ACRM
AMERICAN CONGRESS OF REHABILITATION MEDICINE

Archives of Physical Medicine and Rehabilitation

journal homepage: www.archives-pmr.org

Archives of Physical Medicine and Rehabilitation 2014;95:1127-34

ORIGINAL ARTICLE

Massage Therapy Restores Peripheral Vascular Function After Exertion

Nina C. Franklin, PhD,[a,b] Mohamed M. Ali, MD,[a,b] Austin T. Robinson, MS,[a,b] Edita Norkeviciute, BS,[a] Shane A. Phillips, PT, PhD[a,b,c]

From the Departments of [a]Physical Therapy; [b]Integrative Physiology Laboratory, College of Applied Health Sciences; and [c]Department of Medicine, University of Illinois at Chicago, Chicago, IL.

Abstract

Objective: To determine if lower extremity exercise-induced muscle injury reduces vascular endothelial function of the upper extremity and if massage therapy (MT) improves peripheral vascular function after exertion-induced muscle injury.

Design: Randomized, blinded trial with evaluations at 90 minutes, 24 hours, 48 hours, and 72 hours.

Setting: Clinical research center.

Participants: Sedentary young adults (N=36) were randomly assigned to 1 of 3 groups: (1) exertion-induced muscle injury and MT (n=15; mean age ± SE, 26.6±0.3); (2) exertion-induced muscle injury only (n=10; mean age ± SE, 23.6±0.4), and (3) MT only (n=11; mean age ± SE, 25.5±0.4).

Intervention: Participants were assigned to exertion-induced muscle injury only (a single bout of bilateral, eccentric leg press exercise), MT only (30-min lower extremity massage using Swedish technique), or exertion-induced muscle injury and MT.

Main Outcome Measures: Brachial artery flow-mediated dilation (FMD) was determined by ultrasound at each time point. Nitroglycerin (NTG)-induced dilation was also assessed (0.4mg).

Results: Brachial FMD increased from baseline in the exertion-induced muscle injury and MT group and the MT only group (7.38%±.18% to 9.02%±.28%, $P<.05$ and 7.77%±.25% to 10.2%±.22%, $P<.05$, respectively) at 90 minutes and remained elevated until 72 hours. In the exertion-induced muscle injury only group, FMD was reduced from baseline at 24 and 48 hours (7.78%±.14% to 6.75%±.11%, $P<.05$ and 6.53%±.11%, $P<.05$, respectively) and returned to baseline after 72 hours. Dilations of NTG were similar over time.

Conclusions: Our results suggest that MT attenuates impairment of upper extremity endothelial function resulting from lower extremity exertion-induced muscle injury in sedentary young adults.

Archives of Physical Medicine and Rehabilitation 2014;95:1127-34

Exertion-induced muscle injury is an important consideration, particularly after physical activities that entail high-force and/or repetitive eccentric muscle contractions.[1] This type of injury is associated with muscle pain, soreness, swelling, decreased range of motion (ROM), and reduced muscle strength, which can last from 5 to 7 days.[1] The pathogenesis of exertion-induced muscle injury is related to an inflammatory response triggered by damaged muscle fibers[2,3] that can lead to systemic inflammation and altered endothelial function[4]; however, these effects have not yet been fully elucidated. Currently, there is no universally accepted treatment for exertion-induced muscle injury; however, massage therapy (MT) is often recommended for reducing associated symptoms and has shown to reduce postinjury inflammation.[5]

MT is a well-known comprehensive intervention that involves the utilization of a variety of manual techniques designed to manipulate the soft tissues and joints of the body.[6] Certain techniques are speculated to decrease pain, reduce intramuscular swelling, and increase ROM after muscle injury.[7] It has also been suggested that some forms of MT influence physiological factors associated with muscle injury and recovery by increasing tissue

Supported by the Massage Therapy Foundation; the National Heart, Lung, and Blood Institute (grant nos. K23HL85614, RO1HL095701, and HL095701-01A2S); and the University of Illinois at Chicago, Center for Clinical and Translational Science (award no. UL1TR000050) from the National Center for Research Resources.

The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

No commercial party having a direct financial interest in the results of the research supporting this article has conferred or will confer a benefit on the authors or on any organization with which the authors are associated.

0003-9993/14/$36 - see front matter © 2014 by the American Congress of Rehabilitation Medicine
http://dx.doi.org/10.1016/j.apmr.2014.02.007

blood flow.[6] MT has most frequently been studied within the context of indirect indices of muscle injury, including pain, muscle function (ie, muscular strength, ROM), swelling, markers of muscle damage (ie, creatine kinase, lactate dehydrogenase), and circulating neutrophils.[8]

Recent in vitro studies have revealed that MT attenuates production of inflammatory cytokines in muscle when administered after damage from acute eccentric exercise.[5] Inflammatory cytokines can initiate a systemic inflammatory response resulting in neutrophil activation and adhesion to vascular endothelial cells.[9,10] Such a response can ultimately culminate in impaired endothelial function,[4] an early prognostic indicator for the development of cardiovascular disease.[11,12] Previous research shows that flow-mediated dilation (FMD), a measure of endothelial function, is impaired in healthy but sedentary young adults after an acute bout of strenuous lower extremity resistance exercise involving both eccentric and concentric muscle contractions.[13] As such, MT may attenuate impaired endothelial function after acute eccentric exercise. Therefore, the purpose of this study was to investigate the mechanisms of systemic endothelial dysfunction of the brachial artery, which develops after exertion-induced muscle injury of the lower extremities, and to determine if treatment of the lower extremities with MT reduces endothelial dysfunction. The hypothesis to be tested is that a MT treatment performed after exposure to exertion-induced muscle injury will protect against impaired endothelial function.

