Effects of Cold Modality Application With Static and Intermittent Pneumatic Compression on Tissue Temperature and Systemic Cardiovascular Responses

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Background: In the therapeutic setting, cryotherapy with varying levels of intermittent cyclical compression often replaces an ice bag and elastic wrap. However, little is known about the cardiovascular strain and tissue temperature decreases associated with cooling and intermittent compression.

Hypothesis: The authors hypothesized that higher levels of intermittent compression will result in greater reductions of tissue temperature and that all cold modalities will cause acute increases in cardiovascular strain.

Design: Experimental crossover repeated measure design.

Methods: Ten healthy subjects (23 ± 3 years) volunteered for 4 cryotherapy sessions (30-minute treatments with 30-minute passive recovery). Treatments included ice with elastic wrap and Game Ready (GR) with no, medium (5-50 mmHg), and high compression (5-75 mmHg). Throughout the experiment, oral, skin surface, and intramuscular quadriceps temperatures were measured along with mean arterial pressure, heart rate, rate pressure product, forearm blood flow, and forearm vascular conductance.

Results: Mean arterial pressure increased up to 5 minutes ($P < 0.05$). Forearm blood flow and forearm vascular conductance decreased after baseline ($P < 0.05$), but there were no differences between treatments. Peak intramuscular changes from baseline were $-14 ± 2°C$ (ice), $-11 ± 6°C$ (GR$_{HIGH}$), $-10 ± 5°C$ (GR$_{MED}$), and $-7 ± 3°C$ (GR$_{NO}$). Ice cooled the muscle the most, while GR with medium and high compression cooled more than GR without compression ($P < 0.05$).

Conclusions: The application of cold and intermittent pneumatic compression using GR did not produce acute cardiovascular strain that exceeded the strain produced by standard ice bags/elastic wrap treatment. Greater temperature decreases are achieved with medium- and high-pressure settings when using the GR system.

Clinical Relevance: Type of cold and amount of compression affect tissue cooling in healthy lean subjects. All tested cold modalities caused acute increases in cardiovascular strain; however, these increases are no more than what healthy subjects experience with the onset of exercise.

Keywords: cryotherapy; blood pressure; blood flow

Cryotherapy, the application of cold to the body, is a widely accepted modality used to manage musculoskeletal injuries. The benefits of cryotherapy immediately after application include higher pain threshold,$^1$ pain tolerance,$^1$ and slower nerve conduction velocity.$^{1,4}$ Cryotherapy mitigates inflammatory processes by decreasing tissue metabolic rate,$^{8,10,22,24}$ attenuating ischemic tissue damage,$^9,38$ and reducing microcirculatory impairment and muscle necrosis.$^{29}$ Ice bags with compression are a commonly used cold modality. Various compression methods are used, including Flex-i-Wrap (Cramer Products Inc, Gardner, Kansas)$^{34}$ and elastic wraps.$^{26,30,34}$ It is well known that external static compression with ice increases the magnitude of cooling on the skin surface$^{10}$

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and intramuscularly. Because of the positive therapeutic results of cold and compression, various cryotherapy devices have been marketed to provide continuous cooling with external compression. The Game Ready (Game Ready, Alameda, California) provides the continuous circulation of water (ie, ice water) through a flexible fabric and plastic wrap and dynamic intermittent intermittent pneumatic compression. The therapeutic temperature of the Game Ready system is controlled by the amount of ice and water added to the Game Ready cooler and can be manually adjusted during treatment (ie, with the addition of more ice). To provide cooling, the Game Ready system pumps the ice-cold water from the cooler and air into separate chambers of a therapeutic wrap. The system can be set to cyclically inflate and deflate (~3-minute cycles) at different levels of pressure so that a limb is compressed with pneumatic pressures ranging between 5 to 75 mmHg.

