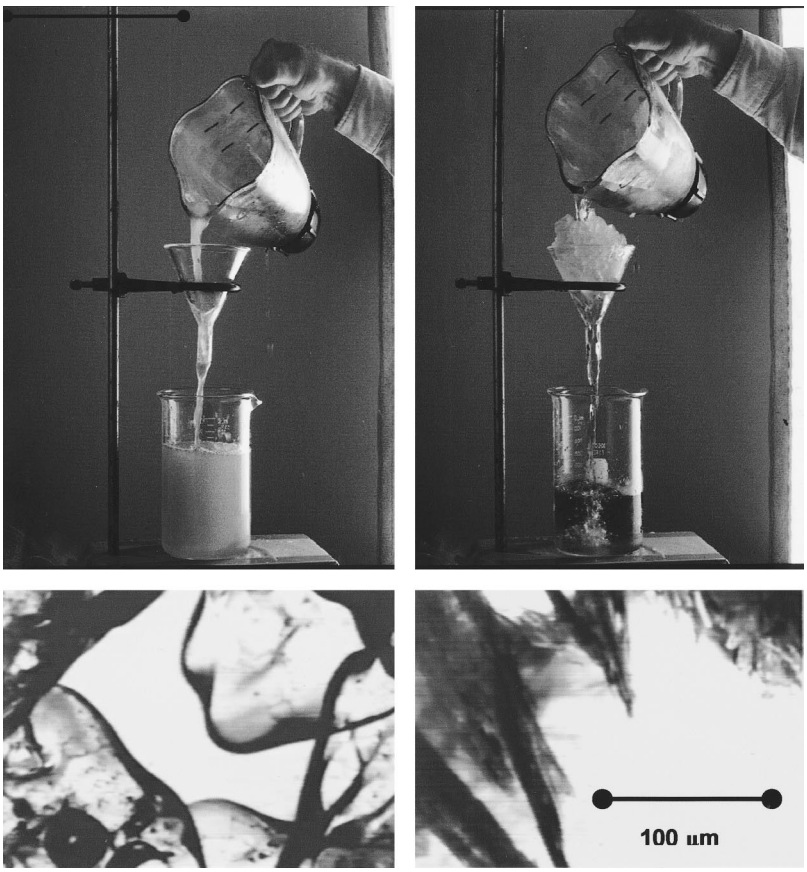

Figure 1. Microparticulate slurry (*left*, *top* and *bottom*) is composed of smooth globular (100 μm) ice particles with superior fluid dynamic properties that make it suitable for pumping through intravenous catheters. Dendritic ice (*right*, *top* and *bottom*), as produced by commercial slush beverage–making machines, cannot be readily pumped, and produces plugging when poured.

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ice particles is used to create a highly flowable MPS that can pass through small-diameter tubing without plugging (21). By contrast, ordinary ice-liquid suspensions (e.g., slush beverages) are composed of dendritic ice crystals that do not flow at high ice-particle loading values without plugging. The prototype MPS yields saline with a salt concentration of 1.5% by weight when fully melted. Although this MPS is necessarily hypertonic, future design improvements will likely yield solutions with decreased salt concentrations.

METHOD

We hypothesized that an intravenous bolus of MPS would induce hypothermia (32–34°C) more quickly than an equal bolus of chilled saline. We studied 11 farm swine, *Sus scrofa domestica*, using a protocol approved by the Institutional Animal Care and Use Committee. The swine were anesthetized with an intramuscular cocktail of ketamine, xylazine, tiletamine, and zolazepam (each at 2.2 mg/kg), followed by 1–2% isoflurane inhalant for maintenance of an appropriate depth of anesthesia during mechanical ventilation. A modified 9-Fr catheter was then placed in the right femoral vein for delivering the cooling solutions. Animals underwent bilateral temporal craniotomies for placement of thermocouples at a depth of 1.25 cm for recording cortical temperatures. Thermocouple probes, embedded in a thermoconductive paste, were inserted into the ear canal to the tympanic membrane for recording bilateral tympanic membrane temperatures. Rectal and inferior vena cava (IVC) temperatures were also recorded. Temperature data were acquired at 1-min intervals.

