A Comparison of the Effects of Heat Therapy and Exercise Training on Vascular Function During Passive and Active Exercise

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A Comparison of the Effects of Heat Therapy and Exercise Training on Vascular Function During Passive and Active Exercise

Taysom Erica Wallace

A thesis submitted to the faculty of Brigham Young University in partial fulfillment of the requirements for the degree of
Master of Science

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ABSTRACT
A Comparison of the Effects of Heat Therapy and Exercise Training on Vascular Function During Passive and Active Exercise

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Master of Science

Recent evidence suggests that heat, a major byproduct of exercise, may be the mediator for many vascular adaptations that come from exercise. Thus, heat therapy that increases muscle temperature in a comparable way to exercise may be an advantageous alternative for enhancing cardiovascular health in individuals where treatment with exercise is either not possible or undesired.

PURPOSE: Compare the effects of exercise and heat training on resistance artery function at rest and during exercise.

METHODS: Thirty-five (18 female) healthy, untrained subjects completed a 6-week training program utilizing either high intensity knee extension (KE) exercise (40 min), localized heat therapy (pulsed shortwave diathermy; 120 min), or a sham heat therapy protocol (120 min). We randomly selected 8 subjects from each group to have a temperature probe inserted into their vastus lateralis muscle during one of their training sessions to evaluate the effect of the interventions on muscle temperature. We assessed resistance artery function at rest with the passive leg movement technique (PLM) prior to and after completion of the training protocols. We assessed peak exercise blood flow (KE peak flow) and peak power output (KE peak power) during the KE graded exercise test and prior to and after completion of the training protocols.

RESULTS: Peak muscle treatment temperature was significantly different between all groups with those assigned to the diathermy heat training exhibiting a higher peak temperature (~40.80°C) than those in the exercise (~37.75°C, P < 0.001) and sham training groups (~36.10°C, P < 0.001). KE peak flow during PLM increased to the same extent (P = 0.625) in both the exercise (~10.5% increase, P = 0.009) and heating groups (~8.5% increase, P = 0.044); but tended to decrease in the sham group (P = 0.087). KE peak flow increased in the exercise group (~19%, P = 0.005), but did not change in the heat group (P = 0.523) and decreased in the sham group (~7%, P = 0.020). Peak vascular conductance during KE significantly increased by ~25% in the exercise (P = 0.030) and heat (P = 0.012) groups. KE peak power increased in the exercise group by ~27% (P = 0.001) but did not significantly change in the heat (P = 0.175) and sham groups (P = 0.111). The change in vascular function, assessed via PLM, showed a correlation with both ∆KE peak flow (R = 0.55, P = 0.01) and ∆KE peak power (R = 0.56, P = .010). Likewise, ∆KE peak flow showed a strong association with ∆KE peak power (R = 0.64, P < 0.001).

CONCLUSION: Localized diathermy heat treatment increased resistance artery function at rest and during exercise to a similar extent as single-leg KE exercise training but did not yield
significant improvements in performance. Thus, heat training mimics some but not all of the benefits associated with exercise and may be used to replace exercise treatment to some extent.

Keywords: heat therapy, passive leg movement, exercise blood flow, vascular function, pulsed shortwave diathermy
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INTRODUCTION

Muscle blood flow is crucial for any form of physical activity or exercise.\(^1\) If blood flow to the muscle is inhibited enough to prevent oxygen from reaching the muscle, or if the metabolic demand exceeds the muscle’s capacity to utilize oxygen, then that level of exercise will be unsustainable.\(^2\) The endothelium, the innermost single layer of cells within blood vessels,\(^3\) helps regulate the extent to which blood flows throughout the body. Endothelial cells, in response to mechanical stress and chemical signaling, secrete vasodilators and vasoconstrictors to alter the blood vessel radius\(^4\) and direct blood flow to organs that have the greatest need.\(^5\)–\(^7\) While endothelial cells are present throughout the vascular tree, the majority of blood flow regulation occurs at the level of the resistance arteries. Not surprisingly, resistance artery endothelial function, as evaluated by passive leg movement (PLM), is independently correlated with peak exercise blood flow and maximum oxygen consumption (ie, \(\dot{V}O_2\) max) during intense exercise.

Exercise training is beneficial for endothelial health\(^8\)–\(^11\) and exercise capacity,\(^10,12,13\) but some individuals are incapable of exercise due to physical ailments or injuries. Additionally, others may choose not to exercise due to social insecurities\(^14\) or a lack of desire. Due to those obstacles, many individuals do not reap the health benefits that accompany exercise. Recent evidence has suggested that heat, a major by-product of exercise, may be the mediator for many of the vascular adaptations that come from exercise.\(^10,15\)–\(^20\) Thus, heat therapy, that increases muscle temperature in a comparable way to exercise, may be an advantageous alternative for enhancing cardiovascular health in individuals where treatment with exercise is either not possible or undesired.
For example, our group recently found that daily heat therapy, in the form of pulsed shortwave diathermy applied directly to the thigh, prevented the deleterious effects of 10 days of single-leg immobilization on resistance artery function. While immobilization was associated with a ~30% decrease in resistance artery function, immobilization accompanied by daily heat treatment was associated with preserved function that tended to increase despite the immobilization. While these data indicate that heat therapy may be useful for maintaining resistance artery function during periods of disuse, it remains unclear if heat therapy can improve resistance artery function in regularly ambulating adults.

