Journal of Athletic Training 2021;56(4):383–388
doi: 10.4085/1062-6050-0146.20

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Cooling Capacity of Transpulmonary Cooling and Cold-Water Immersion After Exercise-Induced Hyperthermia

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Context: Cold-water immersion (CWI) may not be feasible in some remote settings, prompting the identification of alternative cooling methods as adjunct treatment modalities for exertional heat stroke (EHS).

Objective: To determine the differences in cooling capacities between CWI and the inhalation of cooled air.

Design: Randomized controlled clinical trial.

Setting: Laboratory.

Patients or Other Participants: A total of 12 recreationally active participants (7 men, 5 women; age = 26 ± 4 years, height = 170.6 ± 10.1 cm, mass = 76.0 ± 18.0 kg, body fat = 18.5% ± 9.7%, peak oxygen uptake = 42.7 ± 8.9 mL·kg^{-1}·min^{-1}).

Intervention(s): After exercise in a hot environment (40°C and 40% relative humidity), participants were randomized to 3 cooling conditions: cooling during passive rest (PASS; control), CWI, and the Polar Breeze thermal rehabilitation machine (PB) with which participants inspired cooled air (22.2°C ± 1.0°C).

Main Outcome Measure(s): Rectal temperature (T_{REC}) and heart rate were continuously measured throughout cooling until T_{REC} reached 38.25°C.

Results: Cooling rates during CWI (0.18°C·min^{-1} ± 0.06°C·min^{-1}) were greater than those during PASS (mean difference [95% CI] of 0.16°C·min^{-1} [0.13°C·min^{-1}, 0.19°C·min^{-1}]; $P < .001$) and PB (0.15°C·min^{-1} [0.12°C·min^{-1}, 0.16°C·min^{-1}]; $P < .001$). Elapsed time to reach a T_{REC} of 38.25°C was also faster with CWI (9.71 ± 3.30 minutes) than PASS (–58.1 minutes [–77.1, –39.9 minutes]; $P < .001$) and PB (–46.8 minutes [–65.5, –28.2 minutes]; $P < .001$). Differences in cooling rates and time to reach a T_{REC} of 38.25°C between PASS and PB were not different ($P > .05$).

Conclusions: Transpulmonary cooling via cooled-air inhalation did not promote an optimal cooling rate (>0.15°C·min^{-1}) for the successful treatment of EHS. In remote settings where EHS is a risk, access and use of treatment methods via CWI or cold-water dousing are imperative to ensuring survival.

Trial Registry: ClinicalTrials.gov (NCT0419026).

Key Words: rectal temperature, transpulmonary cooling, body cooling, exertional heat stroke

Key Points

- Cold-water immersion had a greater cooling capacity after exercise-induced hyperthermia than that of cooling during passive rest or transpulmonary cooling.
- Transpulmonary cooling via inhalation of cooled air after exercise-induced hyperthermia did not enhance the body's cooling capacity when compared with cooling during passive rest.
- Whole-body, cold-water immersion remained the most effective cooling modality for lowering body temperature in individuals with hyperthermia.

Exertional heat stroke (EHS), an emergency medical condition diagnosed as a rectal temperature (T_{REC}) of >40°C in conjunction with central nervous system dysfunction, requires immediate and aggressive whole-body cooling to limit the time the critical threshold for cell damage (40.83°C) is exceeded and ensure survival.[1–5] The current criterion standard method of treatment and care for EHS is immediate, onsite, whole-body cooling using cold-water immersion (CWI), which has been reported to have an optimal cooling rate (>0.15°C·min^{-1}).[6,7] In treating patients with EHS, selecting a cooling modality with an optimal cooling rate is crucial to limit the time above the critical body temperature threshold of 40.83°C to <30 minutes for the best chance of survival and minimize the severity of the prognosis.