Three groups of animals were studied: saline infusion, MPS infusion, and anesthetized controls. For the saline group, a bolus (50 mL/kg target dose) of chilled (0–1°C) saline (1.5% NaCl by weight) was pumped through insulated tubing using a roller pump at 120 mL/min. During administration, temperatures were recorded at 1-min intervals for 60 mins after the start of the infusion. The animals were then killed. The MPS group received the same volume (50 mL/kg) of the MPS (equilibrium temperature of −1 to 0°C) initially, composed of a 1:1 mixture of distilled ice and H_2O plus 1.5% non-iodinated NaCl by weight. Although the initial ice loading of this mixture is 50%, a substantial amount of melting occurs during slurry processing to yield a delivered value of 15–20% ice by weight. Control data were obtained from animals utilizing the same anesthesia protocol and instrumentation without cooling.

RESULTS

The experimental group characteristics are detailed in Table 1. The weights of the saline and MPS animals were statistically indistinguishable. The average weight of the control group was statistically less than the saline group. Given their smaller thermal mass, the control group would be expected to display increased cooling rates after induction of general anesthesia, thus overestimating the effect of sedation alone on cooling rate (22). The delivered weight-based dosages of intravenous coolants, initial cortical temperatures, infusion time periods, mean arterial pressure, and heart rate were statistically indistinguishable in the saline and MPS groups. All experiments were performed in the same climate-controlled animal surgical suite set for 21–23°C.

With cooling, brain cortex temperatures in the saline and MPS groups decreased rapidly to their minima during the average infusion period of approximately 18 mins (Fig. 1). Minimum cortical temperatures for the MPS group were significantly lower than those of the chilled saline group (Fig. 2, Table 2). The cortex in each of the MPS swine reached temperatures of ≤34°C within an average time period of 7.0 (range, 3–10) mins, with an average absolute change in temperature of 5.3 ± 0.7°C, when the 20% ice-loaded MPS was delivered at a rate of 120 mL/min. The saline pigs achieved a 3°C temperature decrease after an average of 16.3 (range, 13–19) mins when near-0°C chilled saline was delivered at 120 mL/min; however, due to average initial core temperatures of >37°C, none crossed into the target range (32–34°C).

Average initial cooling rates using an infusion rate of 120 mL/min were estimated by averaging linear least-squares

Table 1. Experimental group characteristics

Characteristic	Control	Saline	MPS	*p* Value[a]
n	3	4	4	
Weight, kg	39.0 ± 1.7	45.4 ± 2.0	42.2 ± 2.8	.12
Dose, mL/kg	NA	49.7 ± 0.7	50.4 ± 0.8	.25
Infusion time, min	NA	18.8 ± 0.9	17.7 ± 1.0	.16
MAP, mm Hg	83.8 ± 12	78.3 ± 22	77.2 ± 15	.94
HR, beats/min	109 ± 28	94.5 ± 11	83.0 ± 19	.35

MPS, microparticulate slurry; NA, not applicable; MAP, mean arterial pressure; HR, heart rate.
[a]*p* values for *t*-test comparing saline and MPS groups only; weights of the control and MPS groups were statistically different ($p < .005$). Data are presented as mean ± SD.

