Whole-Body Vibration Stimulates Microvascular Blood Flow in Skeletal Muscle

ANDREW C. BETIK[1], LEWAN PARKER[1], GUNVEEN KAUR[1], GLENN D. WADLEY[1], and MICHELLE A. KESKE[1,2]

[1]*Institute for Physical Activity and Nutrition (IPAN), School of Exercise and Nutrition Sciences, Deakin University, Geelong, AUSTRALIA; and* [2]*Baker Heart and Diabetes Institute, Melbourne, AUSTRALIA*

ABSTRACT

BETIK, A. C., L. PARKER, G. KAUR, G. D. WADLEY, and M. A. KESKE. Whole-Body Vibration Stimulates Microvascular Blood Flow in Skeletal Muscle. *Med. Sci. Sports Exerc.*, Vol. 53, No. 2, pp. 375–383, 2021. **Purpose:** Whole-body vibration (WBV) therapy has been reported to potentially act as an exercise mimetic by improving muscle function and exercise capacity in a variety of healthy and clinical populations. Considering the important role that microvascular blood flow plays in muscle metabolism and exercise capacity, we investigated the muscle microvascular responses of acute WBV to knee extension exercise (KEX) in healthy individuals. **Methods:** Eleven healthy adults (age: 33 ± 2 yr; body mass index: 23.6 ± 1.1 kg·m^{-2}) underwent 3 min of WBV, or 3 min of KEX at 25% of one-repetition maximum, in a randomized order separated by a minimum of 72 h. Femoral arterial blood flow was measured via Doppler ultrasound, and thigh muscle microvascular blood flow was measured via contrast-enhanced ultrasound at baseline and throughout the 3-min postintervention recovery period. **Results:** Both WBV and KEX significantly increased peak microvascular blood flow (WBV, 5.6-fold; KEX, 21-fold; both $P < 0.05$) during the 3-min recovery period. Despite a similar increase in femoral arterial blood flow (~4-fold; both $P < 0.05$ vs baseline) and whole-body oxygen consumption measured by indirect calorimetry (WBV, 48%; KEX, 60%; both $P < 0.05$ vs baseline) in both conditions, microvascular blood flow was stimulated to a greater extent after KEX. **Conclusion:** A single 3-min session of WBV in healthy individuals is sufficient to significantly enhance muscle microvascular blood flow. Despite KEX providing a more potent stimulus, WBV may be an effective method for improving microvascular blood flow in populations reported to exhibit microvascular dysfunction such as patients with type 2 diabetes. **Key Words:** ULTRASOUND, MICROCIRCULATION, HYPEREMIA, FEMORAL ARTERY BLOOD FLOW, OXYGEN CONSUMPTION, MUSCLE ACTIVATION

Downloaded from http://journals.lww.com/acsm-msse by BhDMf5ePHKav1zEoum1tQfN4a+kJLhEZgbsIHo4XMi0hCywCX1AWnYQp/IlQrHD3i3D0OdRyi7TvSFl4Cf3VC1y0abggQZXdtwnfKZBYtws= on 04/12/2021

Exercise has many health benefits, including reducing the risk of chronic diseases (1). Whole-body vibration (WBV) has recently received attention as an alternative or a supplement to traditional exercise due to its proposed exercise mimetic actions. The ability of WBV to act as an exercise mimetic is in part due to oscillations from the vibration causing a reactionary activation of skeletal muscles, activation of sensory and motor neurons (2,3), increased cardiovascular demand (4–6), and oxygen consumption (5,6). This has led to the use of WBV for both acute (7) and long-term therapy (8–10) in healthy and clinical populations. Although it has long been established that muscle performance during exercise is highly dependent on adequate blood flow to the working muscles (11), the muscle hemodynamic responses of WBV have been poorly characterized.

Muscle contraction (or exercise) stimulates both total limb and microvascular blood flow (MBF) in skeletal muscle to facilitate the delivery of nutrients, hormones, and gases (12,13). Although exercise increases both macrovascular blood flow and MBF, it is the effect on the microvasculature that is particularly important for nutrient exchange. This is due to the microvasculature (or capillaries) being in intimate contact with the myocyte allowing for amplified delivery of nutrients during metabolic demand such as contraction (14,15). Muscle contraction potently increases MBF, which occurs even with low levels of muscle contraction (16–19). For example, forearm contraction at 25% of maximal voluntary strength every 20 s has been shown to maximally (or close to maximally) recruit the microvasculature (approximately threefold above baseline) in healthy humans (18,19). Other exercises such as calf raises (plantarflexion exercise) (20,21) elicit a marked increase in skeletal muscle microvascular blood volume (MBV) and MBF. Importantly, many of these studies have shown that increases in total limb blood flow through conduit arteries do not always reflect increases in MBF (18,22–24). Although studies have shown that an acute bout of WBV increases total limb blood flow (4,25,26), it is not known whether WBV also has exercise mimetic actions to increase MBF, which is important for nutrient exchange.

Address for correspondence: Andrew C. Betik, Ph.D., Institute for Physical Activity and Nutrition (IPAN), School of Exercise and Nutrition Sciences, Deakin University, Geelong, Australia; E-mail: Andrew.Betik@deakin.edu.au.
Submitted for publication January 2020.
Accepted for publication June 2020.
Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.acsm-msse.org).

0195-9131/20/5302-0375/0
MEDICINE & SCIENCE IN SPORTS & EXERCISE®
Copyright © 2020 by the American College of Sports Medicine
DOI: 10.1249/MSS.0000000000002463

APPLIED SCIENCES

Copyright © 2021 by the American College of Sports Medicine. Unauthorized reproduction of this article is prohibited.

It is important to determine whether WBV stimulates MBF because of the microvascular-based benefits of traditional exercise. For example, muscle MBF in response to insulin (or a meal) is blunted in type 2 diabetes, which results in impaired muscle glucose uptake and poor glucose regulation (27). Exercise training improves postprandial-related microvascular responsiveness, and this directly improves glycemic regulation in people with type 2 diabetes (28). Given the importance of exercise on microvascular-related health outcomes, it is important to characterize the effect of WBV on MBF to determine whether WBV can be used as an alternative or a supplement to traditional exercise, particularly in people who are unable or have limited capacity to exercise. However, before this, it is first necessary to characterize the muscle hemodynamic responses of WBV in healthy individuals. The aim of this study was to characterize the muscle microvascular responses of an acute bout of WBV compared with knee extension exercise (KEX) when matched for the same femoral artery blood flow response in apparently healthy individuals.