In certain settings and scenarios (eg, wilderness firefighting, military operations, and remote athletics events), it may not be feasible to use CWI to treat a patient with EHS. Although previous researchers[8,9] suggested that a modified approach to CWI (ie, tarp-assisted cooling) yielded optimal cooling rates, this method relies on having ice and water readily available. Human lungs, with a purported surface area-to-body surface area ratio between 16 : 1 and 59 : 1,[10,11] are theorized to be an effective route for heat dissipation.[12–17] This theory, termed *transpulmonary cooling*, is supported by the combined effects of the Fourier law of heat conduction that expresses the rate of heat transfer as a proportion of the negative temperature gradient and overall area available for heat transfer,[18] the overall surface area and associated thinness of the alveolar membrane,[10] and the physiological responses (ie, increased cardiac output and pulmonary ventilation) associated with exercise or passive hyperthermia.[19]

Despite evidence showing that the airway may be an effective route for heat loss in both human[13,17] and animal models,[12,14–16] earlier researchers only performed this work when participants were under anesthesia[12–16] or exposed to passive hyperthermia or exercise that minimized the extent of hyperthermia.[17] Furthermore, in the previous work, the investigators did not compare the cooling capacity of transpulmonary cooling with that of CWI. Therefore, the aim of our study was to compare the cooling capacity of transpulmonary cooling delivered via the inhalation of cooled air, CWI, and cooling during passive rest (PASS) after exercise-induced hyperthermia. We hypothesized that transpulmonary cooling would be an inefficient method of body cooling after exercise-induced hyperthermia when compared with CWI.

METHODS

Participants

Twelve recreationally active individuals (42% female, n = 5; Table 1) volunteered to participate in this randomized, crossover design study (ClinicalTrials.gov Identifier NCT0419026). Participants completed 3 experimental exercise and cooling trials: exercise followed by PASS (control trial), exercise followed by transpulmonary cooling using a microenvironmental air-chiller thermal rehabilitation machine (Polar Breeze [PB]; Statim Technologies LLC), and exercise followed by cooling with CWI. Before the trials, each participant completed a medical history questionnaire to ensure the following criteria were met: (1) no chronic health problems; (2) no fever or illness at the time of testing; (3) no history of cardiovascular, metabolic, or respiratory disease; (4) no current musculoskeletal injury that limited the ability to exercise; (5) no history of exertional heat illness within the 3 years before the study; and (6) self-reported engagement in moderate- to vigorous-intensity exercise 3 to 4 $d \cdot wk^{-1}$ for at least 30 minutes per session. Menstrual status was not measured or used as an exclusionary factor. All participants provided written informed consent, and the study was approved by our university's institutional review board.

Experimental Protocol

Familiarization. Before the start of the exercise trials, participants arrived at the laboratory to become familiarized with the experimental procedures. Each person provided a measure of height, nude body mass (NBM), and body fat percentage. We measured NBM to the nearest 0.1 kg using a digital scale (model WB-800S Plus; Tanita Corp) and height to the nearest 0.1 cm using a wall-mounted stadiometer (model 216; Seca). Body density was measured using the methods established by Jackson and Pollock[20] and Jackson et al.[21] The average of 2 skinfold measures (Lange Skinfold Caliper; Beta Technology Inc) taken at 3 sites on the right side of the body were used; measures were obtained at the chest, abdomen, and thigh sites for men[20] and suprailiac, triceps, and thigh sites for women.[21] Body fat percentage was estimated using the method established by Siri.[22] Participants were also familiarized with the perceptual scales and the use of the PB. After being instructed in the use of the PB, participants performed a graded exercise test on a motorized treadmill (model T150; h/p/cosmos) so that we could assess peak oxygen uptake (VO_2peak). Oxygen uptake and related gas exchange were captured using open-circuit spirometry (model TrueOne 22400; Parvo Medics Inc). The resulting VO_2peak measure and corresponding running speed at which this was achieved were used to identify the participant's relative exercise intensities for each exercise trial.

Table 1. Participant Demographics[a]

Measure	Sex: Male (n = 7)	Sex: Female (n = 5)	Total (N = 12)
Age, y	24 ± 4	27 ± 5	26 ± 4
Height, cm	177.3 ± 5.7	161.3 ± 6.8	170.6 ± 10.1
Mass, kg	87.1 ± 13.9	60.5 ± 9.4	76.0 ± 18.0
Body fat, %	12.2.0 ± 6.5	27.3 ± 5.3	18.5 ± 9.7
Peak oxygen uptake, $mL \cdot kg^{-1} \cdot min^{-1}$	48.5 ± 7.0	34.7 ± 2.3	42.7 ± 8.9

[a] All values are mean ± SD.