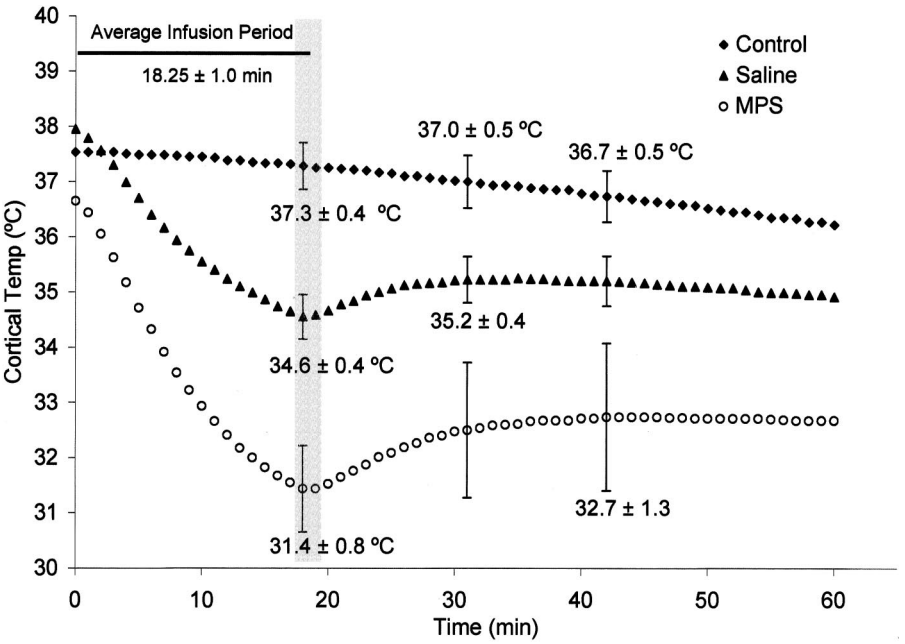

Figure 2. Average cortical temperatures with injection of saline and microparticulate slurry (*MPS*). Data presented as mean ± SD.

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approximations ($R > .95$) of the cortical temperature data sets between the initial and minimum temperature values (Table 2). Because the control pigs did not achieve minimum temperatures, their initial rates were calculated by choosing the temperature at the end of the average infusion period. At the same rate of infusion, the average initial cooling rate for the MPS group was approximately 50% faster than the saline group. After the infusion period, cortical temperatures partially rebounded to temperatures that were still significantly below the minimum cortical temperature of the control group.

Average rectal, tympanic membrane, cortical, and central venous temperatures for the saline group are presented in Figure 3. As expected, the venous temperature (from the thermocouple placed in the IVC) displayed the largest reduction in temperature during the infusion period. Like the cortical temperatures, the IVC and tympanic membrane temperatures reached minima followed by partial rebounds after the cessation of infusion. By contrast, the rectal temperature did not reach a minimum and continued to decrease after infusion (although at a slower rate). After the infusion, the temperatures equilibrated with each other after approximately 40 mins.

MPS induced a more profound instantaneous decrease in IVC temperature before dramatically rebounding to equilibrate with the cortical and tympanic membrane temperatures (Fig. 4). As noted for the cortical temperatures above, the rectal, tympanic membrane, and IVC temperatures did not continue to drop after rebound. Average tympanic membrane temperatures followed cooling trajectories that were qualitatively similar to cortical temperatures, reaching statistically equivalent minima ($p > .90$ for paired t-test) with a 2- to 4-min lag between cortical and tympanic thermocouple readings.

Finally, heart rate, mean arterial pressure, and arterial oxygen saturation remained statistically constant throughout the experimental period. In addition, no qualitative changes in the electrocardiogram wave morphologies were noted.

Table 2. Experimental cortical temperatures and cooling rates

Variable	Control	Saline	MPS	p Value[a]
Temperatures, °C				
Initial	37.5 ± 0.3	38.0 ± 0.4	36.7 ± 1.3	.13
Minimum	37.3 ± 0.3[c]	34.5 ± 0.4	31.4 ± 0.9	.002
Absolute ΔT	0.2 ± 0.1	3.4 ± 0.4	5.3 ± 0.7	.009
Rebound[b]	36.8 ± 0.5[c]	35.3 ± 0.4	32.8 ± 1.3	.028
Time to, mins				
T ≤ 34°C	NA	>60	7.0 ± 2.9	NA
ΔT > 3°C	NA	16.3 ± 2.8	8.3 ± 1.0	<.002
Cooling rate, °C/hr				
Initial 18 mins	−0.89 ± 0.7	−11.6 ± 1.8	−18.2 ± 2.9	<.002
Final 20 mins	−1.62 ± 0.35	−0.89 ± 0.46	−0.18 ± 0.40	.07

MPS, microparticle slurry; ΔT, change in temperature; T, temperature; NA, not applicable.

[a]p values compare saline and MPS groups; [b]rebound temperatures defined as maximum temperature after the infusion; [c]control minimum and rebound defined as temperature at the end of the average infusion period and at 40 mins, respectively. Data are presented as mean ± SD. Initial (18 mins) and final (20 mins) cooling rates were calculated by averaging least-squares linear approximations of individual data sets.