METHODS

Participants and screening. Twelve healthy adults were recruited through community advertisement of which 11 (5 males and 6 females) completed the study with 1 withdrawal. Females were recruited and tested at any stage during their menstrual cycle, and estradiol levels were not measured. Participant characteristics are presented in Table 1. Exclusion criteria for participation included current or previous history of cardiometabolic disease, smoking, and musculoskeletal or other conditions that prevent daily activity. Verbal and written explanations about the study were provided before obtaining written informed consent. Participants were asked to refrain from moderate to vigorous physical activity (48 h) and alcohol and caffeine ingestion (24 h) before all testing sessions. The study was approved by the Deakin University Human Research Ethics Committee. To confirm participants did not have any cardiometabolic risk factors, participants were screened via a medical history, resting blood pressure, and a fasting blood sample, which was analyzed at an accredited commercial pathology laboratory (Australian Clinical Labs, Victoria, Australia) using standard protocols for glucose, insulin, total cholesterol, triglycerides, and glycated hemoglobin (HbA_{1c}).

TABLE 1. Participant characteristics (n = 11).

Anthropometrics	
Age (yr)	33 ± 2
Body mass (kg)	69.2 ± 4.5
Height (cm)	170.5 ± 2.8
Body mass index ($kg \cdot m^{-2}$)	23.6 ± 1.1
Fasting blood	
Glucose ($mmol \cdot L^{-1}$)	4.6 ± 0.1
HbA_{1c} (%)	5.0 ± 0.1
HbA_{1c} ($mmol \cdot mol^{-1}$)	31.4 ± 0.9
Insulin ($mU \cdot L^{-1}$)	5.9 ± 1.0
Total cholesterol ($mmol \cdot L^{-1}$)	5.4 ± 0.3
HDL ($mmol \cdot L^{-1}$)	1.7 ± 0.1
LDL ($mmol \cdot L^{-1}$)	3.2 ± 0.3
Triglyceride ($mmol \cdot L^{-1}$)	1.0 ± 0.1

Data are presented as mean ± SEM. HbA_{1c}, glycated hemoglobin.

Eligible participants were then invited to attend a familiarization session before completing three experimental sessions, separated by a minimum of 72 h.

Overview of study design. Participants completed a familiarization session and three experimental sessions (Fig. 1). The first experimental session was designed to determine and match superficial femoral arterial (total limb) blood flow responses between WBV and knee extension. This was achieved by measuring femoral arterial blood flow of the right leg after a range of vibration frequencies and comparing and matching this response to that elicited by the KEX protocol. Once completed, participants were then randomized (and subsequently crossed over) to undergo two experimental sessions, separated by a minimum of 72 h, to measure and compare the muscle MBF responses to both vibration exposure and knee extension when matched for total leg blood flow.

Familiarization session: WBV familiarization and determination of 25% one-repetition maximum knee extension. Participants arrived at the Deakin University exercise laboratory, and their height and weight were measured via a standard weight scale and stadiometer. A pneumatic bilateral knee extension machine (AIR250; Keiser Corporation, Fresno, CA) was than adjusted for each individual participant, and seat position and leg length settings were documented. Participants were provided instructions on correct knee extension technique and allowed to familiarize themselves with the range of motion of the unloaded machine. The right leg was used for all participants and experimental sessions. After a 5-min warm-up on a cycle ergometer at 50–75 W, participants returned to the knee extension machine, and an initial resistance was selected that was estimated to correspond to their 4–10 repetition maximum. If participants successfully completed more than 10 repetitions, the resistance was incrementally increased between sets, with 5–10 min rest periods, until participants achieved their 4–10 repetition maximum. Twenty-five percent of one-repetition maximum (1RM) was calculated using the Brzycki (29) equation: weight / [1.0278 − (0.0278 × number of repetitions) × 0.25]. After adequate rest, participants were then familiarized with the WBV machine by asking them to stand on a synchronous, side-alternating vibration platform (Galileo Sport; Novotec Medical GmbH, Pforzheim, Germany). Participants were instructed to stand as natural as possible with their feet shoulder width apart with a slight bend in their knees to absorb the vibration and minimize discomfort at higher frequencies. Participants wore sport shoes and stood flat-footed on both legs in an upright position. They were instructed to look forward and not down at the vibration platform and to rest their hands on the support bar but not to grip it. The standing position was not made too prescriptive to ensure that participants would mimic how they would use these platforms at home, in a gym, or in a clinic. For this reason, foot position was not regimented between participants, and thus it is not possible to report on specific amplitude of vibration or acceleration parameters. Based on estimated foot positions, peak-to-peak displacement would be in the range of 6–8 mm, which at 12.5 Hz

Copyright © 2021 by the American College of Sports Medicine. Unauthorized reproduction of this article is prohibited.

