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Plantar vibration improves leg fluid flow in perimenopausal women

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Departments of [1]Pediatrics, [2]Physiology, and [3]Internal Medicine, New York Medical College, Valhalla and [5]Department of Bioengineering, State University of New York at Binghamton, Binghamton, New York; and [4]LDM Associates, San Jose, California

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Stewart, Julian M., Carol Karman, Leslie D. Montgomery, and Kenneth J. McLeod. Plantar vibration improves leg fluid flow in perimenopausal women. *Am J Physiol Regul Integr Comp Physiol* 288: R623–R629, 2005. First published October 7, 2004; doi:10.1152/ajpregu.00513.2004.—Recent studies have indicated that plantar-based vibration may be an effective approach for the prevention and treatment of osteoporosis. We addressed the hypothesis of whether the plantar vibration operated by way of the skeletal muscle pump, resulting in enhanced blood and fluid flow to the lower body. We combined plantar stimulation with upright tilt table testing in 18 women aged 46–63 yr. We used strain-gauge plethysmography to measure calf blood flow, venous capacitance, and the microvascular filtration relation, as well as impedance plethysmography to examine changes in leg, splanchnic, and thoracic blood flow while supine at a 35° upright tilt. A vibrating platform was placed on the footboard of a tilt table, and measurements were made at 0, 15, and 45 Hz with an amplitude of 0.2 *g* point to point, presented in random order. Impedance-measured supine blood flows were significantly ($P = 0.05$) increased in the calf (30%), pelvic (26%), and thoracic regions (20%) by plantar vibration at 45 Hz. Moreover, the 25–35% decreases in calf and pelvic blood flows associated with upright tilt were reversed by plantar vibration, and the decrease in thoracic blood flow was significantly attenuated. Strain-gauge measurements showed an attenuation of upright calf blood flow. In addition, the microvascular filtration relation was shifted with vibration, producing a pronounced increase in the threshold for edema, P_i, due to enhanced lymphatic flow. Supine values for P_i increased from 24 ± 2 mmHg at 0 Hz to 27 ± 3 mmHg at 15 Hz, and finally to 31 ± 2 mmHg at 45 Hz ($P < 0.01$). Upright values for P_i increased from 25 ± 3 mmHg at 0 Hz, to 28 ± 4 mmHg at 15 Hz, and finally to 35 ± 4 mmHg at 45 Hz. The results suggest that plantar vibration serves to significantly enhance peripheral and systemic blood flow, peripheral lymphatic flow, and venous drainage, which may account for the apparent ability of such stimuli to influence bone mass.

plantar vibration; orthostasis; blood flow; lymphatic flow; venous return

THE IMPORTANCE OF BLOOD and interstitial flow in the maintenance of bone mass has long been suggested, although difficulties in studying the interstitial fluid flows in bone has slowed progress in this area. In the mid-1960s, Keck and Kelly (18) demonstrated that increased bone growth was associated with increased venous pressure. These observations led to studies of interstitial flow in bone and to the demonstration of lymphatic vessels in bone directed from the marrow to the periosteal surfaces (36). Subsequently, Kelly's group (19) showed that high venous pressure encouraged bone formation. Later, this same group demonstrated that high venous pressure was associated with increased venous filtration (20). McDonald and Pitt Ford (23) demonstrated that an important effect of mechanical loading was the significant alteration of blood flow in bone. The influence of increased venous pressure and increased filtration on interstitial and lymphatic flow has been confirmed in a rat hindlimb suspension model of microgravity (2). Most recently, Colleran et al. (4) have shown that decreased lower limb perfusion results in decreased cancellous bone formation as well as reduced periosteal bone.

Results from recent studies indicate that a relatively small vibrational stimulus applied to the plantar surface of standing subjects is capable of inhibiting bone loss or even increasing bone mass (34, 43). The effects reported in these studies are similar in magnitude to those obtained in pharmacological trials of similar duration (28) and, therefore, may have clinical implications. At this time, however, the mechanism of action of this plantar stimulation remains unclear, making it difficult to rationalize its use. Because the stimulus magnitude utilized in these studies is so low, it is unlikely that the observed effects are a direct result of the mechanical strain induced into the tissue (30). An alternative mechanism is that the bone tissue response is secondary to vibrational stimulation of postural mechanisms and the skeletal muscle pump effects on blood and lymphatic flow.