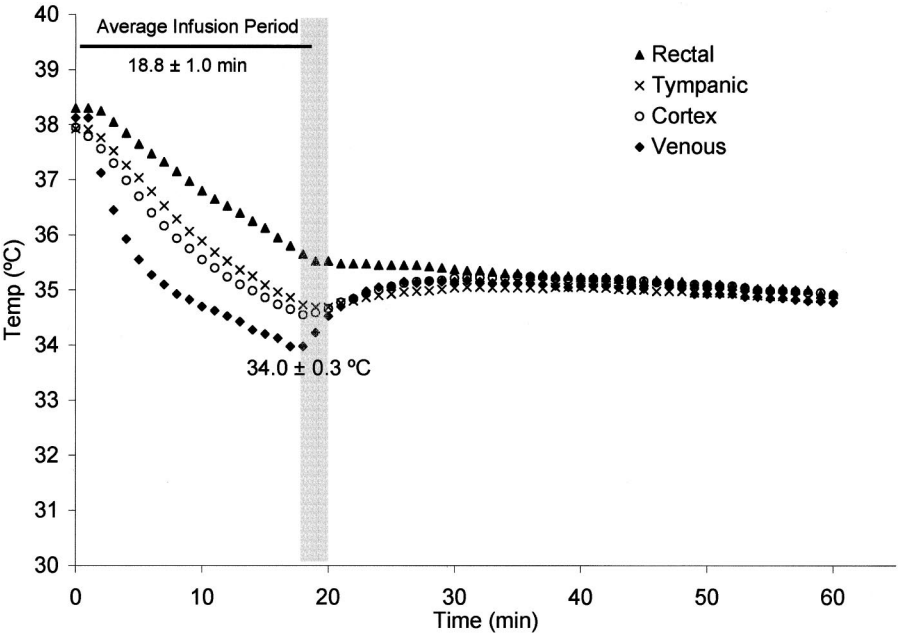

Figure 3. Average rectal, tympanic membrane, cortical, and central venous temperatures during cold saline infusion. Inferior vena cava temperature reached 34.0 ± 0.3°C at 17 mins.

DISCUSSION

The induction of hypothermia has recently been recommended for selected comatose cardiac arrest patients after return of spontaneous circulation (8–10). Given this international advisory statement and its clinical basis, there is a clear need for the development of hypothermia-induction techniques that are rapid, safe, and simple to implement in the emergent setting. Given concerns about fluid volume in resuscitation settings (both for cardiac arrest and hemorrhagic shock), coolants with greater cooling capacities, such as microparticulate ice slurries, may prove useful in this setting.

Characteristics of Intravenous Cooling. Several studies have sought to understand the mechanisms of human thermoregulation through theoretical models and experimental measures (17, 22–25). The simplest models partition the body into core and peripheral compartments. The core compartment, which comprises the highly perfused thoracoabdominal organs and brain, remains at a relatively uniform temperature, despite constant environmental changes. In our study, cortical brain temperatures served as the gold standard for recording core temperature; however, we found good correlation with tympanic membrane temperatures with a 2- to 4-min time lag. As previously observed, we found that rectal temperature was not a good proxy for core temperature (26). The peripheral compartment, which includes the limbs

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and skin, is characterized by a labile temperature that compensates for metabolic and environmental changes.

Temperatures in the anesthetized control animals decreased at absolute rates between 0.9 and 1.6°C/hr, which are consistent with temperature changes noted during the first hour after the induction of general anesthesia in humans. This decrease is primarily the result of redistribution of heat from the core to the periphery rather than environmental loss or decreased metabolic rate (27).

Our data suggest that a large resuscitation volume (50 mL/kg) intravenous bolus of MPS can rapidly induce mild to moderate hypothermia in the core compartment of swine with intact circulation. A bolus of chilled saline did not achieve cortical temperatures of ≤34°C but did produce a significant mean temperature decrease (3.4°C) slightly greater than previous studies utilizing smaller doses (30–40 mL/kg) of chilled saline in human volunteers and patients with cardiac arrest (16, 17).

Unlike surface cooling, intravenous coolants induce extremely rapid cortical cooling rates. In the current study, cortical temperature minima were reached within 1 min after completion of the 50 mL/kg bolus. This result suggests that cooling rate is heavily dependent on the rate of infusion such that increased rates of administration will likely yield faster cooling rates.

After the intravenous bolus, core temperatures uniformly displayed a pronounced partial temperature rebound (Fig. 1). Figure 4 suggests that the observed rebound could be secondary to redistribution of heat from relatively warmer areas such as the rectum, abdominal vessels, or peripheral tissues. Rajek et al. (17) noted a similar rebound effect in their detailed study of intravenous cooling in healthy volunteer subjects. By contrast, they concluded that the rebound was a result of metabolic heat constrained to the core via peripheral vasoconstriction. Despite this partial rebound, the MPS group core temperatures remained at <34°C.