There are contraindications and precautions with the application of all cold modalities, including advanced diabetes, cold allergies, preexisting skin anesthesia, peripheral vascular diseases, uncovered open wounds, and cardiorespiratory conditions. Many investigators have used acute exposure (1-6 minutes) to immersion of the hand or foot in ice water (ie, the cold pressor test) in an effort to elicit an increase in sympathetic neural outflow and the associated increases in arterial pressure. While the cold pressor test has been well characterized experimentally, we do not fully understand the arterial blood pressure and other cardiovascular responses to the application of therapeutic cooling (≥ 30 minutes) and compression. It is also unknown whether the therapeutic combination of cold and different levels of intermittent pneumatic compression will elicit further increases in cardiovascular strain.

The purpose of this study was to investigate the cardiovascular responses and tissue temperature decreases of common therapeutic applications of cryotherapy, including ice bag/elastic wrap and the continuous circulating water and intermittent pneumatic compression provided by the Game Ready system. We examined the intramuscular and skin surface temperature responses as well as several systemic cardiovascular responses to the combination of 30 minutes of cold and compression therapy, following by 30 minutes of passive recovery. We used the ice bags/elastic wrap as our “control” condition, as it serves as the most common therapeutic applications of cryotherapy, including advanced diabetes, cold allergies, preexisting skin anesthesia, peripheral vascular diseases, uncovered open wounds, and cardiorespiratory conditions. Many investigators have used acute exposure (1-6 minutes) to immersion of the hand or foot in ice water (ie, the cold pressor test) in an effort to elicit an increase in sympathetic neural outflow and the associated increases in arterial pressure. While the cold pressor test has been well characterized experimentally, we do not fully understand the arterial blood pressure and other cardiovascular responses to the application of therapeutic cooling (≥ 30 minutes) and compression. It is also unknown whether the therapeutic combination of cold and different levels of intermittent pneumatic compression will elicit further increases in cardiovascular strain.

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**METHODS**

**Study Design**

An experimental crossover design with repeated measures (time) was used. Our independent variables included treatment and time. Treatment included ice bag/elastic wrap (control condition), Game Ready no compression (GR

**Subjects**

Ten healthy subjects (9 men and 1 woman; 23 ± 3 years; 70 ± 11 kg; 173 ± 10 cm; 11.3 ± 3.6 mm, thigh skinfold; mean ± SD) volunteered. The study was reviewed and approved by the Institutional Review Board. Inclusion criteria were men and women 18 to 36 years old with no current or recent (within 12 months) knee, thigh, or lower leg injuries. Exclusion criteria included cardiovascular risk factors, active infection, medication that would affect the cardiovascular system or temperature response of the muscles, hypersensitivity to needles or cold, and thigh skinfold caliper measurement greater than 45 mm. Subjects were also requested to refrain from vigorous physical exercise, alcohol, and caffeine consumption 24 hours prior to scheduled experiment. All 10 subjects completed the 4 therapeutic treatments; however, only 7 subjects’ data were collected for the FBF and VFC data (6 men and 1 woman; 22 ± 4 years; 72 ± 13 kg; 174 ± 9 cm; 10.8 ± 2 mm, thigh skinfold).

**Instrumentation**

**Tissue temperature.** We used an intramuscular-implantable tissue thermocouple (Type IT-18 copper constantan, Physitemp Inc, Clinton, New Jersey) to measure T

**Subcutaneous adipose.** We used a Lange skinfold caliper (Beta Technology, Santa Cruz, California) to assess the skin and subcutaneous adipose layer thickness of the left distal quadriceps.

**Cardiovascular parameters.** An electrocardiogram monitored HR continuously. Automated sphygmomanometry (Tango+,
Suntech Medical, Morrisville, North Carolina) was used to collect blood pressure. Strain gauge plethysmography using venous occlusion (DE Hokanson Inc, Bellevue, Washington) measured FBF as previously described. We chose the forearm as the site of measurement to reflect whole body changes in blood flow and global vascular responses and because these measurements did not interfere with the treated leg. We recorded data using AcqKnowledge Software (BioPac Systems Inc, Goleta, California).