Such a hypothesis is reasonable because loss of bone mass, whether due to aging, bed rest, or spaceflight, is consistently associated with decreased postural musculature. As early as the 1960s, Issekutz et al. (17) demonstrated that bone loss and postural muscle atrophy associated with immobilization or bed rest in young subjects could be inhibited by having study subjects stand quietly for six 30-min sessions per day. This strategy does not work with older subjects (34), for whom quiet standing appears to result in decreased bone density. Standing increases the arterial and venous hemostatic pressure in the lower limbs, causing increased venous pooling and microvascular filtration. Although vasoconstriction modifies this to a degree, the assistance of the skeletal muscle pump is required to effectively return blood and lymph to the heart. On the one hand, the skeletal muscle pump in young individuals is usually healthy, maintaining venous and lymphatic return and aiding in orthostatic tolerance (42). On the other hand, data show that with aging there is a reduction in postural skeletal muscle activity associated with reduction in type IIa fibers and reduction in the efficacy of the muscle pump (16). This reduces venous and lymphatic return during quiet standing in older individuals and reduces the benefit on bone perfusion of hydrostatic pressure. Type IIa fibers contract at rates in the

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range of 20–70 Hz. We proposed that plantar vibration at low levels at frequencies similar to the contraction frequency of type IIa fibers may enhance bone growth and inhibit bone loss through its influence on the skeletal muscle pump (34, 35).

On the basis of these observations, we developed the hypothesis that plantar vibration should have a significant effect on lower limb blood flow and lymph flow, particularly in older women at greatest risk for osteoporosis. Our aim was therefore to study perimenopausal women.

To test this hypothesis in perimenopausal women, we combined vibrational stimulation of the plantar surface with upright tilt table testing while examining blood flow and fluid flow parameters in the lower extremities.

MATERIALS AND METHODS

Subjects. We screened consecutive female subjects aged 45–70 yr who were enrolled in a general internal medicine practice. Subjects were excluded who had a current fracture of the lower appendicular or axial skeleton, history of back pain (which could be exacerbated by the vibration protocol), known peripheral vascular disease, peripheral neuropathy, uncontrolled hypertension (systolic blood pressure >150 mmHg or diastolic blood pressure >95 mmHg despite treatment), congestive heart failure, diabetes, liver or kidney failure, hyperparathyroidism, multiple myeloma, metastatic carcinoma, Cushing syndrome, collagen vascular disease, chronic angioedema or lymphedema, uncontrolled hyperthyroidism, chronic substance abuse, or any condition precluding the subject following the protocol or providing informed consent. Subjects with excessive alcohol use (>2 drinks/day) or who smoked were also excluded. Written informed consent was obtained, and all protocols were approved by the Committee for the Protection of Human Subjects (Institutional Review Board) of New York Medical College.

Laboratory evaluation. All experiments started at 9 AM after a brief fast (4 h). Morning medications were withheld. The right arm and right calf blood pressure were monitored intermittently by oscillometry. A vibrating plate (see below) was placed on the footboard of an electrically driven tilt table (Cardiosystems 600, Dallas, TX). Subjects wore rubber-soled shoes to ensure electrical isolation and were asked to lie supine with their feet flush with the plate, which initially was not oscillating. We designated this situation "0 Hz." Subjects were instrumented to measure blood flow by two forms of measurement: mercury in Silastic strain-gauge phlethysmography (SGP) with venous occlusion congestion cuffs, and impedance plethysmography (IPG). Occlusion cuffs were placed around the lower limb 10 cm above a strain gauge of appropriate size attached to a Whitney-type strain gauge plethysmograph. These are explained further below. Ag/AgCl ECG electrodes for IPG were attached to the left foot and left hand, which served as current injectors, and in pairs representing anatomic segments as follows: ankle to upper calf just below the knee (the calf segment), knee to iliac crest (the pelvic and upper leg segment), iliac crest to midline xyphoid process (the splanchnic segment), and midline xyphoid process to supraclavicular area (the thoracic segment). Output from the strain gauge and impedance leads were interfaced to a personal computer through an analog-to-digital converter with a sampling rate of 200 samples/s per channel. (DataQ Ind, Milwaukee, WI). Data were multiplexed and effectively synchronized.

Subjects had vascular measurements made with plantar stimulation at 0, 15, and 45 Hz with the three frequencies presented in random order for a given subject. At each vibrational frequency, measurements were made supine and at 35° upright tilt.

Peripheral vascular evaluation by SGP. We used SGP to measure calf blood flows, the calf capacitance vessel pressure (venous pressure, denoted P_v), the calf venous volume-pressure capacitance relation, calf venous capacity, and the microvascular filtration (flow-pressure) relation while supine and during upright tilt to 35° in all subjects. Methods were adapted from the work of Gamble et al. (8–10) and have been used extensively by our group (38, 40) and are summarized in Fig. 1.