Exercise Trials. To ensure that participants were properly hydrated, they were instructed to consume an additional 500 mL of water before bed the night before and the morning of their scheduled exercise trial. Upon arrival at the laboratory, participants provided a urine sample for assessment of urine specific gravity (USG) to ensure euhydration (USG <1.020).[23] If the USG was >1.020, he or she was instructed to consume 500 mL of water before the start of the exercise trial to ensure euhydration. They then provided a pre-exercise NBM (PRE_{NBM}), inserted a flexible thermistor (model 401AC; Measurement Specialties) 15 cm past the anal sphincter for assessment of T_{REC},[24] and donned electrodes (model EL503; Biopac Systems Inc) for assessment of heart rate (HR). For all exercise trials, participants wore shorts, T-shirts, and running shoes. Female participants also wore a sport bra.

Participants entered a climatic chamber (model CES-5-43; CANTROL International Inc) set at 40°C and 40% relative humidity and rested passively for 10 minutes to become acclimated to the environmental conditions. After the equilibration period, baseline measures of T_{REC}, HR, rating of perceived exertion (RPE),[25] thermal sensation,[26] and fatigue were taken. Fatigue was measured using an 11-point scale with words anchored at the following numbers: 0, *no fatigue at all*; 1, *very small amount of fatigue*; 2, *small amount of fatigue*; 3, *moderately fatigued*; 4, *somewhat fatigued*; 5, *fatigued*; 7, *very fatigued*; 9, *extremely fatigued*; and 10, *completely fatigued*. On a motorized treadmill, participants then began exercise that consisted of 3 sets of 20 minutes of exercise (a 5-minute walk on a 5% incline at a speed equal to 30% of their VO_2peak, followed by a 15-minute jog on a 1% incline at a speed equal to 70% of their VO_2peak). Exercise continued until (1) T_{REC} equaled 39.99°C, (2) the participant asked to stop, (3) the participant exhibited an altered or uneven gait, (4) HR was >5 beats/min from the participant's maximum for 5 minutes, or (5) 60 minutes of exercise had elapsed.

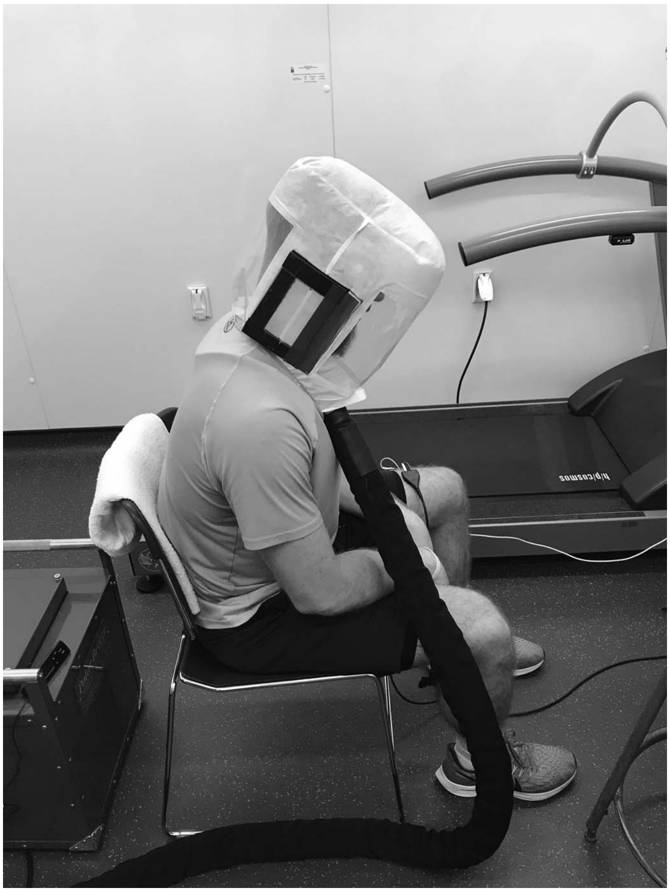

Figure 1. The Polar Breeze (Statim Technologies LLC) thermal rehabilitation machine during operation.

Throughout exercise, T_{REC} and HR were measured continuously, and perceptual scales were assessed periodically.