Cold modalities. The cooling experiment used 4 different cold modalities: 2 standard ice bags (each unfilled bag 26 × 46 cm = 1196 cm²), GRLOW, and GRMED (5 to 50 mm Hg) and GRHIGH (5 to 75 mm Hg) with standard knee sleeve (71 × 43 cm = 3053 cm²). Equal amounts of crushed ice were added to the 2 ice bags and Game Ready cooler. A 6-in double elastic wrap secured the ice bags on the distal thigh. A blood pressure cuff bladder (inflated to ~30 mmHg) was placed on top of the ice bags but under the elastic wrap to standardize the amount of compression. Game Ready provides cyclical pneumatic compression via approximately 3-minute pressure cycles (1 1/2 minutes to pressurize and 1 1/2 minutes to depressurize).

Experimental Procedures

Following arrival in the temperature-controlled laboratory (room temp: 22.7 ± 0.2°C and humidity: 22.7 ± 1.0%), subjects signed the informed consent and completed a health history questionnaire. Each subject’s thigh skinfold was determined for thermocouple depth calculation. Skinfold measures were taken at approximately two-thirds of the distance from the anterior superior iliac spine to the superior aspect of the patella where the vastus lateralis muscle had its most hypertrophy with a maximal isometric contraction.

Subcutaneous adipose layer thickness was calculated by dividing the skinfold average by 2. The thermocouple depth from the skin surface for each subject was then calculated by adding 15 cm to the subcutaneous adipose layer thickness. Thermocouple placement depth remained constant for each laboratory visit at 1.5 cm below the subcutaneous adipose layer. At the site of skinfold assessment, a 3 × 3 cm area was shaved and cleaned with a Povidine-Iodine swab. A 20-gauge, 1.25-in sterile intravenous needle catheter (Medex Inc, Carlsbad, California) was inserted perpendicular to the skin surface. Upon needle removal, an IT-18 thermocouple was threaded through the catheter to a premarked depth of 5 cm. The catheter was removed, and the thermocouple was retracted until the calculated distance of each subject’s thermocouple placement was reached. Each subject had a unique depth of thermocouple placement based on individual subcutaneous adipose tissue amount and the desired 1.5-cm muscular depth required. A second IT-18 thermocouple was placed sublingually for T↓IM. A copper constantan surface thermocouple was secured to the skin’s surface within 3 cm of the insertion site, and another surface thermocouple was placed into the ice bag or the cooler of the cooling device. All thermocouples were connected to Isothermex using standard thermocouple extensions (EXT-6, Physitemp Inc, Clinton, New Jersey).

Cardiovascular instrumentation followed thermocouple placement. Electrocardiogram was collected using a 3-lead setup with Ag/AgCl wet gel electrodes (Nikomed USA, Huntington Valley, Pennsylvania). A fitted upper-arm blood pressure cuff was placed on the right arm. The strain gauge was positioned around the left forearm at the point of greatest circumference. One occlusion cuff was placed around the left upper arm, and one cuff was placed around the wrist to exclude the hand from the circulation during measures of FBF. The left arm was positioned at an angle allowing for maximal forearm drainage.

Data Collection

After instrumentation, subjects rested in the supine position for approximately 30 minutes to achieve temperature and cardiovascular baseline. Baseline T↓IM was determined by maintaining a constant temperature (no more than ± 0.5°C change over a 5-minute period). After baseline, 1 of the 4 treatments was applied. T↓IM, T↓SF, T↓ORAL, and device temperatures were recorded every 5 seconds over the 30-minute treatment and the 30-minute passive recovery. HR was collected continuously. Arm cuff blood pressures were collected at baseline, 0.5, 1.5, 5, 10, 20, 30, 35, 40, 50, and 60 minutes. For FBF collection, the wrist cuff was inflated to ~240 mmHg during all flow measurements, and venous occlusion was achieved by inflating a cuff around the subject’s left upper arm to 40 mmHg intermittently (8 seconds on, 12 seconds off) during the collection period (approximately 2 minutes). FBF trials were performed at baseline, 3-5, 8-10, 18-20, 28-30, 38-40, 48-50, and 58-60 minutes.