After a 30-min resting period, flow measurements were performed in at least triplicate. After flow values returned to baseline, we increased occlusion pressure gradually until limb volume change was just detected. This represents ambient P_v (7). We used the mean arterial pressure (MAP), calculated as 0.33 × (systolic BP) + 0.67 × (diastolic BP), and P_v to calculate the calf arterial resistance to blood flow [in units of mmHg·ml^{-1}·100 ml tissue·min] from the equation (MAP − P_v)/flow. To determine overall calf capacitance, the leg was gently raised above heart level until no further decrease in volume was obtained. After recovery and with the leg flat, we used 10-mmHg

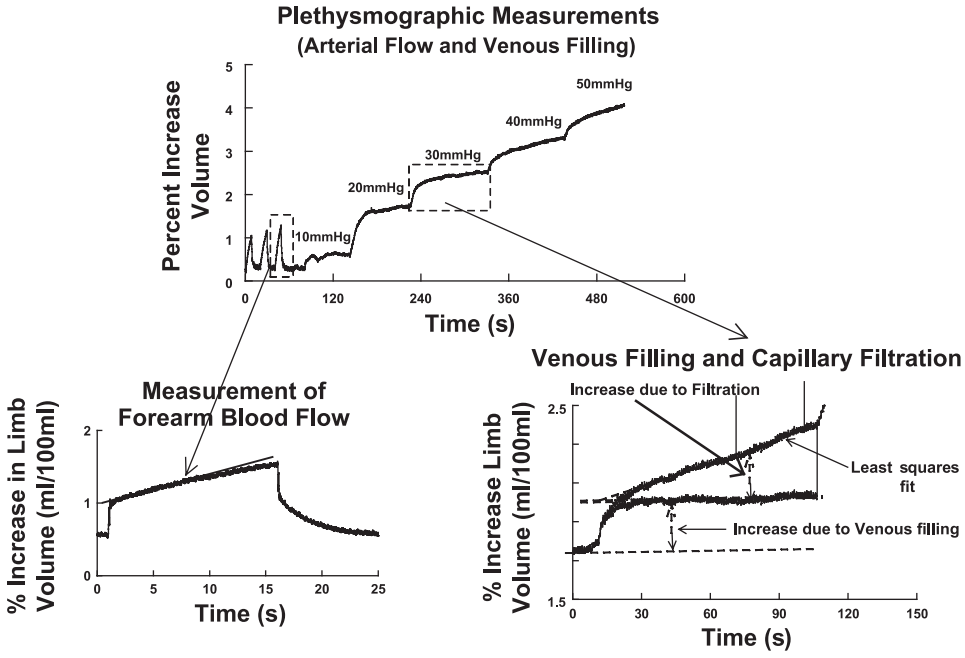

Fig. 1. Supine measurements made during venous occlusion plethysmography. *Top*: a typical experiment in which blood flow is measured in triplicate by venous occlusion followed by incremental occlusions using 10-mmHg steps to determine the volume-pressure relation. *Bottom left*: derivation of limb blood flow by fitting a straight line to the initial portion of the occlusion curve. *Bottom right*: the means by which volume changes during pressure steps can be partitioned into contributions from venous filling and microvascular filtration

steps in pressure, starting at the first multiple of 10 larger than P_v, to a maximum of 60–70 mmHg, resulting in progressive limb enlargement. Independent data indicate that the P_v distal to the congestion cuff approximates the cuff pressure (3). Pressure was maintained for 4 min to reach a steady state. At lower congestion pressures the limb size reached a plateau (Fig. 1). With higher pressures, a plateau is not reached, but (Fig. 1, *bottom right*) after initial curvilinear changes representing venous filling, the limb continues to increase in size linearly with time for a given pressure step. The linear increase represents microvascular filtration. At a critical pressure greater than P_v, denoted by P_i, the lymphatic system fails to compensate for filtration, and the limb interstitium enlarges at a rate proportionate to imposed pressure. This is the pressure threshold for edema formation. At occlusion pressure between P_v and P_i, the change in leg size reaches a plateau. At occlusion, pressures exceeding P_i, pressure increments result in a change in leg size, which is asymptotic to a straight line with positive slope. We used the singular value decomposition technique (29) to fit a least squares straight line to the points comprising the linear microvascular filtration portion of the filling curve at each occlusion pressure, as shown in (Fig. 1, *bottom right*). The linear portion is then electronically subtracted from the total curve to obtain a residual curvilinear portion that reaches a plateau. This residual portion is the change of capacitance vessel filling with each pressure step.

Once the volume response is partitioned, capacitance is calculated from the sum of residual portions shown as "intravascular filling" in Fig. 1 to which is added the estimate of supine venous volume obtained from raising the limb (39). The microvascular filtration relation (filtration rate vs. pressure relation) is constructed for each subject. Normalized volume is measured and expressed in units of milliliters volume change per 100 ml tissue; normalized filtration rate is expressed in units of milliliters per 100 ml tissue per minute; and the normalized filtration coefficient, K_f, the slope in the linear relation, is expressed in units of milliliters per 100 ml tissue per minute per millimeter Hg. The intercept with the pressure axis of the filtration rate-pressure graph is P_i, at which microvascular filtration exceeds lymphatic flow and approximates the net oncotic pressure gradient for microvascular filtration. The work of Pappenheimer and Soto-Rivera (27) established that net filtration does not occur at pressures less than P_i. Thus the extension of the linear fit to negative flow is a "virtual flow," which serves to estimate the *y*-intercept with the filtration axis, the normalized filtered flow at zero hydraulic pressure, comprising contributions from lymphatic flow and osmotically driven filtration. We used SGP to measure P_v, P_i, the volume-pressure relation of the capacitance vessels, and thus overall capacity, and the microvascular filtration relation, including the filtration coefficient K_f.