Immediately after exercise, participants stepped off the treadmill and took a seated position while remaining in the climatic chamber. Participants were randomly assigned to the PASS, PB, or CWI intervention. Cooling ceased after T_{REC} reached 38.25°C to provide an adequate cooling curve for calculation of cooling rates. For PASS, participants sat in a comfortable position in a chair in the climatic chamber and relied on their natural ability to dissipate stored body heat. For PB, participants donned a hood with a volume of 22 240 cm^3 that permitted cooled air (22.2°C ± 1.0°C) to flow into the hood from the thermal rehabilitation machine per the manufacturer's instructions (Figure 1). Ambient air (40°C and 40% relative humidity) inside the climatic chamber was drawn into the intake of the PB, where it passed through a series of thermocouples to cool the air. After being cooled, the air was pumped through the output hose and into the hood for participants to inhale. For CWI, participants sat in a tub of ice water (75.7 L of water, 75.7 L of ice, temperature = 1.45°C ± 2.3°C) and were immersed approximately to the level of the xiphoid process. During cooling, the ice water was continuously circulated to maximize convective cooling.

After cooling ended, we obtained the final physiologic and perceptual measures, and participants exited the climatic chamber. They dried off, removed the rectal thermistor, and provided a final NBM ($POST_{NBM}$) so that we could calculate the extent of body mass loss due to dehydration: $[(POST_{NBM} - PRE_{NBM})/PRE_{NBM}] \times 100$.

Statistical Analysis

All values are presented as mean ± SD unless otherwise noted. We evaluated normality of continuous variables using the Shapiro-Wilk test. For the continuous variables exhibiting a non-normal distribution and for all ordinal-scale perceptual data (RPE, thermal sensation, and fatigue), separate ordinal regression analyses were conducted to assess differences between trials across time. For the perceptual data, we used postcooling measures in PASS as our reference. Cooling rates were calculated using the following equation:

$$\text{Cooling Rate}\left(\mathrm{C}\cdot\mathrm{min}^{-1}\right) = \frac{\text{Precooling } T_{REC} - \text{Postcooling } T_{REC}}{\text{Time to cool to } T_{REC} = 38.25^{\circ}\mathrm{C}}$$

One-way analyses of variances (ANOVAs) were performed to assess differences among pre-exercise USG, percentage of body mass loss, and exercise time for each trial. A condition × time repeated-measures ANOVA was used to assess differences in NBM for each trial. To determine differences in the independent variables (cooling rates and time to cool to the established temperature thresholds between trials), we conducted separate 1-way ANOVAs. When we found a significant difference between trials, Tukey post hoc analyses were used to identify where the differences occurred. The magnitudes of differences were measured using η^2, with effect sizes interpreted as *small* ($\eta^2 < 0.01$), *medium* ($0.01 < \eta^2 > 0.06$), or *large* ($\eta^2 > 0.14$). Mean differences (MDs) and 95% the RPE CIs depicted the magnitude of differences. A post hoc power analysis (G*Power 3.1; Heinrich-Heine Universität, Düsseldorf) comparing the means of the cooling rates for CWI, PASS, and PB (primary outcomes) confirmed that the study was sufficiently powered (0.97). The α level was set a priori at .05. Statistical analyses were performed using SPSS (version 25; IBM Corp, Armonk, NY).

RESULTS

Participant characteristics across all 3 trials are presented in Table 2. The percentage of body mass loss was lower in CWI than PASS (MD [95% CI]; –0.7% [–1.2%, 0.2%]; $P = .02$). We observed no differences among trials for USG, NBM, T_{REC}, or exercise time ($P > .05$; Table 2).

Comparisons of average cooling rates across time for each cooling trial revealed that cooling rates were greater during CWI ($\eta^2 = 0.862$) than during PASS (0.16°C·min^{-1} [0.13°C·min^{-1}, 0.19°C·min^{-1}]; $P < .001$) and PB (0.15°C·min^{-1} [0.12°C·min^{-1}, 0.16°C·min^{-1}]; $P < .001$; Figure 2). The time to reach T_{REC} of 38.25°C was also shorter with CWI ($\eta^2 = 0.711$) than with PASS (–58.1 minutes [–77.1, –39.9 minutes]; $P < .001$) and PB (–46.8 minutes [–65.5, –28.2 minutes]; $P < .001$; Figure 3). Cooling rates and the time to reach a T_{REC} of 38.25°C between PASS and PB were not different ($P > .05$).