Changes in Heat Content. As thermodynamic theory predicts, two-phase MPS induces lower core temperatures than chilled saline. To quantify this thermal advantage, we calculated the amount of heat absorbed by the coolants during each trial. The heat content of a liquid coolant increases as it absorbs energy from the body (Appendix, Eq. 1).

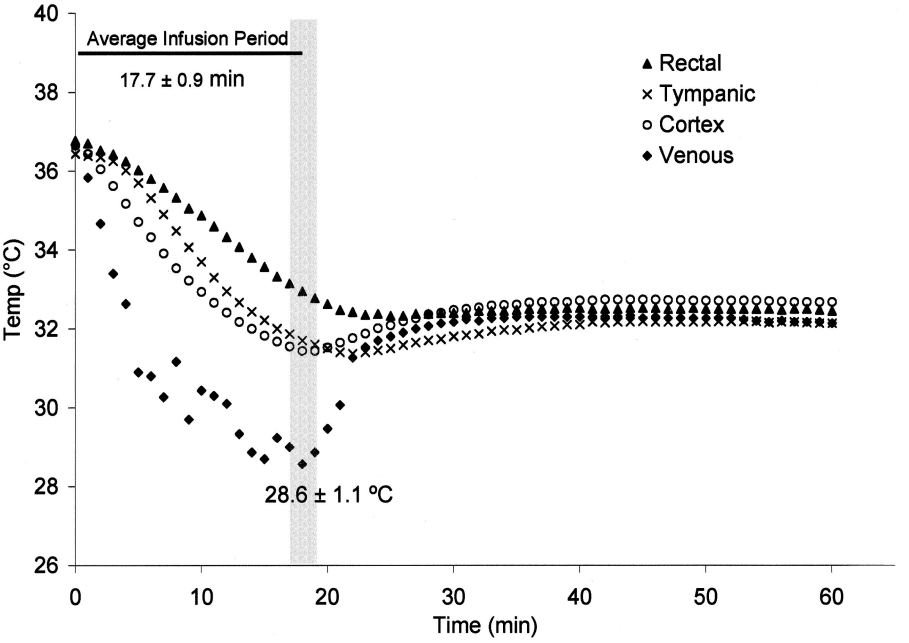

Figure 4. Average rectal, tympanic membrane, cortical, and central venous temperatures during microparticulate slurry infusion. Note that the central venous temperature reached 28.6 ± 1.1°C.

Table 3. Change in core heat content

Change in Heat Content, kcal	Control[a]	Saline	MPS
At minimum temperature			
Pig core	−3.9 ± 2.1	−77.2 ± 6.7	−110 ± 10.3
Coolant	NA	80.1 ± 3.4	103 ± 6.7
(Attributed to core)[b]	NA	(48)	(61)
Excess core cooling	3.9	29	49
At rebound temperature			
Pig core	−14.7 ± 5.5	−61.0 ± 1.5	−81.5 ± 2.4
Coolant total	NA	81.8 ± 3.2	106 ± 6.7
(Attributed to core)[b]	NA	(49)	(64)
Excess core cooling	14.7	12	17.5

MPS, microparticle slurry; NA, not applicable.

[a]Control group heat fluxes calculated using temperatures at 18 (minimum) and 40 (rebound) mins, respectively; [b]coolant heat content change attributed to core (in parentheses) was calculated by multiplying the coolant total by the 60% core partition estimate. Data are presented as mean ± SD.

$$\Delta Q = m \cdot C \cdot \Delta T \qquad [1]$$

Heat content changes for the saline coolant were calculated based on the minimum and rebound temperatures (Table 3). Heat content changes for the MPS coolant were calculated using an estimated ice load of 20% by weight (Appendix, Eq. 2).

$$\Delta Q_{MPS} = m_{MPS} \cdot C \cdot \Delta T + \%_{ice} \cdot m_{MPS} \cdot L \qquad [2]$$

We calculated the energy dissipated by the core compartment by assuming an average tissue-specific heat of 0.83 $kcal \cdot kg^{-1} \cdot °C^{-1}$ and an approximate 60/40 partition between the mass of the core and peripheral compartments for humans (27). Decreases in core compartment heat content for the control, saline, and MPS pig groups were calculated at the minimum and rebound temperatures (Table 3).

