

Brief Muscle Hypoperfusion/Hyperemia: An Ergogenic Aid?

JOSEPH R. LIBONATI,^{1,2} AMY K. HOWELL,¹ NICOLE M. INCANNO,¹
KELLEY K. PETTEE,¹ AND HELENE L. GLASSBERG³

¹Department of Cardiopulmonary Sciences, Human Performance Laboratory, Northeastern University, Boston, Massachusetts 02115; ²BioKinetics Research Laboratory, Department of Kinesiology, Temple University, Philadelphia, Pennsylvania 19122; ³Section of Cardiology, Temple University Hospital, Philadelphia, Pennsylvania 19140.

ABSTRACT

The purpose of this study was to investigate how short-duration forearm hypoperfusion/hyperemia affects isometric wrist flexion maximal voluntary contraction (MVC) in humans. Fourteen subjects (7 men and 7 women) performed isometric wrist flexion MVC on a Biodex ergometer under 2 experimental conditions: (a) without preceding forearm blood pressure cuff occlusion (control), or (b) immediately following forearm blood pressure cuff occlusion (2 minutes at 200 mm Hg) with 10 seconds of hyperemia (postocclusion). The mean MVC was greater in the postocclusion trial for both men (men, control = 267 ± 57 J vs. postocclusion = 303 ± 48 J; $p < 0.05$) and women (women, control = 185 ± 21 J vs. postocclusion = 237 ± 21 J; $p < 0.005$). The delta MVC between control and postocclusion trials was similarly increased in men and women (men, 36 ± 13 J vs. women, 52 ± 11 J; $p =$ not significant [NS] between genders). When men and women were coupled as a single group, the MVC was approximately 20% greater in the postocclusion trial compared with the control trial (control = 226 ± 31 J vs. postocclusion = 270 ± 27 J; $p < 0.0005$). With Doppler/ultrasound imaging, brachial artery flow following 2 minutes of forearm occlusion was five- to sixfold greater than baseline blood flow ($p < 0.0005$). Isometric wrist flexion MVC is improved in both men and women following brief duration forearm cuff occlusion. The hyperemia that follows cuff occlusion may provide this putative effect.

Key Words: muscle strength, blood flow, isometric, ergogenic, hyperemia, ischemia/reperfusion

Reference Data: Libonati, J.R., A.K. Howell, N.M. Incanno, K.K. Pettee, and H.L. Glassberg. Brief muscle hypoperfusion/hyperemia: An ergogenic aid? *J. Strength Cond. Res.* 15(3):362–366. 2001.

Introduction

There is an intricate relationship between skeletal muscle blood flow and muscle force output during

exercise (20). For instance, skeletal muscle performance and metabolism are enhanced when skeletal muscle blood flow (1) and/or arterial oxygen content (9) are increased. Conversely, prolonged exposure to ischemia precipitates the development of skeletal muscle fatigue and may instead induce irreversible cell damage concurrent with microvascular injury (7). The extent and duration of the ischemic exposure is critical in understanding the extent of tissue damage (7), as more prominent tissue necrosis is observed with lengthy periods of tissue hypoperfusion.

When skeletal muscle blood flow is temporarily diminished (i.e., with blood pressure cuff occlusion), there is a prompt reactive hyperemia observed when the occlusion is removed (13). The magnitude of reactive hyperemia is, in part, based on the length of tissue hypoperfusion. We have recently reported that immediately following 2 minutes of forearm occlusion, brachial artery flow increased fourfold from baseline (12), whereas 5 minutes of forearm occlusion elicited a sevenfold brachial artery hyperemic response (13).

Since increasing arterial blood flow is known to enhance muscle performance, we hypothesized that hyperemia following brief blood pressure cuff occlusion may enhance muscle performance if the duration of muscle hypoperfusion was brief enough so as not to impair high-energy phosphate metabolism and/or sarcolemmal ionic distribution. This hypothesis was based on Muller's data suggesting that calf pedaling ergometer performance was enhanced following brief occlusion/hyperemia in the upper leg (16).

The purpose of this paper was to assess how brief forearm occlusion/hyperemia affects peak isometric wrist flexion maximal voluntary contraction (MVC). A secondary aim of this study was to determine if the MVC response to occlusion/hyperemia was different between men and women.