Changes in RPE, thermal sensation, and fatigue during cooling are depicted in Table 3. RPE, thermal sensation, and fatigue were lower across all trials at postcooling than at precooling ($P < .05$). Thermal sensation was lower

Table 2. Participants' Exercise Trial Characteristics[a]

Measure	Trial: Cooling During Passive Rest	Polar Breeze[b]	Cold-Water Immersion
Pre-exercise urine specific gravity	1.013 ± 0.009	1.013 ± 0.008	1.011 ± 0.008
Nude body mass, kg			
Pre-exercise	75.9 ± 17.8	75.9 ± 14.2	76.9 ± 18.7
Postexercise	74.2 ± 17.1	74.5 ± 17.3	75.5 ± 18.2
Body mass loss, %	2.1 ± 0.9	1.8 ± 0.6	1.4 ± 0.5[c]
Rectal temperature, °C			
Pre-exercise	37.45 ± 0.30	37.41 ± 0.32	37.39 ± 0.37
Postexercise	39.83 ± 0.15	39.72 ± 0.30	39.86 ± 0.19
Precooling	39.82 ± 0.21	39.73 ± 0.31	39.94 ± 0.18
Exercise time, min	54.5 ± 6.3	55.6 ± 6.0	53.0 ± 7.0

[a] All values are mean ± SD.
[b] Polar Breeze (Statim Technologies LLC) thermal rehabilitation machine.
[c] Different from cooling during passive-rest trial ($P = .02$).

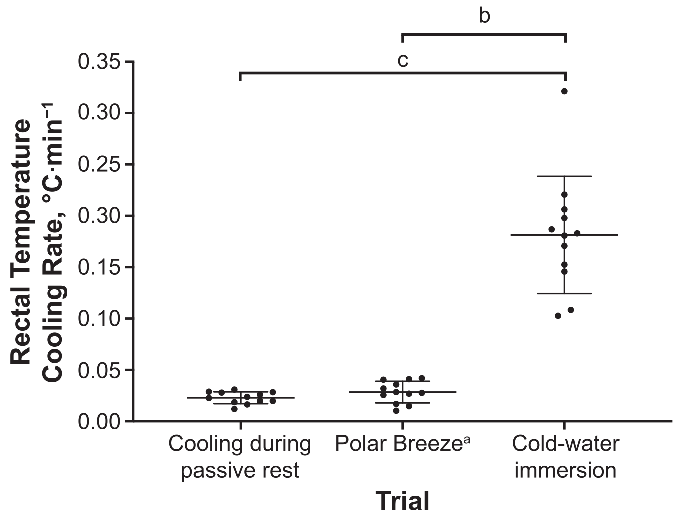

Figure 2. Rectal temperature cooling rates among the experimental trials. The dots represent individual participant cooling rates. The horizontal lines represent mean and associated standard deviation cooling rates. [a] Polar Breeze (Statim Technologies LLC) thermal rehabilitation machine. [b] Difference between the cold-water immersion and Polar Breeze trials ($P < .05$). [c] Difference between cold-water immersion and cooling during passive-rest trials ($P < .05$).

during PB ($P = .03$) and CWI ($P < .001$) than during PASS at postcooling. We observed no differences among trials for RPE and fatigue ($P > .05$).

DISCUSSION

The purpose of our study was to examine the efficacy of transpulmonary cooling in reducing body temperature after exercise-induced hyperthermia. Our primary findings showed that PB cooled the body more slowly (0.03°C·min^{-1}) than CWI (0.18°C·min^{-1}). Furthermore, the cooling rate of PB was not different from that of PASS (MD [95% CI]; 0.01°C·min^{-1} [–0.03°C·min^{-1}, 0.04°C·min^{-1}]; $P > .05$), providing further evidence that the inhalation of cooled air afforded by PB had no added cooling benefit beyond the body's ability to cool passively.