When calculated at the minimum temperature, total increases in coolant heat content are similar to the corresponding decreases in core heat content (Table 3). However, if we assume that heat absorption is proportionally distributed throughout the peripheral and core compartments, the proportional amount of coolant heating attributable to the core is only 60% of the total value (parenthetical values in Table 3). Once adjusted, the core heat loss exceeds the amount proportionally absorbed by the coolant. Such

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Two-phase (liquid plus ice) saline slurry cools more rapidly than an equal volume of cold saline at 0°C.

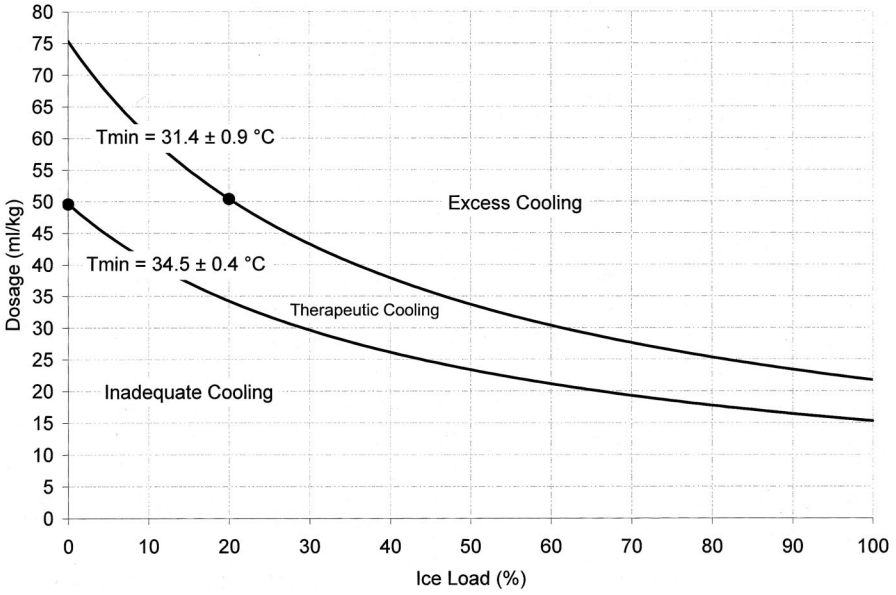

Figure 5. Theoretical dosage vs. ice load extrapolated from saline (*bottom curve*) and microparticulate slurry (*top curve*) cortical cooling minima data points (indicated by *circles*). Microparticulate slurry dosage/ice-load combinations falling between the curves will produce core temperature minimums within a range of 31.4 ± 0.9°C to 34.5 ± 0.4°C.

"excess core cooling," previously described in a study of human intravenous cooling, suggests that the coolant is preferentially constrained to the core compartment (17). Alternatively, this disparity may reflect inaccuracies in our 60/40 compartment partition assumption.

Risks and Benefits of Intravenous Cooling. Clinical studies confirm that humans are difficult to cool. The adult body combats accidental hypothermia by increasing metabolic heat production through shivering and by decreasing environmental losses by thermally isolating the core from the peripheral compartment via peripheral vasoconstriction (17, 22, 28). These compensatory mechanisms are attenuated during induction of general anesthesia, thus facilitating core cooling with surface methods (27, 29). However, in the postarrest setting, thermal isolation between the peripheral and core compartments is likely increased by the overall "adrenergic" state of the postarrest patient after administration of vasoactive medications. Our results suggest that intravenous coolants, when administered through a central catheter, may bypass the peripheral compartment completely. Although intravenous coolants may bypass the thermal resistance of the peripheral compartment, this thermal shunting may be attenuated when they are administered through a peripheral vein.