Methods

Subjects

A total of 14 healthy subjects (7 men and 7 women, age range 21–34 years) volunteered to take part in this study after receiving full written and verbal details of the experimental procedures. All subjects were treated in accord with human subject procedures put forth by the American College of Sports Medicine. All subjects reported to the laboratory in a rested state at least 2 hours following the last meal. All subjects refrained from the use of caffeine and/or alcohol at least 24 hours prior to testing.

Subjects were placed in a seated position with the hip flexed at 90°. The right arm was flexed at the shoulder with the elbow joint angle maintained at 135° of elbow extension. The palm was situated in the anatomical position. Subjects maintained this position for 5–10 minutes prior to the start of the experimental protocol. A Biodex multijoint ergometer (Biodex Inc., Shirley, NY) was used to determine 1 isometric MVC of the wrist flexors. The isometric MVC was held for 20 seconds, and the total force was recorded and analyzed with Biodex software. In order to limit accessory muscle use and extraneous body movement during the MVC, subjects were secured in the Biodex chair with seat restraints around the torso and hips.

Reliability Trial

The first series of experiments were designed to establish the reliability of the experimental protocol. In 2 separate trials, which were separated by a time period of at least 1 week, 12 subjects (7 men and 5 women) performed one 20-second isometric wrist flexion MVC with the right arm. The data were recorded on the Biodex for both trials. Mean data and a reliability coefficient were established.

Brief Occlusion/Hyperemia Protocol

In the second set of experiments, subjects were situated in the position described above. Subjects (7 men and 7 women) performed a singular 20-second, isometric wrist flexion MVC with the right arm under 2 experimental conditions. The experimental conditions were administered in a random fashion with each subject acting as his or her own control. The protocol consisted of performing isometric wrist flexion MVCs following (a) 2 minutes of no forearm occlusion with the sham cuff situated on the forearm (control), or (b) 2 minutes of forearm occlusion induced with a blood pressure cuff inflated to 200 mm Hg and released for 10 seconds prior to the onset of the exercise (postocclusion). In both experimental conditions the blood pressure cuff was placed 0.5 cm below the elbow joint, with the bladder situated anteriorly.

Blood Flow Determination

In order to quantify the magnitude of the hyperemic response following 2 minutes of forearm occlusion, a

third set of experiments was performed utilizing brachial artery Doppler/ultrasound imaging. These methods have previously been reported in detail (12). The hyperemic response of the brachial artery was directly determined in 7 subjects (3 men and 4 women) in a temperature-controlled room (23° C), with the subjects positioned for the above exercise protocol. Brachial artery diameter and flow velocity were determined with a 7.5 MHz linear array transducer ultrasound system (Hewlett-Packard, Sonos 1000, Andover, MA). The brachial artery was imaged at 3–5 cm above the antecubital fossa, and a 1.5 cm segment of artery was continuously imaged throughout the protocol. All images were viewed in a longitudinal plane at an image depth of 4 cm, and great methodological precautions were taken to optimize blood vessel wall definition. Images were maximally magnified, and all Doppler/ultrasound settings were kept constant throughout each experiment. Doppler flow velocity measurements were obtained using an angle of incidence of 60°. All images were recorded on a video tape for analysis on the Sonos 1000 (Hewlett Packard, Andover, MA).

Arterial diameter and blood flow measurements were determined from the video tape recordings by 2 separate observers. Arterial diameter was calculated within the 1.5-cm segment of artery as determined by the measurement of 5 evenly spaced measurements across the distance of the arterial wall/blood interface perpendicular to the arterial long axis. All measurements were determined in the diastolic phase of the cardiac cycle as denoted by a 3-lead electrocardiogram. A total of 3 cardiac cycles were averaged for all diameter measurements at a specific time point of the experimental protocol. Likewise, a mean Doppler flow velocity was calculated from 3 cardiac cycles. Brachial artery blood flow was calculated by multiplying the mean Doppler flow velocity (of 3 consecutive cardiac cycles) by the cross-sectional area of the brachial artery.