The ability to cool the body quickly after exercise-induced hyperthermia, especially when exertional heat illness is suspected, is paramount to ensuring survival.[1,27] Researchers have suggested that the optimal cooling rate to ensure survival from EHS exceeds 0.15°C·min^{-1},[1,4,7,8,27,28] with the goal of reducing the body temperature to 38.89°C within 30 minutes from the moment of collapse.[2,3,27] We confirmed that CWI exceeded the optimal cooling rate recommended for EHS treatment and reduced T_{REC} to our cooling threshold cutoff of 38.25°C in 9.71 ± 3.30 minutes. In comparison, the PASS and PB experimental trials averaged 68.22 ± 27.60 and 56.56 ± 25.52 minutes, respectively, to cool to 38.25°C (Figure 3).

When the cooling threshold cutoff was adjusted to 38.89°C, which aligns with the threshold to cease cooling during EHS care, CWI (6.85 ± 2.48 minutes) remained the best cooling option compared with PASS (38.87 ± 13.13 minutes) and PB (25.08 ± 10.82 minutes). Although PB exhibited an overall cooling time of <30 minutes, T_{REC} at the onset of cooling in PB averaged 39.70°C, which was less than the diagnostic criteria (40°C) for EHS. If these findings were extrapolated to a patient with EHS and an initial T_{REC} of 41.44°C[4] was assumed, 85 minutes (SD range = 63.75–127.5 minutes) would have been needed to cool the patient, which is well past the 30-minute period for ensuring survival.

Mariak et al[13] found that when patients inhaled cool air (22°C) after passive hyperthermia, they exhibited immediate declines in brain and esophageal temperature, providing evidence that the lungs can effectively cool the brain and a valid measure of body temperature used during exercise (ie, esophageal temperature). However, the rate of decline in T_{REC} did not match the former measures. Conversely, Kumar et al[12] noted that inhalation of cooled heliox (70% He, 30% O_2; 0°C ± 2°C) reduced T_{REC} in a swine model at

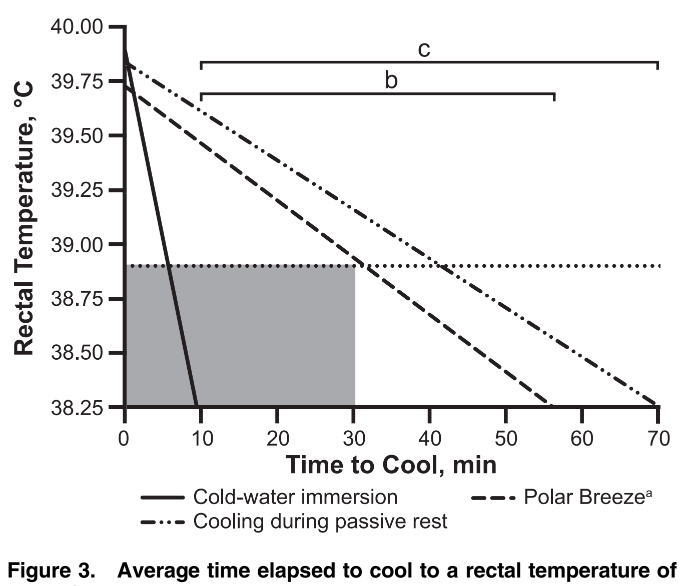

Figure 3. Average time elapsed to cool to a rectal temperature of 38.25°C. The dotted horizontal line depicts the current medical best practices for cooling cessation (38.9°C) in patients with exertional heat stroke. The shaded gray area depicts the area <38.9°C during the first 30 minutes of cooling, which is the current standard for exertional heat-stroke treatment. [a] Polar Breeze (Statim Technologies LLC) thermal rehabilitation machine. [b] Difference between the cold-water immersion and Polar Breeze trials ($P < .05$). [c] Difference between cold-water immersion and cooling during passive-rest trials ($P < .05$).