Methods

Participants and design

Thirty-six sedentary adults aged 18 to 40 years were studied. Subjects were randomly assigned to 1 of 3 groups: (1) MT treatment after exposure to exertion-induced muscle injury (exertion-induced muscle injury and MT group), (2) a control intervention of exertion-induced muscle injury without MT treatment (exertion-induced muscle injury only group), or (3) a control intervention of MT treatment without exertion-induced muscle injury (MT only group). Eligibility was confirmed on completion of a health history questionnaire and physical examination. Inclusion criteria were as follows: $<$150 minutes of moderate physical activity per week, no history of resistance or aerobic training within the past 6 months prior to enrollment, no history of cardiovascular disease or suspected collagen vascular disease (eg, systemic vasculitis, diabetes mellitus, thyroid dysfunction, orthopedic injuries), not pregnant, no history of cancer, no history of smoking (for $\geq$6mo prior to participation), no history of amenorrhea or irregular menses, and no use of vasoactive medications. Written informed consent was obtained from all subjects prior to participation. The study protocol was approved by the Office for the Protection of Research Subjects and the Institutional Review Board of the University of Illinois at Chicago.

List of abbreviations:

FMD	**flow-mediated dilation**
MT	**massage therapy**
NO	**nitric oxide**
NTG	**nitroglycerin**
ROM	**range of motion**
ROS	**reactive oxygen species**
SR	**shear rate**

Initial screening and baseline measurements

Subjects were evaluated in the Clinical Research Center of the University of Illinois at Chicago during a screening visit and at 5 time points before (baseline) and after (90min, 24h, 48h, 72h) the intervention. All measurements were performed after a 12-hour overnight fast. During the initial screening visit, venous blood samples were drawn from an antecubital vein, and plasma was separated by centrifugation for laboratory analysis of total cholesterol, high-density lipoproteins, low-density lipoproteins, and glucose. Total cholesterol, high-density lipoproteins, and low-density lipoproteins were measured using spectrophotometric assays. Glucose concentration was measured using the glucose oxidase procedure.[a] A food frequency questionnaire (Block Brief 2000 Food Frequency Questionnaire) was used to determine dietary intake and nutritional content.[14] Heart rate, systolic and diastolic blood pressures, and anthropometric measurements, including height, weight, and waist circumference, were measured. Body composition was determined by bioelectrical impedance analysis[b] as previously reported.[15]

Brachial artery measurements of FMD and nitroglycerin-induced dilation

Approximately 1 week after the initial screening, subjects who met all inclusion criteria returned to the Clinical Research Center for baseline assessment of endothelial function. Brachial artery FMD was used as a measure of endothelial function using previously described techniques.[13,16] In premenopausal women, FMD may vary during the menstrual cycle[17]; therefore, women underwent study procedures during the early follicular phase of menses. Although subjects were in the supine position in a quiet, temperature controlled room, ultrasound imaging[c] of the brachial artery was performed in a longitudinal plane at a site 1 to 3cm proximal to the antecubital fossa of the dominant arm[18] using a high-frequency (7.5MHz) linear array probe. Measurements were made at a depth of 30 to 50mm according to each subject's frame. The same anatomic distance and examination depth were used for each study visit. The dynamic range and pulse-repetition frequency for all examinations were set at 55 to 60dB (B-mode) and 3.5kHz, respectively. Baseline images were recorded after which a forearm blood pressure cuff was inflated to 50mmHg above systolic blood pressure for 5 minutes. Brachial artery diameter (mm) was determined during peak hyperemia after release of the cuff. To assess dilation, at least 30 seconds of images were captured during the first, second, and third minutes after cuff release. Baseline brachial artery flow velocity and peak velocity after cuff release were recorded using central velocity measures described previously.[19] The velocity detecting range was from -30 to 140cm/s within a sample volume of 2mm. Subjects underwent repeated measures of brachial artery FMD and flow at 4 time points (90min, 24h, 48h, 72h) after the intervention. Nitroglycerin (NTG)-induced dilation was also assessed at these 4 time points. Ten minutes after recording the last brachial artery diameter measurement after hyperemia, 0.4mg of sublingual NTG was administered, and endothelium-independent dilation was assessed for 5 minutes.

Offline analysis of FMD and NTG responses was made using edge-detection software[d] as previously described.[13] Percent FMD and responses to NTG were calculated using the averaged minimum mean brachial artery diameter at baseline compared with the largest mean values obtained after release of the forearm occlusion or administration of NTG. Peak shear rate (SR) was calculated as flow