Baseline brachial artery diameter and blood flow velocity (control) were recorded during an interval of 1 minute following 10 minutes of quiet rest. A blood pressure cuff was placed over the forearm 0.5 cm below the antecubital fossa and inflated for 2 minutes at an occlusion pressure of 200 mm Hg. Both brachial artery diameter and blood flow velocity were measured in the brachial artery proximal to the occlusion. Immediately following cuff deflation (within 10 seconds), blood flow velocity and brachial artery diameter were measured, denoting the peak hyperemic flow. Peak hyperemic flow was calculated as the baseline brachial artery flow subtracted from the brachial artery flow immediately following blood pressure cuff occlusion (reactive hyperemia).

Table 1. Physical characteristics of subjects.*

	Age (y)	Weight (kg)	Height (cm)
Men ($n = 7$)	25 ± 1	81 ± 6	178 ± 2
Women ($n = 7$)	24 ± 1	61 ± 4	157 ± 5

* Data are mean \pm SEM.

Table 2. Individual maximal voluntary contraction (MVC) responses to control or postocclusion in men and women.

Subject	Control (J)	Postocclusion (J)	Change in MVC (J)
1-male	217	290	73
2-male	245	321	76
3-male	332	336	4
4-male	496	485	-11
5-male	392	405	13
6-male	100	150	50
7-male	89	137	48
8-female	133	156	23
9-female	183	248	65
10-female	152	236	84
11-female	175	268	93
12-female	218	254	36
13-female	294	318	24
14-female	138	179	41

Statistics

All data are expressed at mean \pm SEM. The reliability of the isometric wrist flexion MVC protocol was assessed using a Pearson correlation. The mean MVC in both reliability trials was also compared with paired Student *t*-tests. Control and postocclusion MVC were compared in both men and women with paired Student *t*-tests. Postocclusion gender responses and hyperemic blood flow were also compared with paired Student *t*-tests. The alpha level was set at 0.05 for all analyses. All statistics were generated with a commercial statistical package on a Macintosh personal computer (Instat, 2.01, San Diego, CA).

Results

Reliability Trial

The mean MVC among 12 subjects repeating control 2 trials was similar (trial 1 = 200 ± 20 J vs. trial 2 = 209 ± 31 J; $p =$ not significant [NS]). The reliability coefficient between trials was $r = 0.79$; $p = 0.0024$.

MVC in Control and Postocclusion Trials

The physical characteristics of subjects are listed in Table 1. Table 2 shows the individual MVC responses in men and women during the control and postocclusion

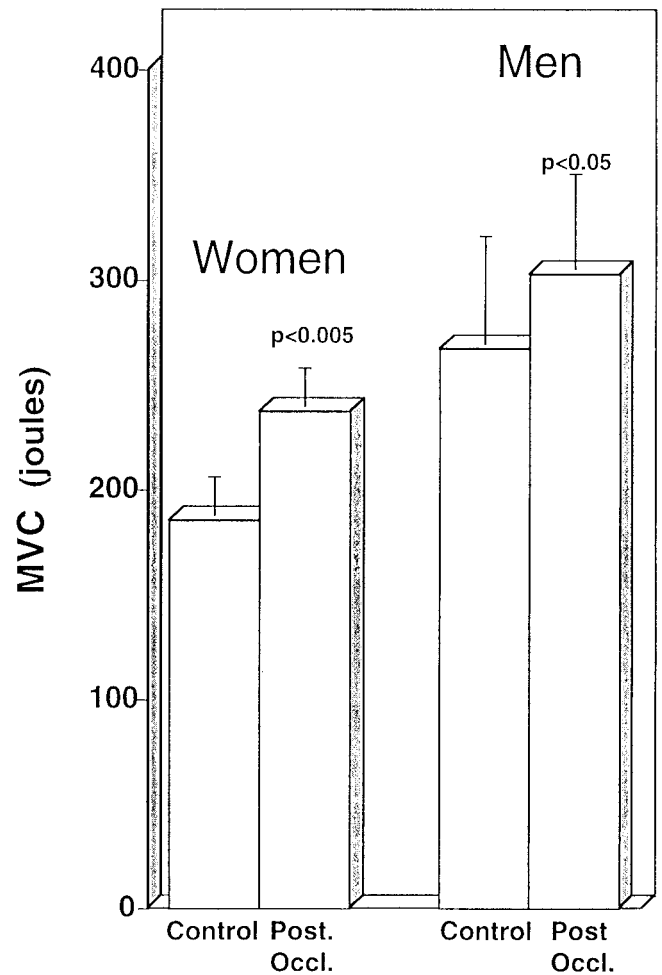


Figure 1. The mean wrist flexion maximal voluntary contraction (MVC) for women ($n = 7$) and men ($n = 7$) under control and postocclusion conditions. In both men and women, MVC during postocclusion was significantly greater than during control conditions. Data are means \pm SEM.