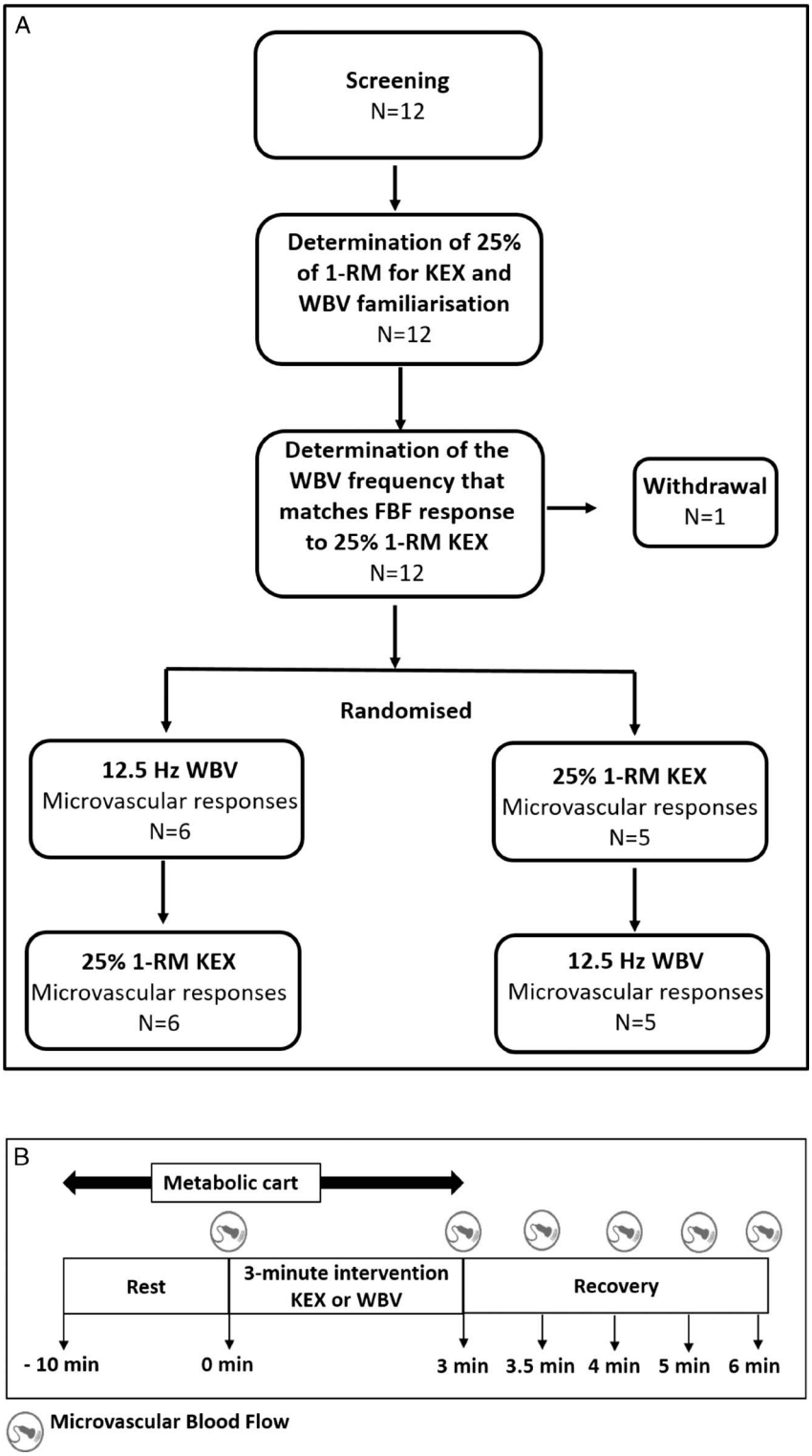

FIGURE 1—A, Overall flow of the study design and participant testing. B, Experimental session overview. Participants underwent 3 min of KEX, or in a randomized crossover fashion, 3 min of WBV at 12.5 Hz. Skeletal muscle MBF of the thigh was measured before, immediately after, and throughout the 3-min postintervention recovery period. Indirect calorimetry was measured via a portable metabolic cart at baseline and during the intervention. FBF, femoral artery blood flow.

gives an acceleration range of 1.9–2.5*g* (where $g = 9.81\ \mathrm{m \cdot s^{-2}}$). The vibration frequency was progressively increased from 5 to 15 Hz, over a 5-min period, to ensure participants were comfortable with the range of frequencies used in the study.

Experimental session 1: the effects of acute WBV and knee extension on superficial femoral artery blood flow. Participants arrived in the laboratory and rested for 10 min before measurement of resting heart rate, blood

APPLIED SCIENCES

Copyright © 2021 by the American College of Sports Medicine. Unauthorized reproduction of this article is prohibited.

pressure, and baseline diameter and blood flow velocity of the superficial femoral artery of the right leg via a high-frequency L12-5 linear array transducer interfaced to an ultrasound machine (Philips iU22 Ultrasound Machine; Philips Medical Systems, Bothell, WA). Participants then underwent 3-min periods of standing on the vibration platform at a frequency set to 5, 7.5, 10, 12.5, and 15 Hz, in a randomized order and interspersed by a minimum of 5 min recovery between frequencies. After the last frequency, and after a minimum of 5 min rest, participants then underwent a 3-min 25% 1RM knee extension protocol consisting of three initial contractions over 3 s, followed by a single contraction every 15 s (15 total contractions). Heart rate, blood pressure, and superficial femoral artery blood flow (artery diameter and blood flow velocity) were measured before and 15 s after each individual vibration frequency and after the KEX protocol. The vibration frequency of 12.5 Hz produced a similar peripheral hemodynamic response (femoral arterial blood flow) to that of the KEX protocol (see Results and Fig. 2). As such, the frequency of 12.5 Hz was selected to be the prescribed frequency for the 3-min WBV intervention in the subsequent experimental session.

Experimental sessions 2 and 3: the effects of acute WBV and knee extension on skeletal muscle MBF and whole-body energy expenditure. On two separate days, participants arrived in the laboratory after an overnight fast and rested on a hospital bed while an intravenous cannula was inserted into an antecubital vein. While rested, a perflutren lipid microsphere injectable suspension contrast agent (Definity; Lantheus Medical Imaging, North Billerica, MA) was infused intravenously to measure resting thigh (vastus lateralis) skeletal muscle MBF of the right leg. Participants then underwent either the 3-min WBV or the 3-min KEX in a randomized order and then crossed over for the subsequent visit. MBF was assessed before, immediately after the 3-min intervention and subsequently at 0.5, 1, 2, and 3 min of recovery after cessation of the WBV or KEX protocols (Fig. 1B). During the KEX, we were able to acquire contrast-enhanced ultrasound (CEU) measurements at 2 and 2.5 min when the leg remained rested between contractions. This gave insight into whether MBF had reached steady state by the end of the 3 min. Because of the continuous leg movements during WBV, it is not possible to collect CEU measurements simultaneously while WBV is occurring. Whole-body oxygen consumption ($\dot{V}O_2$) and carbon dioxide production were measured during the protocol via an indirect calorimetry system (Cortex MetaMax 3B; Cortex Biophysik, Leipzig, Germany).

Real-time CEU. Skeletal muscle MBF was determined by CEU as previously described (23,28). Definity contrast agent (1.5 mL) was diluted in 19 mL of saline and infused intravenously at a constant rate of 1.5–2.2 mL·min^{-1} (infusion rate based on body weight) using a rotating syringe pump (Vue Ject, BR-inf 100; Bracco, Geneva, Switzerland). After 4 min of infusion to allow for whole-body contrast agent equilibrium, baseline MBF was measured via CEU using an L9-3 linear transducer positioned (cross section) over the right vastus lateralis muscle. A series of 3 × 45-s CEU real-time video captures were recorded before commencement of the protocol. Single 30-s CEU videos were captured immediately after the protocol and at 0.5, 1, 2, and 3 min postprotocol. Settings for mechanical index (0.11 for continuous and 1.30 for flash), gain (75%), depth, and focus were identical between trials.

Digital images were analyzed offline using Qlab (QLAB; Philips Medical Systems, Andover, MA). Raw acoustic intensity was background subtracted (0.5 s frame for baseline and 0.25 s frame for postprotocol) to eliminate signal from larger vessels and tissue artifacts (e.g., tissue and fascia). The acoustic intensity measured from a suitable region of interest was then plotted over time and fitted using the equation $y = A\,(1 - e^{-\beta(t - t_b)})$, where y is the acoustic intensity at time t, t_b is the background time, A is the plateau acoustic intensity (MBV), and β is the rate constant (a measure of microvascular refilling rate). MBF was determined by $A \times \beta$ (30).