A handful of studies have investigated the possibility of using heat therapy to elicit exercise-like adaptations in the vascular system, but most have focused on conduit artery function, assessed by flow-mediated dilation (FMD), which is not strongly related to exercise blood flow and VO2 max. For example, a study published in 2016 directly compared the vascular and exercise capacity adaptations resulting from 8 weeks of cycling training (70% of heart rate maximum) to those seen from 8 weeks of warm water immersion treatment (water temperature 42°C). Both interventions included a 30-minute training or treatment session 3 times each week for 8 weeks. Exercise capacity (VO2 max) and endothelial function (FMD) increased in both the exercise training and warm-water immersion treatment groups to the same extent.

Other studies have shown similar increases in conduit artery function for both exercise treatment and heat therapy protocols. However, excluding the study mentioned previously, and another completed by Hesketh, the research is lacking in direct comparison studies between heat and exercise interventions. Furthermore, research comparing localized heating and exercise interventions on resistance artery function, exercise blood flow, and
exercise capacity is currently nonexistent. Pulsed shortwave diathermy, one localized heating technique, has been shown to increase deep muscle temperature and improve mitochondrial function of the treated area.\textsuperscript{15,25} This may allow for greater oxygen utilization within the muscle during exercise and subsequently improve exercise capacity. Thus, the purpose of this study was to evaluate and compare the vascular adaptations within the resistance arteries both at rest (PLM) and during exercise (exercise blood flow) with the adaptations in exercise capacity (KE peak power) that accompany 6 weeks of either exercise training or localized diathermy heat training.

**METHODS**

**Subjects**

Thirty-eight subjects (18 male, 20 female) between the ages of 18 and 35 years old volunteered for this study. These subjects consisted of untrained individuals who had the capacity for exercise. The recruitment of subjects was primarily done on BYU campus and all methods were approved by the Institutional Review Board (IRB). Subjects provided informed, written consent before participating in the study. Three subjects after giving their informed consent and beginning the study were disqualified due to either an inability to give a sufficient muscle biopsy or were later found to not meet the requirements defined by the study. Thus, only 35 of the 38 subjects (17 male, 18 female) completed the full study protocol.

The subjects also met the following exclusion criteria\textsuperscript{26–33} to ensure accurate blood flow and arterial function measurements, as well as to ensure that the heating treatment functioned properly: (1) no history of cardiovascular disease or heart problems; (2) no history of metabolic disease; (3) not currently taking any prescribed medications; (4) healthy; (5) able to endure a new single-leg exercise protocol; (6) thigh skin fold measurement < 40 mm; (7) no history of smoking or illicit drug use; (8) 18 to 35 years old; (9) untrained (had not currently been
participating in any aerobic fitness training; had not participated in a sustained aerobic fitness training in the 3 months before participating in the study; and participated in < 3 hours of low intensity exercise per week).

**Procedures**

The experiment protocol (Figure 1) consisted of 21 visits per subject. The primary visit for each subject was an informed consent meeting which included a description and explanation of the experiment followed by the signing of a consent form. The subsequent visit consisted of baseline evaluations of subjects’ vascular function (Passive Leg Movement, PLM) and exercise blood flow responses, knee extension (KE) exercise capacity (KE peak power), and other biological measurements including a biopsy from the vastus lateralis muscle. After the baseline measures were completed, the subjects were assigned in a partially randomized, balanced design to either the exercise training, the diathermy heat training, or the sham heat training group which they participated in for the next 6 weeks. A midpoint $K_{\text{Emax}}$ assessment was also taken at that point for those subjects assigned to the exercise training group to reevaluate their training intensity. The final visit mimicked the first day of testing allowing for a comparison to the baseline data.

**Anthropometric Measurements**

We took subjects’ height and weight using a digital scale and stadiometer. We took subjects’ leg anthropometric measurements as described by Layec et al while subjects lay supine on a table. Leg circumference measurements were taken using a standard tape measure at the lower (directly above the kneecap), middle (midpoint of the thigh), and upper (upper portion of the thigh coordinating in distance to the distal lower measurement from the midpoint of the thigh) portions of their thighs. We also measured the length of the leg, constituting the distance...
from the anterior superior iliac spine to the mid kneecap, for each subject. We took 3 to 5 measurements at each area and an average was recorded. We took 3 to 5 skinfold measurements using calipers at the anterior midpoint of the thigh. The length, skinfold, and circumference measurements allowed us to determine if the training protocols produced a difference in thigh composition or quadriceps size. The skinfold measurements also served to verify that the diathermy treatment penetrated at least 1 cm deep in the quadriceps muscles of those individuals assigned to the heating treatment. Pulsed shortwave diathermy treatment has been shown to increase tissue temperature up to a depth of 3 to 5 cm. Individuals whose skinfolds exceeded 40 mm were rejected from the study.

**Physical Activity Measurements**

We measured subjects’ physical activity for a period of 5 to 7 days at the beginning and end of the study to determine if physical activity levels had changed. We placed an accelerometer (ActiGraph GT9X Link, ActiGraph, Pensacola, FL, USA) on the lateral side of the subjects’ left ankle for the measurement period. We instructed subjects to keep the accelerometer on during all waking hours other than while showering.

The accelerometer software recorded the number of minutes each day that the subjects spent being sedentary and participating in light, moderate, vigorous, and very vigorous physical activity based upon the Freedson count system. The daily average number of minutes for each category was taken and used to compare the baseline and end-of-study activity levels.