The heat content equation (Appendix, Eq. 2) shows that the cooling capacity of MPS is determined, in part, by the total dosage and ice-loading percentage. We can apply this relationship to the average data from the saline and MPS groups to estimate a range of dosage/ice-load combinations that would induce similar cortical cooling results (Fig. 5). The top curve, which is based on the MPS data, extrapolates the dosage/ice-load combinations that would produce minimum core temperatures approximately equal to the MPS group. The bottom curve combinations would lead to cooling results similar to the saline group. The region between the curves represents combinations that would lead to minimum temperatures between the MPS and saline group minima. Recall that the saline group did not quite reach the target range (32–34°C), whereas the MPS group produced minimum temperatures of <32°C. From the top curve of Figure 5, we can estimate that it would require a bolus of approximately 75 mL/kg of saline (i.e., 0 % ice load) to produce cooling equivalent to 50 mL/kg of 20% ice MPS. Similarly, it would take a bolus of approximately 34 mL/kg of 20% ice MPS to reproduce the saline results 50 mL/kg saline. As illustrated in Figure 5, when MPS ice loads are increased to >20%, the bolus volumes required for a given temperature change decrease significantly. With more highly loaded MPS, we expect smaller volumes to achieve the same degree of cooling. Minimizing the total volume of an intravenous coolant bolus might be important for avoiding pulmonary edema after cardiac arrest and hemodilution of clotting factors after hemorrhagic shock. Supporting this goal of reducing coolant volume, our collaborators at Argonne National Laboratory have recently improved MPS ice loading to levels up to 50% by weight. From Figure 5, we can predict that a 23 mL/kg bolus of 50% ice-load MPS would produce temperature minima similar to those observed in the saline group.

Another important consideration is whether the cooled blood traversing the heart may produce adverse effects. With the MPS group, the IVC reached a minimum temperature of 28.6 ± 1.1°C, which if transmitted to the myocardium, could theoretically induce ventricular fibrillation. Although we saw no adverse effects on hemodynamics or electrocardiogram tracings, this study was not by design powered to detect low-frequency events. A slower infusion rate or smaller bolus would likely attenuate the IVC temperature drop if required. The IVC temperature was almost 5°C lower than the rectal temperature for the MPS group and 2°C in the saline group. This reflects a thermal compartmentalization that could be even more pronounced during the low-flow setting of CPR.

In conclusion, cold intravenous fluids can rapidly induce hypothermia in pigs with intact circulation. A two-phase (liquid plus ice) MPS cools more rapidly and effectively than cold saline at 0°C. Ice slurry could be a significant improvement over other cooling methods when speeds of cooling and low infused volumes are important to the clinician. Further work on methods for the intravenous induction of hypothermia is warranted.

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ACKNOWLEDGMENTS

We thank the staff of the University of Chicago Animal Resources Center and Lynne Harnish for her administrative support.

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APPENDIX

Calculating Heat Content. The heat content of a coolant increases as it absorbs energy from the body. For a single-phase coolant such as saline, this increase in heat content is directly related to the change in coolant temperature (Eq. 1) through a constant known as the specific heat (1 $kcal \cdot kg^{-1} \cdot °C^{-1}$ for saline).

The net amount of energy absorbed by the saline during the initial cooling period is exactly determined by the initial and minimum coolant temperatures. Using an aggregate value for the specific heat of human tissue (0.83 $kcal \cdot kg^{-1} \cdot °C^{-1}$) and a core compartment of approximately 60% of the body, we used Equation 1 to calculate an estimated change in the core compartment's heat content (Table 3) for the control, saline, and MPS groups (27).

Where ΔQ = heat flux (kcal), m = saline coolant (or core) mass (kg), C = specific heat of coolant (or core tissue, $kcal \cdot kg^{-1} \cdot °C^{-1}$), and ΔT = temperature change of coolant (or core, °C).

For the MPS coolant, a term is added to account for the energy required to melt the ice particles during warming (Eq. 2). The energy required to promote this phase change is determined by the latent heat of fusion and mass of ice in solution. Ice particles initially comprise 50% of the MPS mass, although this fraction decreases to approximately 15–20% as a result of the smoothing process. For simplicity, we ignore the negligible amount of energy required to warm slurry ice from −1°C to its 0°C melting point.

Where ΔQ_{MPS} = change in MPS heat content (kcal), m_{MPS} = MPS mass (kg), $\%_{ice}$ = percentage of ice loading (15–20%), C = specific heat of saline (1 $kcal \cdot kg^{-1} \cdot °C^{-1}$), L = latent heat of fusion for ice (80 kcal/kg), and ΔT = change MPS temperature (°C).

Equation 2 can be rearranged to illustrate the inverse relationship between MPS dosage and percentage of ice load (Eq. 3).

$$m_{MPS} = \frac{\Delta Q_{MPS}}{C \cdot \Delta T + \%_{ice} \cdot L} \qquad [3]$$

We can extrapolate combinations of MPS mass and ice load that would produce temperature minima observed in the saline and MPS groups (Fig. 5).

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