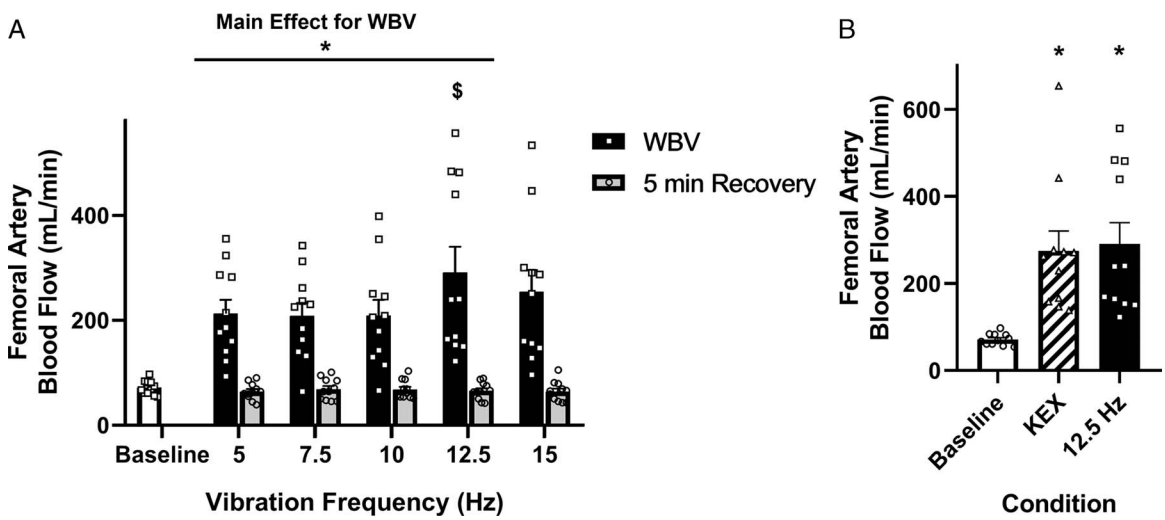

FIGURE 2—Femoral artery blood flow after 3 min WBV at different vibration frequencies (*solid bars*) and showing return to baseline by 5 min (*gray bars*) (A) and after 3 min of KEX compared with 12.5 Hz WBV (B). Values are presented as mean ± SEM. *$P < 0.05$ vs baseline; \$$P < 0.05$ vs 10 Hz.

Copyright © 2021 by the American College of Sports Medicine. Unauthorized reproduction of this article is prohibited.

Statistical methods. Data were analyzed using GraphPad Prism version 8.0.0 (GraphPad Prism, La Jolla, CA). For time course MBF responses, comparisons of multiple means within a condition were examined using a repeated-measures ANOVA with a Holm–Sidak *post hoc* to control for multiple comparisons (all time points vs baseline). Comparisons between interventions of baseline and peak responses for MBF measures, femoral artery blood flow, $\dot{V}O_2$, heart rate, and blood pressure were performed by a two-factor (protocol–time point) repeated-measures ANOVA followed by a Holm–Sidak *post hoc* test where appropriate. *A priori* sample size calculation determined that 12 participants would be needed to detect a twofold increase in MBF after WBV ($\alpha = 0.05$ and power = 90%). One participant withdrew because of a vasovagal episode, and therefore only data from the 11 participants who completed the study were used in the final analysis. Data are reported as mean ± SEM, and statistical analysis was conducted at the 95% confidence interval ($P \leq 0.05$).

RESULTS

Participant characteristics. Six females and five males completed the study (age = 33 ± 2 yr; body mass index = 23.6 ± 1.1 $kg \cdot m^{-2}$). All participants were apparently healthy with normal fasting blood glucose (<5.5 $mmol \cdot L^{-1}$), HbA_{1c} (<6.5%), and insulin (<25 $mU \cdot L^{-1}$) levels. Participants were not on any medication known to affect glucose or lipid levels.

Superficial femoral artery blood flow. The first testing visit was used to determine which vibration frequency would elicit a similar femoral artery blood flow response to the KEX protocol. Compared with standing with no vibration, femoral artery blood flow was significantly higher after all vibration intensities (Fig. 2A). The KEX protocol elicited a fourfold increase in femoral artery blood flow (Fig. 2B). Femoral artery blood flow at 12.5 Hz was the lowest frequency that stimulated a comparable fourfold increase compared with 25% 1RM KEX (Fig. 2B). There was no further increase in femoral artery blood flow at the higher frequency of 15 Hz (Fig. 2A). The effect of WBV and contraction on femoral artery blood flow was acute, and flow returned to baseline values after 5 min (Fig. 2A). In summary, the vibration frequency of 12.5 Hz was used for comparison with the KEX in the main trial.

Skeletal muscle MBF responses. Baseline muscle microvascular responses (MBV, β, and MBF) were similar between KEX and WBV (MBV = 7.2 ± 1.4 vs 8.2 ± 1.9 AI; β = 0.09 ± 0.01 vs 0.08 ± 0.01 $1 \cdot s^{-1}$; MBF = 0.68 ± 0.23 vs 0.65 ± 0.18 $AI \cdot s^{-1}$; $P > 0.05$; Fig. 3), indicating that MBF was not affected by standing on the nonvibrating platform.

Compared with baseline, KEX elicited a significant increase in MBV (fourfold, $P < 0.05$) and β (sixfold, $P < 0.05$; Fig. 3A and B, respectively). Consequently, MBF (which is the product of MBV and β) was markedly elevated above baseline (~23-fold, $P < 0.05$; Fig. 3C). All microvascular responses to exercise were similar in magnitude during the last minute of real-time contraction (2 and 2.5 min) and immediately after the cessation of KEX (3-min time point) (Fig. 3A–C). There was a time-dependent decay in microvascular responses (MBV, β, and MBF), which reached baseline levels 3 min after cessation of KEX (Fig. 3A–C).

Three minutes of WBV did not change MBV when data from all participants were collated together for each time point after WBV (Fig. 3D). However, each participant had a different microvascular time course after WBV, and all participants displayed an increase in MBV at some time point. Five participants had an immediate increase in MBV in response to WBV when compared with baseline, which declined over time (see Figure, Supplemental Digital Content 1, Microvascular blood volume response after 3 min WBV, http://links.lww.com/MSS/C80). The other six participants had the opposite time course with no increase in MBV immediately after WBV when compared with baseline but increasing and peaking to a level above baseline over time (see Figure, Supplemental Digital Content 1, Microvascular blood volume response after 3 min WBV, http://links.lww.com/MSS/C80). Because of the different microvascular time course in response to WBV, the data were also analyzed by assessing the peak response of each participant. Peak muscle MBV in response to WBV was elevated by 2.5-fold above baseline ($P < 0.05$; Fig. 3G) compared with the 4.0-fold increase with KEX ($P < 0.05$). Although WBV produced an exercise mimetic action on MBV, the response to leg exercise was significantly higher than WBV ($P < 0.05$; Fig. 3).

Three minutes of WBV increased MBF velocity (β) 3.4-fold compared with baseline (Fig. 3E) and quickly returned to baseline values within 30 s. Peak β in response to WBV was 3.6-fold higher than baseline ($P < 0.05$; Fig. 3H), whereas KEX elicited a 6.2-fold increase from baseline ($P < 0.05$; Fig. 3H). Although WBV produced an exercise mimetic action on β, the response to KEX was significantly higher than WBV ($P < 0.05$; Fig. 3).