**Vascular Assessments**

We assessed vascular function via blood flow response during a PLM assessment and during the KE exercise. To minimalize variations in blood flow responses, we asked subjects to refrain from intense exercise, caffeine consumption, tobacco use, and alcohol for at least
12 hours prior to each testing day. Additionally, we asked subjects to arrive for testing in a fasted state, having water, but no food for at least 4 hours prior to testing.40

Passive Leg Movement

As described by Gifford and Richardson 2017,41 we performed the PLM assessment by recording the blood flow velocity and artery diameter of the common femoral artery with Doppler ultrasound (Doppler ultrasound 9L probe, General Electric Medical Systems, Milwaukee, WI, USA) at a 60-degree insonation angle, while the subject’s right leg was moved for them. We placed the subject in a raised chair with their feet elevated to approximately the height of their hips, so that their legs were straight. After waiting 15 minutes for their bodies to acclimate to that position, we recorded a baseline measurement for 60 seconds to determine the artery diameter. Subsequently we took a 65-second measurement while a research assistant moved the subject’s leg in a 90° range of motion at a pace of 180°/sec.42 We repeated this measurement 2 to 3 times to establish an average. These repeated measurements have been shown to have an I.C.C of 0.91.23 We spaced out the measurements by 15 minutes for blood flow to return to baseline before the next PLM assessment was taken.41

**Blood Flow Analysis.** The maximum or peak flow during PLM was determined by analyzing velocity on a second-by-second basis and subsequently applying a 3-second rolling average. We considered the highest blood flow rolling average as the peak flow. We took area under the curve (AUC) measurements during the PLM assessments. We determined the AUC flow by taking the cumulative difference in blood flow during PLM versus baseline measurements.
Knee Extension Max Power and Max Blood Flow

After the biopsy and prior to knee extension max (KEmax) blood flow measurements, subjects underwent familiarization with the knee extension cycle ergometer and a warm-up.\textsuperscript{43,44} The warm-up consisted of a 3-minute exercise period at 10 Watts on the knee extension cycle ergometer. The subjects were instructed to maintain a speed of 80 rpm and only contract their muscles during the extension motion. After the 3-minute warm-up, the workload was increased by 5 watts every minute until the subjects were no longer able to maintain a speed of $>74$ rpm, at which point the intensity was lowered and the subjects performed a cool down. We identified the greatest power output maintained for 60 seconds as the KE peak power output.

**Blood Flow Analysis.** We analyzed the maximum or peak exercise blood flow in 10-second bins; a 30-second rolling average was subsequently applied.

**Blood Pressure Measurements**

We measured mean arterial pressure (MAP) as well as heart rate and cardiac output during both the PLM and KE exercise. We recorded the data via sphygmomanometer and finger plethysmography (CNAP, CNSystems, Graz, Austria). We verified systolic and diastolic measurements with a second automated sphygmomanometer (OMRON 3 Series Upper Arm, OMRON, Kyoto, Japan).

**Training Interventions**

**Knee Extension HIIT Protocol**

The subjects assigned to the exercise group completed knee extension HIIT workouts 3 times per week for 6 weeks. Each session was 40 minutes long in duration and was monitored by a member of the research team. During the sessions, the subject sat in the custom-built knee extension ergometer and was strapped to the leg attachment. The workout began with a 6-minute
Warm-up at 20% of the subjects KE peak power. We asked subjects to maintain a speed of 80 rpm throughout the workout. After completion of the warm-up, the subjects completed a 4-minute interval at 80% KE peak power followed by a 4-minute interval at 20% KE peak power. Subjects repeated these intervals 3 more times resulting in 4 intervals at 80% KE peak power and 3 intervals at 20% KE peak power. After completion of the intervals, subjects completed a 6-minute cool down at 20% of their KE peak power.

During the midpoint assessment, if subjects showed an increase in their KE peak power, the 80% and 20% power output values during the training sessions reflected the increase respectively. If any subject showed significant ease during their training sessions (rpm consistently > 80, able to speak and breathe easily during 80% intervals) between the testing days, the research assistant would make a note on the subject’s chart and increase the interval watts by 2 during the next training session. If subjects were not able to maintain a speed of > 74 rpm during the elevated intervals of their training session, the research assistant would decrease the power level by 2 watts until that speed was once again achieved. That power output would then be maintained for the remainder of that 4-minute interval.

*Diathermy Therapy Protocol*

The subjects assigned to the diathermy heat training group completed 18 local diathermy training sessions over the course of 6 weeks. The sessions were 2 hours long and occurred 3 times per week. The diathermy units were placed in a manner that allowed for the treatment of all quadriceps muscles of the subjects’ right legs. Unit one was placed on the proximal lateral portion of the right leg, while unit 2 was placed on the distal medial portion of the same leg. After 20 minutes unit 1 was moved to the distal lateral portion of the quadriceps muscles and unit 2 was moved to the proximal medial portion of the quadriceps muscles. After another 20
minutes the diathermy units were returned to their original placement. The placement of units continued being moved every 20 minutes until the 2-hour session was completed. After completion of each 2-hour session, we asked the subjects to give a heat rating associated with their heating experience. The scale was from 1 to 10: 1 indicating that the subject detected “no heat”; 10 indicating that the heat was so intense that it felt like their “leg was in flames.”