Peripheral vascular evaluation by IPG. IPG was used to measure segmental blood flows (26). IPG has also been used to quantify relative body fluid volumes (14). Relations between impedance and fluid compartmentalization have been established (12). Recently, changes in fluid compartment volumes and transient blood flows have been quantitated during orthostasis (5, 26). We used a tetrapolar IPG device to measure blood flows in the thoracic, splanchnic, pelvic-upper leg, and calf segments during each test sequence. Measurements of baseline impedance, Z_0, and pulsatile impedance changes, ΔZ, were made. A high-frequency (50 kHz), low-amperage (0.1 mA RMS), constant-current signal between the foot and hand electrodes was introduced. Z_0 values were measured in each segment continuously. Pulsatile impedance changes were used to compute the time derivative $\partial Z/\partial t$, which we used to obtain the total (ml/min) and relative (ml·100 ml body tissue^{-1}·min^{-1}) blood flow responses of each body segment to each test condition. Blood flow was estimated for an entire anatomic segment from the formula (11): flow = $[HR \cdot \rho \cdot L^2 \cdot T \cdot \partial Z/\partial t_{max}]/Z_0^2$. In this formula, HR is heart rate, ρ is the density of blood, L is the distance between the centers of the electrodes, T is the ejection period, Z is the impedance, and Z_0 is the baseline impedance.

To obtain IPG flows free of respiratory artifacts, we had the subjects lightly hold their breath for 10 s on exhalation, taking care that they did not perform a Valsalva maneuver. IPG flows are expressed in units of milliliters per minute for an entire anatomic segment. Normalization to tissue volume can be performed.

35° Upright tilt table testing. At each vibration frequency, after supine vascular measurements were complete, the subjects were tilted to 35° for ~15 min to obtain circulatory measurements during orthostasis. Earlier work indicated that strain-gauge measurements were more accurately determined during 35° compared with 70° upright tilt and that the lower angle still produces an adequate orthostatic stimulus (41). Preliminary studies have shown that this angle of upright tilt can be easily tolerated by all subjects (6). Measurements were made after ~5–7 min when blood pressure and heart rate had stabilized. Heart rate measurement, as well as arm and leg blood pressures, was repeated by oscillometry. P_v was remeasured upright. Limb blood flows were measured by SGP and IPG. Segmental blood flows were remeasured by IPG. SGP was used to reassess the volume-pressure relation and the microfiltration relation by increasing occlusion cuff pressure beginning at the new measured value of P_v and increasing in 10-mmHg steps up to a maximum pressure less than the diastolic pressure. P_i, overall capacity, and K_f were obtained by least squares analysis. The vertical height between the congestion cuff and the strain gauge was used to correct for hemostatic load differences. Thus the pressure at the calf strain gauge was adjusted by adding $\rho \cdot g \cdot D \cdot \sin(35°)$, where ρ is the density of blood, g is the gravitational acceleration constant, and D is the distance from the congestion cuff to the strain gauge.

Plantar stimulation. Plantar stimulation was applied using a custom-made apparatus devised by one of us (K. J. McLeod). The device consists of a rectangular-shaped frame constructed with an aluminum top plate against which the subjects place their feet in either a supine or upright position. The plate is circumferentially supported by an array of 12 coil springs. Centrally located on the bottom surface of the plate is an electromechanical actuator. This actuator is capable of delivering sinusoidal 15- to 120-Hz vertical displacements of about 0.004–0.24 mm to the top plate. Attached to the underside of the aluminum plate is an accelerometer, which provides acceleration feedback to the system. Digital electronic control circuitry automatically adjusted the actuator force to provide an acceleration of 2.0 m/s^2 [0.2 *g* point to point (p-p)]. This corresponded to a surface displacement of 240 μm p-p at 15 Hz and a stimulation amplitude of 25 μm p-p at 45 Hz. The platform was mounted on the footplate of the tilt table throughout the protocol. This is a stable and comfortable arrangement.

Statistics. Tabular data were compared by two-way ANOVA, with vibration frequency, position (supine and upright) on the table axes. When significant interactions were demonstrated, paired *t*-tests were used for compared supine and upright changes within-groups comparisons. Results are reported as means ± SD. P values < 0.05 were considered statistically significant.

RESULTS

Over a 1-yr period, we recruited 18 subjects for the current study ranging in age from 45.5–63.3 yr. Subject ages, heights, weights, illnesses, medications, resting blood pressure, and heart rate are shown in Table 1. All enrolled subjects were free of acute illnesses. There were no trained competitive athletes. There were no bedridden subjects.