Table 3. **Changes in Perceived Thermal Sensation, Fatigue, and Perceived Exertion During Cooling**

Measure	Trial	Time	Estimate	95% CI	*P* Value
Rating of perceived exertion	Polar Breeze[a]	Precooling	3.812	2.045, 5.579	<.001[b]
	Polar Breeze	Postcooling	−0.666	−2.400, 1.068	.45
	Cold-water immersion	Precooling	4.286	2.453, 6.118	<.001[b]
	Cold-water immersion	Postcooling	0.846	−0.757, 2.450	.301
	Cooling during passive rest	Precooling	4.398	2.580, 6.216	<.001[b]
	Cooling during passive rest	Postcooling	Reference variable		
Thermal sensation	Polar Breeze[a]	Precooling	2.509	0.918, 4.101	.002[b]
	Polar Breeze[a]	Postcooling	−1.694	−3.242, −0.145	.03[c]
	Cold-water immersion	Precooling	3.378	1.674, 5.082	<.001[b]
	Cold-water immersion	Postcooling	−4.123	−6.042, −2.204	<.001[c]
	Cooling during passive rest	Precooling	3.400	1.721, 5.080	<.001[b]
	Cooling during passive rest	Postcooling	Reference variable		
Fatigue	Polar Breeze[a]	Precooling	2.366	0.847, 3.886	.002[b]
	Polar Breeze[a]	Postcooling	0.185	−1.248, 1.618	.80
	Cold-water immersion	Precooling	2.738	1.161, 4.315	.001[b]
	Cold-water immersion	Postcooling	−0.748	−2.287, 0.791	.34
	Cooling during passive rest	Precooling	3.132	1.549, 4.714	<.001[b]
	Cooling during passive rest	Postcooling	Reference variable		

[a] Polar Breeze (Statim Technologies LLC) thermal rehabilitation machine.
[b] Different from postcooling ($P < .05$).
[c] Different from cooling during passive-rest trial ($P < .05$).

a rate similar to that of esophageal, pulmonary artery, and tympanic membrane temperatures. Our results showed that transpulmonary cooling had no added cooling benefit for T_{REC} compared with passive cooling. An argument could be posed that because we assessed T_{REC}, we would not have been able to capture the acute changes in body temperature that may have occurred in the esophagus or tympanic membrane, as reported by earlier authors. Although this argument may have merit, given the medical literature on the pathophysiological cascade emanating from the gastrointestinal tract with the infiltration of endotoxins into the systemic circulation during EHS[29–32] and the current best medical practices regarding the recognition of EHS,[2,3,27] assessing the effect of transpulmonary cooling on T_{REC} is imperative.

We observed that after exercise-induced hyperthermia, RPE, thermal sensation, and fatigue declined at the postcooling timepoint. Furthermore, thermal sensation was less with both the CWI and PB trials than with the PASS trial at postcooling, which is supported by evidence suggesting that reductions in skin temperature after exercise alleviate thermal discomfort.[33,34] Based on the differences in thermal sensation among trials at postcooling that stemmed from afferent feedback of the thermoreceptors on the skin, we speculated that thermal sensation during PB may have been lower throughout cooling than during PASS, despite no difference in cooling rates. The latter could create a scenario in which thermal sensation may be reduced (ie, a sustained elevated internal body temperature), and another bout of physical activity (eg, following thermal rehabilitation in occupational settings, halftime during sport) may increase the risk profile of exertional heat illness.

Our study had a number of strengths. First, our randomized crossover clinical trial design allowed participants to act as their own controls when we compared the experimental trials. Second, the comparison of the PB with CWI in both men and women after exercise-induced hyperthermia (>39.75°C) allows these results to be directly translated to clinical practice. Third, using a controlled laboratory setting allowed us to control factors that may influence cooling capacity, such as environmental conditions and hydration status.

However, this work was not without limitations. We examined only the utility of the PB on postexercise cooling, which did not provide any evidence on the ability of the PB to attenuate the rise in body temperature from repeated bouts of exercise in a hot environment, such as during firefighting operations or at halftime in an athletic competition. We were also unable to reduce the air temperature from the PB to <22.2°C ± 1.0°C because of the machine constraints in cooling the air from the external environment. Further reducing the temperature of the inspired air may offer added benefits to the body's ability to cool. We were also unable to discern the effect of transpulmonary cooling with the PB given that the cooled air was inspired and then passed over the face and torso of participants.

CONCLUSIONS

After exercise-induced hyperthermia, transpulmonary cooling using the PB did not exhibit cooling rates similar to those of CWI. For the treatment of EHS, whole-body CWI remains the criterion standard.

ACKNOWLEDGMENTS

We acknowledge Statim Technologies for providing funding for this study.

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