Subjects were told before the training session to alert the technician if the diathermy treatment was too hot or uncomfortable and the training would be paused to allow the leg to cool down before continuing the training.

Sham Heat Therapy Protocol

The sham therapy protocol mimicked the diathermy therapy protocol with the exception, that unbeknownst to the subjects, the diathermy unit was not turned on during the 2-hour sessions.

Temperature Probe Insertion

To verify that muscle temperature was raised in both the exercise and heating groups and was maintained in the sham group, we randomly selected 8 subjects from each assigned group to have a temperature probe inserted into their vastus lateralis muscle during 1 of their 18 training sessions. A trained lab assistant first marked the incision site of the temperature probe and then cleaned the site and surrounding area with the antiseptic chlorohexidine. After cleaning the area, the lab assistant numbed the epidermal skin layer and the muscle column affected by the probe with a local anesthesia (1% lidocaine with epinephrine) until the subject no longer had sensation in that area. The technician then inserted an 18-gauge sterile Cathlon I.V. catheter (Smiths Medical, Lancashire, UK) into the muscle site. The temperature probe (Physitemp Instruments, Clifton, NJ; model IT-17:3) was then threaded through the catheter ~3.5 cm deep into the vastus
lateralis muscle. Once the temperature probe was in place, the lab assistant removed the catheter and secured the probe with tape for the remainder of the training period. Then the probe was plugged into an Iso-Thermex machine (Columbus Instruments, Columbus, OH; model 256) which projected the temperature readings for the researchers to record. We recorded the temperature readings at baseline and at 5-minute intervals for subjects in the exercise training group, and at 10-minute intervals for subjects in the heating and sham training groups. The peak and average muscle temperature of each subject was documented.

**Statistical Analysis**

We used a mixed model ANOVA test (2 repeated measures across 3 groups) to determine if the 6-week training programs (exercise, heat, and sham) produced adaptations in vascular health and performance (PLM, max exercise blood flow, KE peak power). In the event of a significant F-statistic, we performed t-tests of planned comparisons. We also used Pearson product correlations to determine the relationship between maximum blood flow during exercise and endothelial function (PLM). The alpha for the statistical procedures were set to 0.05.

**RESULTS**

Thirty-five young, healthy, untrained subjects (17 male, 18 female) completed the full study protocol (Figure 1). We assigned 11 subjects (4 male, 7 female) to the exercise training group; 13 subjects (7 male, 8 female) to the heat training group; and 11 subjects (6 male, 5 female) to the sham training group. We saw no significant differences between the groups in terms of subject age, BMI, physical activity levels, or baseline vascular function and exercise performance (Table 1).
Effect of Interventions on Muscle Temperature, Body Mass, Quadriceps Mass, and Physical Activity

We randomly selected 8 subjects from each intervention to have a temperature probe placed in the vastus lateralis muscle of their treated leg during one of their training sessions. Mixed-model ANOVA revealed a significant time-by-group interaction for both the average treatment temperature (P < 0.001) and peak treatment temperature (P < 0.001). As depicted in Table 2, post hoc analysis showed significant differences in both average and peak treatment temperatures between all groups. Those receiving the diathermy heat training exhibited the highest average temperature (~38.7°C) as compared to those in the exercise (~36.97°C, P = 0.001) and sham (~35.63°C, P < 0.001) training groups. Those in the exercise and sham groups likewise exhibited significantly different average treatment temperatures from each other (P = 0.007). Similarly, peak treatment temperature followed the same pattern as average treatment temperature with those in the heat group having a significantly greater value (~40.80°C) than those in the exercise (~37.75°C, P < 0.001) and sham training groups (~36.10°C, P < 0.001); the peak temperature of those in the exercise group was significantly higher than those in the sham training group (P = 0.006).

We used Mixed Model ANOVA to analyze the chronic effect of the interventions on body mass and quadriceps mass. Analysis revealed no main effects for time or interaction regarding either the change in body mass (F = 0.260, P = 0.613; F = 1.441, P = 0.252) or the change in the mass of the subjects’ quadriceps (F = 0.001, P = 0.974; F = 1.368, P = 0.269). Physical activity, determined by daily step count, likewise showed neither a main effect of time (F = 1.097, P = 0.304) nor a significant time-by-group interaction (F = 1.739, P = 0.194).
Effect of Interventions on Blood Flow Response to PLM

We measured PLM, which assesses the vascular function of the resistance arteries, prior to and after the training interventions. We saw no time effect in the statistical analysis ($F = 2.788, P = 0.105$), however the time-by-group interaction was significant ($F = 6.990, P = 0.003$). As seen in Figure 2, both the exercise and heating interventions produced a similar positive adaptation (~10.5% increase, $P = 0.009$ and ~8.5% increase, $P = 0.044$) regarding peak blood flow during PLM, that did not differ between the heat and exercise groups ($P = 0.625$). The exercise ($P = 0.002$) and heating ($P = 0.004$) groups did show significantly greater adaptations than the sham group, which did not significantly change from pretesting to posttesting.

Delta peak PLM blood flow, or the peak change in blood flow from baseline, exhibited a significant positive time effect ($F = 8.067, P = 0.006$). Whereas the time-by-group interaction, while trending toward significance, did not reach significance ($F = 3.094, P = 0.060$).