Heart rate and pressure measurements. As shown in Table 2, heart rate was not affected by the plantar vibration at either frequency and tended to increase modestly with orthostasis, as expected. Arm MAP was unaffected by vibrational frequency or by orthostasis, while leg blood pressure (BP) increased

Table 1. *Subject data*

Variable	Data
Age, yr	56±5
Height, cm	163±6
Weight, kg	71±18
Supine resting heart rate, beats/min	67±9
Supine mean arterial pressure, mmHg	92±9
n	
Illnesses	
Hypertension	8
Migraine	3
Hypothyroidism	3
GERD	3
Hypercholesterolemia	3
Asthma	1
Seizure disorder	1
No illness	3
Medications	
Statin drugs	4
ACE inhibitors	3
Synthroid	3
Beta blockers	2
SSRI	2
Prevacid	2
SERM	2
ARB	1
Tegritol	1
Albuterol	1
Inhaled steroid	1
Hydrochlorothiazide	1
Proton pump inhibitor	1

Values are means ± SE; *n* is no. of subjects with respective illness or on respective medication; GERD, gastroesophageal reflux disease; ACE, angiotensin-converting enzyme; SSRI, selective serotonin reuptake inhibitor; SERM, specific estrogen receptor modulator; ARB, angiotensin receptor blocker.

during tilt as a result of the hemostatic column imposed by tilting. Leg BP was unaffected by vibrational frequency.

Leg P_v was increased at 15 Hz and at 45 Hz compared with 0 Hz, while supine ($P < 0.04$) but was not different from 0 Hz when upright. Tilt increased P_v similarly at all frequencies.

Peripheral blood flow and resistance measurements. Table 2 shows the expected decrease in calf blood flow measured by SGP with orthostasis, while peripheral arterial resistance increased with upright tilt. SGP recording did not identify any significant increase in calf blood flow with either plantar stimulation frequency when subjects were in the supine position. However, calf blood flow increased during plantar stimulation in the upright position (from 1.2 ± 0.2 at 0 Hz, to 1.6 ± 0.4 at 15 Hz, and to 1.8 ± 0.4 ml·100 ml^{-1}·min^{-1} at 45 Hz, $P < 0.002$ by paired *t*-testing). There was no effect of vibration on arterial resistance when supine or upright. Venous resistance was unaffected by orthostasis but decreased during 45 Hz plantar stimulation in the upright position (from 1.2 ± 0.2 at 0 Hz, to 1.2 ± 0.5 at 15 Hz, and to 0.7 ± 0.1 mmHg·ml^{-1}·100 ml·min, $P < 0.05$)

IPG measurements showed that calf segmental flow was significantly affected both by orthostasis and plantar stimulation. In the supine position, calf flow increased from 137 ± 18 to 150 ± 21 ($P = 0.05$) at 15 Hz, and 178 ± 26 ml/min ($P = 0.05$) at 45 Hz. Orthostasis resulted in a significant reduction in calf flow to 99 ± 15 ml/min ($P = 0.05$ compared with supine). However, plantar stimulation at 15 Hz increased calf flow to 131 ± 31 ($P = 0.005$) and to 146 ± 28 ml/min with 45 Hz stimulation ($P = 0.001$).

Upper leg-pelvic blood flows were unaffected by orthostasis but increased during plantar stimulation while supine (Table 2). With orthostasis, plantar vibration increased pelvic flow from 707 ± 90 at 0 Hz, to 952 ± 123 at 15 Hz, and finally to 940 ± 102 ml/min, at 45 Hz, $P < 0.005$. Splanchnic flow was unaffected by the plantar vibration but decreased during orthostasis at all frequencies ($P < 0.001$).

Thoracic blood flow decreased as expected with orthostasis ($P < 0.05$) and was increased to a similar extent in the supine and upright positions by plantar stimulation (from 3,506 ± 322 at 0 Hz, to 3,990 ± 270 at 15 Hz, and finally to 4,237 ± 366 ml/min at 45 Hz, $P < 0.02$ when supine and from 2,688 ± 287 at 0 Hz, to 3,391 ± 688 at 15 Hz, and finally to 3,670 ± 313 ml/min at 45 Hz, $P < 0.02$ when upright).

Volume-pressure capacitance and microfiltration relations. The volume-pressure relation as depicted in Fig. 2 is unaffected by plantar stimulation and by orthostasis (39). As shown in Table 3, the maximum leg capacity was unaffected by tilt or stimulation.

However, as shown in Fig. 3, the microvascular filtration relation is shifted rightward with plantar stimulation and is