Data Reduction

Temperature data were reduced using 30-second averages around selected time points. HR data were reduced using 30-second averages at the time points of automated blood pressure collection. MAP, RPP, and FVC were calculated using the following equations:

- MAP = diastolic pressure + (systolic pressure-diastolic pressure) / 3
- RPP = systolic blood pressure × HR
- FVC = FBF / MAP

Statistical Analysis

We used NCSS Statistical Software (NCSS, Kaysville, Utah) to analyze all variables of interest. Separate 4 × 15 within-within repeated measures analyses of variance (ANOVA; treatment × time) were used to analyze T↓IM, T↓SF, and T↓ORAL (time: baseline, 0.5, 1.5, 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, and 60 minutes). We used a 1-way ANOVA with treatment as a within factor to assess device temperatures and peak decreases for skin
surface (T_{SF \text{ PEAK}}), intramuscular (T_{IM \text{ PEAK}}), and oral (T_{ORAL \text{ PEAK}}) temperatures. We analyzed HR and MAP using separate 4 × 12 within-within repeated measures ANOVA (time: baseline, 0.5, 1.5, 5, 10, 20, 25, 30, 35, 40, 50, and 60 minutes), and we analyzed FBF and FVC using separate 4 × 8 within-within repeated measures ANOVA (time: baseline, 3-5, 8-10, 18-20, 28-30, 38-40, 48-50, and 58-60 minutes). Analysis time points for temperature and cardiovascular data were determined based on clinical meaningfulness. Because the data failed to meet compound symmetry, we used the Huynh-Feldt adjustment to determine significance. Alpha was set a priori 0.05. A step-down procedure was used for all interactions and main effects. Tukey multiple comparisons were used to isolate the treatments and time points that differed, and only the a priori planned comparisons were investigated. Effect sizes were calculated using eta squared (\eta^2 = SS_{between}/SS_{total}) and Cohen d (d = difference between 2 means divided by the standard deviation for the data [\sqrt{MS error}]).

RESULTS

Device and modality temperatures. Temperature gradients for the different cold modalities were consistent because there were no between treatment differences (P > 0.05) over the 30-minute treatment. The 95% confidence intervals for average temperature treatment were 0.46–0.51°C (ice bags), 0.6–1°C (GR_{NO}), 0.8–1.4°C (GR_{MED}), 0.6–1.1°C (GR_{HIGH}).

Baseline measures. There were no between treatment differences for all temperature and cardiovascular parameter measures at baseline (P > 0.05).

Tissue temperature. There was a significant treatment × time interaction for T_{IM} (P = 0.002, \eta^2 = 0.8, d > 1) (Figure 1). There was a significant treatment × time interaction for T_{SF} (P < 0.001, \eta^2 = 1.04, d > 1) from baseline (Figure 2). There were significant treatment main effects for peak changes from baseline for T_{IM} (P < 0.001, \eta^2 = 1.07, d > 0.99) and T_{SF} (P < 0.001, \eta^2 = 3.8, d > 1) (Table 1). Average oral temperature during treatment was 36.9 ± 0.09°C. For T_{ORAL}, there were not significant interaction (1 – β = 0.05, \eta^2 < 0.1), treatment (1 – β = 0.3, \eta^2 = 0.14), or time effects (1 – β = 0.72, \eta^2 = 0.26).

Cardiovascular parameters. There were no significant treatment × time interactions for HR (1 – β = 0.29, \eta^2 = 0.13), MAP (1 – β = 0.26, \eta^2 = 0.21), RPP (1 – β = 0.40, \eta^2 = 0.12), FBF (1 – β = 0.13, \eta^2 = 0.08), or FVC (1 – β = 0.72, \eta^2 = 0.13). Time effects are presented in Table 2.