Total blood flow response during PLM or area under the curve (AUC) blood flow response did not show a significant time-by-group interaction effect ($F = 1.082, P = 0.352$). However, a significant time effect ($F = 6.73, P = 0.015$) was associated with AUC blood flow response.

Effect of Interventions on Blood Flow During KE Exercise

As illustrated in Figure 3A, steady-state blood flow at 10 watts was unaffected by the interventions, exhibiting no time effect ($F = 0.31, P = 0.581$), no group effect ($F = 0.269, P = 0.766$) and no interaction ($F = 0.853, P = 0.435$). Nevertheless, as illustrated in Figure 3B, steady-state vascular conductance exhibited a significant time effect ($F = 7.046, P = 0.013$), but no group effect ($F = 0.172, P = 0.843$) or interaction ($F = 1.541, P = 0.231$). Post hoc analysis
revealed a significant increase in conductance at 10 watts in the heat group (P = 0.036), and a tendency for an increase in the exercise group (P = 0.056), but not the sham group (P = 0.915).

As illustrated in Figure 3C, we analyzed peak blood flow during the graded exercise test by comparing the maximum hyperemic response during KE exercise. Comparison of the values revealed a significant time effect (F = 5.354, P = 0.027) as well as a significant time-by-group interaction (F = 12.569, P < 0.001). Post hoc analysis showed significant differences in delta KE peak blood flow between all groups respectively: heat and sham (P = 0.014), sham and exercise (P = 0.001), and exercise and heat (P = 0.006). As shown in Figure 3, those in the exercise group exhibited an increase of ~19% (P = 0.005) in their peak blood flow during KEmax. Those in the heat group exhibited no significant change from pretest to posttest KE peak blood flow assessments (P = 0.523). However, those in the sham group exhibited a ~7% decrease in their peak blood flow responses (P = 0.020).

As illustrated in Figure 3D, peak vascular conductance during KE exercise exhibited a significant time effect (F = 11.858, P = 0.002), but no group effect (F = 0.057, P = 0.944) or interaction (F = 1.873, P = 0.173). Post hoc analysis revealed a significant increase in peak conductance in the exercise group (P = 0.030) and the heat group (P = 0.012), but not the sham group (P = 0.699).

**Effect of Interventions on KE Peak Power**

We analyzed the change in KE peak power between interventions. Main effects for time (F = 9.764, P = 0.004) and the time-by-group interaction (F = 13.993, P < 0.001) were seen in the KE peak power analysis. Post hoc analysis revealed that KE peak power increased in the exercise group in comparison to baseline values (see Figure 4) by ~27% (P = 0.001). Those in the heat group showed a ~6% increase in their KE peak power outputs, however, this effect was not
shown to be significant \((P = 0.175)\). Those in the sham group exhibited an 8\% decrease in KE peak power \((P = 0.111)\) which also did not reach significance, which was significantly different from both the exercise \((P < 0.001)\) and heating groups \((P = 0.033)\).

**Relationships Between Changes in Vascular Function, Exercise Tolerance, and Anthropometrics**

We used linear regression to determine if changes in responses to PLM, KE peak flow, KE peak conductance, and KE peak power were associated with each other. As illustrated in Figure 5, the change in resistance artery function, assessed by PLM, was related to the change in multiple indices during KE exercise. Specifically, the change in vascular function, as assessed via PLM, showed a correlation with the change in KE peak blood flow response (Figure 5A, \(R = 0.55, P = 0.010\)) and KE peak conductance (Figure 5B, \(R = 0.50, P = 0.006\)). Furthermore, the greater the increase in PLM, the greater the increase in KE peak power (Figure 5C, \(R = 0.56, P = 0.010\)). Finally, the change KE peak power was significantly related to the change in KE peak blood flow \((R = 0.64, P < 0.001)\).

**DISCUSSION**

Systemic heat therapy has been shown to produce benefits associated with exercise training,\(^8,10,11,45,46\) including increased conduit artery health.\(^10,19,47–49\) However, because the majority of blood flow regulation occurs at the level of the resistance arteries,\(^22,52\) adaptations relating to resistance artery function may be more impactful for exercise capacity and overall health than those relating to conduit artery function. The purpose of this study was to compare the effects of exercise and localized muscle heat training on resistance artery function at rest and during exercise. Overall, localized muscle heat training was able to match some, but not all, of
the benefits that accompanied the exercise training. Context and implications of these treatments and their effects are discussed below.

**How Did the Interventions Affect Resistance Artery Function Assessed with PLM?**

As mentioned previously, the layer of endothelial cells within blood vessels helps to regulate the extent to which blood flows throughout the body.\(^3\) By secreting vasodilators and vasoconstrictors in response to mechanical stress or chemical signaling, they alter the blood vessel radius\(^4\) and direct blood flow to organs that have the greatest need.\(^5\)–\(^7\) While flow-mediated dilation (FMD) illustrates the endothelial function of the conduit artery being examined, PLM assessment evaluates the endothelial function of the downstream resistance arteries.\(^4\)\(^1\) Indeed, PLM-induced hyperemia is dependent upon nitric oxide bioavailability and is strongly related to acetylcholine-induced dilation in young adult populations.\(^4\)\(^1\),\(^5\)\(^3\) Consequently, this technique may be a better representation of an individual’s vascular health because the resistance arteries in the human body exponentially outnumber the conduit arteries; thus, they have a higher impact on blood flow regulation throughout the body during exercise.\(^2\)\(^2\),\(^5\)\(^2\) While other studies evaluating heating and exercise treatments have examined vascular health through the lens of FMD, we utilized the PLM to examine the health of the downstream resistance arteries.