Table 2. *Hemodynamic properties*

	0 Hz	15 Hz, %Change	45 Hz, %Change
HR, beats/min			
Supine	65±2	−1±1	0±2
Upright 35°	72±2†	−3±2†	0±2†
MAP arm, mmHg			
Supine	88±4	7±6	4±5
Upright 35°	92±3	−6±6	1±1
MAP leg, mmHg			
Supine	88±4	7±6	4±5
Upright 35°	124±4†	−2±2†	3±2†
P_v leg, mmHg			
Supine	13±1	14±7*	16±6*
Upright 35°	27±2†	−1±2†	3±2†
SGP calf blood flow, ml·100 ml^{-1}·min^{-1}			
Supine	2.4±.3	12±9	11±8
Upright 35°	1.2±.2†	33±22*†	46±17*†
SGP leg arterial resistance, mmHg·ml^{-1}·100 ml·min			
Supine	41±7	−6±7	−4±5
Upright 35°	126±28	11±15	7±9
SGP leg venous resistance, mmHg·ml^{-1}·100 ml·min			
Supine	1.3±.4	8±12	−10±10
Upright 35°	1.2±.4	11±40	−27±12*†
IPG calf segmental flow, ml/min			
Supine	137±18	10±4*	30±7*
Upright 35°	99±15†	32±12*†	47±14*†
IPG pelvic segmental flow, ml/min			
Supine	707±90	31±15	26±9*
Upright 35°	713±80	22±15	35±11*
IPG visceral segmental flow, ml/min			
Supine	1,906±253	6±9	11±14
Upright 35°	1,288±302†	0±15†	7±14†
IPG thorax segmental flow, ml/min			
Supine	3,506±322	10±5*	20±7*
Upright 35°	2,688±287†	16±8†	17±7*†

Values are means ± SE. HR, heart rate; MAP, mean arterial pressure; SGP, strain-gauge plethysmography; IPG, impedance plethysmography. *$P < 0.05$ compared with 0 Hz; †$P < 0.05$ compared with supine.

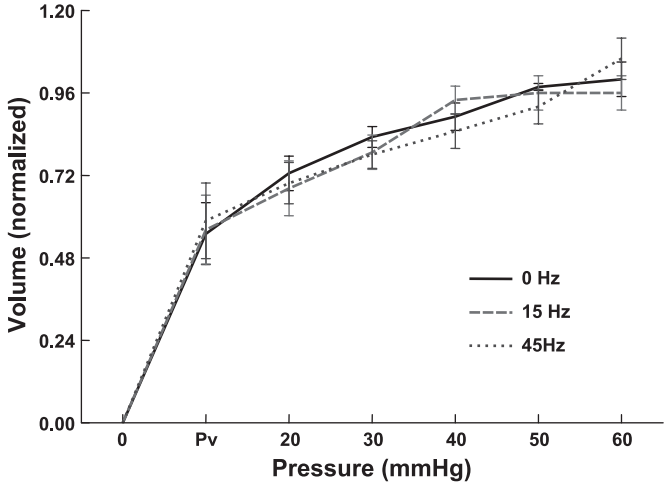

Fig. 2. Effect of plantar vibration on the volume-pressure capacitance relation. The relation displayed is obtained by normalizing all data to the maximum capacity obtained for an individual subject. Systematic deviations are detectable as a shift in the curve. 0 Hz represents no vibration; 15 Hz plantar vibration at 0.2 *g*, and 45 Hz plantar vibration at 0.2 *g* are shown. There is no difference in relations. P_v, venous pressure.

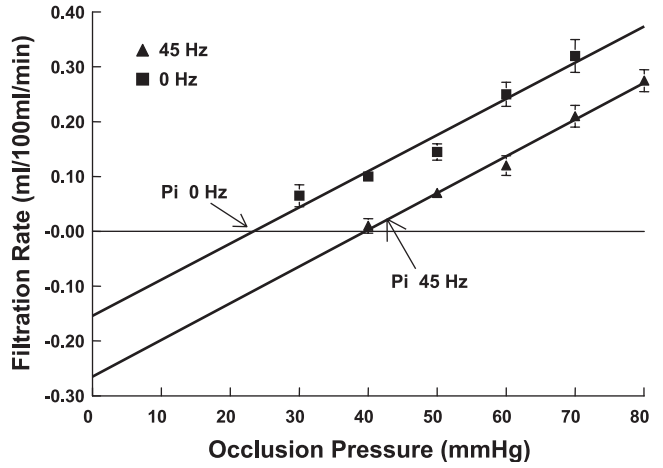

Fig. 3. Alteration of the microvascular filtration relation as a result of plantar vibration. 0 Hz represents no vibration, and 45 Hz plantar vibration at 0.2 g is shown. The slope, K_f, is not affected by the vibration stimulus. However, the absolute values of isovolumetric pressure (P_i) and the absolute value of the *Y*-intercept, which reflect lymphatic flow, are significantly increased by the vibration. Supine data are shown; upright data are similar.

unaffected by upright tilt. As shown in Table 3, there is no change in the slope of the relation, K_f, with vibrational frequency, but a pronounced shift in *x*-intercept (P_i) and *y*-intercept. Thus while supine, P_i increases from 24 ± 2 at 0 Hz to 27 ± 3 at 15 Hz, and to 31 ± 2 mmHg at 45 Hz ($P < 0.01$), and while upright, P_i increases from 25 ± 3 at 0 Hz to 28 ± 4 at 15 Hz, and to 35 ± 4 mmHg at 45 Hz ($P < 0.04$).

Figure 4 shows individual upright subject data as a function of the frequency of plantar vibration. While scatter remains wide, there is significant increase in upright calf blood flow and P_i as a function of vibrational frequency.