trials. The mean MVC increased in both men (men, control = 267 ± 57 J vs. postocclusion = 303 ± 48 J; $p < 0.05$) and women (women, control = 185 ± 21 J vs. postocclusion = 237 ± 21 J; $p < 0.005$; see Figure 1). The change in force between control and postocclusion trials was similar between men and women (men = 36 ± 13 J vs. women = 52 ± 11 ; $p =$ NS). Although the trials were administered randomly, postocclusion force was greater in 93% of subjects (13 of 14 subjects tested). The MVC increased approximately 20% from control to postocclusion when men and women were combined as a single group (no occlusion = 226 ± 31 J vs. postocclusion = 270 ± 27 J; $p < 0.0005$). The control MVC tended to be greater in men vs. women, but this relationship did not reach statistical significance.

Hyperemic Response

Figure 2 represents the hyperemic response of the brachial artery to forearm cuff occlusion. The control

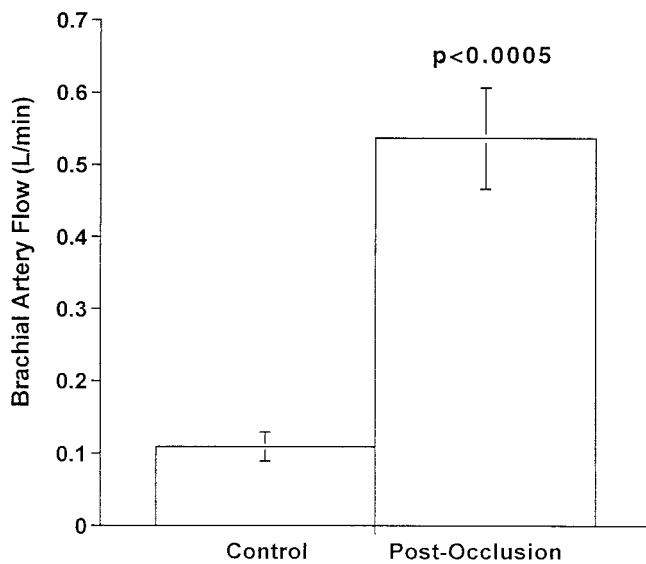


Figure 2. Blood flow in the brachial artery in 7 subjects during control conditions at baseline and following 2 minutes of cuff occlusion (postocclusion). There was a five- to sixfold increase in blood flow during immediate postocclusion conditions. Data are expressed as means \pm SEM.

blood flow was 109 ± 29 ml \cdot min $^{-1}$. Immediately following forearm blood pressure cuff occlusion, brachial artery blood flow increased five- to sixfold (reactive hyperemia) to 536 ± 73 ml \cdot min $^{-1}$ ($p < 0.0005$).

Discussion

The purpose of this study was to determine the effects of a brief period of skeletal muscle hypoperfusion on isometric wrist flexion MVC. Second, it was determined if the MVC response to hypoperfusion was similar between men and women. The results of our study suggest that isometric wrist flexion MVC was enhanced immediately following forearm occlusion (10 seconds), and that both the male and female subjects similarly generated a greater MVC during the postocclusion trial as compared with the control trial. In a separate set of experiments, brachial artery hyperemia was quantified following 2 minutes of forearm cuff occlusion, and it was found that brachial artery flow increased five- to sixfold from the control. It was hypothesized that the reactive hyperemia associated with brief forearm cuff occlusion offered this ergogenic effect.

In his review regarding physiological methods of enhancing work capacity, Muller (16) described that heavy exercise performance could be increased by reducing the blood supply for up to 10 minutes prior to the onset of exercise. In his model using a pedaling ergometer driven by the calf muscles, maximal work time following cuff occlusion of the upper leg was increased in parallel to duration of hypoperfusion. We recently showed that the rate of fatigue in our isomet-

ric forearm model was attenuated following 2 minutes of forearm occlusion (12). However, from our initial study, it was unclear how brief hypoperfusion affected strength and whether or not the response was gender-specific (12).