As illustrated in Figure 2, our study showed evidence that localized heat training improved endothelial health of the resistance arteries by \(\sim8.5\%\). Though their modes of heating and manner of evaluating endothelial health differed from ours, the observed heat-induced increase in endothelial function is in accordance with other studies by Brunt,\(^1\)\(^9\) Carter,\(^4\)\(^7\) and Imamura.\(^4\)\(^8\) The increase in endothelial health seen in our study also corroborated the results in a study recently published by Hyldahl et al\(^2\)\(^1\) which used localized diathermy heat treatment to
minimize the vascular dysfunction induced by limb immobilization. The results of this study and that of Hyldahl et al\textsuperscript{21} indicate that localized muscle heating impacts the function of the resistance vasculature.

Exercise training is known to improve vascular function,\textsuperscript{9,54} but is impractical in some situations. Impressively, our study showed that diathermy heat training (120 min/session) and exercise training (40 min/session) exhibited statistically similar improvements in resistance artery function, assessed by PLM peak flow. Other studies comparing heat and exercise training have also shown similar improvements in endothelial function\textsuperscript{12} and blood flow response.\textsuperscript{10} For example, Bailey et al, performed a time matched training study comparing warm-water immersion and moderate intensity cycling training. Brachial artery FMD response increased by 1.71\% (0.56, 2.19) following both interventions (P = 0.003).\textsuperscript{10} Hesketh et al, compared the effects of heat and exercise training on endothelial function by comparing endothelial nitric oxide synthase (eNOS) content in the subjects’ vastus lateralis muscles before and after chronic passive heat treatment (PHT; heat chamber) and exercise treatment (moderate intensity cycling training (MICT)). The eNOS content increased after both interventions (MICT 12\%, PHT 8\%) with no significant difference between the two interventions.\textsuperscript{12}

While systemic heat therapy previously has been shown to increase conduit artery endothelial function in a similar manner to exercise, this is the first study to compare localized heat and exercise training on resistance artery function. Our results show that it is possible to receive similar improvements to resistance artery function from localized diathermy treatment as from exercise training.
How Do Exercise Training and Heat Training Affect Blood Flow During Exercise?

Since heat and exercise training both improved PLM-induced hyperemia, which is known to be related to exercise blood flow, we next investigated the impact of heat therapy on blood flow and vascular conductance during submaximal and maximal KE exercise. As illustrated in Figure 3A, bulk blood flow through the femoral artery during submaximal exercise (10 watts) was not impacted by any treatments. Nevertheless, both exercise and heat training augmented vascular conductance at 10 watts (Figure 3B). It was expected that KE peak flow would increase in both the exercise and heat groups due to their improvement in endothelial function. However, only the exercise group exhibited a significant increase in exercise blood flow (Figure 3C).

Nevertheless, when considered in terms of vascular conductance, both exercise and heat training increased peak conductance response to KE exercise (Figure 4D). The heat-induced increases in vascular conductance, that were not accompanied by increased blood flow, likely indicate that heat training improved the vasodilatory function of the resistance vasculature to permit the same blood flow with less of an increase in blood pressure.

How Do Exercise Training and Heat Training Affect Exercise Capacity?

To see how the interventions impacted exercise capacity, all subjects completed a graded exercise test while performing single-leg KE exercise prior to and after completing the interventions. Previous studies have illustrated that exercise training tends to increase exercise performance in the form of increased $\dot{V}O_2$ max, increased max workload, and increased critical power. As illustrated in Figure 4, this study mimicked those results with the exercise training group experiencing a ~27% increase in KE peak power. In contrast, those in the heat and sham training groups did not experience a significant change in maximum power. As exercise capacity is influenced by more factors than just vasodilator function, the lack of change in the
heat group may be because heat training failed to stimulate other factors associated with exercise capacity. Further research examining the impact of heat therapy on other factors associated with exercise performance is warranted.

**Do the Changes in PLM-Induced Hyperemia Relate to Improved Exercise Performance?**

Muscle blood flow is crucial for any form of physical activity or exercise. Because the vascular system is integral to this process, it is possible that an improvement in vascular function may lead to an improvement in exercise blood flow and performance. Indeed, Hanson et al, found that resistance artery function (PLM), but not conduit artery function (FMD), was strongly related to maximum exercise blood flow. Gifford et al, in a similar experiment, concluded that 30% of the variance in \( \dot{V}O_2 \) max, a common unit of exercise capacity, could be accounted for by indices of resistance artery function, including PLM. These two studies illustrate that resistance artery function is associated with exercise blood flow at high intensities and exercise performance. However, it still was not clear if changes in those variables would relate to each other. With this line of thought, we sought to examine if changes in resistance artery function brought on by exercise and heat training would correlate with changes in KE peak flow and subsequently changes in KE peak power.