DISCUSSION

In the introductory section, we proposed a mechanism for the maintenance of bone density that depends on hemostatic pressure in the lower extremities to provide for microvascular filtration and a skeletal muscle pump to ensure the adequacy of blood and interstitial flow. We provided past evidence that low-amplitude plantar vibration operating at frequencies similar to postural muscle contraction rates enhances bone growth and inhibits bone loss. We developed the hypothesis that plantar vibration stimulates or simulates skeletal muscle pump function. Here, we successfully tested the prediction that plantar vibration enhances lower body blood flow and lymph flow. Thus a method that promotes peripheral flow in one set of experiments also promotes bone growth in another.

Table 3. *Capacity and microfiltration properties*

	0 Hz	15 Hz, %Change	45 Hz, %Change
Maximum leg capacity, ml/100 ml			
Supine	4.7±0.3	2±2	2±4
Upright 35°	4.5±0.4	4±4	5±4
P_i, mmHg			
Supine	24±2	26±16	40±15*
Upright 35°	25±3	36±24	48±12*
K_f, 10^{-3}·ml·100 ml^{-1}·min^{-1}·mmHg^{-1}			
Supine	5.9±0.6	25±19	2±15
Upright 35°	6.2±0.8	32±40	16±31

Values are means ± SE. P_i, isovolumetric pressure; K_f, microvascular filtration coefficient. *$P < 0.05$ compared with 0 Hz; †$P < 0.05$ compared with supine.

This role of the skeletal muscle pump in maintaining bone mass has been lent support by a recent study on an elderly female population (25). In the latter study, the degree of skeletal muscle pump activity was determined by the surrogate measures of muscle activity (via vibromyography) and postural sway. Bone mineral density in both the femur and lumbar spine was found to be strongly associated with both increased muscle activity during quiet standing and, correspondingly, increased postural sway during standing.

One significant effect of plantar stimulation on circulation in this study was on calf blood flow, which, while significantly decreased by orthostasis, is improved by plantar vibration.

Similarly, upper leg-pelvic blood flow and thoracic flow are significantly increased by vibration and orthostatic changes blunted by plantar stimulation, particularly at 45 Hz. It is likely that the changes in leg-pelvic flow are produced as part of a generalized lower extremity effect affecting calf and thigh alike and that the increase in thoracic IPG flow relates to the increase in overall systemic flow due to improved peripheral flow and venous return. This is entirely consistent with a skeletal muscle pump mechanism in which venous return is ensured by pumping, while forward flow is enhanced by intermittent reduction of venous pressure and increased arteriovenous pressure gradient (32).

Another finding is that the microvascular filtration relation is right-shifted by plantar vibration as a consequence of an increase in P_i, the threshold for edema, while the microvascular filtration coefficient, K_f, remains unchanged. Our prior work indicates that $Y_{intercept} \approx K_f \cdot P_i$ and approximates lymphatic flow (37). Taken together, the results therefore suggest that while microvascular filtration (i.e., K_f) is unaffected by plantar vibration, there is enhanced lymphatic and venous drainage, particularly evident when upright.

Peripheral lymphatic transport is known to be linked to skeletal muscle pump activity. Thus while lymph is formed by

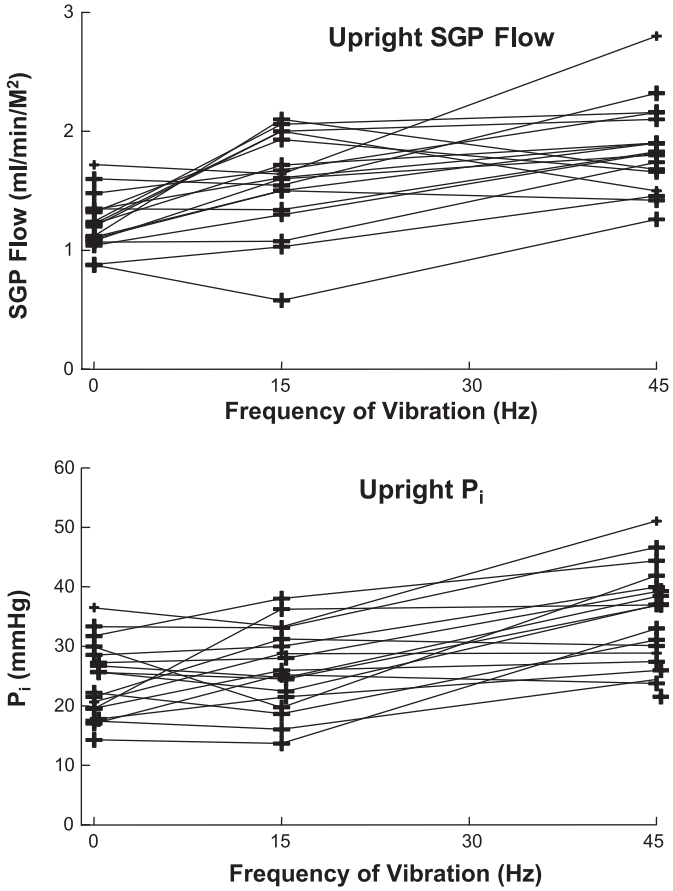

Fig. 4. Individual upright patient data as a function of the frequency of plantar vibration. *Top*: normalized calf blood flow measured by strain-gauge plethysmography (SGP). *Bottom:* P_i, which shows the threshold pressure for edema formation. 0 Hz (no vibration), 15 Hz, and 45 Hz plantar vibration at 0.2 *g* are shown. Calf blood flow and P_i both increase as a function of frequency of the vibration stimulus.