Recent studies in animals have shown that muscle protection from ischemia/reperfusion appears to be proportional to the number of ischemic/reperfusion cycles. Even brief intervals of ischemic "preconditioning" have been found to significantly improve skeletal muscle force, performance, endurance, and contractility of postischemic animal skeletal muscle (2, 5, 6, 15, 18, 19). Several studies have also reported improved myocardial tolerance to ischemic stress following relatively brief intermittent exposures to myocardial ischemia (14, 17, 21).

Various phases of both isotonic and isometric skeletal muscle contraction are known to impede skeletal muscle blood flow during exercise (22). Even at low percentages of the MVC (22), intramuscular pressure far exceeds microvascular pressure and impedes microvascular flow. By increasing blood flow prior to the initiation of muscular contraction (i.e., with cuff occlusion), microvascular hypoperfusion may be attenuated during the actual period of exercise. We have recently shown that peak forearm hyperemia is well correlated with endurance performance (13), and Hughson et al. (10) have reported that the skeletal blood flow response at the onset of exercise directly effects oxidative metabolism through alterations in the transport of oxygen. In the present study, the observed postocclusive hyperemia may have allowed for greater forearm MVC by establishing greater nutritive flow, increasing microvascular pressure, and/or by increasing metabolite washout.

Other possibilities associated with hypoperfusion/hyperemia may include the following: protection by heat shock proteins, alterations in Ca $^{2+}$ metabolism, antioxidant defense systems, as well as the release of vasodilatory mediators such as adenosine, nitric oxide, or prostaglandins (3, 4, 8, 11). The neural effects of cuff occlusion are difficult to determine, although the anesthetic sensation associated with cuff occlusion may also be involved in the improvement of MVC.

The duration of muscle hypoperfusion is an important consideration in understanding the improvement of MVC. Although the brachial artery hyperemic response following 5 minutes of forearm cuff occlusion is considerably greater than the hyperemia following 2 minutes of cuff occlusion (13), we have only observed a reduction of the MVC after 5 minutes of cuff occlusion (unpublished data). One explanation for these observations is that beyond inducing reactive hyperemia, longer duration cuff occlusion may alter ionic balance, pH, and/or high-energy phosphate metabolism. In conclusion, brief cuff occlusion increases wrist flexor isometric MVC. The ergogenic nature of this

phenomena may be secondary to the reactive hyperemia associated with short-term forearm occlusion. Further study using dynamic exercise models is needed to determine the involved putative mechanisms.

Practical Applications

This study shows that brief periods of skeletal muscle occlusion/hyperperfusion can acutely increase muscle force output by approximately 20%. These data may suggest that occlusion/hyperperfusion can be used as an ergogenic aid in activities that rely on short-term strength and power. For instance, performance in sports such as powerlifting or shot putting may be enhanced following occlusion/hyperperfusion. It is extremely important, however, that this study be exclusively interpreted as investigative research. The authors do not recommend that readers self-experiment, extrapolate, or prescribe these techniques to others until further research is conducted.