Immediately after WBV, skeletal muscle MBF was 5.1-fold higher than baseline ($P < 0.05$; Fig. 3F). MBF decreased quickly in the 30 s after WBV, and although it appeared to remain above baseline for the 3 min into recovery, none of the other time points were statistically different from baseline. However, as above, participants had a varied response in the time course of MBF response after WBV. When the peak MBF for each participant was calculated, irrespective of the time, WBV elicited a 5.6-fold increase in MBF above baseline ($P < 0.05$; Fig. 3I). However, the response to KEX (23-fold increase) was significantly higher than WBV ($P < 0.05$; Fig. 3). Representative ultrasound images of the vastus lateralis and representative data with corresponding curve fit results for baseline and postintervention are shown in Figure 4.

Oxygen consumption, heart rate, and blood pressure during WBV and knee extension. Whole-body $\dot{V}O_2$, heart rate, and blood pressure were similar at baseline between WBV and KEX. $\dot{V}O_2$ increased to a similar degree in the first minute for both KEX and WBV and remained significantly elevated throughout the 3-min intervention ($P < 0.05$; Fig. 5). Heart rate did not increase from baseline during WBV (72 ± 3.1 vs 69 ± 2.6 bpm, $P > 0.05$) but was

Copyright © 2021 by the American College of Sports Medicine. Unauthorized reproduction of this article is prohibited.

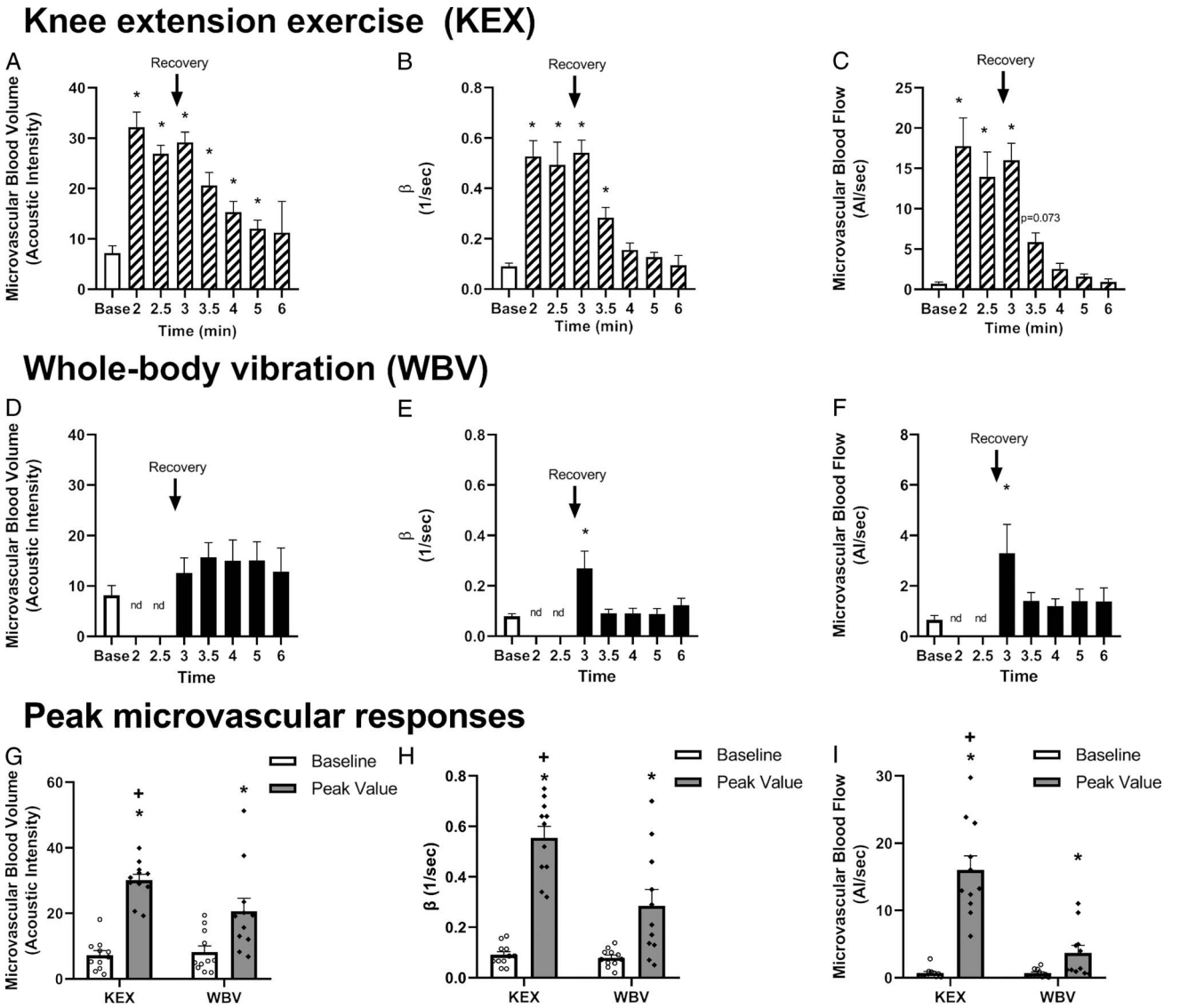

FIGURE 3—CEU results after 3 min of KEX (*top panels*) or WBV (*middle panels*). MBV (A, D), *β* (B, E), and MBF (C, F). Note the different *y*-axis scale for MBF (C, F) when comparing KEX vs WBV. Panels G, H, and I are the peak values recorded after the intervention for MBV, *β*, and MBF, respectively, for both KEX and WBV. For WBV, it was not possible to perform CEU measurements during the vibration so there are no values for 2 and 2.5 min. Values are presented as mean ± SEM. *$P < 0.05$ vs base; +$P < 0.05$ vs WBV. Base, baseline; nd, not determined.

significantly elevated after KEX compared with baseline (73 ± 2.6 vs 81 ± 3.1 bpm, $P < 0.05$). Systolic blood pressure did not change significantly from baseline after either condition (WBV = 119 ± 3.2 vs 120 ± 4.4 mm Hg, KEX = 119 ± 3.2 vs 122 ± 3.1 mm Hg, $P > 0.05$). However, diastolic blood pressure was elevated slightly from baseline after both conditions (WBV = 75 ± 2.6 vs 80 ± 2.2 mm Hg, KEX = 75 ± 2.6 vs 81 ± 3.0 mm Hg, both $P < 0.05$).