After analyzing the results of this study, it became apparent that a relationship does exist between the training-induced changes in PLM peak flow and KE peak flow. Figure 5A illustrates that increases in PLM peak flow were associated with increases in KE peak flow (R = 0.55, P = 0.01). The relationship between training-induced changes in PLM peak flow and KE peak flow persisted even when excluding the exercise group from the correlation (R = 0.60, P = 0.003). Furthermore, changes in PLM peak flow were correlated to the changes in peak conductance, further supporting the notion that exercise and heat-training-induced improvements
in resistance artery function positively impact the blood flow response to exercise. Furthermore, both the change in PLM peak flow (R = 0.56, P = 0.01) and the change in KE peak flow (R = 0.64, P < 0.001) exhibited a positive correlation with the change in KE peak power (Figures 5B and 5C). Again, these correlations persisted when excluding the exercise group suggesting that increased vascular function (ie, resistance artery dilation) leads to the improvements in exercise blood flow and conductance.

**Practical Applications**

The results of this study indicate that diathermy heat training may be used to mimic several benefits of exercise, making it a viable alternative when exercise is not possible. Nevertheless, there are some aspects of the diathermy heat modality that may hinder its practicality. For example, the diathermy intervention used in our study required 2 hours of sedentary behavior per session. In addition to being time consuming, this may reduce physical activity in subjects, which could offset some of the benefits of the treatment. Indeed, 8 out of 13 subjects in the heat group reduced their daily step count by 10% to 20% throughout the study. More time effective heating modalities are needed. Additionally, the diathermy modality can only heat one small area of muscle at a time, making it impractical for improvement of whole-body vascular function. Alternative mechanisms of whole-body muscle heating, like sauna or hot water immersion, may be more practical methods for reaping the vascular benefits associated with heat training.

**Experimental Considerations**

The purpose of this study was to determine if heat training could produce similar benefits as exercise training. We assumed that the exercise training would be significantly more beneficial for blood flow adaptations than the heat training because the heat training would be
more localized in nature. Consequently, we made the heat training sessions (120 min) significantly longer than the exercise training sessions (40 min) to mimic heat\textsuperscript{15,16,21} and exercise training sessions previously used in our lab.

A major benefit of using a localized heating modality (eg, pulsed shortwave diathermy) as opposed to a systemic heating technique (eg, hot-water bath, sauna, etc.) in our training study was that we were able to verify that the vascular changes that occurred during the experiment were due to adaptations within the muscle. While increases in endothelial function and exercise capacity (VO\textsubscript{2} peak) have been reported from systemic heating treatments,\textsuperscript{10,12} it is possible that those adaptations were due to an increase of blood volume, that can accompany chronic systemic heating treatments,\textsuperscript{56,57} rather than an increase in muscle mitochondrial or endothelial function.

In addition to not matching the time for the training sessions, we also did not attempt to match for muscle temperature. Instead, we collected data to compare the temperature of the vastus lateralis muscle from subjects in each training group. There were no significant differences in baseline muscle temperature between the heat, exercise, and sham groups (0.098). However, all groups exhibited significant differences in peak (P < 0.001), average (P < 0.001), and $\Delta$ temperatures (P = 0.004), with the heat group having the highest values in each category (Table 2). The peak temperatures of ~40.8°C for the heat group and ~37.8°C for the exercise group are consistent with previous studies.\textsuperscript{20,25,58}

**Conclusions**

From the results of this study, we can conclude that heat training mimics many, but not all of the vascular benefits associated with exercise training. If an individual can complete either training, exercise training would likely produce greater vascular benefits and a larger increase in exercise capacity. However, in populations where exercise may not be a practical alternative,
such as injured or bedridden individuals, muscle heat training may be a good substitute to maintain or improve resistance artery function.
REFERENCES


Table 1. Subjects’ Baseline Characteristics by Intervention Group

<table>
<thead>
<tr>
<th></th>
<th>Exercise</th>
<th>Heat</th>
<th>Sham</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>22.73 ± 1.74</td>
<td>21.77 ± 1.33</td>
<td>20.55 ± 0.55</td>
<td>0.525</td>
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<tr>
<td>BMI (kg/m²)</td>
<td>23.14 ± 1.33</td>
<td>22.05 ± 1.02</td>
<td>20.64 ± 0.67</td>
<td>0.274</td>
</tr>
<tr>
<td>Physical Activity (steps/day)</td>
<td>5868.67 ± 226.03</td>
<td>7910.62 ± 713.71</td>
<td>6698.91 ± 780.38</td>
<td>0.125</td>
</tr>
<tr>
<td>Quadriceps Mass (kg)</td>
<td>1.73 ± 0.13</td>
<td>1.66 ± 0.08</td>
<td>1.71 ± 0.11</td>
<td>0.900</td>
</tr>
<tr>
<td>PLM Peak Flow (ml/min)</td>
<td>1225.39 ± 141.70</td>
<td>1154.96 ± 99.45</td>
<td>1152.70 ± 106.31</td>
<td>0.884</td>
</tr>
<tr>
<td>KE Peak Power (watts)</td>
<td>35.91 ± 2.22</td>
<td>33.08 ± 2.75</td>
<td>36.36 ± 3.10</td>
<td>0.643</td>
</tr>
<tr>
<td>KE Peak Flow (ml/min)</td>
<td>3860.24 ± 271.01</td>
<td>4059.74 ± 277.13</td>
<td>4282.63 ± 241.56</td>
<td>0.558</td>
</tr>
</tbody>
</table>

BMI: Body Mass Index; PLM Peak Flow: peak blood flow during passive leg movement; KE Peak Power: max power output during knee extension graded exercise test; KE Peak Flow: peak blood flow during the graded exercise test. Values are represented as mean ± standard error.
**Table 2. Temperature Probe Data and Heat Ratings**