References

1. BRECHUE, W.F., J.K. BARCKLAY, D.M. O'DROBINAK, AND W.N. STAINSBY. Differences between $\dot{V}O_2$ maxima of twitch and tetanic contractions are related to blood flow. *J. Appl. Physiol.* 71: 131-135. 1991.
2. CARROLL, C., S. CARROLL, M. OVERGOOR, G. TOBIN, AND J. BARKER. Acute ischemic preconditioning of skeletal muscle prior to flap elevation augments muscle-flap survival. *Plast. Reconstr. Surg.* 100:58-65. 1997.
3. DIETZ, N.M., K.A. ENGELKE, T.T. SAMUEL, R.T. FIX, AND M.J. JOYNER. Evidence for nitric oxide mediated sympathetic forearm vasodilation in humans. *J. Physiol. London* 498:531-540. 1997.
4. ENGELKE, K.A., J.R. HALLIWILL, D.N. PROCTOR, N.M. DIETZ, AND M.J. JOYNER. Contribution of nitric oxide and prostaglandins to reactive hyperemia in the human forearm. *J. Appl. Physiol.* 81:1807-1814. 1996.
5. GURKE, L., A. KUHRMEIER, P. SUTTER, J. SEELIG, S. MARTINOLI, M. HEBERER, AND A. MARX. Ischemic preconditioning improves postischemic function but not energy metabolism of skeletal muscles. *Ann. Italian Chir.* 67:253-255. 1996.
6. GURKE, L., A. MARX, P. SUTTER, A. FRENTZEL, T. SALM, F. HARDER, J. SEELIG, AND M. HEBERER. Ischemic preconditioning improves postischemic skeletal muscle function. *Am. Surg.* 62:391-394. 1996.
7. HARRIS, A.G., R. LEIDERER, F. PEER, AND K. MESSMER. Skeletal muscle microvascular and tissue injury after varying durations of ischemia. *Am. J. Physiol.* 271:H2388-H2398. 1996.
8. HICKNER, R.C., J.S. FISHER, A.A. EHSANI, W.M. KOHRT. Role of nitric oxide in skeletal muscle blood flow at rest and during dynamic exercise in humans. *Am. J. Physiol.* 273:H405-410. 1997.
9. HOGAN, M.C., AND H.G. WELCH. Effect of altered arterial O_2 tensions on muscle metabolism in dog skeletal muscle during fatiguing work. *Am. J. Physiol.* 251:C216-C222. 1986.
10. HUGHSON, R.L., J.K. SHOEMAKER, M.E. TSCHAKOVSKY, AND J.M. KOWALCHUK. Dependence of muscle $\dot{V}O_2$ on blood flow dynamics at onset of forearm exercise. *J. Appl. Physiol.* 81:1619-1626. 1996.
11. LAWSON, C.S., AND J.M. DOWNEY. Preconditioning: State of the art myocardial protection. *Cardiovasc. Res.* 27:542-550. 1993.
12. LIBONATI, J.R., M. COX, N. INCANNO, S. MELVILLE, F. MUSANTE, H.L. GLASSBERG, AND M. GUAZZI. Brief periods of occlusion and reperfusion increase skeletal muscle force output in humans. *Cardiologia* 4312:1355-1360. 1998.
13. LIBONATI, J.R., H.L. GLASSBERG, T. CALDWELL, M. COX, N. INCANNO, A.C. SULLIVAN, AND L.M. HAYWARD. Brachial artery postocclusion hyperemia strongly predicts exercise capacity. *Circulation* 17(Suppl.):I-156. 1998.
14. LIU, Y., AND J.M. DOWNEY. Ischemic preconditioning protects against infarction in the rat heart. *Am. J. Physiol.* 263:H1107-1112. 1992.
15. MATTEI, A., L. GURKE, A. MARX, K. CHALOUKKA, F. HARDER, AND M. HEBERER. Preconditioning with brief ischemia and reperfusion cycles improves ischemia tolerance of skeletal muscle in the rat. *Langenbecks Arch. Chir. Suppl.* 114:495-498. 1997.
16. MULLER, E.A. Physiological methods of increasing human physical work capacity. *Ergonomics* 8:409-424. 1965.
17. MURRY, C.E., R.B. JENNINGS, AND K.A. REIMER. Preconditioning with ischemia: A delay of lethal cell injury in ischemic myocardium. *Circulation* 74:1124-1136. 1986.
18. PANG, C., P. NELIGAN, A. ZHONG, W. HE, H. XU, AND C. FORREST. Effector mechanism of adenosine in acute ischemic preconditioning of skeletal muscle against infarction. *Am. J. Physiol.* 273:R887-R895. 1997.
19. PANG, C., R. YANG, A. ZHONG, N. XU, B. BOYD, AND C. FORREST. Acute ischemic preconditioning protects against skeletal muscle infarction in the pig. *Cardiovasc. Res.* 29:782-788. 1995.
20. ROBERGS, R.A., M.V. ICENOGLU, T.L. HUDSON, AND E.R. GREENE. Temporal inhomogeneity in brachial artery blood flow during forearm exercise. *Med. Sci. Sports Exerc.* 29:1021-1027. 1997.
21. YELLON D.M., A.M. ALKHULAIFI, AND W.B. PUGSLEY. Preconditioning the human myocardium. *Lancet* 342:276-277. 1993.
22. WALLOE, L., AND J. WESCHE. Time course and magnitude of blood flow changes in human quadriceps muscles during and following rhythmic exercise. *J. Physiol.* 405:257-273. 1988.