DISCUSSION

Microvascular perfusion represents the capacity for exchange of nutrients, hormones, and gases as it is the interface between the blood in the capillaries and the tissue. The major findings of this study are that WBV significantly increases muscle MBF but to a much smaller magnitude than exercise, despite WBV and exercise eliciting similar increases in femoral artery blood flow and whole-body oxygen consumption. Although 3 min of WBV produced these hemodynamic and metabolic exercise mimetic actions, knee extension contraction produced stronger effects on the microcirculation with greater increases in MBV, *β*, and MBF. WBV may be a therapeutic option for improving microvascular perfusion in at-risk populations who find it difficult to do traditional exercise.

Although the main objective of this study was to determine whether WBV could increase skeletal muscle microvascular perfusion, it was first necessary to determine a vibration frequency that elicited an increase in leg blood flow, as measured in the superficial femoral artery. We found that leg blood flow increased above baseline (standing quietly on the vibration platform) even at the low frequency of 5 Hz, but a higher blood flow response was achieved at 12.5 Hz with no further

Copyright © 2021 by the American College of Sports Medicine. Unauthorized reproduction of this article is prohibited.

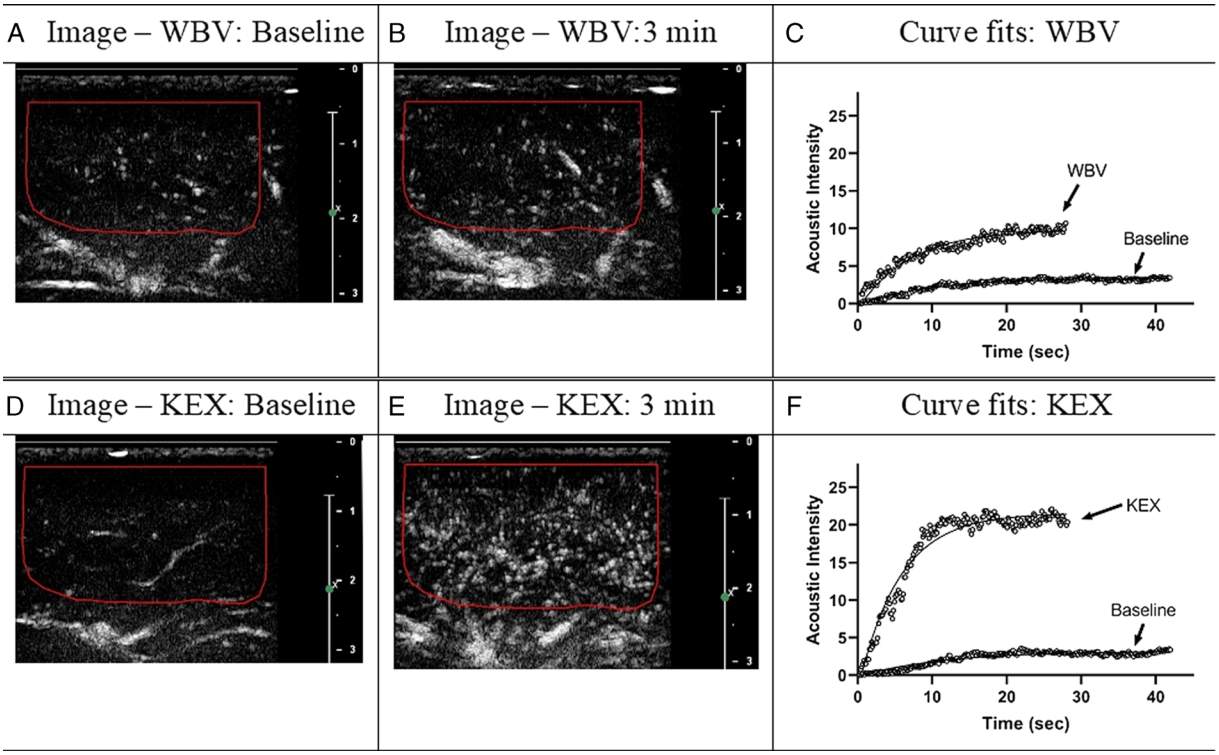

FIGURE 4—Representative images of the vastus lateralis showing intensity of microbubbles and curve fits at baseline and after 3 min of WBV or KEX. Images showing intensity of microbubbles at baseline before WBV (A) and KEX (D) and after 3 min of WBV (B) or knee extension (E). Right-side panels show representative curve fits at baseline and after WBV (C) and KEX (F).

detectable increase at 15 Hz (Fig. 2A). Our observations of an approximate threefold increase in femoral artery blood flow are not too dissimilar with other studies showing a doubling of popliteal artery blood flow velocity after a 26-Hz vibration exposure (4) and approximately three- to fivefold increases in femoral artery mean blood velocity at frequencies of 5–30 Hz (26). Lythgo et al. (2009) also performed a frequency dose-response; however, these were done during 1-min intervals in an isometric squat position and thus difficult to directly compare with this study. Although they found a main effect of vibration to increase mean blood velocity, they did not detect significant differences between the frequencies (26). An increase in skin blood flow in response to WBV has been observed previously in people with type 2 diabetes (31) and during supine WBV (32); however, skin blood flow does not mirror the effects of limb blood flow (28,32). Because 12.5 Hz was the lowest frequency to stimulate a comparable increase in femoral artery blood flow to knee extension contraction, this frequency was chosen to investigate the effects of WBV on skeletal muscle microvascular perfusion.

This is the first study to our knowledge to directly measure microvascular perfusion after WBV and present the novel finding that three min of WBV at 12.5 Hz increases vastus lateralis muscle microvascular responses. Furthermore, individual time course responses after WBV are highly variable as evident by the large variation in the timing of the increase in MBV post-WBV. These different time courses may be reflective of the body position while standing on the platform and the degree of loading on the quadriceps while standing during and after the vibration. A limitation of the study is that acceleration parameters during WBV for each participant were not recorded. Relating acceleration to macrovascular and microvascular responses will be important to follow-up in future studies. An investigation of group characteristics found no group differences in body mass index, body mass, or physical activity status between immediate and delayed responders (see Table, Supplemental Digital Content 2, Participant characteristics for groups identified as immediate or delayed responders, http://links.lww.com/MSS/C81). However, there

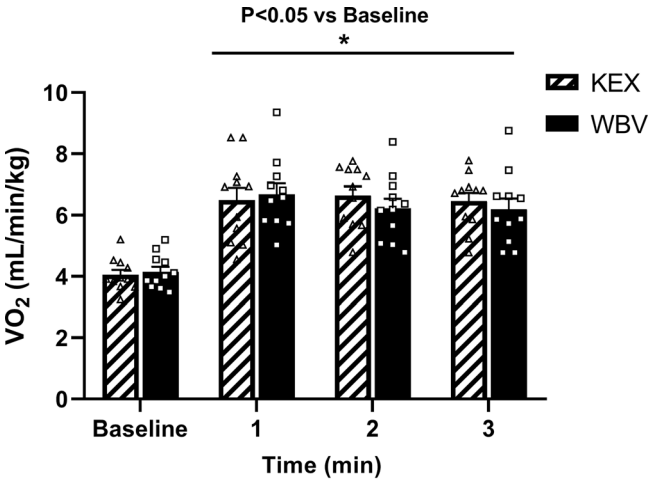

FIGURE 5—$\dot{V}O_2$ response during the 3-min KEX and WBV intervention (mean ± SEM). There was a main effect for time (*P < 0.05 for all time points vs baseline within each condition) and no difference in the response between conditions (WBV vs KEX, P > 0.05).