the translocation of interstitial fluid into the initial lymphatics by osmotic or vesicular transport mechanisms (1), and initial lymphatics may possess some degree of actin-dependent active contractile transport from initial lymphatics to valves containing lymphatic ducts, the bulk of lymphatic flow seems to depend on tissue movement. Thus chronically immobilized tissues have almost no lymphatic flow especially in the extremities (13). Unlike veins, there is apparently little effect of "force from behind" (cardiac muscle and blood pressure) on lymphatic fluid propulsion. Instead lymph flow is enhanced by active and passive limb muscle movements, the skeletal muscle pump (31). Prior work indicates that to create unidirectional flow, these external forces must be intermittent (24). In our subjects enhanced lymphatic flow is stimulated by plantar vibration.

During relaxed standing, postural muscle activity, and correspondingly skeletal muscle pump activity, can be inferred through assessments of postural sway activity, as greater postural sway typically represents higher levels of lower limb muscle activity. While younger individuals are posturally more stable than their elders, we have observed that younger individuals permit themselves to sway more during relaxed standing than older individuals (21, 31). In the absence of movement (i.e., sway), tissue pressures increase in the legs (15, 31).

Type IIa fibers are believed to play a dominant role in skeletal muscle pump activity (33). While type I fibers typically contract at rates below 20 Hz, type IIa muscle fibers have typical contraction rates in the range of 20–60 Hz (16). The efficacy of the higher plantar vibration frequency we tested (45 Hz) in reducing edema pressure and enhancing blood flow in the lower body is consistent with the stimulus triggering type IIa muscle fiber contraction.

We have previously demonstrated age-related decreases in muscle contraction dynamics with a significant decrease in the magnitude of the component of vibromyography associated with type IIa muscle contractions, corresponding to approximately a 1–2% decrease in amplitude per year (16). Our ability to influence skeletal muscle pump activity in this particular population may, therefore, be a reflection of the fact that this group had lost a substantial fraction of their normal muscle pump activity due to the age-related conversion of type IIa fibers to type IIb.

Nonetheless, it would appear that the remaining musculature is sufficient to respond to the vibration stimulus. Stimulated skeletal muscle pump activity produced enhanced upright calf blood flow and enhanced centripetal lymphatic flow.

Limitations. We principally studied the lower extremities. While IPG provides hints about other regional circulations, it is incomplete in this regard and varies from subject to subject, dependent on body habits and other factors. Although other regional circulations could be affected by vibration, one would guess that the most immediate effects of plantar vibration would be on the lower extremities, which along with buttocks (pelvic-upper-leg segment) are important sites for venous pooling during quiet standing (22). Thus the study addresses effects that are important to the orthostatic response.

IPG was used to measure regional blood flow changes. The standard for peripheral flow measurement is SGP. While SGP measures a physical size change (circumference), impedance measures electrical resistance changes. They are not equivalent. However, from a qualitative standpoint, they yield directionally similar data. Also, our main conclusions concerning the effects of plantar vibration on calf blood flow and lymphatic flow when upright were obtained equally well by strain-gauge measurements at 45 Hz.

In addition, low-angle tilts were studied. We required stable conditions during which microvascular filtration and capacitance relations could be measured. Potentially useful information could be missed. Data collection becomes more difficult and biological variability increases at higher angles.

Age and gender limitations to generalizability may exist. Data obtained from perimenopausal women are not representative for younger or older ages, or for men. However, we studied this group because they are at particular risk for vascular and musculoskeletal abnormalities that may affect the lower extremities and may have an impact on osteoporosis.

Some subjects had medical ailments and were maintained on current medications, although this was limited by exclusion criteria. Our rationale is that we wished to study average women and not necessarily perfect physical specimens. Although the results could have been affected by illnesses and medications, all illnesses (e.g., hypertension, hypothyroidism) were controlled, we withheld medications on the day of testing, the subjects represent a cross section of comparably aged women, and we could see no apparent stratification by disease

or medication subtype. In regard to orthostasis and plantar vibration, the subjects served as their own controls (14). The true control group would be older women taking absolutely no medications. However, we have had great difficulty in recruiting a suitably large medication-free population. Several of our subjects had no illnesses and took no medication, while having similar response to vibration.

GRANTS

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