DISCUSSION

Cardiovascular Strain

The application of all cold modalities and the resultant skin and intramuscular tissue cooling resulted in acute increases in cardiovascular strain. HR, MAP, and RPP were greater...
throughout the first 5 minutes of treatment when compared to baseline. However, the addition of various levels of intermittent pneumatic compression to the thigh did not have a different effect on HR, MAP, and RPP responses when compared to the control condition of ice bag/elastic wrap. The magnitude of the HR, MAP, and RPP changes appear to be within the range of the normal responses to daily physical activity. Therefore, the type of cooling and compression does not appear to affect cardiovascular strain or myocardial health risk in young, healthy individuals. Passive skin warming after 30 minutes of cryotherapy with static compression or cycling intermittent pneumatic compression over the thigh musculature does not appear to potentiate clinically significant cardiovascular strain, either. However, the cardiovascular responses for specific patient populations (eg, hypertensive patients or patients with acute inflammatory disorders) remain unknown.

**FBF and Vascular Conductance**

Previous strain gauge plethysmography data reported by Fiscus et al\(^6\) demonstrated no global changes in blood flow of a nontreated leg for both a control condition (no cooling)
Table 2. Cardiovascular parameters during cryotherapy.a

|                      | Heart Rate, bpm | Mean Arterial Pressure, mmHg | Rate Pressure Product, mmHg × bpm | Forearm Blood Flow, mL / 100 mL / min | Forearm Vascular Conductance, mL / 100 mL / min / mmHg × 100 |
|----------------------|----------------|-------------------------------|-----------------------------------|--------------------------------------|-------------------------------------------------------------|
|                      | Mean ± SE | 95% CI | Mean ± SE | 95% CI | Mean ± SE | 95% CI | Mean ± SE | 95% CI | Mean ± SE | 95% CI |
| Baseline             | 61.3 ± 1.4 | 58.5, 64.2 | 78.6 ± 1.3 | 76.1, 81.2 | 6710 ± 176 | 6354, 7065 | 2.4 ± 0.16 | 2.0, 2.7 | 3.1 ± 0.2 | 2.6, 3.6 |
| 0.5 min              | 62.4 ± 1.8 | 58.8, 66.1 | 83.9 ± 1.3 | 81.3, 86.4 | 7817 ± 236 | 7339, 8295 | N/A | N/A | N/A |
| 1.5 min              | 62.0 ± 1.6 | 58.6, 65.3 | 86.1 ± 1.5 | 83.1, 89.1 | 6802 ± 176 | 6446, 7159 | N/A | N/A | N/A |
| 5 min                | 63.4 ± 1.8 | 59.8, 67.0 | 84.6 ± 1.3 | 81.9, 87.2 | 7182 ± 229 | 6720, 7645 | 2.1 ± 0.13 | 1.8, 2.3 | 2.5 ± 0.2 | 2.2, 3.0 |
| 20 min               | 61.3 ± 1.7 | 57.9, 64.6 | 79.6 ± 1.1 | 77.3, 81.8 | 7555 ± 247 | 7056, 8054 | 2.1 ± 0.12 | 1.8, 2.3 | 2.7 ± 0.2 | 2.3, 3.1 |
| 30 min               | 61.3 ± 1.5 | 58.4, 64.3 | 80.9 ± 1.2 | 78.5, 83.2 | 6977 ± 207 | 6559, 7395 | 2.1 ± 0.11 | 1.8, 2.3 | 2.6 ± 0.2 | 2.3, 3.0 |
| 50 min               | 59.7 ± 1.5 | 56.7, 62.7 | 83.0 ± 1.3 | 80.3, 85.6 | 6632 ± 177 | 6273, 6990 | 2.0 ± 0.12 | 1.7, 2.3 | 2.5 ± 0.2 | 2.1, 2.8 |
| 60 min               | 60.2 ± 1.4 | 57.3, 63.2 | 82.1 ± 1.1 | 79.8, 84.4 | 6986 ± 185 | 6612, 7360 | 2.1 ± 0.13 | 1.8, 2.3 | 2.6 ± 0.2 | 2.2, 2.9 |

aSelected data points were chosen based on clinical meaningfulness. Time points 0.5 to 5 minutes represent acute changes; 20 and 30 minutes represent changes toward the end of treatment and at the end of treatment; and 50 and 60 minutes represent the changes after passive recovery. SE, standard error; CI, confidence interval.