APPLIED SCIENCES

Copyright © 2021 by the American College of Sports Medicine. Unauthorized reproduction of this article is prohibited.

was a trend for more males to be in the immediate response group (four males, one female) and more females in the delayed response group (one male, five females; see Figure, Supplemental Digital Content 1, Microvascular blood volume response after 3 min WBV, http://links.lww.com/MSS/C80). We are unaware of any sex-specific explanation for a differential time course in microvascular response but do note that the baseline MBV values in the females appear to be higher. Despite an apparent difference in timing of response, the total peak response was similar between the groups, so in this regard the significance in sex differences may be minimal. Although this study is not statistically powered for sex-specific comparisons, this observation is worth noting and worthy of future investigation. A limitation of the study is that females were not tested during the same phase of the menstrual cycle, and estradiol levels were not measured, which are important to follow-up.

Despite a significant increase in microvascular responses with WBV, the increase in the microcirculation with knee extension was substantially greater. Contraction at 25% of 1RM every 15 s increased perfusion (MBF) by greater than 20-fold, although the task was of light-to-moderate intensity and not demanding. This level of contraction was used in the current project because it has been shown in the forearm flexors to produce near maximal microvascular recruitment, otherwise known as MBV (18,19). These disparities in microvascular responses between WBV and KEX occurred despite a comparable increase in femoral artery blood flow in both conditions. As we have pointed out that changes in MBF do not always mirror changes in femoral artery blood flow, it is possible that higher vibration frequencies could induce greater MBF responses than reported here (12.5 Hz), although femoral artery blood flow does not increase. Limits on the number/volume of microbubbles than can be safely infused into humans prevented us from measuring MBF at different vibration frequencies, but this is worthy of further investigation.

It is well known that skeletal muscle blood flow increases to meet the metabolic demand of contracting muscle (33–35) although the precise molecular pathways are not fully resolved. Metabolic biproducts (e.g., inorganic phosphate, carbon dioxide, and nitric oxide) and reduced oxygen tension that occurs during contraction can cause vasodilation of the precapillary arterioles, increasing the number of open capillaries (capillary recruitment) (13,36,37) and reducing vascular resistance. Whether WBV increases skeletal muscle blood flow using similar mechanisms is unknown. The reason why WBV elicited a similar but smaller microvascular response than KEX, despite comparable whole-body energy demands, is likely due to the fact that KEX exercise (a dynamic movement) was isolated to a small muscle group of higher metabolic demand, which was the specific site that microvascular measurements were taken, whereas WBV (a more static movement) likely activated muscles of the entire lower limb and stabilizing muscles of the trunk. Although we did not measure it directly, standing with WBV likely requires much less than 25% of vastus lateralis muscle strength, which was required by KEX. We, and others, have shown that bulk blood flow does not always reflect skeletal muscle MBF (17,18,23,24) for which these data further support such disparity.

To this end, it is noteworthy that both the WBV and the knee extension elicited similar total leg blood flow (Fig. 2B) and oxygen consumption (Fig. 5), suggesting similar metabolic demands for both activities. Whole-body $\dot{V}O_2$ and femoral artery blood flow were increased after WBV, which corroborates other published data (4,6). In possibly the most convincing data for WBV increasing $\dot{V}O_2$, Rittweger et al. used three conditions of increasing load with and without WBV and found across all three conditions a ~3.5-mL·kg^{-1}·min^{-1} increase in $\dot{V}O_2$ with the addition of WBV. In our study, we observed a slightly lower increase of ~2.1 mL·kg^{-1}·min^{-1}, which may be explained by the lower vibration frequency in our study compared with theirs (12.5 Hz vs 26 Hz). It has been reported that the increases in peripheral blood flow with WBV are minimized with vibration frequencies above 25 Hz (25,26), potentially through greater sympathetic stimulation (25). We report that WBV did not result in an increase in heart rate or blood pressure compared with standing quietly, an observation seen by others of similar study design (4).

This study is the first to show that even just a short 3-min bout of WBV can increase muscle microvascular perfusion in healthy individuals. Although KEX provides a more potent stimulus for muscle MBF, WBV may be a suitable and effective method for stimulating muscle MBF in populations that commonly exhibit microvascular dysfunction, such as patients with type 2 diabetes or heart failure. Future research is required to establish whether the reported cardiometabolic benefits, both acute and chronic, of WBV therapy are in part due to muscle microvascular-related improvements or adaptations. For example, it would be useful to know if an acute exposure to WBV was able to improve glycemic control after a meal or if long-term repeated exposure could improve microvascular networks and/or function.

Funding provided by a grant from the Institute for Physical Activity and Nutrition (IPAN) SEED. L. P. is funded by the NHMRC and the National Heart Foundation Early Career Fellowships.

There are no actual or perceived conflicts of interest and no relationships with any company that could benefit from this study. The results do not constitute endorsement by the American College of Sports Medicine. They are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation.

APPLIED SCIENCES

REFERENCES

1. Weston KS, Wisloff U, Coombes JS. High-intensity interval training in patients with lifestyle-induced cardiometabolic disease: a systematic review and meta-analysis. *Br J Sports Med*. 2014;48(16):1227–34.
2. Wakeling JM, Nigg BM, Rozitis AI. Muscle activity damps the soft tissue resonance that occurs in response to pulsed and continuous vibrations. *J Appl Physiol*. 2002;93(3):1093–103.

Copyright © 2021 by the American College of Sports Medicine. Unauthorized reproduction of this article is prohibited.