<table>
<thead>
<tr>
<th></th>
<th>Exercise</th>
<th>Heat</th>
<th>Sham</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BL Temp (°C)</td>
<td>35.49 ± 0.28</td>
<td>36.27 ± 0.16</td>
<td>35.80 ± 0.27</td>
<td>0.098</td>
</tr>
<tr>
<td>Peak Temp (°C)</td>
<td>37.75 ± 0.25(^H,S)</td>
<td>40.80 ± 0.58(^E,S)</td>
<td>36.10 ± 0.19(^E,H)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>(\Delta) Temp (°C)</td>
<td>2.26 ± 0.33(^H,S)</td>
<td>4.53 ± 0.73(^E,S)</td>
<td>0.31 ± 0.21(^E,H)</td>
<td>0.004</td>
</tr>
<tr>
<td>Avg. Temp (°C)</td>
<td>36.97 ± 0.21(^H,S)</td>
<td>38.69 ± 0.43(^E,S)</td>
<td>35.63 ± 0.26(^E,H)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Heat Rating</td>
<td>n/a</td>
<td>3.56 ± 0.48(^S)</td>
<td>1.50 ± 0.27(^H)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

BL Temp: vastus lateralis (VL) temperature at baseline; Peak Temp: highest temperature of the VL during training intervention; \(\Delta\) Temp: the change in VL temperature from baseline to peak temperature; Avg. Temp: the average temperature of the VL during training intervention; Heat Rating: the average heat rating given by subjects during their training interventions from 1–10 (1 – no heat detected, 10 – felt like their leg was in flames). E: significantly different than Exercise group. H: Significantly different than Heat group. S: Significantly different than Sham Group. Values are represented as mean ± standard error.
Table 3. Effect of Interventions on Anthropometric Measurements, Baseline Flow, and Physical Activity

<table>
<thead>
<tr>
<th></th>
<th>Exercise</th>
<th>Heat</th>
<th>Sham</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>△ Body Weight (kg)</td>
<td>−0.30 ± 0.56</td>
<td>−0.47 ± 0.18</td>
<td>0.42 ± 0.40</td>
<td>0.252</td>
</tr>
<tr>
<td>△ Quadriceps Mass (kg)</td>
<td>0.05 ± 0.08</td>
<td>−0.08 ± 0.07</td>
<td>0.03 ± 0.02</td>
<td>0.269</td>
</tr>
<tr>
<td>△ Leg Mass (kg)</td>
<td>0.17 ± 0.25</td>
<td>−0.26 ± 0.22</td>
<td>0.10 ± 0.08</td>
<td>0.268</td>
</tr>
<tr>
<td>△ Artery Diameter (mm)</td>
<td>0.06 ± 0.01&lt;sup&gt;H,S&lt;/sup&gt;</td>
<td>0.02 ± 0.01&lt;sup&gt;E&lt;/sup&gt;</td>
<td>0.01 ± 0.01&lt;sup&gt;E&lt;/sup&gt;</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>△ Baseline Flow (ml/min)</td>
<td>0.45 ± 34.86</td>
<td>−4.22 ± 39.10</td>
<td>−81.67 ± 39.32</td>
<td>0.252</td>
</tr>
<tr>
<td>△ Physical Activity (steps/day)</td>
<td>283.06 ± 651.27</td>
<td>−1080.4 ± 880.70</td>
<td>−275.43 ± 516.75</td>
<td>0.442</td>
</tr>
</tbody>
</table>

E: significantly different than Exercise group. H: Significantly different than Heat group. S: Significantly different than Sham Group. △: change in value from pretest to posttest intervention. Values are represented as mean ± standard error.
**Figure 1**: Study Schematic. An illustration of the protocol and timing of interventions and assessments associated with this study. PLM: Passive Leg Movement; KEmax: Knee extension maximum power output assessment.
**Figure 2:** Impact of Exercise Training and Heat Training on Resistance Artery Function Assessed by Passive Leg Movement (PLM). S = change in group is different than change in Sham; E = change in group is different than change in Exercise; H = change in group is different than change in Heat; * = significantly change from Pre; P = 0.08: sham group almost significantly decreased vascular function.
Figure 3: Impact of Exercise Training and Heat Training on Blood Flow and Vascular Conductance During Submaximal and Maximal Knee Extension Exercise. A) Blood flow and B) Vascular conductance during submaximal knee extension (KE) at 10 watts. C) Blood flow and D) Vascular conductance during maximal knee extension exercise (KEmax). S = change in group is different than change in Sham; E = change in group is different than change in Exercise; H = change in group is different than change in Heat; * = significantly changed from Pre.
Figure 4: Impact of Exercise Training and Heat Training on Maximum Power Achieved During Knee Extension Exercise. S = change in group is different than change in Sham; E = Change in group is different than change in Exercise; H = Change in group is different than change in Heat; * = significantly changed from Pre.
Figure 5: The Relationship Between Changes in Resistance Artery Function and the Blood Flow Response to Maximal KE Exercise. Linear regression analysis regarding the relationships between the % changes in A) PLM Peak Flow and KE Peak Flow; B) PLM Peak Flow and KE Peak Conductance; and C) PLM Peak Flow and KE Peak Power ($R = 0.64$, $P < 0.001$). PLM: Passive Leg Movement; KEmax: Knee extension maximum power output assessment.