and lower leg cooling in 13°C water. We observed an ~16% decrease in FBF and ~20% decrease in FVC from baseline to the end of the experiment for all cooling treatments using modalities ≤ 2°C to the thigh/knee. These decreases were likely caused by global vasoconstriction triggered by sympathetic neural activation in response to the cold stimulus on the skin. The nature of the discrepancy between the findings of the current study and the findings of Fiscus et al are not readily apparent but may be due to differences in the cooling stimuli as well as the nontreated limb investigated (ie, nontreated arm vs nontreated leg). It is expected that the reduction in blood flow observed in the nontreated limb would also be evident at the site of cold modality application as both Ho et al.28 and Karunakara et al15 have reported reductions in intramuscular temperature reductions and that skin temperature decreases are not indicative of intramuscular cooling.29 Overall, 30 minutes of various cryotherapy/compression treatments followed by 30 minutes of passive recovery produced skin surface temperatures between 4°C to 15°C and intramuscular temperatures between 22°C to 31°C. T IM remained well below baseline measures (≥ 5°C decrease) after a passive recovery of 30 minutes, which is consistent with Myrer et al.20 Therefore, 30 minutes of cryotherapy with any of our chosen modalities was adequate to produce moderate to complete skin analgesia but inadequate to produce significant lowering of a muscle’s metabolic functions.2

**Limitations**

All subjects were young and apparently healthy and did not necessarily represent a clinically injured or “typical” diseased population. Consequently, the hemodynamic responses of subjects experiencing acute inflammation at the site of the cold modality treatment or those with hypertensive or other circulatory conditions may not be similar. In addition, our subjects were at rest; therefore, caution is warranted when applying results to athletes who just finished exercise.21 Finally, we did not include a noncryotherapy condition, because we were interested in clinically relevant treatments.
CONCLUSIONS

The benefits of cryotherapy, including decreased pain intensity, reduced postoperative edema, accelerated rate of recovery post surgery, and faster return to full range of motion, are often linked to decreases in tissue temperatures; however, we still have little evidence regarding the tissue temperature benchmarks for these clinical or physiological changes. Our data provide us with more evidence regarding the therapeutic cooling of lean subjects when different cold modalities are applied. When using cryotherapy devices that allow for continuous cooling and combined compression, both levels of intermittent pneumatic compression (GRCC, or GRPCM) appear adequate to achieve intramuscular cooling to ~25°C. Clinically meaningful reductions in skin temperature (12°C to 17°C) were achieved within 5 minutes using ice and within 10 to 15 minutes using Game Ready system with or without compression. Finally, while increases in HR, MAP, and RPP were observed during Game Ready system with or without compression. Finally, within 5 minutes using ice and within 10 to 15 minutes using reductions in skin temperature (12°C to 17°C) were achieved intramuscular cooling to ~25°C. Clinically meaningful compression (GRCC, or GRPCM) appear adequate to achieve intramuscular cooling to ~25°C. Clinically meaningful reductions in skin temperature (12°C to 17°C) were achieved within 5 minutes using ice and within 10 to 15 minutes using Game Ready system with or without compression. Finally, while increases in HR, MAP, and RPP were observed during the early stages of tissue cooling, they did not exceed typical elevations reported during exercise or experimental cold exposure. Therefore, 30-minute cold treatments with added static or intermittent pneumatic compression appear relatively safe in otherwise healthy individuals.

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