3. Cardinale M, Lim J. Electromyography activity of vastus lateralis muscle during whole-body vibrations of different frequencies. *J Strength Cond Res*. 2003;17(3):621–4.
4. Kerschan-Schindl K, Grampp S, Henk C, et al. Whole-body vibration exercise leads to alterations in muscle blood volume. *Clin Physiol*. 2001;21(3):377–82.
5. Rittweger J, Ehrig J, Just K, Mutschelknauss M, Kirsch KA, Felsenberg D. Oxygen uptake in whole-body vibration exercise: influence of vibration frequency, amplitude, and external load. *Int J Sports Med*. 2002;23(6):428–32.
6. Rittweger J, Schiessl H, Felsenberg D. Oxygen uptake during whole-body vibration exercise: comparison with squatting as a slow voluntary movement. *Eur J Appl Physiol*. 2001;86(2):169–73.
7. Bosco C, Iacovelli M, Tsarpela O, et al. Hormonal responses to whole-body vibration in men. *Eur J Appl Physiol*. 2000;81:449–54.
8. Mulder ER, Stegeman DF, Gerrits KH, et al. Strength, size and activation of knee extensors followed during 8 weeks of horizontal bed rest and the influence of a countermeasure. *Eur J Appl Physiol*. 2006; 97(6):706–15.
9. Blottner D, Salanova M, Püttmann B, et al. Human skeletal muscle structure and function preserved by vibration muscle exercise following 55 days of bed rest. *Eur J Appl Physiol*. 2006;97(3):261–71.
10. Ebing J, Gast U, Hauptmann C, Felsenberg D, Belavý DL. Hypertrophy and explosive-reactive functioning in sedentary men after 10 weeks of whole-body vibration. *J Strength Cond Res*. 2018;32(1):27–36.
11. Wahren J, Saltin B, Jorfeldt L, Pernow B. Influence of age on the local circulatory adaptation to leg exercise. *Scand J Clin Lab Invest*. 1974;33(1):79–86.
12. Dawson D, Vincent MA, Barrett EJ, et al. Vascular recruitment in skeletal muscle during exercise and hyperinsulinemia assessed by contrast ultrasound. *Am J Physiol Endocrinol Metab*. 2002; 282(3):E714–20.
13. Honig CR, Odoroff CL, Frierson JL. Capillary recruitment in exercise: rate, extent, uniformity, and relation to blood flow. *Am J Physiol Heart Circ Physiol*. 1980;238(1):H31–42.
14. Federspiel WJ, Popel AS. A theoretical analysis of the effect of the particulate nature of blood on oxygen release in capillaries. *Microvasc Res*. 1986;32(2):164–89.
15. Mathieu-Costello O. Comparative aspects of muscle capillary supply. *Annu Rev Physiol*. 1993;55(1):503–25.
16. Hong YH, Betik AC, Premilovac D, et al. No effect of NOS inhibition on skeletal muscle glucose uptake during in situ hindlimb contraction in healthy and diabetic Sprague-Dawley rats. *Am J Physiol Regul Integr Comp Physiol*. 2015;308(10):R862–71.
17. St-Pierre P, Keith LJ, Richards SM, Rattigan S, Keske MA. Microvascular blood flow responses to muscle contraction are not altered by high-fat feeding in rats. *Diabetes Obes Metab*. 2012;14(8):753–61.
18. Vincent MA, Clerk LH, Lindner JR, et al. Mixed meal and light exercise each recruit muscle capillaries in healthy humans. *Am J Physiol Endocrinol Metab*. 2006;290(6):E1191–7.
19. Womack L, Peters D, Barrett EJ, Kaul S, Price W, Lindner JR. Abnormal skeletal muscle capillary recruitment during exercise in patients with type 2 diabetes mellitus and microvascular complications. *J Am Coll Cardiol*. 2009;53(23):2175–83.
20. Lindner JR, Womack L, Barrett EJ, et al. Limb stress-rest perfusion imaging with contrast ultrasound for the assessment of peripheral arterial disease severity. *JACC Cardiovasc Imaging*. 2008;1(3):343–50.
21. Meneses AL, Nam MCY, Bailey TG, et al. Leg blood flow and skeletal muscle microvascular perfusion responses to submaximal exercise in peripheral arterial disease. *Am J Physiol Heart Circ Physiol*. 2018;315(5):H1425–33.
22. Hildebrandt W, Schwarzbach H, Pardun A, et al. Age-related differences in skeletal muscle microvascular response to exercise as detected by contrast-enhanced ultrasound (CEUS). *PLoS One*. 2017; 12(3):e0172771.
23. Sjoberg KA, Frosig C, Kjobsted R, et al. Exercise increases human skeletal muscle insulin sensitivity via coordinated increases in microvascular perfusion and molecular signaling. *Diabetes*. 2017;66(6):1501–10.
24. Zhang L, Vincent MA, Richards SM, et al. Insulin sensitivity of muscle capillary recruitment in vivo. *Diabetes*. 2004;53(2):447–53.
25. Games KE, Sefton JM, Wilson AE. Whole-body vibration and blood flow and muscle oxygenation: a meta-analysis. *J Athl Train*. 2015; 50(5):542–9.
26. Lythgo N, Eser P, De Groot P, Galea M. Whole-body vibration dosage alters leg blood flow. *Clin Physiol Funct Imaging*. 2009;29(1):53–9.
27. Clark MG, Wallis MG, Barrett EJ, et al. Blood flow and muscle metabolism: a focus on insulin action. *Am J Physiol Endocrinol Metab*. 2003;284(2):E241–58.
28. Russell RD, Hu D, Greenaway T, et al. Skeletal muscle microvascular-linked improvements in glycemic control from resistance training in individuals with type 2 diabetes. *Diabetes Care*. 2017; 40(9):1256–63.
29. Brzycki M. Strength testing—predicting a one-rep max from reps-to-fatigue. *J Phys Educ Recreat Dance*. 1993;64(1):88–90.
30. Russell RD, Hu D, Greenaway T, et al. Oral glucose challenge impairs skeletal muscle microvascular blood flow in healthy people. *Am J Physiol Endocrinol Metab*. 2018;315(2):E307–15.
31. Johnson PK, Feland JB, Johnson AW, Mack GW, Mitchell UH. Effect of whole body vibration on skin blood flow and nitric oxide production. *J Diabetes Sci Technol*. 2014;8(4):889–94.
32. Lohman EB 3rd, Petrofsky JS, Maloney-Hinds C, Betts-Schwab H, Thorpe D. The effect of whole body vibration on lower extremity skin blood flow in normal subjects. *Med Sci Monit*. 2007;13: CR71–6.
33. Segal SS, Kurjiaka DT. Coordination of blood flow control in the resistance vasculature of skeletal muscle. *Med Sci Sports Exerc*. 1995; 27(8):1158–64.
34. Saltin B, Radegran G, Koskolou MD, Roach RC. Skeletal muscle blood flow in humans and its regulation during exercise. *Acta Physiol Scand*. 1998;162(3):421–36.
35. Laughlin MH, Armstrong RB. Muscular blood flow distribution patterns as a function of running speed in rats. *Am J Physiol Heart Circ Physiol*. 1982;243(2):H296–306.
36. Segal SS. Regulation of blood flow in the microcirculation. *Microcirculation*. 2005;12(1):33–45.
37. Rattigan S, Wheatley C, Richards SM, Barrett EJ, Clark MG. Exercise and insulin-mediated capillary recruitment in muscle. *Exerc Sport Sci Rev*. 2005;33(1):43–8.

Copyright © 2021 by the American College of Sports Medicine. Unauthorized reproduction of this article is prohibited.